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Case Report

Echoes of a Cytokine Storm: HLH-Associated Bi-Ventricular Failure in a Young Woman with Lupus – A Case Report.

Chiedozie Nnabue Uwakwem[1], Samuel Clark[2]

[1] Clinical Research Fellow in Critical Care and Echocardiography, Critical Care Department, University College London Hospitals NHS Foundation Trust. 235 Euston Road, London. United Kingdom, NW1 2BU, [2] Consultant Anesthetist and Critical Care, University College London Hospitals; Echocardiography Fellowship & Research Lead. 235 Euston Road, London. United Kingdom, NW1 2BU

Abstract

Haemophagocytic lymphohistiocytosis (HLH) is a rare hyperinflammatory syndrome that can lead to rapid multiorgan failure. Cardiovascular involvement is under-recognised but may manifest as acute, reversible cardiomyopathy, particularly in patients with autoimmune disease. Early identification of cardiac complications is essential to guide timely immunosuppression and supportive therapy.

A 33-year-old woman with systemic lupus erythematosus (SLE) was transferred for specialist management of HLH. After initial stabilisation, she developed chest pain and haemodynamic compromise. Transthoracic echocardiography revealed severe bi-ventricular failure (EF 18%) and torrential tricuspid regurgitation. She was readmitted to ICU and managed with levosimendan, glyceryl trinitrate, and milrinone. Immunosuppression was escalated with IV methylprednisolone, IVIG, anakinra, etoposide, and rituximab.

Cardiac function improved rapidly, guided by serial echocardiography and biomarker monitoring. She was discharged with normalised EF and good functional recovery on tapering steroids and mycophenolate.

This case demonstrates that HLH can cause severe but reversible cardiomyopathy, particularly in patients with autoimmune disease. Early echocardiographic assessment and prompt initiation of immunosuppression alongside cardiovascular support enabled full recovery of cardiac function. Timely, multidisciplinary management is essential to prevent irreversible multiorgan dysfunction in HLH.

Keywords: Haemophagocytic lymphohistiocytosis, cardiomyopathy, systemic lupus erythematosus, cytokine storm, echocardiography, acute heart failure, tricuspid regurgitation.

***Correspondence:** Dr. Chiedozie Uwakwem, Email: chiedozie.uwakwem@nhs.net, ORCID: 0009-0001-5772-8284

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Quick Response Code:

Introduction

Haemophagocyticlymphohistiocytosis (HLH) is a rare but severe hyperinflammatory syndrome characterised by uncontrolled activation of cytotoxic T cells and macrophages, resulting in excessive cytokine release and rapid multiorgan dysfunction [2]. Although HLH is well recognised in paediatrics, adult secondary HLH is increasingly identified in association with infections, malignancy, and autoimmune conditions such as systemic lupus erythematosus (SLE) [2,5]. Mortality remains high, particularly when diagnosis is delayed or complications involve the cardiovascular or central nervous systems [2].

The classical clinical spectrum of HLH—cytopenias, fever, hepatosplenomegaly, liver dysfunction, and hyperferritinaemia—forms the basis of current diagnostic frameworks. However, cardiac involvement is not routinely emphasised in diagnostic criteria, despite emerging evidence that myocardial dysfunction may be both under-recognised and clinically significant [6]. Reported cardiac manifestations include global systolic dysfunction, myocarditis, takotsubo-like patterns, conduction abnormalities, and acute right heart failure in the context of pulmonary hypertension [6,7]. Distinguishing HLH-associated cardiomyopathy from sepsis-induced cardiomyopathy or lupus myocarditis is challenging due to overlapping inflammatory pathways and biomarker profiles [5].

Pathophysiologically, cytokine storm plays a central role in myocardial injury. Excessive levels of interleukin-1, interleukin-6, interferon-γ and tumour necrosis factor-α have been linked to myocardial oedema, impaired contractility, and reversible cytotoxic effects on cardiac myocytes [3,10]. This inflammatory phenotype aligns with the reversible pattern observed in HLH-related cardiomyopathy, where recovery often follows prompt immunosuppressive escalation and haemodynamic support.

