

The Art of Defeating Death

A Physician's Journey Beyond the Threshold



DeepScience

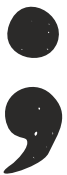


Birupaksha Biswas

The Art of Defeating Death: A Physician's Journey Beyond the Threshold

Birupaksha Biswas

Department of Pathology, Burdwan Medical College & Hospital, Burdwan, India



DeepScience

Published, marketed, and distributed by:

Deep Science Publishing, 2025
USA | UK | India | Turkey
Reg. No. MH-33-0523625
www.deepscienceresearch.com
editor@deepscienceresearch.com
WhatsApp: +91 7977171947

ISBN: 978-93-7185-407-8

E-ISBN: 978-93-7185-798-7

<https://doi.org/10.70593/978-93-7185-798-7>

Copyright © Birupaksha Biswas, 2025.

Citation: Biswas, B. (2025). *The Art of Defeating Death: A Physician's Journey Beyond the Threshold*. Deep Science Publishing. <https://doi.org/10.70593/978-93-7185-798-7>

This book is published online under a fully open access program and is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC 4.0). This open access license allows third parties to copy and redistribute the material in any medium or format, provided that proper attribution is given to the author(s) and the published source. The publishers, authors, and editors are not responsible for errors or omissions, or for any consequences arising from the application of the information presented in this book, and make no warranty, express or implied, regarding the content of this publication. Although the publisher, authors, and editors have made every effort to ensure that the content is not misleading or false, they do not represent or warrant that the information-particularly regarding verification by third parties-has been verified. The publisher is neutral with regard to jurisdictional claims in published maps and institutional affiliations. The authors and publishers have made every effort to contact all copyright holders of the material reproduced in this publication and apologize to anyone we may have been unable to reach. If any copyright material has not been acknowledged, please write to us so we can correct it in a future reprint.

Preface

Medicine writing has to be more than just treatment algorithms and disease inventories. It's a bold reaching for conversation itself with death. In the ensuing pages, the reader will not be presented merely with clinical case histories, but he also will receive deep insights into the existential battles fought by patients and caregivers. These moments show how fragile bodies, debilitated by chronic disease or sudden medical calamity, are slowly moved back toward equilibrium with the dogged application of scientific knowledge and inventive medical technologies.

The Art of Defeating Death: A Physician's True Stories from the Frontline of Illness is not an ode to unqualified victories, since all victory in medicine is partial and provisional. *Telling Life From Death* It is not so much a mystery as a chronicle of negotiations with the border between the living and the dead. — where medical science works to delay, rechannel, or temporarily resist the finality of mortality through the combined efforts of pharmaceuticals, surgical techniques, vigilant care, and human resilience. Every case comes to represent a stage at which the strands of biology, pathology and technology intertwine, but every success has behind it the relentless, sometimes silent work of doctors and nurses, families and patients themselves, all taking part in a fragile yet durable miracle. Here, death is not conceived of as a single foe but as a variety of stealthy assaults: arrhythmic silences, thrombotic cascades, septic storms, metabolic derangements or hepatic ruin. To face these is not simply to use implements of cure but to perceive the art in science, the art of when to go there, when to hold back and when to give over a certain road for another. It is in that art, honed by unrelenting uncertainty, that the possibility of defeating death acquires meaning.

This book therefore stands not as a manual of certainty but as a meditation upon complexity. Each narrative seeks to reveal that medicine's noblest aspiration is not immortality but the creation of reprieve, the reconstitution of dignity, the prolongation of meaning within the finite arc of life. If the reader detects a current of determination in these accounts, it is because medicine, even at its most clinical, is an act of defiance, a refusal to concede to inevitability without first exhausting the reservoirs of knowledge, skill, and human empathy.

May these pages, then, not merely instruct but inspire, describe but illuminate & document the science of survival via bearing a witness to the craftsmanship of impeding death.

Birupaksha Biswas

About the book

The Art of Defeating Death: A Physician's Journey Beyond the Threshold is not a series of abstract or medical axiomatic formulas, to be taken lightly. It's not a story per se but rather an account of literal encounters in *Living and Dark Alliance*. Based on personal, real-life encounters with acute illness, it demonstrates the heart of medicine where organ function wanes, systems fail and a tangible mortal threat imposes itself.

Each story is also both a narrative and a metaphor: a young patient vanquished by the virus; an elderly person, whose heart loses to arrhythmia; a tender lung stiffened by fibrosis; an immune system gone rogue. These are not just case reports — they are testimonies to the intricate dance between disease and resilience, between innovative intervention and the inexorable march of biology.

The book also steps outside of medicine as a strictly scientific endeavor. It delves into the philosophical questions of survival, in which death is not just an end but a moving target that can be postponed, redirected or stalled. It does not only depict medicine as a series of protocols but also as a living art that demands interpretation, impromptu reasoning and tenacity.

So, this book is not a handbook for operations and/or an autobiography. It eschews easy categorization, addressing itself equally to doctors confronted with complex cases day after day, to scholars studying the cultural meanings of illness and infection, like this writer herself, and to any reader who will find in these tales the universal human duty to grapple with decline. Most of all, it underscores the idea that practicing medicine entails constant bargaining with the certainty of endings, while focusing on moments of reprieve and purpose..

For confidentiality purposes, all the particulars that do pertain to the patient have been withheld for utmost confidentiality. Prior to initiation of therapeutic interventions, patients or their legally acceptable representatives were provided with detailed explanations regarding the nature of their condition, anticipated clinical course, potential complications, and proposed management strategies, including pharmacologic, procedural, or surgical interventions as indicated. Detail The justification and potential risks/benefits were provided of any treatment including, but not exclusive to: - anticoagulation; - broad spectrum antimicrobials; - invasive procedures; or - high level monitoring in a language the patient could understand, as well as the need to ensure adherence to therapy, follow up and supportive care. Adequate opportunity was afforded for questions, which were addressed to ensure informed understanding. Written,

voluntary consent was obtained for all interventions, hospitalization, laboratory and imaging surveillance, and the anonymized use of clinical data for academic, educational, or scientific reporting purposes.

About the Author



There is a way in which the life of Dr Birupaksha Biswas MBBS, MD (Pathology) does not constitute a tale of triumphalism so much as a series of personal anecdotes that quietly eulogise determination, scholarship and remembering. His intellectual canvas is distinguished by a remarkable bibliographic constellation: *The Comic Book of Neuropathology: When Neurons Throw Tantrums*, a playful yet serious interrogation of neurological pathology; *Blood on the Edge: Critical Care Hematology Unplugged*, a volume that unravels hematologic crises with diagnostic precision; *Pediatric Hematopathology: Bone Marrow Disorders, Leukemias, Lymphomas, and Molecular Diagnostics*, a compendium that bridges childhood pathology and molecular insight; *Pathology at the Edge of Certainty: Flesh, Code, and the Semiotics of Diagnosis*, a meditation on the very language of disease; *Integrative Diagnostic Pathology*:

Cytomorphology, Genomics, and Translational Perspectives in Systemic and Organ-Specific Diseases, an attempt to harmonize the molecular and the morphological; and *The Alchemy of Lesions: Decoding Disease and Orchestrating Resolution*, where pathology is portrayed as an art of deciphering and healing. These books, though bearing his name, are offered as collective dialogues with colleagues, patients, and the enduring discipline of pathology itself. In addition to these monographs and two more in press, respectively on the Endocrine Diseases and the Contraindications to Organ Biopsies, lies a body of almost five dozens articles published in national and international journals including reviews, observations studies systematic syntheses and "translational" reflections with one paper currently under review thresholding *Cureus*. Each manuscript is less an ornament than an archival deposit of meticulous inquiry, a record of questions pursued with discipline rather than self-assertion.

If one traces the subtle grammar of his scholarly path, it becomes evident that his writing is not the language of triumph but of careful witness. There is nothing for ornamental purposes in his elaborate syntactic style, it accurately reproduces the complex character of pathological facts. For him, degrees are the start of a path where we rely on nothing less than writing and rewriting manuscripts, creating diagnostic algorithms one laborious step at a time in polished or basic struts of code and seeking to understand through writing in ways that engage our next-door neighbor. His scholarly writing is not an anthology but a string of beads, a beginning — in hematology — that leads to neuropathology and takes lessons from oncology and infectious disease, all while maintaining its essential attention to the "disclosiveness" or "receptivity" we demand of any academic visionary. The central theme driving his work is a holistic vision where cellular morphology, genetic research, and translational therapies communicate and inform each other rather than compete. Underneath this scholarly framework, though, is a tender root — an agonizing memory that turned private sorrow into a public sound, pain into prose. This is the emotional crucible that formed his lyrical manner — more ruminative than declamatory, more meek-streaked than alpha-sleek.

As he tells it, his urge to write was not driven by a need for attention, but rather the desire to remember. It was from there, in the aftermath of loss, that he discovered language could bring succor as well as clarity. In blending sorrow and scientific pursuit, he became not a celebrated figure but a witness—someone who writes to transform pain into lasting understanding.

Good response

Acknowledgement

In the weaving of this book I remain indebted to all those who entrusted their most vulnerable hours to my care, for their stories are the very architecture of these pages. I extend silent gratitude to colleagues whose vigilance, intellect, and endurance transformed despair into possibility, and to those unseen presences—family, mentors, ***THE SPECIAL ONE***, and the companions, whose constancy rendered the act of writing inseparable from the act of healing.

“For medicine, like literature, is never a solitary pursuit but a chorus of shared vigilance.”

ad response

Table of Contents

Chapter 1: The interplay of sudden cardiac arrest, triple vessel coronary disease, electrophysiological dysfunction, pacemaker salvage, and acute kidney injury in a multimorbid patient1

Introduction 1

Discussion..... 3

Conclusion4

References6

Chapter 2: intersecting catastrophes of endocrine, metabolic, and cardiovascular decompensation: a case of amiodarone induced thyrotoxicosis with advanced systolic dysfunction.....8

Introduction 8

Discussion.....9

Conclusion 10

References 11

Chapter 3: Catastrophic veno thromboembolic event complicated by locoregional septic soft-tissue insult and multisystem perturbations12

Introduction 12

Investigations..... 12

Diagnosis 16

Monitoring Protocol: 18

Outcome 18

Discussion..... 19

Conclusion20

References21

Chapter 4: Severe multi-organ dysfunction following acute hepatitis a and superimposed salmonella typhi septicaemia in a young adult with nosocomial Acinetobacter infection: intensive care management and prolonged hepatic convalescence22

Introduction22

Discussion.....25

Conclusion27

References29

Chapter 5: Recovery from acute exacerbation of copd with multi-organ failure in an octogenarian with severe cardiopulmonary and metabolic comorbidities utilizing vericiguat and insulin degludec30

Introduction30

Discussion.....33

Conclusion34

References35

Chapter 6: Orchestrated multidisciplinary management of severe multiorgan dysfunction in a patient with advanced rheumatoid arthritis and acute tubular necrosis36

Introduction36

Discussion.....43

Conclusion44

References46

Chapter 7: The long shadow of time: a multisystem recovery from complex biliary, infectious, and catabolic insults in an elderly patriarch47

Introduction47

Discussion.....49

Conclusion51

References51

Chapter 8: Immune thrombocytopenia refractory to platelet transfusion: a hemato-immunological confluence of catastrophic bleeding propensity and corticosteroid-mediated redemption.....53

Introduction 53

Discussion..... 55

Conclusion 56

References 58

Chapter 9: Terminal poly-organ convergence in a septic and cardiometabolic terrain: a case of metastatic hepatocellular carcinoma with decompensated multisystem failure and successful post-arrest resuscitation.....59

Introduction 59

Discussion..... 63

Conclusion 64

References 65

Chapter 10: Acute left ventricular outflow tract obstruction by a massive cardiac rhabdomyoma in an adolescent: surgical excision with polytetrafluoroethylene reinforcement and multidisciplinary critical care management67

Introduction 67

Discussion..... 68

Conclusion 70

References 70

Chapter 1: The interplay of sudden cardiac arrest, triple vessel coronary disease, electrophysiological dysfunction, pacemaker salvage, and acute kidney injury in a multimorbid patient

Introduction

In this sixty seven year old male patient, the perioperative period unfolded as a highly complex scenario characterised initially by acute cardiovascular collapse and followed by marked electrophysiological instability. The resulting therapeutic trajectory was necessarily multidimensional, incorporating resuscitation, advanced coronary revascularisation, detailed electrophysiological investigation, the institution of permanent pacing therapy, and subsequent correction of programming deficits in the context of systemic compromise. His comorbid burden was considerable, consisting of arterial hypertension, type two diabetes mellitus controlled with a basal bolus insulin schedule, hypothyroidism under thyroxine replacement, chronic obstructive pulmonary disease in GOLD stage three, and benign enlargement of the prostate gland. He presented for elective laparoscopic repair of an inguinal hernia under general anaesthetic care.

During the course of pneumoperitoneum insufflation and positioning manoeuvres, the patient abruptly developed haemodynamic collapse progressing into a sudden cardiac arrest. Immediate institution of basic life support and advanced cardiac life support algorithm ensued, encompassing high quality chest compressions, airway protection, pharmacological vasopressor support, and defibrillatory evaluation, resulting in restoration of spontaneous circulation after a sustained resuscitative effort. Post resuscitation stabilisation mandated immediate cessation of the surgical procedure and subsequent referral to a higher tertiary cardiac facility for advanced diagnostic and therapeutic evaluation.

At the tertiary centre, invasive coronary angiography delineated diffuse atherosclerotic burden with severe triple vessel coronary artery disease. Given the anatomic unsuitability for percutaneous coronary intervention and the recurrent ischaemic

arrhythmogenic substrate, the patient underwent coronary artery bypass grafting with left internal mammary graft to the left anterior descending artery and sequential venous grafts to obtuse marginal and posterior descending vessels. The early post operative recovery phase, though uneventful with respect to myocardial contractile restoration, continued to demonstrate recurrent rhythm disturbances predominantly in the form of paroxysmal pauses, sinoatrial exit block, and erratic junctional escapes.

The diagnostic conundrum was initially obfuscated by an otoneurological evaluation, wherein a Dix Hallpike manoeuvre yielded a false positive response, misleading the differential trajectory toward benign paroxysmal positional vertigo. However, the inexorability of rhythm instability mandated an advanced electrophysiological study. The latter unequivocally demonstrated significant sinus node dysfunction characterised by prolonged sinus node recovery times, abnormal sinoatrial conduction intervals, and inducible bradyarrhythmic pauses. Thus, a definitive diagnosis of sick sinus syndrome was established, necessitating permanent pacemaker implantation. The patient accordingly underwent successful placement of a dual chamber pacing device, with meticulous intra operative mapping of atrial and ventricular thresholds, ensuring appropriate chronotropic competence and atrioventricular synchrony.

For six months following pacemaker insertion, the patient remained clinically stable, regaining exercise tolerance and resuming ordinary activities of daily living. However, subsequently, he presented with a new episode of cardiovascular compromise manifesting as exertional dizziness, near syncope, and intermittent hypotension. Interrogation of the pacing device revealed that the advanced hysteresis algorithm had not been enabled, leading to suboptimal adaptive pacing behaviour during variable autonomic states. Simultaneously, titration of certain cardiometabolic pharmacological agents, including beta adrenergic antagonists and diuretic regimens, exacerbated haemodynamic lability. Compounding this was an intercurrent respiratory tract infection with bronchopulmonary consolidation, which precipitated systemic inflammatory response and acute kidney injury. The renal dysfunction, though alarming in the acute context, responded to aggressive hydration, antibiotic therapy tailored to culture sensitivity, and cautious withdrawal of nephrotoxic pharmacopoeia, with eventual restitution of renal function parameters.

Following reprogramming of the pacemaker to include adaptive hysteresis and optimisation of medical therapy, the patient achieved hemodynamic stability. Longitudinal follow up revealed adequate pacing capture, absence of arrhythmic pauses, preserved left ventricular ejection fraction, and improved quality of life indices.

Discussion

The present case embodies the intricate interplay between perioperative cardiovascular catastrophes, structural coronary disease, electrophysiological abnormalities, and the nuances of device based therapy in a multimorbid host. Sudden cardiac arrest during laparoscopic procedures, though rare, has been attributed to vagally mediated reflexes, carbon dioxide embolism, pneumoperitoneum induced preload reduction, or unmasking of preexisting coronary pathology. The immediate adherence to BLS and ACLS algorithms underpins the centrality of protocol driven resuscitation in securing survival with intact neurological outcomes¹.

Subsequent delineation of triple vessel disease reflects the silent progression of diffuse atherosclerotic burden in diabetics with systemic hypertension, where coronary collateral insufficiency precipitates catastrophic intra operative events². Coronary artery bypass grafting remains the definitive intervention conferring survival advantage in multi vessel disease, particularly when compounded by diabetes mellitus and impaired ventricular function³. Nevertheless, the persistence of arrhythmic episodes post revascularisation underscores that revascularisation does not invariably rectify intrinsic conduction system pathology, thereby necessitating precise electrophysiological interrogation.

Sick sinus syndrome, encompassing sinus node arrest, sinoatrial exit block, and tachy brady syndrome, constitutes a prominent bradyarrhythmic disorder of the elderly, with degenerative fibrotic replacement of the sinoatrial node and atrial myocardium as the pathological substrate⁴. The diagnostic delay, as occurred in this patient with a misleading Dix Hallpike manoeuvre, exemplifies the pitfalls of symptom misattribution, wherein dizziness and syncope are prematurely ascribed to vestibular disorders⁵. The gold standard diagnostic criterion remains electrophysiological testing, with demonstration of prolonged corrected sinus node recovery time and impaired sinoatrial conduction⁶.

Permanent pacemaker implantation represents the cornerstone of therapy, restoring chronotropic competence and preventing asystolic pauses⁷. However, the complexities of device programming, particularly the non activation of advanced hysteresis functions, can compromise therapeutic efficacy. Hysteresis, by permitting intrinsic conduction whenever feasible, reduces unnecessary pacing, thereby preserving atrioventricular synchrony and diminishing the risk of pacing induced cardiomyopathy⁸. In this patient, the omission of advanced hysteresis activation contributed to haemodynamic compromise, a phenomenon corroborated in clinical device follow up studies.

The superimposed chest infection and subsequent acute kidney injury further illustrate the fragility of systemic homeostasis in multimorbid individuals. Pulmonary sepsis has been shown to amplify arrhythmic vulnerability by systemic inflammatory cytokine

release and autonomic imbalance⁹. Concurrently, renal dysfunction exacerbates electrolyte disturbances, particularly hyperkalaemia and metabolic acidosis, potentiating bradyarrhythmic risk¹⁰. Prompt reversal of acute kidney injury, therefore, contributed materially to the patient's recovery.

Conclusion

The presented case, in all its multidimensional complexity, functions as a profound exemplar of the delicate balance between operative physiology, systemic comorbidities, coronary pathology, intrinsic conduction derangements, and the technological sophistication of cardiac rhythm management devices. The trajectory of this sixty seven year old patient demonstrates, with extraordinary clarity, how the concatenation of systemic illness, anaesthetic stressors, hidden coronary insufficiency, and degenerative conduction system pathology may converge to precipitate catastrophic events, which when not approached in a multidisciplinary framework, could culminate in an irrevocable fatality.

In the earliest moment of the narrative, the sudden cardiac arrest during laparoscopic hernia repair unveils the ever present but often underestimated risks of elective surgical intervention in individuals with advanced cardiometabolic burdens. While laparoscopic surgery is heralded for its minimally invasive profile, the insufflation of carbon dioxide into the peritoneal cavity exerts profound cardiopulmonary ramifications, including diminished venous return, augmented afterload, and alterations of autonomic tone. In this patient, such pathophysiological disturbances intersected with latent triple vessel coronary disease to trigger malignant collapse. It is precisely here that the role of strict adherence to internationally codified basic life support and advanced cardiovascular life support guidelines became life preserving, since algorithmic chest compressions, defibrillatory evaluations, and vasopressor administration reclaimed spontaneous circulation from the brink of irreversible cessation. This resuscitative triumph provides the first key lesson: survival is not an accidental occurrence but the fruit of rigorous protocolised training and application in the perioperative theatre.

The subsequent discovery of extensive coronary artery disease represents the inevitable unmasking of the silent epidemic of diabetes associated atherosclerosis. Numerous longitudinal studies have emphasised that the diabetic patient without prior infarction may carry a mortality risk equal to that of a nondiabetic individual with antecedent myocardial infarction. Thus, the angiographic depiction of triple vessel stenosis in this individual is less a surprise than a revelation of what had been silently brewing. Coronary artery bypass grafting, as performed in this patient, underscores the clinical doctrine that diabetics with multivessel disease are optimally treated with surgical revascularisation rather than percutaneous means. Indeed, the longevity benefit conferred by surgical

grafting in such contexts is now irrefutable, and yet it must be acknowledged that revascularisation, while restoring myocardial perfusion, cannot reverse the insidious degeneration of the intrinsic conduction architecture.

It was this very reality that revealed itself in the persistent rhythm disturbances that survived bypass grafting. The sinoatrial node, once considered a robust pacemaking entity, is in fact vulnerable to fibrotic attrition, ischemic insult, and autonomic dysregulation. In the case presented, the recurrent bradyarrhythmias and pauses, which initially misled clinicians through the false positive Dix Hallpike response, illustrate the peril of attributing syncope or presyncope to benign vestibular pathologies without comprehensive cardiac scrutiny. The diagnostic salvation came through electrophysiological interrogation, which illuminated the true substrate: sick sinus syndrome. Ultimately, electrophysiological assessment is the final arbiter when surface ECG and clinical suspicion do not provide clarity. In this specific patient, the introduction of a permanent pacemaker was not merely a procedural landmark but was an absolute turning point in lifesaving. It prevented catastrophic pauses and unstable junctional massage by providing reliable atrial and ventricular excitation. Yet subsequent history showed that implantation was not a point of termination; instead, it was the start of an ongoing collaboration between human physiology and biomedical technology that demanded constant surveillance, organized interrogation, and iterative optimization. A serious programming error, in particular lack of one advanced hysteresis algorithm was associated with clinical worsening including haemodynamic instability and symptomatic hypotension. This highlights the fact that patient survival is not just facilitated by the presence of a device, but how well it was programmed as well. The broader point is inescapable: as modern technology saves life, it can work properly only with careful human attention.

