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FULMINANT IDIOPATHIC HYPEREOSINOPHILIC SYNDROME PRESENTING WITH CARDIAC, NEUROLOGIC AND HAEMATOLOGIC INVOLVEMENT

Nawras Ibrahim, Abboud Batri, Robert Rueda Rivera, Amer Zwein

HCA Houston Healthcare Clear Lake/University of Houston College of Medicine, Houston, USA

Corresponding author's e-mail: nawras.ibrahim@hcahealthcare.com

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ABSTRACT

Introduction: Hypereosinophilic syndrome (HES) is a rare condition characterised by persistent peripheral eosinophilia and associated with multi-organ damage. The most common sources of both morbidity and mortality in HES patients relate to cardiac or neurologic complications, necessitating early recognition and intervention.

Case description: A 44-year-old male was admitted with acute chest pain followed by progressive encephalopathy which worsened, indicating the need for intubation. Laboratory studies were significant for marked hypereosinophilia, massive troponin elevation and profound thrombocytopenia. Brain magnetic resonance imaging (MRI) revealed bilateral watershed infarcts. Despite normal ventricular function and mobility on echocardiography, the onset of peak troponin levels concurrently with eosinophilia, resolving promptly after treatment, led us to consider probable acute eosinophilic myocarditis (EM). Thorough workup excluded secondary (parasitic, autoimmune) clonal causes, thus fulfilling consensus-defined criteria for idiopathic HES. High-dose intravenous corticosteroids (methylprednisolone 1 g/day × 3 days) resulted in rapid, synchronous normalisation of eosinophilia, troponin levels and platelet counts, confirming a steroid-responsive, eosinophil-driven pathology. The patient was left with persistent severe neurologic deficits.

Conclusion: This case highlights the destructive potential of acute eosinophil degranulation across multiple organs. The rapid improvement with corticosteroids underscores the importance of early recognition and immediate immunosuppressive therapy to limit organ damage. Clinicians should maintain high suspicion for HES in adults with unexplained eosinophilia and multi-organ involvement.

KEYWORDS

Hypereosinophilic syndrome, eosinophilic myocarditis, watershed stroke, thrombocytopenia, corticosteroids

LEARNING POINTS

- Maintain suspicion for HES in unexplained eosinophilia with multi-organ dysfunction.
- Eosinophilic myocarditis may present with high troponin despite normal echocardiogram.
- Bilateral watershed infarcts reflect microvascular hypoperfusion due to eosinophilic endothelial injury.
- Thrombocytopenia often resolves rapidly with corticosteroids.
- Early immunosuppression prevents irreversible organ damage.

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INTRODUCTION

Hypereosinophilic syndrome (HES) – a heterogeneous, rare set of disorders – is defined by the presence of peripheral blood eosinophilia exceeding 1,500 cells/µl with eosinophil deposition, degranulation and consequent tissue damage after the exclusion of secondary (or reactive), or clonal causes[1]. Essentially, HES is broadly classified into three major subtypes: myeloproliferative, lymphocytic and idiopathic[1]. Among these, idiopathic HES, which comprises less than 20% of all HES, is diagnosed if an exhaustive investigation does not show a molecular or phenotypically distinct aetiology[2]. The main cause of HES-associated morbidity and mortality is cardiac or neurologic complications[3,4].

Myocardial damage by eosinophil degranulation can potentially progress through necrotic, thrombotic and fibrotic stages, leading to life-threatening outcomes such as heart failure, mural thrombi or restrictive cardiomyopathy[3]. Additionally, for neurologic consequences such as stroke, embolism or a hyperthrombotic state, eosinophil activation is mainly responsible[4]. Thrombocytopenia can occur consequently upon bone marrow suppression by eosinophilic infiltration, consumption or peripheral destruction[5].

The diagnosis of HES requires persistent eosinophilia, organ involvement and the systematic exclusion of both secondary and clonal aetiologies[6]. Early recognition and aggressive management, particularly cardiac and neurologic manifestations, are crucial for favourable outcomes[6]. Corticosteroids are the first-line therapy, especially in acute organ-threatening presentations, and should be initiated promptly – often before the complete diagnostic workup is finalised[6]. Effective management necessitates a coordinated multidisciplinary approach due to the multisystem nature of the disease.

We present a severe, multi-organ case of idiopathic HES manifesting as probable eosinophilic myocarditis (EM), bilateral watershed strokes and acute thrombocytopenia, emphasising the importance of high clinical suspicion and rapid intervention.