SLE is a well-established trigger of secondary HLH, and the combination of lupus-related immune dysregulation with cytokine storm may predispose to profound cardiovascular decompensation [2,5]. Patients with SLE are also susceptible to a range of cardiac manifestations—including pericarditis, myocarditis, valvular disease, and pulmonary hypertension—compounding diagnostic uncertainty when they deteriorate acutely.

Despite an increasing number of HLH cases being recognised in adults, cardiac involvement remains a poorly described and under-appreciated complication, particularly in resource-limited settings. Reports of severe, reversible bi-ventricular failure triggered by HLH in adults with autoimmune disease are scarce, and most existing literature focuses on paediatric or malignancy-associated HLH. This gap highlights the need for detailed clinical descriptions to improve early recognition, guide echocardiographic monitoring, and support timely immunomodulatory escalation.

We present the case of a young woman with SLE who developed sudden, severe bi-ventricular failure and torrential tricuspid regurgitation during treatment for HLH, despite initially preserved cardiac function. This case underscores the need for early cardiovascular assessment, incorporation of serial echocardiography and cardiac biomarkers into HLH monitoring strategies, and timely, adaptive immunomodulation to reverse cardiac injury and prevent irreversible organ failure [1,4].

Subjects, Materials and Methods.

This report describes a single adult patient with systemic lupus erythematosus (SLE) who was admitted to a tertiary care centre for evaluation and management of suspected haemophagocyticlymphohistiocytosis (HLH). All clinical information was obtained from the electronic health record, including vital signs, laboratory investigations, imaging studies, prescribed therapies, and multidisciplinary team documentation. As this is a single-patient case report, the findings are inherently limited in generalisability and should be interpreted as descriptive rather than representative of broader patient populations.

Diagnostic evaluation adhered to institutional standards for suspected HLH and was guided by established literature [2,5]. Serial investigations included complete blood counts, metabolic panels, inflammatory markers, ferritin measurements (Figure 4), coagulation studies, and haemolysis profiles. Cardiovascular assessment incorporated serial transthoracic echocardiography (TTE) using Simpson's biplane method to evaluate left ventricular ejection fraction (LVEF), global longitudinal strain (GLS) analysis to assess subclinical myocardial dysfunction (Figure 1 & 2), and tricuspid annular plane systolic excursion (TAPSE) to quantify right-ventricular performance—an approach supported by intensive care echocardiography guidelines [1,4].

Cardiac biomarkers, including N-terminal pro-B-type natriuretic peptide (NT-proBNP) and Troponin T, were trended throughout admission to monitor myocardial stress and guide haemodynamic management (Figure 3). Additional imaging included PET-CT to evaluate systemic inflammatory activity, CT pulmonary angiography to exclude pulmonary embolism, and cardiac MRI performed according to standardised acquisition protocols to evaluate myocardial oedema, fibrosis, or structural abnormalities.

Therapeutic interventions were delivered according to clinical need and emerging diagnostic information. HLH-directed treatment included intravenous corticosteroids, intravenous immunoglobulin (IVIG), anakinra, etoposide, and rituximab, following recommended approaches for severe or refractory HLH [3,8]. Cardiovascular support comprised levosimendan, glyceryl trinitrate, and milrinone, selected for their inotropic and vasodilatory profiles in the context of inflammatory cardiomyopathy. Treatment response was monitored through serial laboratory trends, echocardiographic parameters, and haemodynamic assessments.

This case was conducted in accordance with institutional policies for case reporting. The patient provided written informed consent at the time of admission, permitting the use of anonymised clinical data and medical images for research, education, and publication purposes. Ethical approval was not required as per local guidelines governing single-patient case reports.

Ethical Considerations and Consent

This case report was conducted in accordance with institutional policies for the use of anonymised clinical information for research and educational purposes. As this is a single-patient case report without experimental intervention, formal ethical approval was not required under local guidelines.