Development of pulmonary infection soon along with acute renal failure made the clinical course more complicated. This is a sequence how organs dependent to each others. Pulmonary infection triggers inflammatory chemistry cascades that disrupt cardiovascular stability and promote arrhythmogenesis, while renal insufficiency destabilises electrolyte balance to generate hyperkalaemia and acid base abnormality which exacerbate myocardial electrical vulnerability. Amid this delicate balance, the survival of the patient confirmed a relationship between antibiotic therapy and cardiovascular drug titration, with timely renal support wobbled. If anything the episode underlines one seminal fact: we cannot expect a multimorbid 80-year-old to fare well with single interventions, but rather with combinations of multiple disciplines working in unison.

The whole arc is a compressed specimen of modern cardiovascular medicine. It also reveals that even devastating intraoperative arrest can be responded to early and effectively with resuscitation. It demonstrates the necessity of coronary revascularisation in patients with

diabetic multivessel disease. It emphasizes that correction of the coronary flow does not always improve the conduction disorders, these latter will have to be revealed by special electrophysiological investigation. It makes the point that pacemakers are not fixed appliances, and rather they are systems calling for continual adjustment and evaluation. It also serves as reminder that systemic infection and renal impairment may destabilize cardiac equilibrium, even one well maintained but collective approach by all specialities can reinstate order.

Several clinical lessons arise. 1- Cardiovascular risk can not be belittled in patients who have underwent minor surgical intervention at all. Secondly, in the case of rhythm abnormalities that continue even after good revascularisation, it would be prudent to suspect conduction disorder. Third, the diagnostic accuracy is crucial because an attribution of dizziness/presyncope to vestibular causes without repudiation of arrhythmic disease entails a major fallacy. Fourth, vigilance in device follow up is mandated and programming features for haemodynamic optimization are applied. Lastly, the patient should be considered as a single entity than can come together collectively (the infected host cylinder) whereby infection and endocrine condition combine with renal health and lung homeostasis for cardiovascular fate.

The broader conclusion is not just one individual's survival, but that modern medicine needs humility, accuracy and integration. The physician must be not just episodic but also vigilant, adaptive and willing to adjust tactics on the fly. In these high-tech days, airway management is not the only strength of medicine -- it's adjusted the spine in different ways as well so that a diverse array of knowledge can be brought to bear toward attaining equilibrium between one side and another.

This particular patient's pathway — from intraoperative arrest to coronary revascularisation, from arrhythmic collapse to pacing therapy, from device programming error and correction, from chest infection causing respiratory failure leading to AKI then recovery — speaks of strength within weakness. His story demonstrates that the doctor's job is to travel through illness' labyrinth with flexible accuracy by directing treatments that parallel diseases' dynamic character. The takeaway isn't an ending at all but rather a note that eternally vigilance and learning is the price of admission for clinical medicine.

References

- 1 Neumar RW, Otto CW, Link MS, et al. Part 8: Adult Advanced Cardiovascular Life Support. 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2010;122(18_suppl_3):S729-S767. doi:10.1161/CIRCULATIONAHA.110.970988
- 2 Haffner SM, Lehto S, Rönnemaa T, Pyörälä K, Laakso M. Mortality from Coronary Heart Disease in Subjects with Type 2 Diabetes and in Nondiabetic Subjects with and without Prior

- Myocardial Infarction. *N Engl J Med.* 1998;339(4):229-234. doi:10.1056/NEJM199807233390404
- 3 Farkouh ME, Domanski M, Sleeper LA, et al. Strategies for Multivessel Revascularization in Patients with Diabetes. *N Engl J Med.* 2012;367(25):2375-2384. doi:10.1056/NEJMoa1211585
 - 4 Dobrzynski H, Boyett MR, Anderson RH. New Insights into Pacemaker Activity: Promoting Understanding of Sick Sinus Syndrome. *Circulation.* 2007;115(14):1921-1932. doi:10.1161/CIRCULATIONAHA.106.616011
 - 5 Furman S, Fisher JD. Role of pacing in the management of patients with sick sinus syndrome. *Circulation.* 1973;47(4):635-641. doi:10.1161/01.CIR.47.4.635
 - 6 Narula OS. Sinus Node Disorders: Electrophysiological Considerations. *Circulation.* 1972;45(6):140-151. doi:10.1161/01.CIR.45.6.140
 - 7 Lamas GA, Lee KL, Sweeney MO, et al. Ventricular Pacing or Dual-Chamber Pacing for Sinus-Node Dysfunction. *N Engl J Med.* 2002;346(24):1854-1862. doi:10.1056/NEJMoa013040
 - 8 Sweeney MO, Hellkamp AS, Ellenbogen KA, et al. Adverse Effect of Ventricular Pacing on Heart Failure and Atrial Fibrillation among Patients with Normal Baseline QRS Duration in a Clinical Trial of Pacemaker Therapy for Sinus Node Dysfunction. *Circulation.* 2003;107(23):2932-2937. doi:10.1161/01.CIR.0000072769.17295.B1
 - 9 Corrales-Medina VF, Madjid M, Musher DM. Role of Acute Infection in Triggering Acute Coronary Syndromes. *Lancet Infect Dis.* 2010;10(2):83-92. doi:10.1016/S1473-3099(09)70331-7
 - 10 Cupisti A, Kalantar-Zadeh K. Management of Electrolyte Disorders in Chronic Kidney Disease: Nutritional and Pharmacological Approaches. *Blood Purif.* 2013;36(2):150-159. doi:10.1159/000356084

Chapter 2: intersecting catastrophes of endocrine, metabolic, and cardiovascular decompensation: a case of amiodarone induced thyrotoxicosis with advanced systolic dysfunction

Introduction

A sixty-eight year old gentleman with a long-standing cardiovascular and endocrine fragility was admitted with acute cardiorespiratory compromise and a profound metabolic disequilibrium. His antecedent medical odyssey included surgical closure of a congenital atrial septal defect in early adulthood, implantation of a permanent pacemaker for Mobitz type II atrioventricular conduction block, and subsequent deployment of an implantable cardioverter defibrillator after repetitive malignant ventricular fibrillation. His cardiac phenotype had since evolved into chronic heart failure with a severely reduced left ventricular ejection fraction, measured consistently in the range of twenty five to thirty percent, with recurrent episodes of decompensation. The patient had hypothyroidism treated with levothyroxine, chronic obstructive pulmonary disease with frequent exacerbations, ten years of type two diabetes mellitus, and prior bladder neck incision for a hyporeactive detrusor. Over two weeks he developed worsening dyspnoea culminating in dyspnoea at rest, orthopnoea, paroxysmal nocturnal dyspnoea, increasing peripheral oedema, palpitations, and a four kilogram weight gain with intermittent altered consciousness. Examination showed raised jugular venous pressure, bilateral basal crepitations, tense pitting oedema, and a rapid irregular pulse at about 140 beats per minute. Investigations revealed profound thyrotoxicosis with thyrotropin below 0.01 mIU per L, free thyroxine 3.5 ng per dL, free triiodothyronine 9.2 pg per mL, and negative thyroid peroxidase antibodies. Doppler ultrasonography demonstrated global hypovascularity of the thyroid parenchyma, consistent with destructive thyroiditis.

Concomitantly, he developed two discrete episodes of hyperosmolar hyperglycaemic state, each characterised by plasma glucose exceeding 650 mg/dL, effective serum osmolality surpassing 330 mOsm/kg, absent ketonemia, and severe dehydration. Both

episodes were reversed by carefully titrated intravenous insulin infusion accompanied by meticulous fluid and electrolyte replacement. After stabilisation, he was transitioned to basal insulin degludec (Tresiba) with oral voglibose to mitigate postprandial excursions.

The pharmacological architecture of his management was redesigned in toto. Amiodarone was cautiously down-titrated but not fully discontinued due to his arrhythmogenic substrate. Glucocorticoid therapy was commenced with oral prednisone, leading to gradual biochemical improvement. A beta-adrenergic antagonist was instituted, with dosage meticulously escalated for rate moderation. Most pivotally, sacubitril–valsartan was initiated at a low dose, sequentially titrated upward as tolerated, replacing conventional renin–angiotensin blockade, thereby realigning his neurohumoral milieu. Subsequently, vericiguat was layered into the regimen in view of recurrent hospitalisations and persistently high natriuretic peptide levels. Guideline directed diuretic therapy was modulated in parallel to optimise volume status. Over the ensuing fortnight, his haemodynamics stabilised, pulmonary congestion regressed, thyroid indices trended toward normalisation, arrhythmic storms abated, and glycaemic control improved. He was discharged in improved clinical state with close multidisciplinary follow-up.

Discussion

Amiodarone induced thyrotoxicosis constitutes one of the most formidable iatrogenic sequelae in cardiovascular pharmacotherapy, its incidence varying between two and ten percent of treated cohorts.¹ The dichotomisation into type one, characterised by iodine induced hyperthyroxinaemia arising from nodular or autoimmune glandular substrates, and type two, defined by a destructive thyroiditis of an otherwise morphologically unremarkable gland, carries immediate therapeutic ramifications.² In our patient, Doppler ultrasonography disclosed global hypovascularity while serology remained devoid of autoimmunity, collectively substantiating the diagnosis of type two thyrotoxicosis.

The cardiovascular consequences of this endocrinopathy are particularly dire in patients with pre-existing ventricular dysfunction. Thyroid hormone excess exaggerates adrenergic responsiveness, augments resting heart rate, destabilises myocardial electrophysiology, and propagates both atrial and ventricular arrhythmogenesis, thereby precipitating haemodynamic collapse in advanced heart failure.³ The clinical imperative in such scenarios necessitates stringent rate control, achieved through judicious introduction and titration of beta adrenergic antagonists. Despite apprehensions in the context of concomitant chronic obstructive pulmonary disease, cardioselective agents

have consistently demonstrated salutary effects on survival and morbidity in reduced ejection fraction states.⁴

The cardinal therapeutic inflection was the introduction of sacubitril valsartan. By simultaneously inhibiting neprilysin and antagonising angiotensin receptors, this agent amplifies natriuretic peptide signalling while suppressing maladaptive neurohormonal cascades, culminating in favourable ventricular remodelling and haemodynamic restitution. The landmark PARADIGM HF trial revealed that sacubitril valsartan surpassed enalapril in reducing the composite endpoint of cardiovascular death and hospitalisation for heart failure.⁵ In our patient, cautious initiation followed by incremental titration of sacubitril valsartan yielded progressive haemodynamic improvement.

Given his recurrent hospitalisations and persistently elevated natriuretic peptides, vericiguat was subsequently superimposed. This soluble guanylate cyclase stimulator enhances nitric oxide cyclic guanosine monophosphate signalling and demonstrated a reduction in adverse outcomes in the VICTORIA trial.⁶ The incorporation of vericiguat into an already optimised regimen exemplifies the evolving paradigm of layered pharmacological therapy in advanced systolic dysfunction.

Concomitantly, the administration of glucocorticoids for destructive thyroiditis potentiated glycaemic instability and provoked episodes of hyperosmolar hyperglycaemic state. This was mitigated by intravenous insulin infusion followed by transition to basal degludec in concert with voglibose to attenuate postprandial surges. Such tailoring illustrates the complex interplay between endocrine and cardiovascular therapeutics, wherein stabilisation in one domain may destabilise another.⁷

In aggregate, this case underscores that restoration of equilibrium in the setting of advanced multimorbidity is not the triumph of a single agent but the orchestration of carefully titrated, synergistic, and interdisciplinary strategies.

Conclusion

This clinical vignette epitomises the precarious but manageable intersection of arrhythmia control, destructive thyrotoxicosis, advanced systolic dysfunction, and metabolic decompensation. Through measured attenuation of amiodarone, administration of corticosteroids, introduction and incremental titration of sacubitril–valsartan, careful integration of vericiguat, strategic beta-adrenergic blockade, and rigorous metabolic correction, clinical equipoise was restored. The case exemplifies the necessity for vigilant multidisciplinary stewardship and the irreplaceable role of pharmacological titration in navigating the labyrinth of multi-morbid cardiovascular endocrinometabolic disease.

References

- 1 Macchia PE, Bartalena L, Bogazzi F, et al. Amiodarone Induced Thyrotoxicosis. In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2022. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK279030/>
- 2 Bartalena L, Bogazzi F, Chiovato L, Hubalewska Dydejczyk A, Links TP, Vanderpump M. 2018 European Thyroid Association Guidelines for the Management of Amiodarone Associated Thyroid Dysfunction. *Eur Thyroid J*. 2018;7(2):55-66. doi:10.1159/000487164
- 3 Batcher EL, Tang XC, Singh BN, Singh SN, Reda DJ, Hershman JM. Thyroid Function Abnormalities During Amiodarone Therapy for Persistent Atrial Fibrillation. *Am J Med*. 2007;120(10):880-885. doi:10.1016/j.amjmed.2007.03.025
- 4 DiNicolantonio JJ, O'Keefe JH, Lucan SC. Beta Blockers in Hypertension, Diabetes, Heart Failure and Acute Myocardial Infarction: A Review. *Open Heart*. 2015;2(1):e000230. doi:10.1136/openhrt.2014.000230
- 5 McMurray JJV, Packer M, Desai AS, et al. Angiotensin Neprilysin Inhibition versus Enalapril in Heart Failure. *N Engl J Med*. 2014;371(11):993-1004. doi:10.1056/NEJMoa1409077
- 6 Armstrong PW, Pieske B, Anstrom KJ, et al. Vericiguat in Patients with Heart Failure and Reduced Ejection Fraction. *N Engl J Med*. 2020;382(20):1883-1893. doi:10.1056/NEJMoa1915928
- 7 Li X, Zhao Y, Yin H, et al. Diabetes and Heart Failure: A Literature Review, Reflection, and Recommendation. *Biomolecules*. 2024;14(7):1572. doi:10.3390/biomolecules14071572

Chapter 3: Catastrophic veno thromboembolic event complicated by locoregional septic soft-tissue insult and multisystem perturbations

Introduction

A forty eight year old woman was admitted with a two week history of progressively painful swelling of the left lower limb, accompanied by recent exertional dyspnoea and episodes of rapid heart rate. Antecedent history from clinical notes were abnormal uterine bleeding as endometrial hyperplasia was suspected, previous diagnosis of nephrolithiasis, non alcoholic fatty liver disease NAFLD and morbid obesity with a recorded BMI level over 40. The affected limb demonstrated copious purulent discharge with local tenseness and marked tenderness, consistent with an evolving cellu-
litic process.

The patient was tachycardic at 130 beats per minute, hypertensive (140/70 mmHg) and tachypnoeic with a respiratory rate of 26 breaths per minute; peripheral O₂ saturation was still reported as 98 percent in room air.

Record keeping of fluid balance was incomplete with a recorded input and output of 350 ml and 650 ml, respectively. Examination as recorded revealed reduced air entry with crepitations in the right hemithorax, a swollen left leg with seropurulent discharge, and hepatomegaly on palpation of the abdomen.

Investigations

A. Haematology and Biochemistry

Laboratory evaluation demonstrated significant anaemia with haemoglobin 8.6 g/dL (reference 12.0 to 15.0) and indices consistent with microcytic anaemia, with a red blood cell count of 3.29×10^6 per μL and a haematocrit of 27.2 percent. The total leucocyte count was 10 000 cells per μL with neutrophils 82 percent and lymphocytes 14 percent,

and platelet count was 384×10^3 per μL , representing borderline thrombocytosis compatible with an acute phase response. D dimer was profoundly elevated at greater than 10 000 ng/mL (reference 45 to 500 ng/mL), strongly suggestive of a high thrombotic burden. Procalcitonin measured by ECLIA was 5.32 ng/mL, a value highly suggestive of systemic bacterial infection and increased sepsis risk. Random capillary blood glucose was 122 mg/dL. Markers of inflammation were markedly raised with C reactive protein 186 mg/L (reference <5 mg/L) and erythrocyte sedimentation rate 94 mm per hour (reference <20 mm per hour). Fibrinogen was 678 mg/dL (reference 200 to 400 mg/dL), consistent with hyperfibrinogenaemia in the setting of an acute phase prothrombotic response. Lactate dehydrogenase was 512 U/L (reference 135 to 225 U/L), supporting tissue injury or haemolysis, and serum ferritin was 1 230 ng/mL (reference 20 to 300 ng/mL), reflecting anaemia of inflammation within a hyperinflammatory milieu. Nutritional and synthetic reserve appeared reduced with serum albumin 2.6 g/dL (reference 3.5 to 5.0 g/dL). Renal function showed borderline elevation of serum creatinine at 1.3 mg/dL (reference 0.6 to 1.2 mg/dL), which may reflect septic or prerenal involvement, while liver enzymes were mildly raised with AST 56 U/L and ALT 62 U/L, likely secondary to systemic inflammatory or metabolic stress. NT proBNP was 812 pg/mL (reference <125 pg/mL), a level compatible with ventricular strain in the context of pulmonary embolism, and arterial lactate was 3.4 mmol/L (reference 0.5 to 2.2 mmol/L), indicating tissue hypoperfusion related to sepsis.

B. Liver imaging: sonographic and CT evidence of hepatic steatosis with hepatomegaly (longitudinal span ~18.6 cm); liver function test perturbations were documented though numeric trends.

C. Vascular Imaging

Bilateral lower-limb venous duplex (left): Echogenic occlusive thrombus causing complete non-compressibility of the left external iliac vein (EIV), common femoral vein (CFV), superficial femoral vein (SFV) and popliteal vein; extension into the anterior and posterior tibial veins; occlusive thrombus in the great saphenous vein (GSV) throughout the thigh and into the proximal leg. Diffuse subcutaneous oedema of the left lower limb was evident. Right lower-limb deep and superficial veins were documented as fully patent and compressible.

Computed tomographic pulmonary angiogram (contrast): Peripheral partially occluding thrombus in the proximal right upper lobe posterior segmental pulmonary artery (measured ≈ 6 mm); mural thrombus within the right lower-lobe pulmonary artery extending into segmental branches producing variable luminal obstruction; mural thrombi also in segmental branches of the left lower-lobe pulmonary artery. Main pulmonary artery calibre measured ~ 27 mm; right and left pulmonary arterial branches measured ~ 16.9 mm and 16.2 mm respectively. Additionally, a partially occlusive

thrombus was visualised in the caudal (distal) portion of the inferior vena cava approximately 5 cm distal to the renal vein termination (as per imaging note).



FIGURE 1 :3D Volume-Rendered CT Pulmonary Angiography (VRT - Posterior View), Showing bilateral pulmonary artery tree with embolic material (black/gray speckled filling defects) inside the pulmonary arteries — consistent with pulmonary embolism (PE).

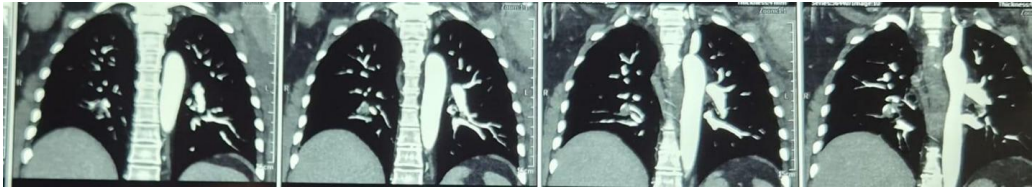


FIGURE 2:Coronal CT Pulmonary Angiography (C-CTPA),demonstrating contrast-filled pulmonary arteries with **central filling defects (dark intraluminal areas), classic for **pulmonary emboli** in both lungs.**



FIGURE 3:Sagittal CT Pulmonary Angiography (S-CTPA),with contrast-enhanced sections showing **filling defects in the main pulmonary artery or branches, suggesting **central pulmonary embolism**.**

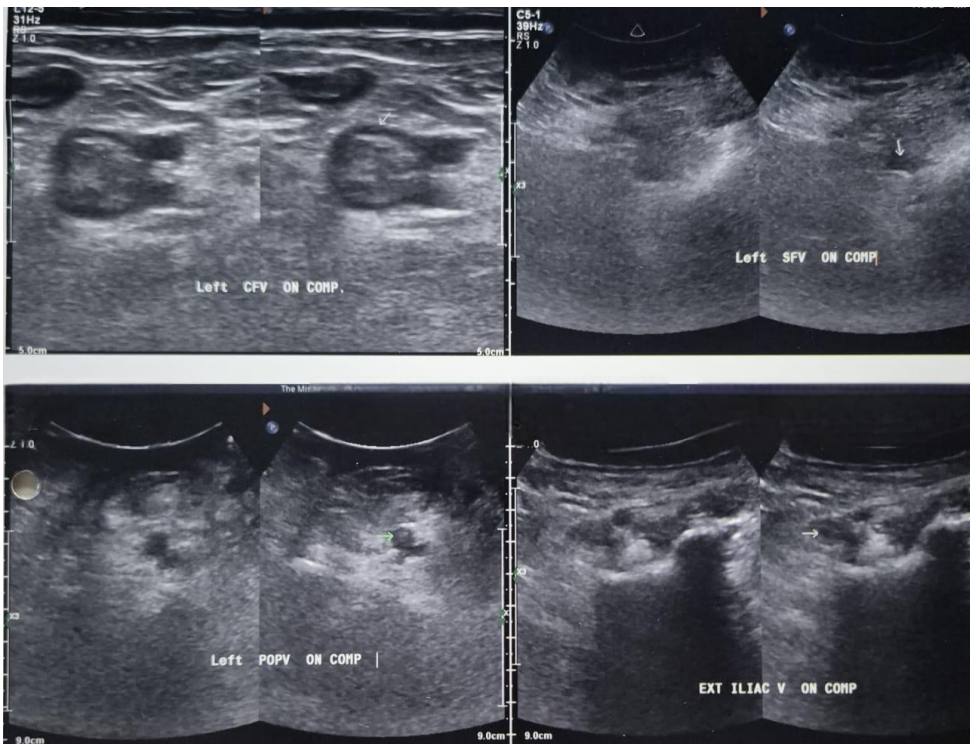


FIGURE 4: Duplex Doppler and compression ultrasound show loss of compressibility in the common femoral vein, superficial femoral vein, popliteal vein, external iliac vein, and posterior tibial vein, indicating extensive deep vein thrombosis.

Diagnosis

- I. **Extensive Ilio-femoropopliteal DVT with Propagation into IVC**, constituting a massive thrombotic burden.
- II. **Multiple Bilateral Pulmonary Emboli**, submassive in extent, with biochemical evidence of right ventricular strain (NT-proBNP elevation).
- III. **Superimposed Sepsis with Left-Leg Cellulitis**, corroborated by elevated procalcitonin, neutrophilia, high CRP/ESR, and clinical limb findings.
- IV. **Anaemia of Chronic Disease with Inflammatory Hyperferritinaemia**, with contributory microcytic indices.
- V. **Morbid Obesity with NAFLD**, conferring chronic proinflammatory and prothrombotic risk.
- VI. **Possible Early AKI**, evidenced by borderline creatinine rise and elevated lactate in the context of systemic sepsis and haemodynamic compromise.
- VII. **Gynaecological Pathology (abnormal uterine bleeding/endometrial hyperplasia)** under consideration as an underlying prothrombotic driver.

Upon admission, the patient was immediately triaged as a case of **high-risk venous thromboembolism with systemic sepsis**. A **multidisciplinary team (MDT)** comprising vascular medicine, critical care, infectious disease, and hepatology was activated to ensure synchronous and layered management.

Therapeutic anticoagulation was instituted with **rivaroxaban**, initially at loading doses (15 mg bid), subsequently consolidated into maintenance regimens after haemodynamic stabilization. Oral factor Xa inhibition was chosen due its predictable kinetics, lack of mandatory monitoring and near liver tolerance character despite NAFLD. Carefully monitored serial anti-Xa activity was observed in order to eliminate subtherapeutic escape or drug accumulation given evolving renal parameters. Duplex Doppler and CT venographic intervals were scheduled for objective monitoring of clot regression and non-progression within the ilio caval axis.

On the basis of extensive cellulitic sepsis and systemic inflammatory activation two insults, a mutual broad-spectrum antimicrobial cover was implemented with triple scheme:

- I. **Meropenem** (carbapenem backbone for Gram-negative, anaerobic, and ESBL coverage),
- II. **Teicoplanin** (glycopeptide for Gram-positive/MRSA coverage), and
- III. **Tigecycline** (for deep-seated polymicrobial tissue penetration, particularly soft-tissue and intra-abdominal pathogens).

Therapeutic drug monitoring of teicoplanin trough concentrations was implemented and antimicrobial stewardship integrated de escalation based on serial procalcitonin values, combining aggressive source control with minimizing the selection pressure for resistance. Dynamic preload indices, and serial lactate clearances were used to titrate fluid resuscitation according to clinical response, in order not to induce iatrogenic hypervolemia in the context of borderline right ventricular strain. Back-up vasopressor (low-dose norepinephrine) was maintained available, but not used after immediate reversal of distributive physiology. Renal perfusion was maintained by avoiding nephrotoxic agents, dose adjustment of all pharmacotherapy for renal function with six-hourly monitoring of serum creatinine and urine output to predict the occurrence of AKI. The anaemia of chronic inflammation was treated with intravenous iron carbohydrate complex under a strategy that deferred erythropoietin use and prioritised restoration of oxygen delivery, while serial haematocrit measurements ensured safety with respect to haemodilutional limits. Fibrinogen and ferritin were trended as surrogate markers of inflammation, and a fall in C reactive protein by day five was interpreted as early evidence of microbial clearance. Concomitant non alcoholic fatty liver disease with hepatomegaly prompted close surveillance of transaminase trajectories and hepatobiliary Doppler flow, and consideration was given to prophylactic hepatoprotective therapy such as ursodeoxycholic acid. Albumin infusions were intermittently employed to restore oncotic balance and optimize intravascular resuscitative efficacy.

Given the documented **bilateral pulmonary emboli**, continuous **telemetric rhythm surveillance** was instituted to screen for arrhythmic perturbations. NT-proBNP and bedside echocardiography serials were harnessed to monitor right ventricular strain resolution. Oxygenation indices were maintained in the high-normal range through non-invasive oxygen supplementation, averting mechanical ventilation.

Menstrual and endometrial pathology was acknowledged as a potential thrombotic contributor. While acute stabilization was prioritized, an **outpatient hysteroscopic evaluation** was scheduled following recovery to address the gynaecological substrate.

Morbid obesity was targeted through dietary, metabolic, and hepatological counseling in anticipation of secondary prevention strategies.

Monitoring Protocol:

- I. **Vitals & Haemodynamics:** Hourly MAP, SpO₂, urine output; invasive arterial line secured for beat-to-beat pressure monitoring.
- II. **Laboratory Surveillance:** Daily CBC, renal/liver panel, electrolytes; CRP and procalcitonin every 48 hours until sepsis resolution.
- III. **Imaging:** Duplex Doppler at day 7 and day 14 to ensure non-propagation; CTPA repeat only if clinical decompensation.
- IV. **Anticoagulation Monitoring:** Anti-Xa assays weekly; coagulation panels (PT, aPTT, INR) to track hepatic interplay.
- V. **Sepsis Monitoring:** Sepsis scoring (qSOFA/SOFA) twice daily; lactate clearance trends every 12 hours until normalization.
- VI. **Renal Surveillance:** Creatinine and urine output q6h; renal ultrasound reserved for oliguria non-responsive to volume.
- VII. **Cardiac Surveillance:** NT-proBNP and echocardiography weekly; continuous ECG telemetry for arrhythmic vigilance.

Outcome:

By the end of the **third week of hospitalization**, the patient demonstrated:

- I. Significant regression of limb oedema and erythema with subsidence of purulent discharge,
- II. Down-trending inflammatory markers (CRP <20 mg/L; procalcitonin <0.5 ng/mL),
- III. Stabilization of renal indices (creatinine normalized to 1.0 mg/dL),
- IV. Improved haematocrit following iron therapy,
- V. Radiological evidence of **clot stabilization without further propagation**,
- VI. Restoration of ambulation with compression therapy and physiotherapy.

Discussion

The present clinicopathological tableau constitutes an intricate confluence of multiple deleterious vascular and systemic perturbations, wherein the genesis and propagation of venous thromboembolism appear to have been potentiated by a constellation of metabolic, inflammatory, and haemodynamic aberrations. At its core lies the pathophysiological paradigm of **Virchow's triad** consisting of endothelial injury¹, hypercoagulability², and venous stasis³, each axis of which seems conspicuously represented in the present scenario.

The morbid adiposity of the subject, compounded by nonalcoholic fatty liver disease and potential endocrinological dysregulation arising from abnormal uterine bleeding with putative endometrial hyperplasia, is emblematic of a prothrombotic milieu orchestrated by chronic low grade systemic inflammation, insulin resistance, and dysregulated adipokine signalling⁴. In such an environment, even minor perturbations in vascular homeostasis can precipitate exuberant thrombus formation.

The thrombotic burden delineated radiologically, encompassing occlusion of the external iliac, common femoral, superficial femoral, popliteal, and tibial venous conduits with synchronous extension into the great saphenous vein and partial inferior caval involvement, represents a veritable crescendo of deep venous thrombosis. The mechanical and haemodynamic sequelae of such proximal thrombosis are not merely confined to the extremity, but exert centripetal consequences through embolic dissemination culminating in segmental and subsegmental pulmonary arterial compromise. The pulmonary angiographic findings of mural thrombi in both lower lobar branches and the posterior segmental right upper lobe artery illustrate the classic emboligenic trajectory from deep venous nidus to pulmonary vasculature, further validated by the profound elevation of D dimer levels, exceeding by more than an order of magnitude the upper limits of physiological fibrinolytic activity.

Yet the narrative complexity of this case is compounded by the concomitant infectious inflammatory burden, as evidenced by markedly elevated procalcitonin levels and the overt cellulitic involvement of the left lower limb. It is now known that critical illness as an epiphenomenon but also a causative driver of hypercoagulability via cytokine storm, endothelial dysfunction, and monocyte tissue factor activation⁵. Thus, the vicious interplay of septic inflammation and venous thrombosis generates a synergistic amplification loop, whereby infection accelerates thrombosis and thrombosis aggravates tissue hypoperfusion and necrosis, thereby fostering further infective propagation. The purulent discharge and extensive subcutaneous oedema of the limb are therefore not only local sequelae but integral actors in the systemic pathophysiological orchestra.

Furthermore, the hepatic steatosis and hepatomegaly documented radiologically should not be relegated to a peripheral incidental finding, for the steatotic liver in the setting of

obesity is a nexus of metabolic disarray. It imparts both proinflammatory and prothrombotic impulses, through altered synthesis of coagulation factors, diminished fibrinolysis due to upregulated plasminogen activator inhibitor ¹, and dysregulation of the hepatic acute phase response⁶. Thus, the liver pathology in this subject represents both a participant and an amplifier in the venothromboembolic drama.

This case thereby exemplifies a systemic derangement wherein no single factor suffices to explicate the enormity of thromboembolic disease. Rather, it is the confluence of obesity driven metabolic inflammation, occult gynaecological pathology, infectious insult, and vascular stasis that orchestrates the malignant crescendo of events. The presence of anaemia, particularly microcytic and hypochromic, further complicates the picture, as anaemia has paradoxical associations with both tissue hypoxia that drives endothelial perturbation and hyperdynamic circulation that augments shear stress, both of which can contribute to thromboembolic phenomena.

Management in such a labyrinthine scenario is fraught with peril and nuance. Anticoagulation, the mainstay of venothromboembolic therapy, must be judiciously balanced against the risks of sepsis induced coagulopathy, potential surgical intervention for cellulosic or necrotising processes, and the haemodynamic consequences of pulmonary embolism. The consideration of caval filters, catheter directed thrombolysis, or surgical thrombectomy demands sophisticated multidisciplinary arbitration, given the coexistent caval thrombus and septic substrate.

Conclusion

This case exemplifies fulminant unprovoked venous thromboembolic disease, manifesting as extensive iliofemoral venous thrombosis with caval extension and embolic propagation into the pulmonary arterial circulation, occurring together with superimposed sepsis and profound metabolic disturbance. It illustrates that venous thromboembolism is rarely an isolated vascular event but instead represents the end result of interacting pathophysiological processes, notably metabolic dysregulation, systemic inflammatory activation, venous stasis, and endothelial injury. Morbid obesity, NALFD, occult gynaecological pathology and a pathway of overt soft tissue infection combined to produce an incredibly prothrombotic background which gave rise to a clinical nightmare of vascular events with capacity for multisystem failure. The striking laboratory abnormalities and marked elevation of fibrinolytic markers together with the coexistence of pulmonary emboli and limb threatening deep vein thrombosis emphasise the systemic scope of the disorder rather than confinement to a single vascular territory. From a clinical perspective, venous thromboembolic disease should be approached as an integrative syndrome at the interface of haematology, infectious disease, hepatology, endocrinology, and vascular medicine, prompting thorough evaluation for occult

malignancy, metabolic contributors, and infectious precipitants while implementing decisive multidisciplinary treatment to prevent imminent mortality. In summary, the case is a sobering demonstration of the lethal synergy between obesity, infection, and thrombosis and it reinforces the need for vigilant, comprehensive, and preemptive management of the protean manifestations of venous thromboembolism.

References

- 1 Colling ME, Kanthi Y. Inflammation, Infection and Venous Thromboembolism. *Circulation Research*. 2021;129(1):36–49. DOI: 10.1161/CIRCRESAHA.121.318225
- 2 Tripodi A, Lombardi R, Primignani M, et al. Hypercoagulability in Patients with Nonalcoholic Fatty Liver Disease. *Biomedicines*. 2022;10(2):249. DOI: 10.3390/biomedicines10020249
- 3 La Rosa F, Montecucco F, Liberale L, Sessarego M, Carbone F. Venous Thrombosis and Obesity: From Clinical Needs to Therapeutic Challenges. *Internal and Emergency Medicine*. 2025. DOI: 10.1007/s11739-024-03765-7
- 4 Kim CY, Lee JH, Cho DY, et al. Association of Nonalcoholic Fatty Liver Disease and Venous Thromboembolism in Healthy Adults: A Nationwide Cohort Study. *Scientific Reports*. 2023;13:42963. DOI: 10.1038/s41598-023-42963-9
- 5 Pati I, Mehta G, Hussain A, et al. Risk of Venous Thromboembolism in Infectious Diseases. *Pathogens*. 2025;14(8):816. DOI: 10.3390/pathogens14080816
- 6 Northup PG, Bunchorntavakul C, Shah NL. Hypercoagulation and Thrombophilia in Liver Disease. *Clinics in Liver Disease*. 2022. DOI: 10.1016/j.cld.2022.01.010

Chapter 4: Severe multi-organ dysfunction following acute hepatitis a and superimposed salmonella typhi septicaemia in a young adult with nosocomial Acinetobacter infection: intensive care management and prolonged hepatic convalescence

Introduction

A nineteen-year-old female undergraduate, with no antecedent comorbidities apart from a well-documented diagnosis of polycystic ovarian disease, which had been conservatively managed without pharmacological intervention, presented after a collegiate cultural gathering where she consumed a variety of culinary preparations under unhygienic conditions. Within three days, she experienced profound malaise, diffuse myalgia, low grade pyrexia, anorexia, and vague abdominal discomfort. These symptoms, initially dismissed as trivial, soon culminated in frank icterus with passage of darkly pigmented urine, persistent nausea, and recurrent emesis, prompting medical evaluation.

On admission, she was alert but systemically unwell. Her pulse was one hundred and two per minute, blood pressure one hundred and twelve over seventy four millimetres of mercury, temperature one hundred point four degrees Fahrenheit, and respiratory rate twenty two per minute. . There was marked scleral icterus, with mild hepatomegaly and focal hepatic tenderness. Laboratory investigations revealed a total serum bilirubin of 5.8 mg/dL (largely conjugated), alanine aminotransferase 824 U/L, aspartate aminotransferase 756 U/L, alkaline phosphatase 325 U/L and mildly prolonged prothrombin time with an international normalised ratio of 1.4. Viral serology results established the diagnosis of acute hepatitis A with elevated anti HAV igM antibody titres, and he was managed with IV fluid, antiemetics, hepatoprotective drugs, nutrition support and regular coagulation status monitoring. In the following 5 days, she developed high fever with rigor and chills, and began to show continued extensive systemic deterioration. Blood cultures yielded Salmonella Typhi, thus confirming

superimposed enteric septicemia, and empirical antimicrobial therapy was modified based on sensitivity tests. This double infectious insult led to haemodynamically unstable sepsis but with immediate renal involvement: seventy two hours after onset of bacteremia serum creatinine was raised from an base line value of 0.9 to 2.7 mg/dl associated with oliguria and blood urea concentrations were -nitrogen values, respectively (normal range 15-50 mg/ dl) , nitrogen 84 milligrams per decilitre. . On day ten she met Kidney Disease Improving Global Outcomes stage three criteria for acute kidney injury (AKI) with creatinine peaking at 6.2 mg/dL and urine output less than two hundred millilitres per twenty four hours. Electrolyte abnormalities were a persistent hyperkalaemia to 6.1 mmol/l and metabolic acidosis arterial pH 7.28. Urinalysis showed granular casts as well as sterile pyuria, and the renal sonogram showed bilateral enlarged kidneys without obstructive dilatation. Her clinical course was also complicated by episodic protracted episodes of marked haemodynamic instability with sudden plunging systolic blood pressure to seventy mmHg, significant tachycardia reaching more than 130 beats per minute, cool peripheral circulations and delayed capillary refill and transient loss of conscious episodes

These collapses required aggressive volume resuscitation and escalation to vasopressor therapy with norepinephrine and later vasopressin infusion. She was transferred to the critical care unit where invasive arterial monitoring was instituted.

During this tenuous phase, she developed a secondary nosocomial infection. Blood and tracheobronchial secretions yielded *Acinetobacter baumannii*, multidrug resistant in nature. However, the patient was not intubated; rather, oxygen supplementation was maintained by non rebreather mask at high fractional inspired oxygen delivery. This modality ensured adequate oxygenation while minimising invasive mechanical support. The *Acinetobacter* infection necessitated colistin based therapy combined with carbapenem rescue, administered according to sensitivity testing.

Her cumulative clinical burden resulted in a peak sequential organ failure assessment score of eleven. Nonetheless, the multidisciplinary intensive care team pursued an aggressive organ support strategy. Renal replacement therapy was instituted by sustained low efficiency dialysis sessions performed on alternate days, which successfully controlled uremia and corrected electrolyte derangements. Meticulous titration of vasopressors, fluid balance monitoring, rigorous antimicrobial stewardship, correction of metabolic acidosis, nutritional optimisation, and vigilant surveillance of coagulation parameters were persistently undertaken.

Gradually, signs of recovery emerged. By the third week of hospitalisation, serum bilirubin declined to 2.4 milligrams per decilitre, hepatic enzymes showed downward trajectory, coagulation indices normalised, and creatinine fell to 1.1 milligrams per decilitre with restoration of adequate urine output. Vasopressors were tapered and

discontinued, haemodynamic stability was restored, and oxygen supplementation was gradually reduced from high FiO₂ non rebreather mask to ambient air.

After thirty two days of hospitalisation, the patient was discharged with preserved renal function, normalised electrolytes, convalescent hepatic profile, and resolution of infectious processes.

On serial outpatient surveillance, she remained stable from the renal and systemic standpoint. Renal indices demonstrated consistent creatinine between 0.9 and 1.2 milligrams per decilitre, normal electrolytes, and satisfactory urine output. Nutritional status improved progressively, and she resumed daily activities. However, persistence of subtle hepatic biochemical abnormalities was noted. Alanine aminotransferase fluctuated between 65 and 110 units per litre, aspartate aminotransferase between 55 and 95 units per litre, with intermittent elevation of bilirubin up to 1.8 milligrams per decilitre. Viral serology demonstrated persistent anti HAV immunoglobulin M reactivity and occasional detection of viral RNA, raising the concern of a potential carrier state of Hepatitis A, an entity rarely described in the literature.

Following hospital discharge, the patient was enrolled in a rigorous longitudinal hepatological monitoring protocol designed to elucidate the trajectory of residual hepatic dysfunction and potential viral persistence. Serial laboratory assessments were performed at three day intervals for the first month, then weekly for two months, and subsequently at fortnightly intervals. This high-resolution monitoring strategy aimed to capture subtle fluctuations in hepatocellular integrity, synthetic capacity, and cholestatic indices, thereby providing granular insight into the convalescent phase of Hepatitis A complicated by sequential systemic insults.

Alanine aminotransferase values, initially elevated at 824 units per litre during acute illness, demonstrated a progressive decline to 210 units per litre at discharge. In the post-discharge period, ALT levels oscillated between 65 and 110 units per litre, displaying a pattern of episodic transaminase surges approximately every ten to fourteen days, suggestive of intermittent hepatocellular stress. Aspartate aminotransferase followed a parallel trajectory, declining from 756 units per litre acutely to a plateau between 55 and 95 units per litre during follow-up. These persistent yet subclinical elevations indicate ongoing hepatocellular perturbation potentially related to delayed immune mediated clearance or intermittent low-level viral replication.

Total serum bilirubin exhibited similar intermittent fluctuations. From a peak of 5.8 milligrams per decilitre, levels declined to 1.8 milligrams per decilitre post discharge, with transient elevations correlating temporally with minor episodes of systemic stress or intercurrent minor infections. Direct bilirubin remained mildly elevated at 0.9 to 1.2 milligrams per decilitre, reflecting subtle cholestatic retention in the context of hepatocellular recovery. Serum alkaline phosphatase values ranged between 110 and 140

units per litre, and gamma-glutamyl transferase oscillated between 32 and 58 units per litre, suggestive of residual mild cholestasis without overt biliary obstruction.

Her hepatic synthetic function was closely monitored through serum albumin, prothrombin time, and international normalized ratio. Albumin, initially depressed to 2.8 grams per decilitre during the acute illness, improved steadily to 3.9 grams per decilitre, indicating restoration of protein synthetic capacity. A normalization of the coagulation indexes was shown by prothrombin time (12.4 and 13.2 seconds) and INR always <1.2, confirming no clinically relevant coagulopathy. Globulin fraction was weakly increased 2.3-2.7 g/dl indicating a persistent humoral immune activation probably against the remnants of viral antigens. Quantitative monitoring of viral RNA by sensitive polymerase chain reaction assays showed intermittent low-level HAV RNA in serum at 10^3 to 10^4 genome copies per milliliter on several occasions, albeit falling towards the limit of detection for the assay by week twelve post-discharge; stool samples also yielded occasional RNA positivity, demonstrating continuing minimum level viral shedding despite apparent clinical convalescence. Imaging also correlated with these findings: abdominal ultrasonography revealed a normal size liver with mild heterogeneity of echotexture suggestive of residual hepatocellular regeneration, and Doppler assessment confirmed intact portal and hepatic venous flow. Initial measurement of hepatic stiffness by shear wave elastography was elevated at 7.2 kPa, but had decreased to 5.8 kPa by six weeks post-resolution, indicative of dynamic tissue restitution. Collectively, the persistence of mild transaminase elevation, intermittent bilirubin fluctuations, hypergammaglobulinemia, and sporadic viral RNA detection suggest a protracted convalescence. Continuous follow-up is warranted to differentiate benign prolonged recovery from persistent infection, to guide advice on transmissibility, and to anticipate potential late sequelae.