The patient provided written informed consent at the time of admission permitting the use of anonymised clinical data, laboratory results, and imaging for research, educational dissemination, and publication. All identifying information has been removed to preserve confidentiality. The preparation of this case report adheres to the ethical principles outlined in the Declaration of Helsinki and complies with relevant data protection regulations.

Result/Case Presentation.

Case

A 33-year-old woman with systemic lupus erythematosus (SLE, diagnosed 2011), Sjögren's syndrome, musculoskeletal and renal lupus, and recurrent urinary tract infections was transferred to our tertiary centre with progressive cytopenias, transaminitis, hyperferritinaemia, and suspected haemophagocytic lymphohistiocytosis (HLH). She had recently undergone adjustments to her immunosuppressive regimen and had declined hospital admission twice in August 2024 due to fatigue and arthralgia. Initial management at the referring hospital included intravenous (IV) methylprednisolone, anakinra, and supportive therapy.

Clinical Findings

On arrival to the ICU (10/10/2024), she was haemodynamically stable. Baseline transthoracic echocardiography (TTE) showed preserved biventricular systolic function (LVEF 58%) with normal right ventricular (RV) dimensions and function. HLH markers initially improved.

During the next five days on the ward, she developed progressive tachycardia and new pleuritic chest pain. Examination demonstrated cool peripheries, delayed capillary refill, and oliguria. On 15/10/2024, she deteriorated abruptly with biochemical evidence of hypoperfusion (lactate 5.6 mmol/L) and a narrow pulse pressure.

Repeat TTE revealed fulminant cardiac deterioration: severe global left ventricular systolic dysfunction (EF 18% by Simpson's biplane; GLS –5.0), a dilated RV with reduced function (TAPSE 1.3 cm), and torrential tricuspid regurgitation due to leaflet malcoaptation. Right atrial enlargement was present, and pulmonary hypertension was likely underestimated because of the near-free-flowing TR jet. These findings were consistent with acute bi-ventricular failure in the context of HLH.

Extensive microbiological investigations, including blood cultures, viral screening, and cross-sectional imaging, identified no infectious source, supporting HLH-driven inflammatory cardiomyopathy as the cause of acute decompensation.

Timeline

A detailed chronological summary of clinical events, imaging, biomarker trends, and interventions from July to December 2024 is presented in **Table 1.**

Table 1. Chronological timeline of clinical events, diagnostics, interventions, and biomarker trends in a patient with HLH-associated bi-ventricular failure.

Date	**Event**	**Relevant Investigations**	**Key Biomarkers / Echo Findings/Cardiac Imaging**
10/10/2024	Transfer to UCLH ICU for HLH management	Initial TTE	EF 58%, NT-proBNP 13,116 ng/L
15/10/2024	Acute decompensation, ICU readmission, Anakinra dose increased	Repeat TTE	EF 18%, TAPSE 1.3 cm, NT-proBNP 92,060 ng/L, Troponin T 136 ng/L, Lactate 5.6 mmol/L
16/10/2024	Post-levosimendan	TTE	EF 30%, troponin 64 ng/L
17/10/2024	Started on milrinone	TTE	EF 11%, NT-proBNP 33,963 ng/L
18/10/2024	Etoposide, Rituximab given	TTE with contrast	EF 38%, troponin 44 ng/L

21/10/2024	Milrinone weaned	TTE	EF 40%, NT-proBNP 12,228 ng/L
23/10/2024	Recovery of function	TTE	EF 57%, GLS –14.4%
24/10/2024	Anakinra stopped	HLH bloods	Downtrending markers
25/20/2024	Rituximab given	HLH bloods	Downtrending markers
26/10/2024	Stepped down from ICU to ward	Clinical reassessment	EF improving off inotropes, NT-proBNP trending down
28/10/2024	Stable function	TTE	EF 55–60%
22/11/2024	Cardiac MRI	CMR	Findings supported recovery phase of myocardial dysfunction (possible resolving takotsubo vs cytokine injury)
23/11/2024	CTPA	CTPA	No PE, pulmonary artery dilation
17/11/2024	Near-complete recovery	TTE	EF 60%, NT-proBNP 181 ng/L
13/12/2024	Discharged	Final bloods	Ferritin 668 ug/L, Troponin 62 ng/L

Clinical Timeline – HLH-Associated Cardiac Complication

Diagnostic Assessment

Investigations included serial TTE (Figures 1 and 2), cardiac biomarkers (Figure 3) with peak NT-proBNP of 92,060 ng/L and Troponin T of 136 ng/L, and ferritin trends (Figure 4). Additional imaging included PET-CT, CT pulmonary angiography, and bone marrow aspirate showing left-shifted granulopoiesis, 3% blasts, dyserythropoiesis, and occasional haemophagocytosis. The differential diagnosis included HLH-associated myocarditis, takotsubo cardiomyopathy, and antiphospholipid syndrome. Cardiac MRI on 22/11/2024 showed no fibrosis, oedema, or apical ballooning, supporting a reversible inflammatory cardiomyopathy consistent with recovery-phase HLH.

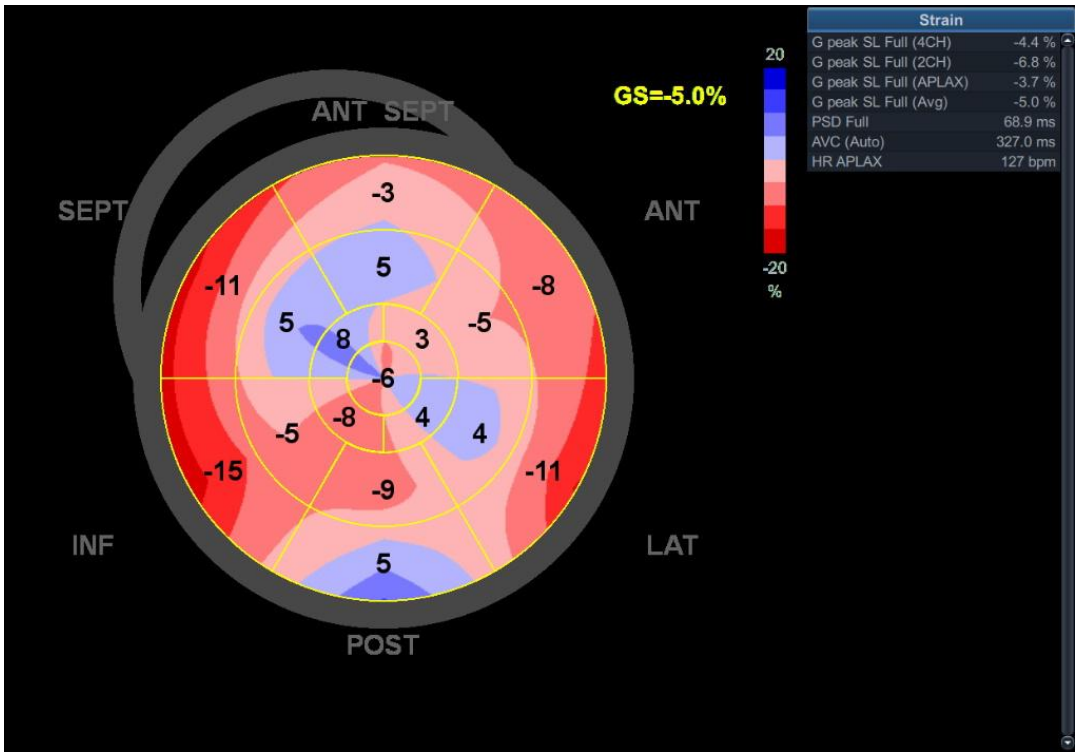

Figure 1. Bull's eye strain map from 15/10/2024, showing a global longitudinal strain (GLS) of –5.0%.