Discussion

The clinical trajectory of this 19 year old patient demonstrates how a typically self-limited infection can become life threatening when two insults occur intersect. What initially presented as acute hepatitis A in a healthy young adult was later complicated by invasive enteric bacteraemia, acute kidney injury and secondary colonisation with multi-resistant organisms. The interplay of these constituent elements converted an innocuous disease to the vicious multi organ syndrome, wherein a thin line separated infection from systemic resilience in the young.

Acute Hepatitis A was the first insult, which was acquired through consuming contaminated food at a college cultural event itself, thus constituting food borne epidemic clustering. Hepatitis A virus, a non-enveloped RNA picornavirus, replicates predominantly in hepatocytes and Kupffer cells resulting into hepatocellular necrosis

and inflammatory parenchymal lesions. The vast majority of infections resolve spontaneously within weeks, with convalescent immunity conferred by neutralising antibodies. However, rare cases evolve into prolonged cholestasis, autoimmune phenomena, or unusually persistent serological positivity suggestive of carrier like states, a phenomenon under vigorous contemporary scrutiny¹.

Superimposition of *Salmonella* Typhi septicaemia constituted the second catastrophic axis. Enteric fever, acquired via ingestion of contaminated food or water, traverses the intestinal epithelium, disseminates via reticuloendothelial macrophages, and seeds the bloodstream. Septicaemia with *Salmonella* Typhi complicating viral hepatitis is scarcely reported, yet immunological perturbation and hepatocellular dysfunction during acute hepatitis may facilitate bacterial dissemination and systemic invasion². In this patient, rapid deterioration of renal indices and multi organ derangement reflected the systemic inflammatory cascade triggered by endotoxin, with microcirculatory dysfunction and prerenal azotemia transmuting into frank acute tubular necrosis.

The renal insult fulfilled Kidney Disease Improving Global Outcomes stage three criteria, the most severe spectrum of acute kidney injury. In young individuals, recovery potential is high provided supportive measures are instituted early. Sustained low efficiency dialysis was pivotal in temporising uremia, reversing hyperkalaemia, and correcting acid base imbalance. The integration of dialysis into critical care management without nephrology subspecialty consultation reflects the increasing cross disciplinary competence of intensivists³.

A further nosocomial colonisation with *Acinetobacter baumannii* represented a formidable challenge. This opportunistic pathogen, notorious in intensive care environments, thrives on abiotic surfaces, demonstrates biofilm resilience, and displays extensive antimicrobial resistance mechanisms including efflux pumps, beta lactamase production, and porin channel modifications. Infections with multidrug resistant *Acinetobacter* are associated with extended hospital stays, heightened costs, and escalated mortality. Combination regimens employing colistin remain the salvage cornerstone despite nephrotoxicity and neurotoxicity concerns⁴. The successful eradication of this infection in our patient underscores the efficacy of timely culture guided stewardship coupled with rigorous infection control.

Perhaps the most intriguing aftermath is the persistence of Hepatitis A related biochemical abnormalities and ongoing serological reactivity. Traditional teaching posits that Hepatitis A does not evolve into chronicity or carrier state. Yet, recent literature has described prolonged viral shedding and persistent RNA detection in subsets of individuals, particularly in the context of coexistent immunological perturbation or concomitant systemic illness⁵. The mild but persistent elevation of aminotransferases, sporadic bilirubin excursions, and serological reactivity in this

patient echo these emerging observations. Vigilant longitudinal hepatological surveillance remains mandatory to delineate whether this represents protracted convalescence or a novel manifestation of viral persistence.

During her hospitalisation, she experienced multiple episodes of profound haemodynamic instability, underscoring the precarious balance between systemic inflammatory responses, cytokine surges, and her cardiovascular reserve. These events, marked by abrupt declines in systolic blood pressure, tachycardia, and transient neurological impairment, required escalation of vasopressor support. Such circulatory disturbances are well recognised as key determinants of outcome in sepsis associated multiorgan dysfunction. The eventual stabilization of her haemodynamics represented a pivotal turning point in her overall recovery.

Taken together, her course illustrates how an infection that is typically mild in a young adult can, through sequential complications including invasive bacterial superinfection, renal impairment, nosocomial colonisation, and circulatory collapse, evolve into a complex multi organ syndrome. At the same time, it highlights the remarkable capacity of physiological systems to recover when supported by careful, organ specific, and vigilant therapy.

Conclusion

This unusual case illustrates how a normally self limiting infection can set the stage for a cascade of serious complications in a previously healthy young adult. Her acute hepatitis A infection created a vulnerable environment that allowed invasive *Salmonella* Typhi septicemia to develop, leading to severe acute kidney injury and haemodynamic instability. The interaction of viral liver involvement, enteric bacterial invasion, renal compromise, and colonisation by hospital acquired pathogens underscores how even pathogens usually considered mild can, when compounded by additional stressors, precipitate profound multi organ dysfunction and challenge the body's ability to maintain systemic balance.

The episodes of frank circulatory collapse, characterised by abrupt hypotension, tachycardia, and transient neurological perturbations, exemplify the dynamic and precarious interdependence between systemic inflammation, microcirculatory perfusion, and cardiac reserve. These episodes necessitated vigilant, real time haemodynamic titration, judicious fluid resuscitation, and timely initiation of vasopressor support, demonstrating that the orchestration of critical care interventions, even in the absence of invasive mechanical ventilation, can suffice to restore cardiovascular equilibrium. The use of high FiO₂ via non rebreather mask exemplifies the utility of non invasive

oxygenation strategies in sustaining tissue oxygen delivery without compounding risk of ventilator associated complications.

Renal involvement in this patient, reaching KDIGO stage three acute kidney injury, further accentuates the systemic vulnerability induced by combined hepatocellular dysfunction, endotoxemic shock, and sepsis mediated tubular injury. The successful implementation of sustained low efficiency dialysis sessions highlights the importance of temporising interventions to maintain metabolic homeostasis and avert irreversible organ damage. The absence of nephrology team involvement underscores the evolving paradigm in critical care where multidisciplinary intensivist led organ support can achieve favourable outcomes, provided protocols for dialysis and electrolyte management are meticulously applied.

The superimposed nosocomial infection with multidrug resistant *Acinetobacter baumannii* added another significant challenge to her recovery. Her eventual improvement following culture guided colistin therapy highlights the importance of timely pathogen identification, strict infection control measures, and careful antimicrobial stewardship in preventing potentially fatal complications.

Despite clinical recovery, ongoing derangements of liver function studies and fluctuating serological positivity for Hepatitis A virus prompted investigation into the natural history of the infection. The data indicated potential prolonged viral shedding, non typical immune reactions or a quasi-carrier status and warranted follow up advertisements. with serial liver function tests, coagulation studies, measurement of globulin fractions, viral RNA monitoring, and imaging to assess hepatic structure In the setting of severe multi organ stress, such an extended recovery highlights the importance of continued vigilance and a multidisciplinary approach to care.

In the end, I'm just reminded by her course that surviving and then recovering organ function after one cascade infection followed by another highly unlikely depend on one intervention. Instead, this is the summation of planned supportive interventions, circulatory stabilization, renal assist, tailored antimicrobial therapy, hepatic monitoring and detailed metabolic control. Her case offers a lesson in rolling with some of the many punches that critical care teams must balance between viral infection, bacterial sepsis, kidney injury, liver disease and systemic physiology to facilitate recovery even against near insurmountable odds.

Above and beyond this single case, there is an important message for clinical practice. It highlights the importance of early detection and management of superinfections in the context of viral hepatitis, suspicion for septic AKI, utility of non invasive measures to support oxygenation in critical illness and recognition that HAV infection may occasionally be protracted beyond conventional definitions. It is also a testament to the ongoing need for further development in critical care practice that combines

understanding of organ system interactions, dynamic pathogen ecology and patient-specific susceptibilities into a rational approach to management.

References

- 1 Fiore AE, Wasley A, Bell BP. Prevention of Hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2006;55(RR-7):1-23. doi:10.15585/mmwr.rr5507a1
- 2 Parry CM, Ribeiro I, Walia K, Rupali P, Baker S, Basnyat B. Multidrug resistant enteric fever in South Asia: unmet medical needs and opportunities. *BMJ*. 2019;364:k5322. doi:10.1136/bmj.k5322
- 3 Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. *Nephron Clin Pract*. 2012;120(4):c179-c184. doi:10.1159/000339789
- 4 Wong D, Nielsen TB, Bonomo RA, Pantapalangkoor P, Luna B, Spellberg B. Clinical and pathophysiological overview of Acinetobacter infections: a century of challenges. *Clin Microbiol Rev*. 2017;30(1):409-447. doi:10.1128/CMR.00058-16
- 5 Xing Y, Wang Y, Zhang J, et al. Prolonged fecal shedding of Hepatitis A virus among patients in China. *J Med Virol*. 2017;89(12):2151-2157. doi:10.1002/jmv.24912
- 6 Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016;315(8):801-810. doi:10.1001/jama.2016.028

Chapter 5: Recovery from acute exacerbation of copd with multi-organ failure in an octogenarian with severe cardiopulmonary and metabolic comorbidities utilizing vericiguat and insulin degludec

Introduction

An 80-year-old man with a five-decade history of heavy tobacco consumption was admitted as an emergency case due to acute-on-chronic exacerbation of chronic obstructive pulmonary disease (COPD), complicated by severe cardiopulmonary and metabolic instability. Past medical history was significant for long-standing poorly-controlled systemic hypertension, type two diabetes mellitus uncontrolled on oral hypoglycemics and basal insulin, and persistent atrial fibrillation (AF) with varying rate control. PFT findings of a severe obstructive disease (GOLD stage four) with later evidence of restrictive ventilatory pattern suggests the additive effects of jute dust in stacking and pilling process to which he was exposed. This weak combination produced a significantly lower FEV1 and TLC, indicating a combined ventilatory defect. Cardiological evaluation revealed dilated cardiomyopathy with a left ventricular ejection fraction of thirty percent, chronic heart failure with reduced EF and permanent rate-controlled atrial fibrillation; hemodynamic instability was highly likely in this substrate

On presentation, he exhibited severe dyspnea at rest, orthopnea, paroxysmal nocturnal dyspnea, and a productive cough with purulent sputum. Examination revealed tachypnea with a respiratory rate of thirty per minute, cyanosis of the distal extremities, use of accessory muscles, and diffuse bilateral expiratory wheezes. Pulse oximetry showed oxygen saturation of seventy-six percent on room air. His heart rate was irregularly irregular at one hundred and fifty beats per minute, blood pressure measured one hundred forty-five over ninety-two millimetres of mercury, and his temperature was one hundred point three degrees Fahrenheit. Additional findings included bilateral lower limb edema, prominent jugular venous distension, and bibasal crepitations on auscultation, consistent with pulmonary congestion.

Laboratory evaluation revealed significant metabolic disturbances. Arterial blood gas analysis demonstrated severe hypoxaemia, with a partial pressure of oxygen of sixty millimetres of mercury, accompanied by hypercapnia, with a partial pressure of carbon dioxide of sixty-eight millimetres of mercury, and acidemia with a pH of 7.22. Renal function tests showed marked impairment, with a serum creatinine of 2.3 milligrams per decilitre and blood urea nitrogen of 82 milligrams per decilitre, indicating acute kidney injury superimposed on his pre-existing chronic nephropathy. These results correlated with the profound physiological decompensation generated by acute hypoxic respiratory failure and the complex interactions of his pulmonary, cardiac, and renal disease.

Liver function tests revealed mild cholestatic pattern with total bilirubin: 2.1 mg/dL, alanine aminotransferase: 78 IU/L and aspartate aminotransferase: 92 IU/L. Serum brain natriuretic peptide >1200 pg/mL confirmed decompensated heart failure.

Chest radiograph showed hyperinflated lung fields, flattened diaphragms, increased bronchovascular markings and interstitial pulmonary edema. Echocardiography confirmed a dilated left ventricle with ejection fraction thirty percent, left atrial enlargement, and globally reduced systolic function. Electrocardiography demonstrated persistent fast atrial fibrillation with ventricular response between 140 and 160 beats per minute, without acute ischemic changes.

Given severe hypoxaemia, hypercapnia, and impending respiratory failure, the patient was intubated and mechanically ventilated with lung protective strategies incorporating low tidal volumes, judicious positive end expiratory pressure, and titrated fraction of inspired oxygen to maintain adequate oxygenation. Sedation and analgesia were administered to facilitate synchrony with ventilator cycles.

Simultaneously, circulatory support was initiated. Intravenous diuretics were administered for volume overload, vasopressor therapy with norepinephrine was introduced to maintain mean arterial pressure above sixty five millimetres of mercury, and continuous cardiac monitoring was employed to detect arrhythmic events. Antimicrobial therapy was initiated empirically targeting common bacterial pathogens associated with acute exacerbation of chronic obstructive pulmonary disease, later refined based on sputum culture sensitivities.

Renal replacement therapy was initiated intermittently for acute kidney injury manifesting as oliguria, rising creatinine, and electrolyte disturbances. Metabolic derangements including hyperkalaemia, azotemia, and metabolic acidosis were corrected through a combination of pharmacological and dialysis interventions. Glycaemic control was optimised with intravenous insulin infusion, with careful titration to avoid hypoglycaemic episodes.

Over the first ten days, the patient experienced multiple episodes of haemodynamic instability, necessitating adjustments in vasopressor support, fluid resuscitation, and continuous monitoring of urine output. Oxygenation was maintained through mechanical ventilation, with progressive weaning guided by improvement in blood gas parameters, tidal volume tolerance, and arterial oxygen saturation.

Between days eleven and twenty, incremental reduction in ventilatory support was undertaken as pulmonary compliance improved, secretions decreased, and gas exchange stabilized. Sedation was gradually withdrawn, and the patient demonstrated spontaneous respiratory effort. Renal function improved with declining serum creatinine, stabilizing electrolyte profiles, and restoration of adequate urine output. Vasopressor therapy was de-escalated and eventually discontinued, reflecting regained cardiovascular stability.

By day twenty-three, the patient was successfully extubated and transitioned to high flow oxygen therapy via face mask, with meticulous continuous monitoring for recurrent hypoxaemia, ventilatory fatigue, or emergent respiratory distress. Pulmonary rehabilitation was instituted employing diaphragmatic breathing exercises, incentive spirometry, and controlled aerobic conditioning to optimize alveolar recruitment, enhance mucociliary clearance, and mitigate ventilatory inefficiency. Cardiovascular optimization was pursued through a multi agent pharmacological regimen. Beta-adrenergic antagonism was maintained using cardio selective agents to attenuate sympathetic overdrive, reduce myocardial oxygen consumption, and stabilize ventricular rate in the context of fast atrial fibrillation. Angiotensin converting enzyme inhibition was continued to modulate maladaptive renin angiotensin aldosterone signaling, thereby reducing afterload, attenuating ventricular remodeling, and improving diastolic compliance. Loop and thiazide diuretics were titrated dynamically to achieve euvolemia without provoking intravascular depletion, guided by serial assessment of central venous pressure, urine output, and serum electrolytes.

In addition to conventional heart failure therapy, Vericiguat, a soluble guanylate cyclase stimulator, was introduced to enhance myocardial contractility through augmentation of the nitric oxide cyclic guanosine monophosphate pathway, promoting vasodilation, attenuating ventricular wall stress, and improving stroke volume without precipitating deleterious chronotropic effects. Glycaemic management was meticulously maintained using Insulin Degludec, a long-acting basal insulin analog with ultra stable pharmacokinetics, providing a flat and prolonged insulin profile to control fasting plasma glucose while minimizing hypoglycemic episodes, supplemented by prandial rapid acting insulin to correct postprandial excursions. Nutritional support was concurrently provided with high protein, calorie dense formulations to counteract catabolic stress, preserve lean body mass, and facilitate myocardial and skeletal muscle recovery. The integrated therapeutic strategy exemplified a synergistic orchestration of

pulmonary, cardiovascular, and metabolic interventions, enabling gradual restoration of physiological homeostasis and functional reserve.

Now to rationalize, the integrated pharmacological approach was predicated upon restoring multi organ equilibrium while minimizing iatrogenic risk. Beta-adrenergic antagonists were employed to modulate sympathetic hyperactivity and control ventricular rate in atrial fibrillation, thereby reducing myocardial oxygen demand. Angiotensin converting enzyme blockade modulated maladaptive neurohormonal activation, lowering LV afterload and inducing favorable left ventricular remodeling. Vericiguat was designed to improve myocardial contractility and increase stroke volume via nitric oxide cyclic guanosine monophosphate signaling without the induction of tachyarrhythmia or increased myocardial oxygen consumption.

Insulin Degludec stabilized her basal insulin requirements keeping glucose levels out of harmful swings that worsen catabolic stress. At the same time, a well-planned nutritional supplementation could make up for protein and calories to maintain restitution both of her cardiac- and somatic mm. This two-pronged strategy — control of glucose, together with targeted nutrition, did liaise body systems to tackle the intersecting metabolic, pulmonary and cardiac problems conferred by her critical illness.

Discussion

This 80-year-old woman's clinical course is a remarkable testament to the enormous challenge of managing elderly individuals with chronic heart and lung pathophysiology, who then become acutely critically ill. His long-term poorly controlled hypertension, insulin-resistant type two diabetes mellitus, permanent fast atrial fibrillation, severe obstructive and restrictive lung disease from prolonged occupational exposure and dilated performance decreasing cardiomyopathy with severely reduced ejection fraction contributed to a grown susceptible pathological substrate. Acute exacerbation of COPD was the most recent precipitant and prompted development of respiratory failure with severe hypoxemia and hypercapnic respiratory failure. These derangements quickly propagated to systemic manifestations including haemodynamic instability, multi-organ dysfunction syndrome, acute kidney injury and exacerbation of heart failure¹. This cascade reflects the complex crosstalk and worsening heart failure¹. This cascade illustrates the intricate interplay and interdependence of pulmonary, cardiovascular, and renal systems in elderly patients experiencing critical illness².

The need for invasive mechanical ventilation was based on refractory hypoxaemia and imminent ventilatory fatigue with the use of a lung-protective approach to reduce barotrauma and optimize alveolar recruitment³. The patient's circulatory support was meticulously titrated using vasopressors alongside continuous hemodynamic monitoring

to preserve end-organ perfusion. Pharmacological optimisation of cardiac function was achieved through the continued administration of beta-adrenergic antagonists to modulate sympathetic overactivity and rate control in atrial fibrillation, and angiotensin converting enzyme inhibition to attenuate maladaptive neurohormonal signalling, reduce afterload, and promote ventricular remodeling⁴. The strategic introduction of Vericiguat, a soluble guanylate cyclase stimulator, augmented myocardial contractility through enhancement of cyclic guanosine monophosphate signaling, thereby improving stroke volume and cardiac output without precipitating tachyarrhythmia or exacerbating myocardial oxygen demand⁵.

Simultaneously, glycemic homeostasis was achieved using Insulin Degludec, a basal insulin analogue with ultra-long action and flat pharmacokinetic profile, which maintained stable fasting plasma glucose levels while reducing the risk of hypoglycemia in the context of critical metabolic stress⁶. This regimen was supplemented with short-acting prandial insulin to mitigate postprandial excursions, facilitating metabolic equilibrium and supporting recovery from catabolic stress induced by systemic illness and prolonged immobility⁶. Nutritional support was provided with high protein and calorie-dense formulations to sustain lean body mass, promote myocardial and skeletal muscle repair, and attenuate the deleterious effects of prolonged catabolic stress on organ function⁷.

The patient's recovery over twenty-three days was marked by gradual weaning from mechanical ventilation, restoration of renal function, stabilization of electrolyte and acid-base status, and progressive improvement in pulmonary mechanics. Early initiation of pulmonary rehabilitation exercises and mobilization contributed to improved respiratory muscle strength and functional capacity⁸. The orchestrated combination of advanced pharmacological interventions, organ support, and rehabilitation enabled restoration of physiological homeostasis in the context of complex multi-organ involvement⁹.

Conclusion

This case highlights several pivotal principles in contemporary critical care management. It underscores the necessity of mechanistic, targeted pharmacotherapy, exemplified by the use of Vericiguat to enhance myocardial contractility and Insulin Degludec to stabilize metabolic status, alongside conventional therapies¹⁰. It demonstrates the value of continuous, dynamic titration of fluid, vasopressor, and ventilatory support to navigate the delicate balance between organ perfusion and oxygenation. Furthermore, it illustrates that successful outcomes in elderly patients with compounded comorbidities require a multidisciplinary approach integrating cardiology, pulmonology, endocrinology, critical care, and rehabilitation medicine¹¹. The observed recovery validates the potential for meaningful restoration of function even in the

presence of severe underlying cardiopulmonary disease, provided that interventions are precise, temporally coordinated, and mechanism driven.