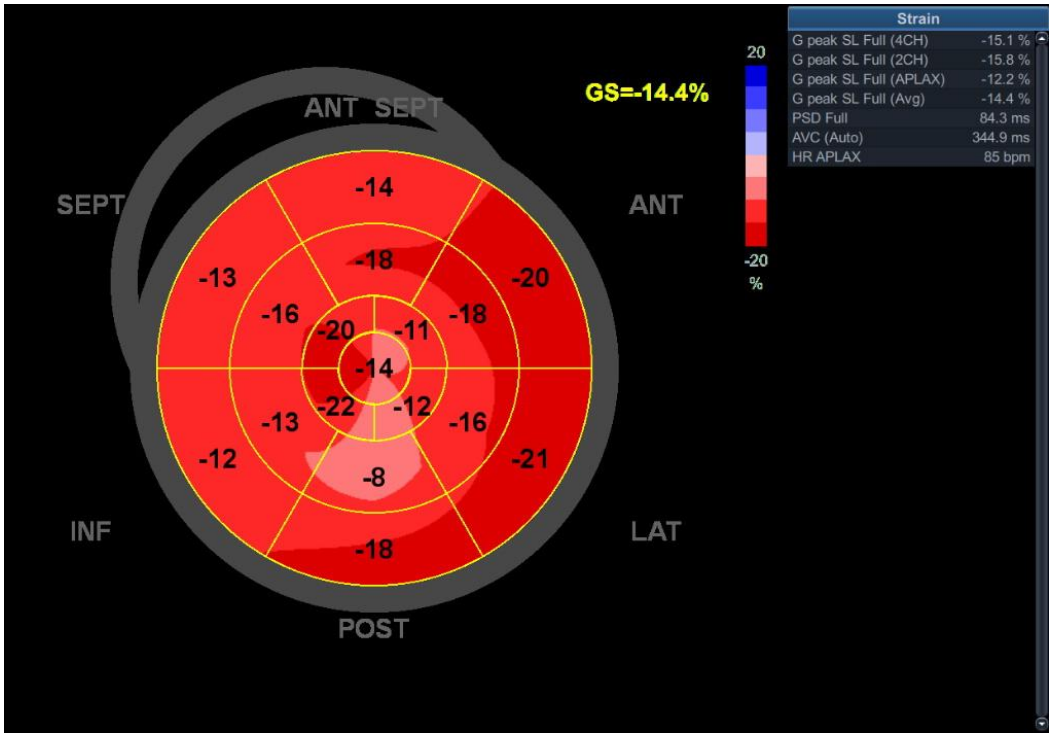

Figure 2. Follow-up bull's eye strain map from 23/10/2024, showing significant functional recovery with improved GLS of –14.4%.

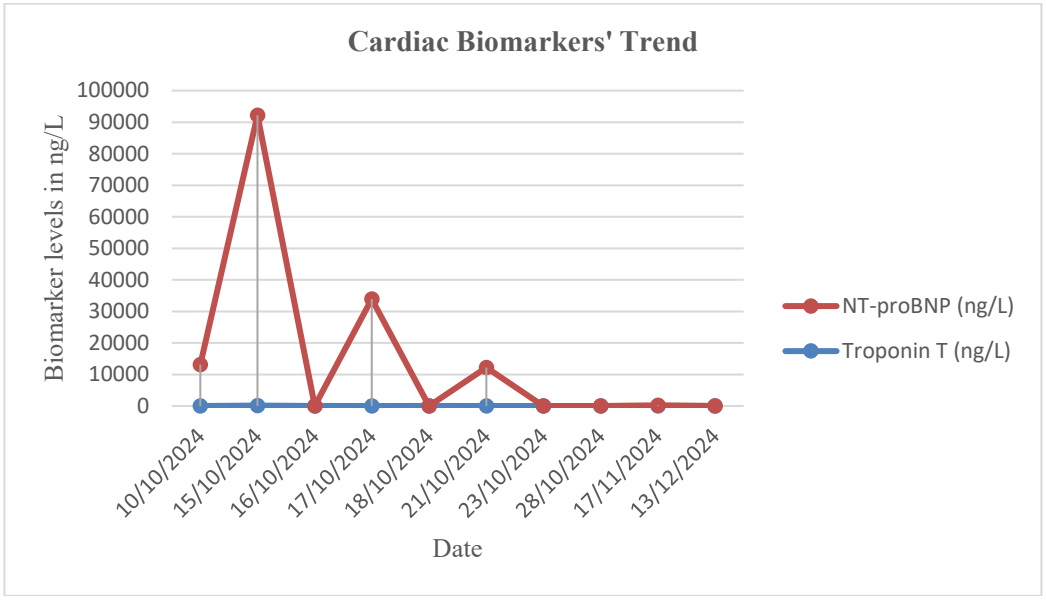

Figure 3.NT-proBNP and Troponin T trends showing a sharp rise during acute bi-ventricular failure on 15/10/2024, followed by steady decline after inotropic and immunomodulatory therapy, reflecting myocardial stress and recovery in HLH.

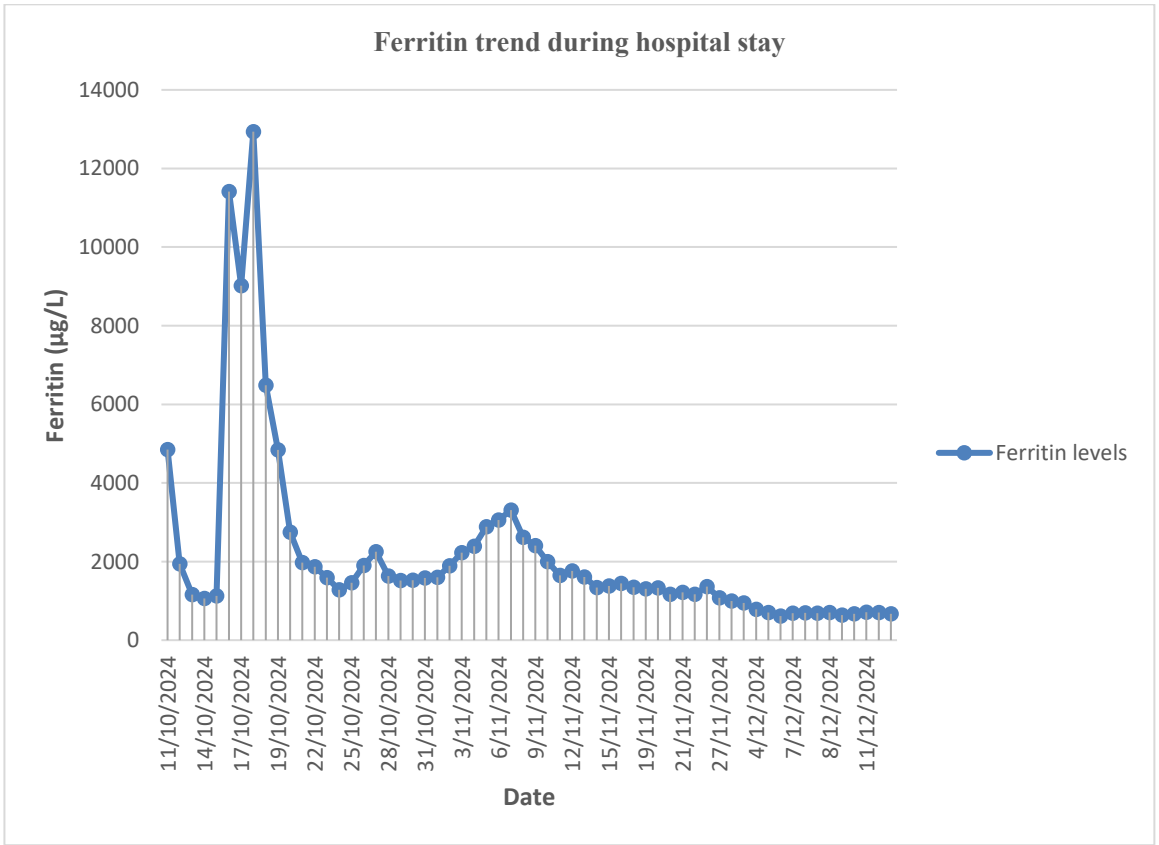

Figure 4.Ferritin trend showing marked hyperferritinaemia at presentation consistent with active HLH, followed by steady decline with immunosuppressive therapy.