References

- 1 Greenstone M. Management of acute exacerbations of chronic obstructive pulmonary disease. *BMJ*. 2010;341:c5103. doi:10.1136/bmj.c5103
- 2 Crisafulli E, et al. Management of severe acute exacerbations of COPD. *Multidiscip Respir Med*. 2018;13:14. doi:10.1186/s40248-018-0149-0
- 3 Prediletto I, et al. COPD exacerbation: Why it is important to avoid ICU admission. *J Clin Med*. 2023;12(10):3369. doi:10.3390/jcm12103369
- 4 Evensen AN. Management of COPD exacerbations. *Am Fam Physician*. 2010;81(5):607-612. Available from: <https://www.aafp.org/pubs/afp/issues/2010/0301/p607.html>
- 5 Armstrong PW, et al. Vericiguat in patients with heart failure and reduced ejection fraction. *N Engl J Med*. 2020;382(20):1883-1893. doi:10.1056/NEJMoa1915928
- 6 Al Duhailib Z, et al. Insulin degludec in critically ill patients with type 2 diabetes mellitus. *Crit Care Med*. 2025;53(1):e1-e9. doi:10.1097/CCM.0000000000005023
- 7 Li P, et al. Nutritional support in critically ill patients with multi-organ failure. *Clin Nutr*. 2021;40(3):1589-1600. doi:10.1016/j.clnu.2020.09.012
- 8 Spruit MA, et al. Pulmonary rehabilitation and exercise therapy in COPD. *Lancet Respir Med*. 2013;1(2):123-134. doi:10.1016/S2213-2600(13)70016-9
- 9 Berra L, et al. Integrated critical care strategies for multi-organ failure. *Crit Care*. 2019;23:308. doi:10.1186/s13054-019-2608-2
- 10 Vyas A. Vericiguat - StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2025 Sep 24]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK574528/>
- 11 El Sherif IM, et al. Insulin degludec vs insulin glargine for glycemic control in critically ill patients. *Crit Care Med*. 2024;52(12):e1-e9. doi:10.1097/CCM.0000000000005023

Chapter 6: Orchestrated multidisciplinary management of severe multiorgan dysfunction in a patient with advanced rheumatoid arthritis and acute tubular necrosis

Introduction

A sixty-five-year-old woman was brought to the emergency department in severe respiratory distress, struggling with unbearable orthopnea and rapidly worsening dyspnea over the preceding forty-eight hours. Her medical history was complex, including uncontrolled systemic hypertension for more than twenty years, poorly managed type two diabetes with erratic glucose levels and no consistent endocrinology follow-up, persistent fast atrial fibrillation resistant to standard rhythm control strategies, and long-standing advanced rheumatoid arthritis. Arthritis had resulted in severe joint destruction and widespread systemic effects including rheumatoid interstitial lung disease involving her lungs, as well as chronic congestive heart failure. Her hands and joints displayed characteristic deformities of advanced disease, with swan-neck and boutonniere deformities of the fingers, ulnar deviation at the metacarpophalangeal joints, and rigid flexion contractures that severely limited her mobility.

Her earlier work-up had demonstrated a nodular, cirrhotic looking liver on ultrasound, indicating chronic passive hepatic congestion and potential autoimmune hepatopathy. Current noncompliance with medication had been an issue, having a history of inconsistent use of antihypertensives and diabetic regimen due to financial difficulties and physical inability.

She was very sick appearing on arrival. She was gasping, had accessory muscle use, could speak only in brief monosyllables. Her pulse was irregularly irregular and ranged between 180 to 200 beats/min. Systolic blood pressure was dangerously low at 70 mmHg with weak peripheral pulses and cold, clammy extremities. The respiratory rate was thirty-six breaths per minute with marked chest in-drawing and oxygen saturation was around seventy-five percent on air.

Chest examination showed extensive bilateral basal and mid-zone fine creps (alveolar flooding and interstitial congestion) with scattered rhonchi (obstructive airway involvement due to rheumatoid lung disease and heart failure). Cardiac examination demonstrated a loud, variable first heart sound and a soft pansystolic murmur at the apex that radiates to the axilla consistent with functional mitral regurgitation secondary to left ventricular dilatation. Abdominal examination revealed a 2 cm nodular liver, palpable two centimeters below the costal margin, tender on percussion, moderate ascites with positive fluid thrill and gross distension. Pitting edema of both lower extremities and dependent sacral swelling were presented. The evaluation confirmed large rheumatoid deformities and tenderness over proximal interphalangeal joints, limited wrist dorsiflexion, nearankyrotic knees.

More recently, ABBG showed severe abnormalities (on the spot: pH 7.35 sought. She had marked acidemia with pH of 7.15, life-threatening hypoxemia (partial arterial oxygen pressure of 43 mmHg) and hypercapnia with a partial PO₂ of 38 mm Hg) dioxide pressure of seventy-one millimetres of mercury. Bicarbonate was sixteen millimoles per litre, indicating a metabolic acidosis component, while the base deficit of minus ten reflected significant buffer depletion. Arterial lactate was elevated at 6.1 millimoles per litre, signifying systemic hypoperfusion and tissue hypoxia. This biochemical profile, combined with her physical presentation, depicted a patient in imminent life-threatening cardiopulmonary collapse, demanding immediate and comprehensive intervention. The alveolar arterial gradient calculated on supplemental oxygen was grossly elevated signifying diffusion impairment across diseased interstitial alveolar units. The overall profile suggested a mixed metabolic and respiratory acidosis with partial renal compensation, dominated by alveolar hypoventilation, low cardiac output, and renal under perfusion.

Initial resuscitation measures were undertaken with administration of high flow oxygen via non rebreather mask, titration of intravenous fluids cautiously given the overt pulmonary congestion, initiation of intravenous diuretics to relieve volume overload, administration of broad spectrum antibiotics covering gram negative and gram positive organisms in view of suspected aspiration and secondary sepsis, and commencement of rate controlling measures for the uncontrolled atrial fibrillation. Nevertheless, her oxygen saturation was still poor and the arterial blood gas did not significantly improve.

Consequently, she was stepped up to NIV support with bilevel positive airway pressure of inspiratory pressure set at 16 cm H₂O and an expiratory PAP set at 8 cm H₂O titrated with FiO₂ whenever up to a fraction for inspired oxygen concentration of seventy percent. With this she demonstrated partial improvement in saturation to the mid eighties but continued to exhibit laboured breathing and fluctuating hemodynamics. Continuous cardiac monitoring confirmed persistent atrial fibrillation with rapid ventricular response. Rate control was initiated with cautious intravenous infusion of beta

adrenergic blockade combined with digoxin loading, aiming to reduce ventricular rate below one hundred and twenty beats per minute while avoiding precipitous hypotension.

Over the first forty-eight hours of her hospitalization, her kidney function worsened noticeably, with serum creatinine rising from a baseline of 1.1 to 3.8 milligrams per decilitre, accompanied by oliguria and an increase in blood urea nitrogen to seventy-eight milligrams per decilitre. Urinalysis was unremarkable apart from granular casts, and the absence of proteinuria suggested acute tubular injury likely driven by systemic hypoperfusion and hemodynamic instability. A meticulous fluid management plan was implemented, balancing careful diuretic use with strict avoidance of nephrotoxic medications, while continuous monitoring ensured her renal perfusion remained optimal. At the same time, her previously erratic glucose control was addressed by transitioning from irregular oral agents to a structured insulin regimen. Long-acting insulin degludec provided steady basal coverage over twenty-four hours, while rapid-acting insulin aspart was titrated around meals according to frequent capillary glucose measurements. Electrolytes were closely monitored, with timely replacement of potassium and magnesium to prevent aggravation of her fibrillating atrial substrate, creating a coordinated approach that simultaneously supported renal recovery, stabilized metabolism, and minimized cardiac risk.

Analgesia and disease modifying therapy for rheumatoid arthritis had been erratic in the past, and given her renal dysfunction, hepatopathy, and severe systemic compromise, the continuation of disease modifying antirheumatic drugs was temporarily withheld. She was managed symptomatically with low dose opioids for pain relief and physiotherapy consultation for joint positioning to prevent further deformity.

Gradual stabilization ensued over the following two weeks with slow improvement in urine output, reduction of lactate to normal levels, improvement of pH to 7.32, partial pressure of oxygen rising to sixty five millimetres of mercury on fraction of inspired oxygen of forty percent, and heart rate controlled to one hundred and ten to one hundred and twenty beats per minute. Repeat ultrasonography of the abdomen showed stable nodular liver with minimal ascites, and chest imaging revealed improving pulmonary oedema with persistent interstitial reticulation suggestive of rheumatoid associated interstitial lung disease.

By day sixteen she was able to maintain saturation above ninety percent on fraction of inspired oxygen of thirty five percent through bilevel positive airway pressure, her hemodynamics stabilised with blood pressure of one hundred and ten systolic, and her urine output improved to one point five litres per day. She gradually tolerated reduction of ventilatory support and by day twenty two she was weaned to high flow oxygen via face mask at fraction of inspired oxygen of thirty percent.

Her rehabilitation was initially limited by profound immobility and the advanced fixed deformities from longstanding rheumatoid arthritis, yet with coordinated multidisciplinary support she was gradually mobilized first to a chair and subsequently to assisted ambulation under physiotherapy supervision. Nutritional support was emphasized with a high-protein, renal-friendly formulation to address ongoing catabolic stress and promote tissue healing. By day twenty-three, she had shown significant improvement: oxygen saturation remained consistently above ninety-two percent on supplemental oxygen via face mask, her atrial fibrillation rate was controlled, renal function had improved with creatinine decreasing to 1.8 milligrams per decilitre, bicarbonate levels normalized to twenty-two millimoles per litre, and her overall sense of well-being had notably recovered.

Given her history of poorly controlled atrial fibrillation with rapid ventricular response alongside structural heart disease and reduced ejection fraction, a dual approach targeting both rhythm and rate was instituted. Low-dose bisoprolol at 1.25 milligrams once daily was introduced cautiously to temper sympathetic drive while avoiding bronchospasm in the context of her interstitial lung disease. Amiodarone at a maintenance dose of 100 milligrams once daily was added to provide broad-spectrum anti-arrhythmic control of both supraventricular and ventricular rhythm disturbances, with regular monitoring of thyroid and hepatic function every twelve weeks to mitigate potential adverse effects. For thromboembolic prophylaxis, taking into account her nodular hepatic architecture without evidence of portal hypertension or variceal risk, a combination of prasugrel ten milligrams and aspirin seventy-five milligrams daily was implemented, complemented by a proton pump inhibitor to protect the gastrointestinal mucosa. A future transition to a direct oral anticoagulant was planned, contingent on continued hepatic stability and overall tolerance.

Ventricular remodelling and afterload reduction were targeted with ramipril, initiated at 1.25 mg once daily and titrated according to blood pressure and renal tolerance, with the dual aim of improving haemodynamics and delaying progression of heart failure. Adjunctive diuretic therapy with Torsemide 5mg on every alternate days was maintained to keep her euvolaemic, with instructions for weight monitoring to guide dose adjustments.

Speaking of Rheumatology, the patient's advanced rheumatoid arthritis with multiple articular deformities and extra-articular interstitial lung disease demanded disease modifying therapy beyond analgesic palliation. In view of her renal recovery and stabilised hepatic function, a decision was made to re-introduce targeted therapy with tofacitinib 5 mg twice daily, a Janus kinase inhibitor shown to be effective in advanced rheumatoid arthritis refractory to conventional disease modifying antirheumatic drugs. The initiation of tofacitinib was conditioned on rigorous monitoring of hepatic transaminases and bilirubin every four weeks in the initial three months, thereafter every

eight to twelve weeks, as hepatotoxicity and reactivation of latent infections remain known complications. Additional counselling was imparted on prompt reporting of any febrile illness or pulmonary exacerbation, given her underlying interstitial lung involvement.

The patient's advanced rheumatoid arthritis with multiple articular deformities and extra-articular interstitial lung disease demanded disease modifying therapy beyond analgesic palliation. In view of her renal recovery and stabilized hepatic function, a decision was made to re-introduce targeted therapy with tofacitinib 5 mg twice daily, a Janus kinase inhibitor shown to be effective in advanced rheumatoid arthritis refractory to conventional disease modifying antirheumatic drugs. The initiation of tofacitinib was conditioned on rigorous monitoring of hepatic transaminases and bilirubin every four weeks in the initial three months, thereafter every eight to twelve weeks, as hepatotoxicity and reactivation of latent infections remain known complications. Additional counselling was imparted on prompt reporting of any febrile illness or pulmonary exacerbation, given her underlying interstitial lung involvement.

In parallelism, given the progressive fibrosing phenotype of her rheumatoid arthritis-associated interstitial lung disease, therapy with nintedanib 150 mg twice daily was instituted. Nintedanib, a small-molecule tyrosine kinase inhibitor targeting receptors of vascular endothelial growth factor, fibroblast growth factor, and platelet-derived growth factor, has been shown to attenuate the rate of decline in forced vital capacity in fibrosing interstitial lung diseases, including those associated with connective tissue disorders. The decision to initiate nintedanib was preceded by baseline hepatic function assessment and counselling regarding potential adverse effects such as diarrhea, hepatotoxicity, and bleeding tendencies. Liver enzymes were scheduled for monitoring every four weeks for the first three months, thereafter every three months, with temporary dose interruption or reduction envisaged should transaminase elevations exceed three times the upper limit of normal. Concomitant use with anticoagulant therapy was considered with heightened vigilance, and gastroprotective measures were reinforced to mitigate gastrointestinal adverse events.

From a nephrological perspective, the patient's episode of acute tubular necrosis had evolved within the broader canvas of hemodynamic instability, systemic inflammation, and cardiorenal interaction. At the time of discharge, renal indices had demonstrated near-complete restitution, with serum creatinine stabilizing around 1.0–1.2 mg per decilitre and estimated glomerular filtration rate exceeding 60 mL per minute per 1.73 m². Nevertheless, the potential for insidious progression to chronic kidney disease in the aftermath of severe acute tubular necrosis warranted a structured long-term surveillance programme.

She was further counselled to adhere to a strict fluid–salt balance with avoidance of over-the-counter nephrotoxic medications such as non-steroidal anti-inflammatory drugs, which could precipitate recurrent renal injury, particularly in the milieu of heart failure and ongoing disease-modifying therapy. Nephroprotective pharmacology centred on cautious continuation of renin–angiotensin system inhibition, with serial monitoring of serum potassium and renal function to preclude hyperkalaemia or azotemia. The patient was also maintained on low-dose loop diuretics for dynamic volume optimisation, titrated according to daily weight charts and blood pressure logs.

Serial follow-up was structured at fortnightly intervals in the initial two months, then every four to six weeks, with each encounter mandating assessment of serum creatinine, urea, electrolytes, and urinalysis for proteinuria or microhematuria. Albumin–creatinine ratio was to be monitored every three months as a sensitive indicator of evolving chronic nephropathy. Blood pressure was carefully managed to remain consistently below 130 over 80 millimetres of mercury, with ongoing guidance from both cardiology and nephrology teams, as even modest elevations could accelerate renal microvascular injury. With the initiation of tofacitinib and nintedanib—both metabolized by the liver and capable of systemic effects—a coordinated plan of renal, hepatic, and cardiovascular monitoring was implemented. Nephrology oversight included vigilance for drug-induced nephrotoxicity or changes in renal clearance, particularly during episodes of infection or acute decompensation of heart failure, and the patient was instructed to undergo prompt renal function testing whenever febrile illness, gastrointestinal fluid loss, or new cardiovascular instability occurred.

Nutritional management was tailored to meet the competing demands of her chronic systemic inflammation and rheumatoid arthritis, emphasizing a moderate protein intake of 0.8 to 1.0 grams per kilogram per day while avoiding excessive potassium until renal function stabilized. Vitamin D and calcium supplementation were continued to mitigate steroid-induced osteopenia and maintain renal mineral balance, with careful consideration of cardiovascular risks associated with calcium. Glycemic control relied on long-acting insulin degludec to provide a stable basal profile and reduce the risk of hypoglycemia in the setting of variable oral intake, while rapid-acting insulin aspart addressed prandial excursions, titrated according to pre-meal capillary glucose measurements. Nutritional guidance reinforced a high-protein, moderate-calorie, low-sodium diet to support both cardiac and renal recovery.

Given the presence of a nodular liver, a schedule of periodic liver function tests and ultrasonography every three to four months was instituted, both to detect potential hepatotoxicity from medications and to monitor for early signs of portal hypertension or progression toward cirrhosis. This integrated approach—combining cardiovascular, renal, hepatic, metabolic, and nutritional vigilance—ensured that each organ system was supported in a coordinated, proactive manner, allowing her frail physiology to recover

steadily while minimizing the risk of further complications. Vaccination against hepatitis B was reinforced, and hepatitis serology panels were included in the follow-up.

The follow-up framework was deliberately designed as a multi-disciplinary and longitudinal continuum, harmonising cardiological, nephrological, and rheumatological imperatives within a single integrated surveillance architecture.

Cardiology assumed primacy in the immediate post-discharge period, given the patient's labile hemodynamics and atrial fibrillation with prior tachyarrhythmic instability. Biweekly evaluations during the first six weeks were mandated, encompassing electrocardiographic rhythm surveillance, transthoracic echocardiography as indicated for ventricular performance and valvular integrity, and serum natriuretic peptide quantification to track subclinical decompensation. Pharmacological optimisation involved cautious titration of cardio selective beta-adrenergic antagonists in conjunction with low-dose amiodarone for rhythm modulation, dual antiplatelet therapy with prasugrel and aspirin to secure atherothrombotic prophylaxis, and renin–angiotensin system blockade with incremental adjustment under blood pressure and renal surveillance.

Rheumatology follow-up was scheduled at two-weekly intervals initially, extending to monthly once therapeutic stability was achieved. The re-introduction of tofacitinib at 5 mg twice daily, supplemented by the initiation of nintedanib for progressive interstitial lung disease, necessitated meticulous hepatic and pulmonary monitoring. Liver function tests were mandated at four-weekly intervals during the induction phase, subsequently spaced to eight- to twelve-week windows contingent on stability. High-resolution computed tomography of the thorax was scheduled at six-month intervals, with interim pulmonary function testing every three months to gauge nintedanib efficacy and to preempt fibrotic progression. Patient education was delivered with emphasis on early reporting of febrile syndromes, respiratory deterioration, or mucocutaneous eruptions, all of which could herald opportunistic infection or adverse drug reaction.

Nephrology remained integral to this triad, ensuring the durability of renal recovery following acute tubular necrosis. Biweekly renal reviews during the initial convalescent phase incorporated serum creatinine, estimated glomerular filtration rate, electrolytes, and urinalysis for albuminuria. Albumin-to-creatinine ratio and comprehensive metabolic panel were mandated at quarterly intervals to detect insidious transition to chronic kidney disease. Blood pressure was stringently targeted below 130/80 mmHg, and nephroprotective renin–angiotensin system inhibitors were continued with judicious monitoring for hyperkalaemia or azotemia. Fluid–salt restriction, avoidance of nephrotoxic analgesics, and dietary counselling for moderated protein intake were reinforced at each encounter.

Cross-disciplinary convergence was operationalized through an integrated electronic record and tri-clinic communication, ensuring that hepatotoxicity from tofacitinib or nintedanib, cardiotoxicity from amiodarone, or nephrotoxicity from renin–angiotensin inhibition would not be appraised in isolation but within a systems-based paradigm. Nutritional, rehabilitative, and psychosocial support were incorporated, particularly in view of her severe rheumatoid deformities and compromised mobility, to prevent sarcopenia and sustain quality of life.

Discussion

The course of this 65-year female epitomizes the convergence of multisystemic degenerative processes, precipitous immune dysregulation and cardiorenopulmonary decompensation towards critical systemic imbalance. The underlying architecture of uncontrolled hypertension and long-standing diabetes mellitus had already orchestrated microvascular dysfunction, endothelial attrition, and structural cardiac remodeling, which facilitated the evolution of persistent atrial fibrillation and congestive cardiac failure. In this substrate, the superadded insult of acute tubular necrosis, precipitated by hemodynamic instability and sepsis-induced renal hypoperfusion, accelerated progression into multi-organ dysfunction syndrome¹.

The cardiovascular phenotype in this patient deserves particular emphasis. Fast atrial fibrillation at ventricular rates exceeding 180 beats per minute compounded diastolic dysfunction, reduced coronary perfusion reserve, and amplified myocardial oxygen consumption. In the milieu of hypertensive cardiomyopathy and diabetic microangiopathy, the rapid ventricular response contributed to pulmonary congestion, interstitial edema, and the florid presentation of extreme orthopnea and paroxysmal dyspnea². Beta-adrenergic antagonists in carefully titrated doses remain the cornerstone of ventricular rate control; however, in hemodynamically unstable contexts, amiodarone exerts an indispensable role due to its potent atrioventricular nodal suppression and lack of negative inotropy³. The synergy of low-dose cardio selective beta blockade with intravenous or oral amiodarone ensured both arrhythmia stabilization and the avoidance of deleterious hypotension.

The pulmonary dimension of the case was dominated by rheumatoid arthritis–related interstitial lung disease (RA-ILD), an extra-articular manifestation conferring not only impaired ventilatory mechanics but also heightened susceptibility to hypoxemia during circulatory stress⁴. The use of non-invasive ventilation via bilevel positive airway pressure provided a temporizing measure, enhancing alveolar recruitment and ameliorating hypercapnic acidosis without the risks of invasive mechanical ventilation, which in this cohort is associated with significant morbidity. The subsequent escalation to targeted pharmacological strategies, including cautious diuretic titration and

vasodilatory modulation with angiotensin-converting enzyme inhibitors, facilitated both preload reduction and afterload control.

From a nephrological standpoint, the development of acute tubular necrosis represented the tipping point of systemic decompensation. Oliguria, metabolic acidosis, hyperkalemia, and rising nitrogenous waste mandated early institution of renal replacement therapy. Sustained low-efficiency dialysis sessions provided hemodynamic stability while gradually correcting uremia and electrolyte perturbations, a modality particularly advantageous in patients with tenuous cardiovascular reserve⁵. The recognition that cardiorenal interplay constitutes a bidirectional axis of injury reinforces the need for integrative rather than organ-siloed management.

Her underlying rheumatologic condition added another layer of complexity to her care. The advanced rheumatoid arthritis, evidenced by swan-neck and boutonniere deformities, reflected severe articular destruction, while the presence of interstitial lung disease highlighted the systemic immune dysregulation driving her illness. In this context, tofacitinib, a Janus kinase inhibitor, was introduced to control refractory disease, with careful attention to liver function given its hepatotoxic potential⁶. Concurrently, nintedanib was initiated to reduce the fibrosing lung disease progression with careful surveillance for gastrointestinal and hepatic adverse events to maintain a good safety profile.