Therapeutic Intervention

Initial HLH therapy included anakinra, IV methylprednisolone, and IVIG. Following cardiac decompensation on 15/10/2024, she was treated with levosimendan and glyceryl trinitrate, followed by milrinone for a persistent low-output state. Immunosuppression was escalated with two doses of rituximab and a single dose of etoposide. Anakinra was discontinued on 24/10/2024. Prednisolone was tapered gradually, and mycophenolate mofetil (MMF) was introduced during ward-based recovery.

Follow-up and Outcomes

Cardiac function improved rapidly. By 23/10/2024, LVEF had increased to 57%, and by 28/10/2024 stabilised at 55–60%. NT-proBNP declined to 181 ng/L by 17/11/2024. Residual findings included mild RV dysfunction and persistent pulmonary hypertension. The patient was discharged on MMF, low-dose carvedilol, and tapering corticosteroids. Multidisciplinary outpatient follow-up with rheumatology, cardiology, and rehabilitation was arranged. No major adverse drug reactions occurred.

Discussion

This case illustrates the rare but potentially life-threatening cardiac complications associated with haemophagocyticlymphohistiocytosis (HLH). Although HLH is classically characterised by cytopenias, hyperferritinaemia, organomegaly, and hepatic dysfunction, its cardiovascular manifestations remain under-recognised and are poorly integrated into current diagnostic guidelines [2,5,6]. The acute bi-ventricular failure and torrential tricuspid regurgitation observed in our patient, in the absence of coronary disease, structural valve pathology, or myocardial fibrosis on cardiac MRI, reinforces the understanding that HLH can precipitate a cytokine-mediated, reversible cardiomyopathy [3,10]. The profound improvement in function with immunomodulation and targeted cardiovascular support further supports this mechanism.

The clinical picture in this case overlapped with myocarditis and takotsubo cardiomyopathy—conditions with shared inflammatory pathways—yet lacked hallmark imaging features such as apical ballooning or late gadolinium enhancement. This highlights the diagnostic complexity of inflammatory cardiomyopathies in HLH. Serial echocardiography, particularly global longitudinal strain (GLS) and right-ventricular markers such as TAPSE, combined with biomarker trends (NT-proBNP and troponin), were essential for tracking disease trajectory and guiding dynamic haemodynamic management [1,4].

A key observation is the potential for latent or delayed cardiac collapse in HLH. Despite initial haemodynamic stability, our patient deteriorated rapidly within days of ICU step-down. Normotension can therefore be misleading, and subtle signs such as rising lactate, narrowing pulse pressure, fatigue, or cool peripheries should prompt urgent re-evaluation. This is clinically important, as delayed recognition of cardiac involvement increases the risk of preventable multiorgan failure [2,5].

Management of HLH-associated cardiomyopathy remains non-standardised due to its rarity and heterogeneous clinical presentations. In this case, immunomodulatory therapies—including IL-1 inhibition (anakinra), IVIG, corticosteroids, rituximab, and etoposide—were combined with tailored cardiovascular support using levosimendan, glyceryl trinitrate, and milrinone. The patient's rapid cardiac recovery underscores the value of integrating targeted immunosuppression with carefully selected inotropes. Early haemodynamic deterioration with beta-blockers highlights the need for caution when applying conventional heart-failure regimens during hyperinflammatory states [1].

Relevance to Sub-Saharan Africa

This case holds particular significance for Sub-Saharan Africa, where HLH remains significantly under-diagnosed due to limited awareness, constrained diagnostic infrastructure, and the high prevalence of infections that mimic HLH. Conditions such as severe malaria, disseminated tuberculosis, HIV-associated

inflammatory syndromes, and viral haemorrhagic fevers share overlapping features—cytopenias, fever, hepatosplenomegaly, and coagulopathy—often leading to misdiagnosis.

Cardiac involvement in HLH is even less recognised in the region, largely due to restricted access to advanced echocardiography (including strain analysis), cardiac biomarkers, PET-CT, and cardiac MRI. As a result, HLH-associated cardiomyopathy may be mistakenly attributed to septic cardiomyopathy, HIV-associated myocarditis, or peripartum cardiomyopathy. Such misclassification can delay treatment, even though HLH-related myocardial dysfunction is often reversible with timely intervention.

HLH can cause sudden yet reversible cardiomyopathy, even in patients who appear initially stable. Early detection using echocardiography and biomarkers such as NT-proBNP is critical, while conventional heart-failure therapies—especially beta-blockers—may worsen perfusion during hyperinflammation. Awareness of HLH-associated cardiac involvement is particularly important in Sub-Saharan Africa, where limited diagnostic resources and overlapping infectious presentations can delay recognition and treatment.

Furthermore, autoimmune diseases such as SLE are increasingly diagnosed across Sub-Saharan Africa, and HLH is an important yet frequently overlooked complication. Improving clinician awareness of HLH-associated cardiac manifestations could enhance early recognition, guide appropriate imaging, and reduce mortality.

Conclusion

HLH can cause sudden and severe cardiac decompensation, even in patients who initially appear stable. This case underscores the importance of early echocardiography, biomarker-guided monitoring, and timely escalation of immunosuppression, particularly in individuals with underlying autoimmune disease. These insights are especially relevant in Sub-Saharan Africa, where HLH remains under-recognised and diagnostic resources are often limited; improving clinical awareness and ensuring early ICU involvement may meaningfully enhance patient outcomes.

References

1. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A. 2023 focused update of the 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2023;44(7):761–821.
2. Hayden A, Park S, Giustini D, Lee AY, Chen LY. Hemophagocytic lymphohistiocytosis: a review of clinical characteristics and critical management considerations. J Intensive Care Med. 2017;32(4):223–35.
3. Wohlfarth P, Agis H, Gualdoni GA, Leitner E, Baldinger C, et al. Interleukin-1 blockade with anakinra in patients with hemophagocytic lymphohistiocytosis. Ann Hematol. 2021;100(8):2057–65.
4. Vieillard-Baron A, Price S, Matthay MA, Sanfilippo F, et al. Echocardiography in the ICU: a critical tool for acute hemodynamic management. Intensive Care Med. 2020;46:216–31.
5. Machowicz R, Janka G, Wiktor-Jedrzejczak W. Similar but not the same: differential diagnosis of HLH and sepsis. Crit Rev Oncol Hematol. 2017;114:1–12.
6. Khalid M, Saleem S, Idrees A, et al. Haemophagocyticlymphohistiocytosis (HLH): a rare hyperinflammatory syndrome with cardiac involvement. Clin Med (Lond). 2021;21(4):e402–6.
7. Ullah W, Abdullah HM, Haq S, et al. Takotsubo cardiomyopathy secondary to haemophagocyticlymphohistiocytosis: case report and review of literature. BMJ Case Rep. 2019;12(4):e226599.

8. Chinnici A, Guarino M, Macagno T, et al. Approaching haemophagocyticlymphohistiocytosis: laboratory and diagnostic tools. Front Immunol. 2023;14:1210041.
9. Wu Y, Sun X, Kang K, et al. Hemophagocytic lymphohistiocytosis: current treatment advances, emerging targeted therapies and underlying mechanisms. J Hematol Oncol. 2024;17:106.
10. Bist P, Khan RS, Limaye AM, et al. Cytokine storm and cardiac dysfunction: emerging insights into inflammatory cardiomyopathy. Cardiovasc Res. 2022;118(9):1973–86.

Informed Consent

At the time of admission, the patient provided written informed consent for participation in clinical research under hospital protocols, including permission for the use of anonymised clinical data and biological samples in ethically approved studies such as the UK Biobank, the use of de-identified clinical images, and reports for educational and research purposes.