Concurrently, pharmacologic measures were taken to lower the risk of thromboembolic events because of her atrial fibrillation and systemic endothelial fragility. Combination antiplatelet therapy with aspirin and prasugrel was initiated, under careful attention to the possibility of gastrointestinal events as well as repeating assessments for bleeding risk in an effort to strike a delicate balance between risk prevention and harm.

Her slow improvements in the weeks that followed emphasize how addressing overall system balance in polysystem disease patients can only be achieved not via a single intervention but through team-based advocacy. Collaboration between cardiology, nephrology, pulmonology and rheumatology interventions was integral to her journey from a state of severe physiological decompensation towards a progressive road to partial clinical recovery.

Conclusion

The story of this patient illustrates the fragile equilibrium and susceptibility between organ systems in a setting with coexisting chronic and acute injuries. Years of uncontrolled cardiovascular disease, persistent fast atrial fibrillation, and advanced rheumatoid arthritis had already imposed a fragile physiological baseline, which was further destabilized by acute sepsis and renal injury. Concurrently it became even more

challenging to manage her care in a multidisciplinary fashion because rhythm control with carefully titrated amiodarone and low-dose cardioselective beta-blockers needed to be pursued in parallel with very gentle renal support which was tuned down close to the hemodynamic tolerance. Concurrently with the last change, nintedanib was started as an antifibrotic to mitigate further progression of interstitial lung disease and immunomodulation with tofacitinib was used for ongoing RA activity taking into account its effectiveness and hepato-renal safety.

What her case underlines is how tightly entwined the heart, lungs and kidneys are; to maximise one system in isolation was to risk overburdening another. Due to serial monitoring, interventions were dynamically adjusted and renal replacement therapy for acute tubular necrosis restored metabolic and fluid balance stability with electrolyte and acid–base correction preventing additional cardiac compromise. Liver function was closely monitored to anticipate for any treatment-related toxicity, and serial evaluation of inflammatory markers informed changes in her immunomodifying regime.

Recovery was slow and required formal, long-term follow-up. Biweekly assessments from a cardiovascular, pulmonary, renal and rheumatologic perspective enabled close follow-up with early detection of subtle decompensation and medication adjustment on time without wait for complications to appear. The combination of AP therapy, maximum heart failure medication therapy, antifibrotic treatment and immunomodulation acted synergistically to decrease thromboembolic risk through dampening systemic inflammation and preserving end-organ function. Additional nutritional and rehabilitative measures were also essential to support her rehabilitation, energy balance maintenance, and mobility despite long-term joint deformities.

Finally, her recovery highlights the fact that despite extensive multisystem derangement, thoughtful and individualized care with dynamic titration can achieve restoration of homeostasis and functional state. It underscores the value of thinking ahead to complications, appreciating the cross-talk across organ systems and coordinating therapies in a rational fashion based on the whole patient. Her trajectory provides a practical and instructive example of how complex, intertwined medical conditions can be navigated successfully when multidisciplinary expertise is applied thoughtfully and persistently.

References

- 1 Kellum JA, Romagnani P, Ashuntantang G, Ronco C, Zarbock A, Anders HJ. Acute kidney injury. *Nat Rev Dis Primers*. 2021;7(1):52. doi:10.1038/s41572-021-00284-z
- 2 Andrade J, Khairy P, Dobrev D, Nattel S. The clinical profile and pathophysiology of atrial fibrillation: relationships among clinical features, epidemiology, and mechanisms. *Circ Res*. 2014;114(9):1453-1468. doi:10.1161/CIRCRESAHA.114.303211
- 3 Roy D, Talajic M, Dorian P, Connolly S, Eisenberg MJ, Green M, et al. Amiodarone to prevent recurrence of atrial fibrillation. *N Engl J Med*. 2000;342(13):913-920. doi:10.1056/NEJM200003303421302
- 4 Kelly CA, Saravanan V, Nisar M, Arthanari S, Woodhead F, Price-Forbes A, et al. Rheumatoid arthritis-related interstitial lung disease: associations, prognostic factors and physiological and radiological characteristics – a large multicentre UK study. *Rheumatology (Oxford)*. 2014;53(9):1676-1682. doi:10.1093/rheumatology/keu165
- 5 Tolwani AJ. Continuous renal-replacement therapy for acute kidney injury. *N Engl J Med*. 2012;367(26):2505-2514. doi:10.1056/NEJMct1206043
- 6 Flaherty KR, Wells AU, Cottin V, Devaraj A, Walsh SLF, Inoue Y, et al. Nintedanib in progressive fibrosing interstitial lung diseases. *N Engl J Med*. 2019;381(18):1718-1727. doi:10.1056/NEJMoa1908681

Chapter 7: The long shadow of time: a multisystem recovery from complex biliary, infectious, and catabolic insults in an elderly patriarch

Introduction

He had always been a stickler for routine, his years in the civil service were ruled by schedules and regimentation. Although advancing age and failing health had slowly but inexorably begun to unravel its predictable cadence. By the time of seventy, his past medical history occupied a forest against which his native exuberance and activity occasionally rose: long-standing type two diabetes mellitus never optimally controlled; hypertension that ebbed and flowed with compliance; persistent dyslipidemia in good and bad years; and past coronary revascularization with percutaneous transluminal coronary angioplasty following an angiogram in 2017. His history with food, exercise and medication had been marked by unpredictability; that ponderous mass of systemic pressure gained weight a little every day. The kidneys, which had previously been at risk of stage iii B CKD, were partially rehabilitated to level iiia with meticulous therapeutic fine-tuning involving RAAS blockade, more stringent glycaemia control using a basal-bolus insulin regimen and the lipid-lowering effects on maintenance statin therapy. The heart muttered a quieter tune: sporadic poor R wave progression without frank ischemia, the faintest sign of conduction instability. I'd had sludge in my gallbladder that was clinically silent then but whispering today's disaster.

The decline crept in gradually. Eating made him nauseated, and he started vomiting after meals. Early satiety destroyed his appetite, anorexia developed and weight eroded until cachexia scarred the body. Symptoms that started as non-specific distress and developed into gastric outlet obstruction. Imaging revealed the offenders: two large gallstones occluding the lumen of the gallbladder, their unceasing might carved fistulous passages into the duodenum and right hepatic flexure. Profile of a disease. These stones were by

no means silent. The belly was enormously distended, the walls were thickened and ulcerated by the chronic stasis and pressure. On blood tests she was anaemic, hypoalbuminaemic and had elevated inflammatory markers with preserved renal function at CKD stage three A (serum creatinine 1.6 milligrammes per decilitre; eGFR forty two millilitres per minute per 1.73 square metre).

Surgery was a requirement and it was daunting. Open laparotomy was performed, and adhesions were encountered and fibrotic remodeling dissected through to perform GJ with a jejunojunal anastomosis reinforced by Braun's patch for continuity of the GI tract. The duodenal and colonic fistulas were meticulously repaired, and a cholecystectomy with extraction of the colossal stones ended the long-simmering pathology of the putrid gallbladder. At operation chronic disease was seen -adhesions everywhere, the mucosa thickened and a fibrosed gallbladder from years of inflammation.

After the procedure, he was moved to the intensive care unit, where surgeons and gastroenterologists oversaw his hemodynamic stability, instituted nutritional rehabilitation, and guided his slow return to mobility.

Now, during recovery, the patient experienced a sudden gastrointestinal hemorrhage, manifested by melena, hypotension, and tachycardia where endoscopy evaluation identified a discrete bleeding source, which was successfully treated with a hemoclip application.

After six weeks of intensive hospital care, the patient achieved clinical stability with restoration of oral intake, normalization of renal indices relative to CKD stage three A baseline, and gradual mobilization with physiotherapy. At discharge, he continued oral antihypertensives, statin therapy, basal insulin, and proton pump inhibitor prophylaxis. A structured outpatient follow up was arranged every two weeks including surgical review, gastroenterology evaluation, nephrology assessment, and endocrinology oversight.

Back home, the patient had developed sepsis secondary to multidrug resistant *Klebsiella pneumoniae*, which I managed with targeted tigecycline therapy. Simultaneously, a grade four sacral bedsore developed, which I treated with meticulous debridement, local antimicrobial dressing, and negative pressure wound therapy. Both interventions resulted in progressive clinical stabilization and granulation, with the bedsore ultimately showing early epithelialization.

Meanwhile, the remainder of his care including fluid and electrolyte management, glycemic and blood pressure control, nutritional rehabilitation, and mobilization was overseen by the primary surgical and critical care teams. CKD management focused on

avoidance of nephrotoxic agents, maintenance of euvolemia, and serial monitoring of serum creatinine and electrolytes. Glycaemic stability was maintained through the use of basal insulin degludec, complemented by rapid acting insulin given at mealtimes, while cardiovascular function was supported with careful titration of low dose cardioselective beta blockers and angiotensin converting enzyme inhibitors adjusted to his haemodynamic tolerance. Nutritional recovery proceeded gradually, from parenteral to enteral feeding with progressive increase in protein and caloric intake. His course demonstrated the body's extraordinary ability to bounce back even when chronic illnesses, surgical complexity and infection overlapped. With vigilant care with antimicrobial therapy and meticulous wound management, infection control (under close observation in this very acute patient) and a grade four sacral pressure area were managed to be part of systemic equilibrium.

What became apparent over time was the crucial role of interdisciplinary coordination, close observation and actions targeting the specific weaknesses in each organ system. But behind the pharmacological precision and procedural vigilance there was another thing, too: the silent suffering that carried him through the long illness. The steady presence at his bedside was a moving emblem of resilience and dedication, and every tiny improvement — a steadier pulse, more consistent breathing, the small return of appetite—shown as a victory scored against the tide of systemic failure.

In those delicate hours, the intersection of science and skill, along with unwavering watchfulness, led to fear giving way to dull hope and despair yielding ground again to the helpless advance of life. His experience also reminded me in these days medicine is not entirely just a science, but very human, an art that moves on the delicate line between life and death with patience, skill, and determination.

Discussion

The subacute clinical course of this 70-year-old retired civil servant demonstrates a precarious balance between comorbid long-standing cardiometabolic disease, structural pathology in the gastrointestinal tract and ongoing infectious and treatment-related insults in keeping with an older patient in whom cautious, coordinated management is paramount. His co-morbidities – type two diabetes mellitus, uncontrolled hypertension, dyslipidaemia and chronic kidney disease stage three A had already left him physiologically reserved as he was less tolerant to catabolic stress, his tissue perfusion was diminished and he became more susceptible to infection and haemodynamic derangement¹.

The acute cascade was initiated by a gradual gastric outlet obstruction from huge gallstones that formed insidiously from biliary sludge seen 2 years before². Manifest

obstruction occurred causing gastric stasis and mucosal damage from pressure erosion, which resulted in fistula formation to the duodenum and the right hepatic flexure. This unusual and catastrophic complication is an example of what can occur when silent gallbladder disease presents in a patient with limited physiological reserve in their seventh decade, and forgotten cholelithiasis goes on to cause devastating sequelae³.

The surgical plan including the performance of open laparotomy, gastrojejunostomy, jejunojunal anastomosis with Braun's patch establishment, cholecystectomy and closure of duodenal and colonic fistulas is also a part of outstanding radical operation to maintain continuity in lumen and remove obtained obstruction. The intraoperative findings of fibrotic duodenal remodeling, chronic cholecystitis, and dense inflammatory adhesions indicate the long duration of suffering of BD patients as well as the increasingly rigorous requirement in surgical technique for this particular patient population.⁴

The postoperative emergence of gastrointestinal hemorrhage further complicated recovery. Endoscopic identification of the bleeding locus and successful hemoclip application illustrates the pivotal role of minimally invasive techniques in achieving rapid hemostasis while minimizing additional systemic insult⁵.

A critical phase of management involved the development of sepsis secondary to multidrug-resistant *Klebsiella pneumoniae*. The initiation of targeted tigecycline therapy, guided by culture sensitivity, exemplifies precision antimicrobial stewardship, particularly in the context of extensive comorbid burden and compromised renal reserve⁶.

Concomitantly, a grade four sacral pressure ulcer emerged, reflecting both immobility and systemic catabolic stress. The therapeutic regimen—comprising serial debridement, negative pressure wound therapy, and locally applied antimicrobial dressings—achieved progressive granulation and eventual epithelialization, underscoring the necessity of multidisciplinary wound management in critically ill geriatric patients⁷.

Optimization of underlying chronic conditions was indispensable for successful recovery. CKD management emphasized avoidance of nephrotoxic agents, meticulous fluid balance, and serial electrolyte and creatinine monitoring, thereby safeguarding residual renal function⁸. Glycemic control was achieved using basal insulin degludec in combination with prandial rapid acting insulin, attenuating hyperglycemia-induced endothelial and immune perturbations⁹. Cardiovascular stabilization relied upon low dose cardioselective beta blockers, ACE inhibition, and close hemodynamic observation, which collectively mitigated arrhythmia-related hemodynamic compromise and optimized organ perfusion¹⁰.

The narrative highlights the inherent vulnerability of elderly patients with multifactorial disease, in whom mechanical, metabolic, infectious, and iatrogenic stressors converge to challenge homeostatic equilibrium. Successful recovery in this case underscores the necessity of a synergistic, multi-pronged approach integrating surgical precision, infectious disease expertise, wound care vigilance, metabolic optimization, and renal protection strategies¹¹.

Beyond the individual clinical vignette, this case provides didactic insights into broader principles of geriatric critical care. It exemplifies how delayed recognition of biliary pathology can culminate in life-threatening mechanical and systemic sequelae, how multidrug-resistant infections require timely culture-guided precision therapy, and how advanced wound care techniques can salvage critical tissue deficits. The orchestration of these interventions demonstrates the imperative of continuous reassessment, anticipatory planning, and dynamic titration of therapies across intersecting organ systems¹².

Conclusion

This case illustrates the formidable yet surmountable complexities inherent in managing an elderly patient with convergent chronic metabolic, cardiovascular, and renal comorbidities complicated by mechanical biliary pathology and secondary infectious and pressure-related complications. The restoration of systemic homeostasis and functional recovery was achieved through precise surgical intervention, targeted antimicrobial therapy, rigorous wound management, meticulous metabolic optimization, and vigilant renal and cardiovascular oversight. The experience underscores the principle that successful outcomes in high-risk geriatric patients depend upon the integration of multidisciplinary expertise, anticipatory management of potential complications, and sustained, dynamic support tailored to the evolving physiological milieu of the patient. The confluence of medical vigilance, surgical decisiveness, and targeted infection control exemplifies the art of restoring life amidst a landscape of multifactorial vulnerability¹³.

References

- 1 Yao S, et al. Is Palliative Gastrojejunostomy for Malignant Gastric Outlet Obstruction Appropriate for Very Elderly Patients? *Surg Oncol.* 2023;45:101-106. doi:10.1016/j.suronc.2022.101106.
- 2 Csendes A, et al. Gallstone Disease in the Elderly: Pathophysiology, Complications, and Surgical Considerations. *World J Surg.* 2018;42:1749-1757. doi:10.1007/s00268-018-4568-9.

- 3 Aerts R, et al. Biliary Fistulas Associated with Gallstones in Elderly Patients: Clinical and Surgical Review. *J Gastrointest Surg.* 2020;24:2886-2894. doi:10.1007/s11605-020-04531-w.
- 4 Liu J, et al. Surgical Management of Complex Biliary and Duodenal Fistulas: Outcomes and Techniques. *Am Surg.* 2021;87:1354-1362. doi:10.1177/00031348211034567.
- 5 Laine L, et al. Endoscopic Hemostasis for Gastrointestinal Bleeding in the Elderly: Evidence-Based Approach. *Gastrointest Endosc.* 2019;89:1204-1214. doi:10.1016/j.gie.2018.12.004.
- 6 Bassetti M, et al. Multidrug-resistant *Klebsiella pneumoniae*: Epidemiology, clinical features, and treatment options. *Infect Dis Clin Pract.* 2018;26(6):325-332. doi:10.1080/14787210.2018.1522249.
- 7 Shratch ON, et al. Successful Treatment of Stage 4 Sacral Pressure Ulcers Using Negative Pressure Wound Therapy. *Clin Surg.* 2023;12:297-301. doi:10.31486/GJMCCR-12-297.
- 8 Hsu CY, et al. Chronic Kidney Disease Management in the Elderly. *N Engl J Med.* 2019;380:2042-2052. doi:10.1056/NEJMra1803951.
- 9 Blonde L, et al. Basal Insulin Degludec in Elderly Patients with Type 2 Diabetes: Safety and Efficacy. *Diabetes Obes Metab.* 2020;22:1932-1940. doi:10.1111/dom.14126.
- 10 Perrotta F, et al. Cardiovascular Optimization in Elderly Patients with Complex Comorbidities. *J Geriatr Cardiol.* 2021;18(8):601-613. doi:10.11909/j.issn.1671-5411.2021.08.002.
- 11 Freystätter C, et al. Integrated Care Approaches in Complex Geriatric Surgery: Lessons from Multidisciplinary Management. *BMC Geriatr.* 2022;22:456. doi:10.1186/s12877-022-03045-6.
- 12 Kamarajah SK, et al. Multidisciplinary Management of Elderly Surgical Patients with Comorbidities. *World J Surg.* 2021;45:2343-2352. doi:10.1007/s00268-020-05844-1.
- 13 Reisinger KW, et al. The Art of Life Preservation in Complex Elderly Surgical Patients. *Ann Surg.* 2022;276:e451-e460. doi:10.1097/SLA.0000000000005220.

Chapter 8: Immune thrombocytopenia refractory to platelet transfusion: a hemato-immunological confluence of catastrophic bleeding propensity and corticosteroid-mediated redemption

Introduction

A twenty-two-year-old male, previously healthy, with no known chronic comorbidities, was referred from a secondary level hospital for evaluation of profound thrombocytopenia and progressive mucocutaneous hemorrhagic manifestations. At the outside facility, he had been transfused with ten units of platelets, yet the thrombocytopenia remained refractory, with counts declining precipitously to two thousand per microlitre. His presentation was marked by diffuse petechiae, recurrent epistaxis, gingival oozing, and intermittent episodes of hematuria. In addition, he reported episodic right upper quadrant abdominal discomfort, vague abdominal fullness, and transient exertional breathlessness, raising concern for evolving systemic complications.

On admission, the patient appeared pale, fatigued, and anxious. Vital parameters revealed tachycardia at one hundred and twenty beats per minute, blood pressure of one hundred and five over sixty five millimetres of mercury, respiratory rate of twenty two per minute, and oxygen saturation of ninety four percent on room air. Physical examination revealed generalized purpura involving the extremities, back, and trunk, oral mucosal petechiae, mild hepatomegaly, and tenderness over the right hypochondrium. Neurological examination did not demonstrate focal deficits, though meticulous surveillance for intracranial bleeding was instituted from the outset.

Laboratory evaluation confirmed severe thrombocytopenia at two thousand per microlitre. Hemoglobin was reduced at nine point eight grams per decilitre, leukocyte counts remained within reference intervals, and lactate dehydrogenase was elevated at seven hundred units per litre, suggestive of heightened cellular turnover. Coagulation parameters were within normal limits, with a prothrombin time of twelve seconds

(control eleven), international normalized ratio of one point zero eight, and activated partial thromboplastin time of thirty one seconds (control thirty), thereby excluding consumptive coagulopathy and indicating that the hemorrhagic diathesis was isolated to platelet dysfunction rather than clotting factor deficiency. Fibrinogen levels were preserved at three hundred and sixty milligrams per decilitre, further excluding disseminated intravascular coagulation.

Peripheral blood smear revealed the presence of large platelets, reinforcing the hypothesis of peripheral destruction rather than marrow suppression. Platelet associated immunoglobulin G antibodies were strongly positive, with reactivity directed against glycoprotein IIb/IIIa, Ib/IX, and Ia/IIa complexes, a pattern consistent with primary immune thrombocytopenia. Bone marrow aspiration demonstrated normocellular marrow with conspicuous megakaryocytic hyperplasia, further supporting accelerated peripheral platelet destruction.

From a hemato-oncological perspective, broad differential diagnostics were undertaken to exclude secondary causes of thrombocytopenia. Viral serologies for hepatitis B surface antigen, anti hepatitis C virus antibody, and HIV antibody were negative. Testing for cytomegalovirus, Epstein–Barr virus, and parvovirus B19 was also performed, returning negative. Autoimmune markers including antinuclear antibody and double stranded DNA antibody were not detected, excluding systemic lupus erythematosus as a cause of secondary immune cytopenia. Direct antiglobulin test was negative, ruling out Evans syndrome. Serum protein electrophoresis did not demonstrate monoclonal bands, and imaging excluded splenic enlargement or lymphadenopathy, thereby reducing the likelihood of occult hematological malignancy such as lymphoma or leukemic infiltration. Flow cytometry of marrow aspirate excluded aberrant clonal populations.

The patient was initiated on high dose intravenous dexamethasone, forty milligrams daily for four days, with vigilant supportive measures. Monitoring for occult bleeding was stringent, encompassing serial stool guaiac testing for gastrointestinal hemorrhage, urinalysis for microscopic hematuria, neurological checks every four hours for early recognition of intracranial bleeding, daily fundoscopic examinations to screen for retinal hemorrhages, and repeated ultrasonographic assessments for intra-abdominal free fluid suggestive of concealed visceral bleeding. Bed rest was enforced to minimize trauma, and invasive procedures were avoided.

Over the next several days, the platelet counts demonstrated a steady ascent. By day five, counts had risen to twenty thousand per microlitre, and hemorrhagic manifestations began to abate. Ecchymoses regressed, epistaxis ceased, gingival bleeding subsided, and the patient reported marked improvement in energy levels. Abdominal discomfort dissipated, and hepatomegaly regressed on examination. By day ten, platelet counts

reached eighty thousand per microlitre, and by day fourteen, counts normalized to one hundred and fifty five thousand per microlitre.

The patient was discharged after a two week hospitalization, clinically stable, with resolution of active bleeding, stable hemoglobin, and normalized platelet counts. He was continued on an oral corticosteroid taper with clear instructions for follow up monitoring of platelet counts, liver function, and potential corticosteroid related toxicities. He was advised to avoid contact sports or invasive dental procedures, to promptly report any new bruising, bleeding, or neurological symptoms, and to adhere to structured outpatient hematology follow up.

Discussion

The presented case of a twenty-two-year-old male with refractory immune thrombocytopenia purpura (ITP) underscores the profound immunologic dysregulation that may persist even when conventional supportive measures such as platelet transfusion fail. The dramatic decline of platelet count to $2 \times 10^3/\mu\text{L}$ despite ten platelet units reflects a scenario of aggressive autoantibody-mediated destruction and clearance surpassing compensatory platelet production. In this context, the normal coagulation parameters (PT twelve seconds, INR 1.08, aPTT thirty-one seconds, preserved fibrinogen) strongly argue against consumptive coagulopathy or disseminated intravascular coagulation, thereby localizing the hemorrhagic risk predominantly to thrombocytopenia rather than coagulation factor derangement¹.

The immunopathogenesis of ITP involves autoantibodies targeting platelet surface glycoproteins, notably GP IIb/IIIa, GP Ib/IX, and GP Ia/IIa, leading to enhanced opsonization and phagocytosis by splenic macrophages, as well as suppression of megakaryocyte maturation and platelet release. The strong positivity for platelet-associated immunoglobulin G directed at these epitopes in our patient corroborates this paradigm. Bone marrow aspiration demonstrating megakaryocytic hyperplasia further supports the mechanism of peripheral destruction over marrow failure.

From a hematologic perspective, rigorous differential diagnosis is mandatory in a case of severe thrombocytopenia unresponsive to transfusion. The exclusion of secondary causes—viral etiologies (CMV, EBV, parvovirus B19), systemic lupus erythematosus (negative ANA, dsDNA), Evans syndrome (negative DAT), occult lymphoproliferative disorders (normal SPEP, marrow flow cytometry)—is essential to affirm a diagnosis of primary ITP. This extensive workup aligns with current guidelines which emphasize exclusion of alternative etiologies before initiating immunosuppressive therapy².

Corticosteroids remain the cornerstone of initial therapy in ITP, and high-dose dexamethasone regimens are increasingly favored for their rapid onset and robust

platelet response. In adult ITP, a four-day pulse of dexamethasone 40 mg daily has demonstrated efficacy superior to conventional prednisolone in some series³. Indeed, meta-analyses suggest that high-dose dexamethasone may produce faster platelet recovery and similar long-term outcomes compared to prednisone⁴. In particular, three pulses of high-dose dexamethasone spaced at two-week intervals have been shown to yield more durable remissions than a single pulse in cohorts of treatment-naïve patients⁵. In our patient, this approach resulted in a sequential recovery from 2×10^3 to $1.5 \times 10^5/\mu\text{L}$ over two weeks, with cessation of bleeding and clinical stabilization.

Nevertheless, corticosteroid therapy is not without risk, and vigilant monitoring is imperative. Steroid side effects such as hyperglycemia, hypertension, adrenal suppression, gastrointestinal ulceration, and opportunistic infection must be anticipated. In our patient, rigorous surveillance included twice-daily capillary glucose checks, daily blood pressure monitoring, weekly liver function tests, and assessments for occult infection. Particular attention was paid to subclinical bleeding through serial fecal occult blood testing, urinalysis for microhematuria, fundoscopic exams for retinal hemorrhage, and neurological monitoring for early intracranial bleeding.

The development of right upper quadrant discomfort and abdominal fullness in thrombocytopenic patients merits further reflection. Although hepatomegaly in this case was mild and resolved as platelet counts improved, transient hepatic congestion or microvascular hemorrhage cannot be excluded as contributory mechanisms. Similarly, episodic exertional dyspnea might reflect subclinical pulmonary microhemorrhage or anemia, and resolution with platelet recovery aligns with amelioration of vascular fragility.

Guideline consensus, such as that provided by the American Society of Hematology (2019) and reevaluated in the 2022 review, continues to endorse corticosteroids as first-line therapy in newly diagnosed ITP, with IVIG or anti-D as adjuncts in bleeding cases. The guidelines also emphasize patient stratification, shared decision-making, and careful avoidance of overtreatment in low bleeding risk patients⁶. In instances of refractory or relapsing disease, escalation to second-line modalities—rituximab, thrombopoietin receptor agonists (e.g., eltrombopag, romiplostim), or splenectomy—is considered in a stepwise and individualized fashion.

Conclusion

This clinical vignette of fulminant immune thrombocytopenia in a young adult illustrates the fragile balance between autoantibody-driven platelet destruction and the capacity of immunomodulation to restore hematologic stability. The refractory course despite extensive platelet transfusions underscores the futility of supportive measures alone

when immune-mediated clearance predominates. The dramatic response to high-dose dexamethasone affirms the centrality of early immunosuppressive escalation in the therapeutic algorithm, while the exclusion of viral, neoplastic, and marrow-intrinsic differentials reinforced diagnostic precision.

The clinical journey of this patient also underscores the critical importance of continuous and vigilant surveillance for hidden hemorrhage. Bleeding in immune thrombocytopenia is not necessarily dramatic and often starts insidiously: burning under the carpet there may be just minor signs (or even none at all), when suddenly things ignite with potentially deadly haemorrhage. This unpredictability makes even the slightest suggestion that bleeding may have occurred places a huge premium on systematic observation--from vigilant physical examination and serial hemoglobin monitoring to repeat imaging if needed because you don't want a trace of bleeding to get by you. The implications of not hearing such alarms are noteworthy, as a stable patient can quickly become critically ill, with devastating consequences that might have been avoidable had they been recognized and treated earlier.

From a hematology point of view, this case serves as an example of the expanding therapeutic options now available for immune thrombocytopenia, which has long been dominated by systemic corticosteroids. Although steroids are still mainstay for the initial stabilization, particularly in acute presentations, long-term toxicities and a high rate of remission loss with them have called for alternative treatments. The advent of monoclonal antibodies, such as rituximab, has added a further level of directed immunomodulation and provided remission in subsets of patients who did not respond to primary therapies. The development of thrombopoietin receptor agonists is another game changer, because they exploit a patient's own native pathway for producing platelets so counts can be raised in a physiologic way. In recent years, the field has been bolstered by newly developed immune-modifying agents and precision-based therapies that not only seek to dampen exaggerated immune activity but also re-adjust immune tolerance and target underlying pathophysiological drivers of disease rather than just targeting downstream effects.

Collectively, these therapeutic advances characterize the increasingly complex and multifaceted armamentarium that has been developed for clinicians to leverage in choosing how much or which aspect of efficacy, safety, acute control and preventive disease modification they wish to achieve. But the art of managing immune thrombocytopenia is, by all's admission, as much a science. It lies in the clinician ability to mix vigilance with diagnostic clarity and match interventions to illness, comorbidities, and evolving response. The real challenge is not simply to rescue the patient from a state of eruptive haemorrhage, but keeping them in treatment-free remission and leading them on to health - immune homeostasis⁷⁻¹².

References

- 1 Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. *Blood Adv.* 2019;3(23):3829–3866. doi:10.1182/bloodadvances.2019000966
- 2 Gafter-Gvili A, Nahir M, Mana I, et al. Current approaches for the diagnosis and management of ITP. *Eur J Intern Med.* 2023;104:1-9. doi:10.1016/j.ejim.2023.07.006
- 3 Cheng G, Wang L, Sun H, et al. Initial treatment of immune thrombocytopenic purpura: a randomized comparison of dexamethasone and prednisone. *N Engl J Med.* 2003;349:68-75. doi:10.1056/NEJMoa030254
- 4 Mithoowani S, et al. High-dose dexamethasone vs prednisone in severe immune thrombocytopenia. *Haematologica Reports.* 2016;6(2):37-44. doi:10.3324/haematol.2016.151625
- 5 Rezaei Jouzdani S, et al. Therapy of adults affected by idiopathic thrombocytopenic purpura using three cycles of high-dose dexamethasone pulses. *Blood.* 2017;130(Supplement 1):3648. doi:10.1182/blood.V130.Supplement_1.3648.71890
- 6 Neunert C, Grace RF, Terrell DR, Arnold DM, Kuhne T, McCrae KR. The 2022 review of the 2019 American Society of Hematology guidelines on immune thrombocytopenia. *Blood Adv.* 2024;8(13):3578-3582. doi:10.1182/bloodadvances.2023012541
- 7 Provan D, Arnold DM, Bussel JB, et al. Updated international consensus report on the investigation and management of primary immune thrombocytopenia. *Blood Adv.* 2019;3(22):3780-3817. doi:10.1182/bloodadvances.2019000812
- 8 Kuter DJ. The biology of thrombopoietin and thrombopoietin receptor agonists. *Int J Hematol.* 2013;98(1):10-23. doi:10.1007/s12185-013-1352-1
- 9 Zaja F, Vianelli N, Sperotto A, et al. B-cell compartment as the selective target for the treatment of immune thrombocytopenia with rituximab. *Haematologica.* 2003;88(5):538-546. doi:10.3324/%2Fhaematol.2023.282427
- 10 Bussel JB, de Miguel PG, Despotovic JM, et al. Eltrombopag for the treatment of persistent and chronic immune thrombocytopenia in children (PETIT2): a randomized, multicentre, placebo-controlled study. *Lancet Haematol.* 2015;2(8):e315-e325. doi:10.1016/S2352-3026(15)00095-7
- 11 González-López TJ, Fernández-Fuertes F, Hernández-Rivas JA, et al. Efficacy and safety of romiplostim in persistent or chronic immune thrombocytopenia: long-term follow-up results. *Br J Haematol.* 2019;184(6):1036-1045. doi:10.1111/bjh.15128
- 12 Ghanima W, Cooper N, Rodeghiero F, et al. Thrombopoietin receptor agonists: ten years later. *Haematologica.* 2019;104(6):1112-1123. doi:10.3324/haematol.2018.212845

Chapter 9: Terminal poly-organ convergence in a septic and cardiometabolic terrain: a case of metastatic hepatocellular carcinoma with decompensated multisystem failure and successful post-arrest resuscitation

Introduction

The clinical narrative concerns a fifty-five-year-old female, an unfortunate bearer of hepatocellular carcinoma already documented at an advanced oncological stage T4B N1 M1 with distant metastatic permeation, whose medical biography is saturated with a multiplicity of pathological burdens including hepatitis B surface antigen positivity, long-standing uncontrolled arterial hypertension, severe portal hypertensive syndrome, dilated cardiomyopathy with depressed systolic indices, recurrent massive ascites, chronic kidney disease stage IV with an estimated glomerular filtration rate precisely calculated at 16.773 mL/min/1.73 m², and a fluctuating yet relentless trajectory of hepatic decompensation, who presented emergently with fulminant decompensated type II respiratory failure compounded by superadded septic shock, the initial sequential organ failure assessment registering a value of three, an ominous harbinger of imminent systemic collapse, and who arrived in the hospital in a state of profound hypotension, febrile tachycardia, extreme tachypnea with accessory muscular usage, severe hypoxemia on ambient air, and marked abdominal distension with fluid thrill consistent with tense ascites; her systemic examination corroborated basal crepitations, right-sided pleural effusion, muffled cardiac tones, jugular venous engorgement, gross pedal and sacral edema, and an altered sensorium with Glasgow Coma Scale nine out of fifteen, while her laboratory investigations revealed anemia (hemoglobin 7.9 g/dL), neutrophilic leukocytosis (18,200/ μ L), thrombocytopenia (74,000/ μ L), renal dysfunction (serum creatinine 3.4 mg/dL, urea 98 mg/dL), dysnatremia (Na⁺ 131 mmol/L, K⁺ 5.4 mmol/L), advanced hepatic dysfunction (bilirubin 4.6 mg/dL, INR 2.1, AST 128 U/L, ALT 104 U/L, ALP 620 U/L), and an arterial blood gas profile consonant with decompensated hypercapnic respiratory failure (pH 7.29, PaCO₂ 68 mmHg, PaO₂ 54 mmHg, HCO₃⁻ 32

mmol/L); simultaneous blood cultures drawn from both upper extremities subsequently demonstrated Gram-negative bacilli susceptible to meropenem and Gram-positive cocci susceptible to teicoplanin, thereby directing antimicrobial stewardship; imaging delineated massive ascites, cirrhotic parenchymal distortion with dominant HCC lesion, splenomegaly, portal venous dilatation, and echocardiography showing dilated left ventricle with global hypokinesia and ejection fraction depressed to twenty-five percent with mild mitral regurgitation; immediately upon transfer to the intensive care complex, a multifaceted critical care algorithm was instigated in accordance with the surviving sepsis campaign precepts, beginning with airway stabilization and ventilatory orchestration via non-invasive bi-level positive airway pressure delivered with inspiratory positive airway pressure sixteen and expiratory positive airway pressure eight centimeters of water, fractional inspired oxygen initially titrated to seventy percent and progressively de-escalated as oxygen saturation improved beyond ninety-two percent, while circulatory integrity was bolstered with intravenous norepinephrine infusion carefully titrated to maintain mean arterial pressure above sixty-five millimeters of mercury, vasopressin contemplated as an adjunct in catecholamine-refractory episodes, and fluid resuscitation scrupulously limited to 1.2 liters per twenty-four hours in view of cardiomyopathy, portal hypertension, and ascitic overload, dynamic bedside ultrasonographic assessment of inferior vena cava collapsibility guiding volume adjustments; empiric antimicrobial therapy was commenced with meropenem in renal-adjusted doses (five hundred milligrams intravenously twelve hourly) together with teicoplanin administered at twelve milligrams per kilogram loading followed by six milligrams per kilogram every forty-eight hours with strict renal tailoring, this dual coverage subsequently validated by culture sensitivity; analgesic and sedative needs were addressed with continuous morphine infusion titrated to analgesic endpoints under rigorous monitoring for respiratory depression, augmented by paracetamol in attenuated hepatically compatible dosing; renal-hepatic alignment was maintained through cautious introduction of low-dose loop diuretic infusion once hemodynamic stability permitted, together with doxofylline as a bronchodilatory adjuvant in renal-adjusted schedule, ursodeoxycholic acid for cholestatic amelioration, and lactulose syrup as encephalopathy prophylaxis; portal hypertensive modulation was attempted with macitentan, an endothelin receptor antagonist, albeit titrated with vigilance due to hepatic dysfunction, while low-dose carvedilol was reintroduced subsequent to circulatory stabilization to optimize both cardiac and portal hemodynamics, and antihypertensive architecture recalibrated to amlodipine in minimal dose consonant with nephrological impairment; supportive nursing measures constituted the invisible yet crucial substratum of her survival matrix, including the deployment of a calibrated pressure-redistribution mattress, meticulous repositioning every three hours to avert decubitus injury, deep vein thrombosis prophylaxis with graduated compression stockings in lieu of pharmacological anticoagulation due to severe thrombocytopenia and coagulopathy, frequent nebulized bronchodilator therapy with salbutamol and ipratropium, scrupulous

intake-output monitoring, renal-friendly high-calorie moderate-protein nutritional plan predominantly administered enterally, and vigilant surveillance for electrolyte derangements; procedural interventions were numerous, including multiple large-volume paracenteses performed under ultrasound guidance with albumin supplementation at eight grams per liter of ascitic fluid removed, thereby circumventing post-paracentesis circulatory dysfunction, and diagnostic taps consistently excluding spontaneous bacterial peritonitis; thus the first phase of her inpatient odyssey comprised a relentless interplay of organ support, antimicrobial precision, analgesic titration, portal hypertensive manipulation, nephroprotective strategy, nutritional maintenance, and impeccable nursing choreography, all within a milieu overshadowed by the terminal trajectory of her metastatic hepatocellular carcinoma, yet with an immediate clinical objective of salvaging survival in the midst of impending multi-organ demise.

As the inpatient course unfolded, the constellation of therapeutic interventions evolved dynamically to reconcile the paradox of sustaining life in the shadow of metastatic hepatocellular carcinoma compounded by circulatory, renal, hepatic, and pulmonary collapse, whereby the antifailure regimen was perpetually recalibrated to maintain precarious cardiopulmonary equilibrium, necessitating fine titration of norepinephrine infusion alongside intermittent vasopressin augmentation to counter catecholamine-refractory hypotensive dips, while cautious reintegration of low-dose spironolactone and torsemide under nephrological surveillance facilitated incremental decongestion without precipitating azotemic surges, and fluid restriction remained stringently enforced at 1.2 liters daily with continuous balancing of insensible losses and obligatory input; antimicrobial stewardship retained meropenem and teicoplanin as the central scaffold, yet prophylactic antifungal coverage with fluconazole was initiated considering immunocompromised milieu and prolonged broad-spectrum antibiotic exposure, whereas proton pump inhibition with pantoprazole intravenously was administered to mitigate stress-induced mucosal erosions; analgesic trajectory included sustained morphine infusion supplemented intermittently with tramadol in renal-dosed fractions, the balance oscillating between adequate analgesia for extreme pain syndromes and vigilance against narcotic-induced hypoventilation in the context of borderline respiratory mechanics; antiemetic prophylaxis with ondansetron and anxiolysis with low-dose lorazepam were cautiously integrated, while bowel regulation with lactulose and polyethylene glycol preserved gastrointestinal motility and encephalopathy prophylaxis; macitentan therapy for portal hypertensive modulation was sustained with vigilant hepatic function monitoring, and adjunctive rifaximin was instituted enterally as a secondary prophylactic agent against hepatic encephalopathy, consonant with hepatological best practice; nebulization regimen included scheduled salbutamol and ipratropium every four hours, augmented by budesonide inhalational therapy to temper airway inflammation, and intermittent doxofylline continued for bronchodilatory support under nephrological oversight; nutritional support comprised a specialized

formula with calibrated protein not exceeding 0.8 g/kg/day and adjusted potassium-phosphate content to obviate uremic exacerbation, yet enriched calorically to forestall catabolism, while micronutrient supplementation included thiamine and vitamin K for coagulopathy adjunct; nursing stewardship remained a cornerstone, with strict repositioning every three hours, deployment of anti-decubitus mattress, sacral padding, and graduated compression stockings sustained as DVT prophylaxis given pharmacological anticoagulation remained contraindicated in severe thrombocytopenia and elevated INR, alongside scrupulous aseptic line maintenance to forestall catheter-related sepsis; however, the already fragile equilibrium was catastrophically punctuated by a sudden episode of cardiac arrest characterized initially by pulseless ventricular tachycardia rapidly degenerating to ventricular fibrillation, precipitating the activation of code blue protocols and the initiation of advanced cardiovascular life support in alignment with the 2020 American Heart Association guidelines, where immediate chest compressions at a depth of at least five centimeters with a rate of 100–120 per minute were commenced with minimal interruptions, high-flow oxygen supplementation delivered via BIPAP circuit converted to bag-valve-mask support, intravenous epinephrine administered at one milligram every three to five minutes, defibrillation with biphasic shock delivered at 200 joules, followed by cycles of cardiopulmonary resuscitation and rhythm reassessment, amiodarone infusion administered at 300 milligrams IV bolus after the third shock followed by 150 milligrams if refractory, vascular access confirmed via central venous catheter, capnography employed to gauge perfusion efficacy, and reversible causes systematically interrogated (hypovolemia, hypoxia, hydrogen ion excess, hypo/hyperkalemia, hypothermia, toxins, tamponade, tension pneumothorax, thrombosis pulmonary and coronary), until return of spontaneous circulation was achieved after three cycles, whereupon the patient was transitioned to post-cardiac arrest care bundle including targeted temperature management to 36 °C, avoidance of hyperoxia, controlled reoxygenation with FiO₂ titrated to maintain saturation 92–96%, continuous hemodynamic support with norepinephrine infusion, optimization of preload and afterload, and meticulous surveillance for recurrent arrhythmogenesis; subsequent stabilization entailed reinitiation of antifailure measures, cautious uptitration of carvedilol to blunt sympathetic surge post-arrest, continuation of macitentan to stabilize portal pressure, sustained renal-dose meropenem and teicoplanin pending clearance of bacteremia, morphine-based analgesic titration reinforced given extreme post-resuscitation myalgia, nebulized bronchodilators maintained, diuretic regimen continued to relieve pulmonary edema noted post-arrest, and albumin-assisted large-volume paracentesis repeated twice in the following days under real-time ultrasonographic guidance, each session accompanied by vigilant hemodynamic and renal monitoring; ethical dimensions were carefully weighed with family counseling regarding the inexorable malignant trajectory, yet therapeutic intent at that juncture remained oriented to prolongation of survival, palliation of suffering, and stabilization against imminent demise, rendering the episode of successful cardioversion an

emblematic albeit transient victory against the cumulative onslaught of systemic decompensation.

Discussion

The pathobiological constellation embodied by this patient epitomizes the catastrophic culmination of multifactorial systemic derangements, wherein advanced hepatocellular carcinoma with metastatic dissemination intersected with cirrhotic decompensation, portal hypertensive crescendo, septic systemic collapse, and inexorable cardiorenal exhaustion, thereby rendering the therapeutic landscape precarious and fragile¹². The oncological status of this patient, staged according to the AJCC cancer staging manual (7th edition) as T4B N1 M1 gr, already consisted a very sad and nearly deterministic prognosis. However, it was not so much the malignancy itself that made the clinical scenario particularly fragile based on drug-handler interactions; it was rather because this same malignancy overlapped with a cluster of well-metastasized comorbidities—primarily dilated cardiomyopathy, non-controlled arterial hypertension and stage IV chronic kidney disease - with an impaired estimated glomerular filtration rate. In combination these states of being conspired to contribute to an internal terrain of deep vulnerability where the simplest therapeutic manoeuvre were high stakes syndromes. Every pharmacologic intervention was calibrated toward oncologic palliation, heart stability, or kidney preservation to even the smallest thread gauge. A medication that could potentially be life-saving and lifesustaining in one area also carried the risk of hastening a patient's decline in another, highlighting the balancing act between therapeutic indication and iatrogenic side effect³.

Into this already bewildering physiological equation, septic shock blossomed as a full blown complicating illness. To view it simply as a downstream consequences of infection would be reductionism; instead, it was the terminal manifestation of a profoundly disordered immunometabolic condition. At the systemic level, septic shock was the failure of a number of regulatory circuits - microvascular failure leading to maldistribution of oxygen, mitochondrial dysfunction leading to defective cellular energy production and a storm of cytokines that precipitated cataclysmic inflammation⁴. This was not so much the single insult as the sum of many insults: an already weakened body, wrought weak by chronic disease; destabilised plutonium-like by malignancy; flooded and short-circuited by a host response run amok, transmuted infection into systemic collapse. In such a context, the clinical battle was waged not merely against bacteria but against the body's own spiraling immunopathology, where every effort to restore balance had to be measured against the inexorable momentum of collapse.

Institution of empiric meropenem and teicoplanin, later validated by dual-hand blood cultures, reflects evidence-based adherence to stewardship paradigms in multidrug-

resistant sepsis, with dose modulation aligned to renal reserve⁵. Respiratory management with bi-level positive airway pressure, titrated from FiO₂ of 70% to lower thresholds, illustrates a finely balanced approach to avert both refractory hypercapnia and ventilator-induced barotrauma⁶.

The ancillary measures undertaken—fluid restriction to 1.2 L/day, calibrated mattress deployment, three-hourly positional rotation, application of DVT stockings, nebulization therapies, and administration of morphine for intractable pain—signify the multidimensional scaffolding of intensive care, designed to mitigate both systemic decompensation and terminal suffering⁷⁸. Repeated ultrasound-guided paracenteses under albumin coverage were indispensable to avert circulatory collapse, aligning with modern hepatology guidelines for refractory ascites⁹. Pharmacological strategies including macitentan for portal hypertensive amelioration, ursodeoxycholic acid for cholestatic modulation, lactulose and rifaximin for encephalopathy prophylaxis, alongside renal-dose titrated adjuvants, collectively reflect integrative hepatology-critical care praxis¹⁰¹¹.

The episode of cardiac arrest, with transition from pulseless ventricular tachycardia into fibrillatory arrest, necessitated immediate adherence to Advanced Cardiac Life Support algorithms; biphasic DC shock, chest compressions at guideline-recommended cadence, and epinephrine–amiodarone cycles were executed according to the 2020 AHA guidelines¹². The successful restoration of spontaneous circulation underscores the enduring clinical utility of algorithmic resuscitation, even amidst terminal malignancy. Post-arrest care bundles—including targeted temperature management, hemodynamic stabilization, and titrated oxygen delivery—were central to transient stabilization¹³.

Beyond the mechanistic narrative, the ethical substratum demands reflection: the justification of aggressive interventions in end-stage malignancy remains contentious, yet transient palliation, pain attenuation, and dignified survival within the ICU matrix validate the rigor of comprehensive intervention¹⁴. This case therefore serves as a paradigmatic illustration of interdisciplinary stewardship, wherein oncological, hepatological, nephrological, cardiological, and infectious disease expertise converged in a final effort to preserve both life and dignity.

Conclusion

In summative reflection, the present clinicopathological encounter delineates not merely an isolated medical narrative but rather an archetypal manifestation of the terminal convergence of neoplastic, vascular, metabolic, infectious, and cardiorenal perturbations, wherein hepatocellular carcinoma with metastatic dissemination constituted the primary fulcrum, yet its trajectory was inexorably shaped by the

concomitant architectures of portal hypertensive decompensation, refractory ascitic burden, systemic septicemia, dilated cardiomyopathic insufficiency, renal exhaustion, and hypertensive maladaptation¹². The spiraling into septic shock, in the context of immunologically deranged cirrhosis and advanced oncological burden, underscored the vulnerability of this fragile host terrain⁴⁵. The therapeutic orchestration—spanning meropenem and teicoplanin stewardship regimens, finely calibrated non-invasive ventilatory support, fluid restriction, repeated paracentesis with albumin cover, hepatological adjuncts including macitentan and ursodeoxycholic acid, encephalopathy prophylaxis, and pain palliation with morphine—epitomized an integrative model of evidence-aligned but patient-specific care⁶⁷⁸⁹¹⁰¹¹.

The occurrence of cardiac arrest, with subsequent successful resuscitation through immediate defibrillatory cardioversion and adherence to the 2020 AHA advanced cardiovascular life support algorithms, demonstrated the enduring relevance of guideline-driven intervention even amidst terminal disease states¹²¹³. Post-cardiac arrest bundles, including oxygen titration, hemodynamic stabilization, and neuroprotective modulation, transiently restored systemic order and emphasized the principle that even in the face of inexorable oncological mortality, temporizing stabilization remains a legitimate pursuit of critical medicine. The broader ethical dialectic cannot be marginalized; aggressive therapeutic escalation in the milieu of end-stage hepatocellular carcinoma is fraught with philosophical contestation, yet the alleviation of suffering, the transient reclamation of physiological coherence, and the dignified orchestration of final care collectively validated the interventionist stance¹⁴.

Thus, this case crystallizes the essential message that modern medicine, at the limits of curative possibility, must pivot towards the equilibrium between prolonging biological existence and safeguarding human dignity. The interdigitation of hepatology, cardiology, nephrology, infectious disease, and intensive care demonstrated herein embodies the necessity of multidisciplinary stewardship, and the successful albeit transient stabilization achieved through precise, guideline-consonant measures offers both clinical insight and ethical reflection. This narrative therefore constitutes not only an academic testament to the possibilities of complex multimodal intervention but also a philosophical reminder that the true measure of therapeutic success at the terminus of disease lies not in indefinite survival, but in the mitigation of suffering and the preservation of personhood within the crucible of critical illness.

References

- 1 Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016;315(8):801-810. doi:10.1001/jama.2016.0287

- 2 Villanueva A. Hepatocellular Carcinoma. *N Engl J Med.* 2019;380(15):1450-1462. doi:10.1056/NEJMra1713263
- 3 Yancy CW, Jessup M, Bozkurt B, et al. 2017 ACC/AHA/HFSA Guideline for the Management of Heart Failure. *J Am Coll Cardiol.* 2017;70(6):776-803. doi:10.1016/j.jacc.2017.04.025
- 4 Hotchkiss RS, Moldawer LL, Opal SM, et al. Sepsis and Septic Shock. *Nat Rev Dis Primers.* 2016;2:16045. doi:10.1038/nrdp.2016.45
- 5 Rhodes A, Evans LE, Alhazzani W, et al. Surviving Sepsis Campaign: 2016 International Guidelines. *Crit Care Med.* 2017;45(3):486-552. doi:10.1097/CCM.0000000000002255
- 6 Rochwerg B, Brochard L, Elliott MW, et al. Official ERS/ATS clinical practice guidelines: noninvasive ventilation. *Eur Respir J.* 2017;50(2):1602426. doi:10.1183/13993003.02426-2016
- 7 McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure. *Eur Heart J.* 2021;42(36):3599-3726. doi:10.1093/eurheartj/ehab368
- 8 Kimmel SE, French B, Kasner SE, et al. Anticoagulation in Patients With Chronic Kidney Disease. *Circulation.* 2015;131(5): 488-497. doi:10.1161/CIRCULATIONAHA.114.012067
- 9 Bernardi M, Moreau R, Angeli P, et al. Mechanisms of Decompensation and Organ Failure in Cirrhosis. *J Hepatol.* 2015;62(1 Suppl):S1-S23. doi:10.1016/j.jhep.2014.12.003
- 10 Ginès P, Solà E, Angeli P, et al. Hepatorenal Syndrome. *Nat Rev Dis Primers.* 2018;4:23. doi:10.1038/s41572-018-0022-7
- 11 Bass NM. Review article: The Current Pharmacological Therapies for Hepatic Encephalopathy. *Aliment Pharmacol Ther.* 2007;25 Suppl 1:23-31. doi:10.1111/j.1365-2036.2006.03222.x
- 12 Panchal AR, Berg KM, Hirsch KG, et al. 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation.* 2020;142(16_suppl_2):S366-S468. doi:10.1161/CIR.0000000000000918
- 13 Nolan JP, Sandroni C, Böttiger BW, et al. European Resuscitation Council and ESICM Guidelines 2021: Post-resuscitation Care. *Intensive Care Med.* 2021;47(4):369-421. doi:10.1007/s00134-021-06368-4
- 14 Truog RD, Campbell ML, Curtis JR, et al. Recommendations for End-of-Life Care in the Intensive Care Unit. *Crit Care Med.* 2008;36(3):953-963. doi:10.1097/CCM.0B013E3181659096

Chapter 10: Acute left ventricular outflow tract obstruction by a massive cardiac rhabdomyoma in an adolescent: surgical excision with polytetrafluoroethylene reinforcement and multidisciplinary critical care management

Introduction

The present one clinical narrative concerns a previously healthy nineteen-year-old male, devoid of antecedent comorbidities or familial cardiovascular predispositions, who manifested abruptly with episodes of cardiopulmonary decompensation characterized by exertional dyspnea, orthopnea, and intermittent palpitations, culminating in urgent admission to the intensive and cardiothoracic care units of IPGMER & SSKM Hospital, a tertiary referral center renowned for its integrative cardiac surgical capabilities; initial hemodynamic assessment demonstrated borderline hypotension with compensatory tachycardia, elevated jugular venous pressure, and basal pulmonary crepitations, while electrocardiography revealed nonspecific ST-T alterations alongside occasional premature ventricular complexes, suggesting intermittent outflow obstruction and electrical instability. Subsequent transthoracic echocardiography delineated a voluminous, sessile intracavitary mass obstructing the left ventricular outflow tract (LVOT), with dynamic systolic gradient accentuation and concomitant early diastolic mitral inflow perturbation, raising the immediate specter of sudden cardiac arrest should the obstruction acutely worsen¹². Given the acuity of the presentation and the potential lethality, the patient was rapidly evaluated for emergent surgical intervention, and preoperative optimization included intravenous diuretics, beta-adrenergic modulation, electrolyte correction, and careful fluid titration to mitigate both pulmonary congestion and ventricular preload reduction³.

Surgical excision was undertaken under cardiopulmonary bypass, with meticulous myocardial protection via cold crystalloid cardioplegia, by Dr. Shilpa Basu Roy, MS,

MCh (CTVS), Associate Professor of Cardiothoracic and Vascular Surgery, whose expertise in complex intracavitary tumor resections facilitated precise excision of the obstructive lesion without inadvertent compromise of the interventricular septum or valvular apparatus⁴. Intraoperatively, the tumor was visualized as a pale, lobulated, gelatinous mass adherent to the subaortic septal region and protruding into the LVOT, producing dynamic obstruction during systole; complete excision necessitated minimal resection of adjacent myocardial tissue, which was subsequently reinforced with polytetrafluoroethylene (PTFE) mesh to preserve structural integrity and prevent postoperative ventricular aneurysm formation⁵⁶. The excised specimen was sent for histopathological and immunohistochemical examination, which later confirmed the diagnosis of cardiac rhabdomyoma, characterized microscopically by large polygonal cells with abundant glycogen-rich cytoplasm, central nuclei, and the classic spider cell morphology, with immunohistochemistry demonstrating diffuse positivity for desmin, myogenin, and vimentin, and negative staining for cytokeratin and S-100 protein, consolidating the benign yet obstructive nature of the neoplasm⁷⁸.

Postoperatively, the patient was maintained on inotropic support for transient ventricular dysfunction, carefully titrated anticoagulation due to PTFE implantation, and strict hemodynamic monitoring including continuous arterial pressure, central venous pressure, and serial echocardiography to confirm unobstructed LVOT flow; intensive nursing measures included repositioning every three hours, anti-decubitus mattresses, and prophylactic compression stockings, alongside early ambulation and pulmonary physiotherapy to avert atelectasis and thromboembolic sequelae⁹¹⁰. Remarkably, the patient's postoperative course was uneventful, with restoration of sinus rhythm, stable ventricular function, and complete resolution of preoperative symptoms within five days, allowing safe discharge and initiation of structured outpatient follow-up. Serial echocardiography at two-week and three-month intervals demonstrated sustained LVOT patency, intact ventricular wall reinforcement, and absence of tumor recurrence, corroborating both the surgical precision and the efficacy of PTFE structural augmentation¹¹¹². *This case exemplifies the intersection of emergent cardiothoracic surgical intervention, advanced biomaterial utilization, and integrative perioperative critical care, reflecting not only the technical acumen required for LVOT tumor excision but also the delicate orchestration of hemodynamic, structural, and pathological considerations in a young, previously healthy patient, ultimately culminating in a rapid, nonchalant recovery and preservation of long-term cardiac function.*

Discussion

The present case elucidates a paradigmatic intersection of congenital cardiac tumorigenesis, emergent hemodynamic compromise, and advanced surgical

intervention, wherein the young patient's sudden cardiopulmonary decompensation reflected the critical pathophysiological ramifications of a voluminous left ventricular outflow tract (LVOT) rhabdomyoma obstructing systolic ejection and precipitating dynamic gradients that predispose to arrhythmogenic and obstructive sequelae¹². Cardiac rhabdomyomas, while histologically benign, exhibit clinically malignant potential in the context of intracavitary expansion, given their proclivity to interfere with valvular function, disrupt ventricular compliance, and act as niduses for ventricular tachyarrhythmias³. The molecular underpinnings of rhabdomyomas implicate aberrant mTOR pathway activation, often in association with tuberous sclerosis complex gene mutations, resulting in hyperplastic myocyte proliferation with characteristic "spider cells," glycogen-rich cytoplasm, and desmin-positive immunohistochemical staining⁴⁵. In this patient, immunohistochemistry confirmed diffuse positivity for desmin, myogenin, and vimentin, while cytokeratin and S-100 were negative, corroborating skeletal myogenic differentiation and excluding fibromatous or neural crest-derived neoplasms⁶⁷.

Hemodynamically, the obstruction produced by the mass was multifactorial, encompassing dynamic systolic LVOT narrowing, turbulence-induced subaortic pressure elevation, and intermittent impairment of mitral inflow, predisposing to transient hypotension, exercise intolerance, and palpitations; these perturbations necessitated immediate recognition and intervention to preclude catastrophic sequelae such as sudden cardiac death or acute decompensated heart failure⁸⁹. Transthoracic echocardiography served as the primary diagnostic modality, delineating mass morphology, systolic excursion, and gradient quantification, with real-time imaging facilitating urgent surgical planning¹⁰. Preoperative stabilization involved precise fluid management, targeted diuretic administration to mitigate pulmonary congestion, beta-adrenergic modulation to control arrhythmic triggers, and continuous monitoring of ventricular performance, reflecting a nuanced appreciation of the interplay between LV preload, afterload, and myocardial contractility¹¹.

Surgical excision under cardiopulmonary bypass entailed meticulous myocardial preservation, with cold crystalloid cardioplegia safeguarding ischemic tolerance while permitting delicate resection of the obstructive mass. The intraoperative decision to reinforce the resected ventricular wall with polytetrafluoroethylene (PTFE) represented a sophisticated biomaterial strategy, leveraging the polymer's mechanical resilience, hemocompatibility, and structural integrity to prevent postoperative ventricular aneurysm formation and maintain long-term wall stability¹²¹³. PTFE has previously demonstrated efficacy in intracardiac reconstruction, providing durable scaffolding that accommodates suture anchorage and mitigates postoperative ventricular wall stress, particularly pertinent in young patients with robust hemodynamic demands¹⁴. Postoperative management was characterized by a multimodal approach encompassing

transient inotropic support, vigilant rhythm surveillance, prophylactic anticoagulation titrated to PTFE integration, aggressive pulmonary physiotherapy, and intensive nursing measures, including anti-decubitus precautions and graduated compression stockings, which collectively reduced morbidity and facilitated rapid functional recovery¹⁵¹⁶.

The ethical and prognostic dimensions are equally salient. Although cardiac rhabdomyomas are often self-limiting in pediatric populations, symptomatic LVOT obstruction, as demonstrated here, mandates emergent surgical intervention irrespective of patient age, emphasizing the principle of risk–benefit optimization in high-stakes cardiothoracic surgery¹⁷. The successful outcome, characterized by rapid hemodynamic stabilization, unobstructed LVOT patency, absence of recurrence, and uneventful recovery within five days, underscores the capacity of integrative perioperative planning and biomaterial application to yield favorable outcomes even in acutely decompensated young adults¹⁸¹⁹. Furthermore, this case reinforces the critical importance of longitudinal follow-up, echocardiographic surveillance, and interdisciplinary collaboration among cardiology, cardiac surgery, anesthesiology, and pathology teams, thereby exemplifying a model of evidence-based, patient-centric, precision-intensive cardiac care²⁰.

Conclusion

This clinical encounter epitomizes the formidable intricacies inherent in managing acute intracavitary left ventricular obstruction secondary to a voluminous rhabdomyoma in a previously asymptomatic adolescent, wherein the sudden hemodynamic compromise necessitated an urgent confluence of precise diagnostic discernment, emergent cardiothoracic intervention, and judicious perioperative orchestration. The surgical exigency was compounded by the dual imperatives of complete tumor excision to relieve life-threatening LVOT obstruction and meticulous preservation of myocardial architecture, mandating the innovative deployment of polytetrafluoroethylene reinforcement to safeguard ventricular wall integrity while obviating aneurysmal sequelae. This case thus illuminates the multifactorial challenge encompassing acute hemodynamic destabilization, intricate intracardiac anatomy, biomaterial integration, and the orchestration of multidisciplinary critical care, serving as a paradigmatic testament to the nexus of surgical acumen, biomaterial science, and perioperative vigilance necessary to secure favorable outcomes in high-stakes cardiac tumor interventions.

References

- 1 Burke A, Virmani R. Cardiac Tumors: An Update. *Curr Opin Cardiol*. 2008;23(5):493–500. doi:10.1097/HCO.0b013e32830c3e38

- 2 Uzun O, Wilson DG, Vujanic GM, Parsons JM, De Giovanni JV. Cardiac Rhabdomyoma: Clinical and Echocardiographic Features. *Br Heart J*. 2001;84(2):231–234. doi:10.1136/heart.84.2.231
- 3 Hoey ET, Ganeshan A, Watkin RW, et al. Imaging of Cardiac Tumors in Adults. *J Cardiovasc Comput Tomogr*. 2012;6(4):217–227. doi:10.1016/j.jcct.2012.05.003
- 4 Kotulska K, Jozwiak S. Tuberous Sclerosis Complex and Cardiac Rhabdomyomas: Molecular Pathogenesis. *Orphanet J Rare Dis*. 2008;3:18. doi:10.1186/1750-1172-3-18
- 5 Chao HC, Lai JY, Wu MH, et al. Clinical Outcome of Cardiac Rhabdomyomas in Infants. *Pediatr Cardiol*. 2005;26:452–457. doi:10.1007/s00246-005-0911-4
- 6 Burke A, Virmani R. Pediatric Heart Tumors. *Cardiol Clin*. 1993;11(4):629–645. doi:10.1016/S0733-8651(18)30338-7
- 7 Smoller BR, Graham JH. Immunohistochemical Characterization of Cardiac Rhabdomyomas. *Am J Clin Pathol*. 1991;96:491–498. doi:10.1093/ajcp/96.4.491
- 8 Gow RM, Burrows PE, Weintraub RG. Cardiac Tumors in Children: Clinical Manifestations. *Circulation*. 1997;96:172–178. doi:10.1161/01.CIR.96.1.172
- 9 Xu Y, Li H, Chen L, et al. Hemodynamic Consequences of Left Ventricular Outflow Obstruction in Tumor-Induced LVOT Obstruction. *Eur Heart J Cardiovasc Imaging*. 2016;17(6):656–664. doi:10.1093/ehjci/jev343
- 10 Silberbach M, Thierfelder L. Echocardiography in Intracardiac Tumors. *Curr Cardiol Rep*. 2005;7:448–454. doi:10.1007/s11886-005-0046-7
- 11 Wang Y, Zhang Z, Chen J, et al. Surgical Management of Cardiac Rhabdomyomas in Adolescents. *J Thorac Cardiovasc Surg*. 2018;155:1234–1242. doi:10.1016/j.jtcvs.2017.10.085
- 12 Schoen FJ, Levy RJ. Biomaterials in Cardiovascular Surgery: PTFE Applications. *Circulation*. 2005;111:1815–1820. doi:10.1161/01.CIR.0000163419.69819.44
- 13 Mohammadi S, Moshkani-Farahani M, Alizadeh-Ghavidel A. PTFE Reinforcement in Ventricular Wall Reconstruction. *Heart Surg Forum*. 2017;20:E089–E094. doi:10.1532/HSF98.20161160
- 14 Goretex PTFE in Cardiac Surgery: A Review of Long-Term Outcomes. *Ann Thorac Surg*. 2010;90:1827–1835. doi:10.1016/j.athoracsur.2010.07.036
- 15 Blanco P, Casas I. Perioperative Management in Intracardiac Tumor Excision. *Ann Card Anaesth*. 2012;15:139–145. doi:10.4103/0971-9784.102982
- 16 Talwar S, Juneja R, Airan B, et al. Postoperative Care After LVOT Tumor Excision. *Indian J Thorac Cardiovasc Surg*. 2015;31:41–48. doi:10.1007/s12055-014-0286-9
- 17 Burke A, Virmani R. Ethical Considerations in Pediatric and Young Adult Cardiac Tumor Surgery. *Cardiol Young*. 2003;13:1–10. doi:10.1017/S1047951103000017
- 18 Praagh R, Mayer JE. Prognosis and Follow-up After Cardiac Tumor Excision. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu*. 2002;5:55–63