CASE DESCRIPTION

A 44-year-old man with a history of chronic amphetamine use disorder was admitted for acute onset of substernal chest pain radiating to the left arm. The patient denied the presence of asthma, skin rash, disease or previous episodes of neurologic disorders. Initially on admission, the patient's vitals remained highly unstable, with blood pressure fluctuating between 90/60 mmHg and 183/116 mmHg, and heart rate between 80 and 110 bpm. The patient remained afebrile. The chest pain gradually resolved in five days. However, the level of neurologic functioning progressively deteriorated from fully awake (Glasgow coma score of 15) to severe encephalopathic state (Glasgow coma score of 4) within a week, prompting urgent intubation. The admission ECG showed ST-segment depression in leads V3–V6 *(Fig. 1)*.

Laboratory findings showed a critical triad (Table 1):

1. *Hypereosinophilia:* total leukocyte count ranged from 9.5 to 24 $\times 10^9$/l, with absolute eosinophils peaking at 6,700 cells/µl, exceeding the diagnostic threshold for hypereosinophilic syndrome (HES)[1,6].
2. *Myocardial injury:* The troponin T levels rose from 2,533

Parameter	Result	Comment
White blood cells ($\times 10^3$/µl)	9.5–24	22–30% eosinophils; AEC 2,500–6,700/µl
Platelets ($\times 10^9$/l)	112 → 31	Nadir; normalised after steroids
Haemoglobin (g/dl)	12.5	Mildly low
Troponin (ng/l)	2,533 → 12,952 → 89	Peak day 7; rapid fall post-steroids
BNP (pg/ml)	506	Mildly elevated
Lactate dehydrogenase (U/l)	1,058 → 713	Fell after steroids
ANA/ANCA	Negative	Supports against systemic vasculitis
Immunoglobulin E (IU/ml)	133	Not elevated
Vitamin B12 (pg/ml)	508	Unremarkable for clonal mast cell disease
Tryptase (ng/ml)	5.5	Unremarkable for clonal mast cell disease
Peripheral smear	Eosinophil predominance	No blasts or dysplasia
Infectious testing	Stool ova and parasite, strongyloides immunoglobulin G negative	No parasitic cause identified

Table 1. Laboratory findings.

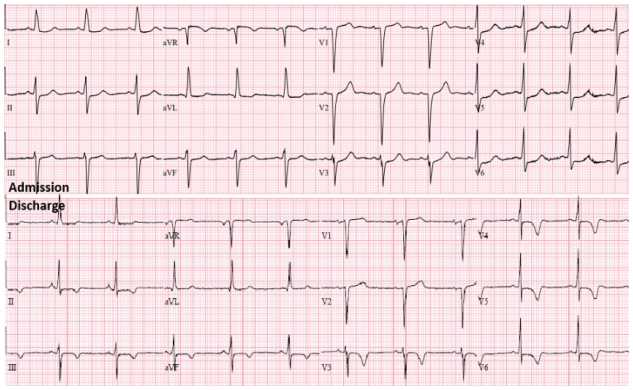


Figure 1. ECG at admission and transfer to long-term acute care; diffuse T-wave inversion noted during recovery; no pathological Q waves.

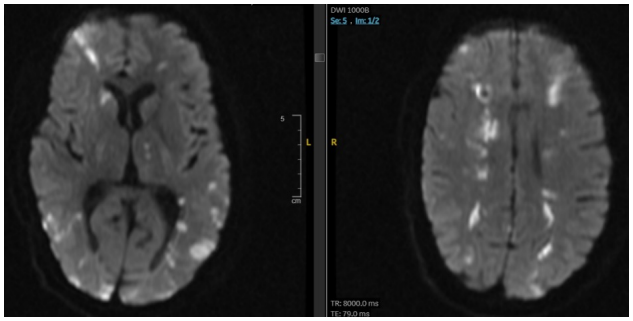


Figure 2. Brain MRI (DWI/ADC) showing bilateral watershed infarcts.

ng/l on admission to 12,952 ng/l on hospital day seven, which indicated significant acute myocardial necrosis; the B-type natriuretic peptide (BNP) was mildly elevated (506 pg/ml).

3. *Haematologic dysfunction:* the platelet count dropped to a nadir of 31 ×10^9/l, indicating severe thrombocytopenia.

Under cardiac imaging, a transthoracic echocardiogram showed preserved left ventricular systolic function (left ventricular ejection fraction 55–60%) without regional wall motion abnormalities, valvular disease or mural thrombi. This was compatible with EM in its early stages[3]. However, a coronary angiogram could not be performed due to patient's refusal, making it difficult to exclude obstructive coronary artery disease.

Under neurologic imaging, the head computed tomography (CT) scan and brain magnetic resonance imaging (MRI) revealed acute/subacute ischaemic infarctions in both watershed regions involving the cerebral hemispheres, thalami, basal ganglia and cerebellum *(Fig. 2)*. A magnetic resonance angiogram did not show large-vessel occlusion, which indicated that the pathophysiological mechanism was microvascular hypoperfusion.

Secondary (reactive) causes were excluded – stool ova, parasites and strongyloides immunoglobulin G were negative. Autoimmune testing (antinuclear antibody – ANA and antineutrophil cytoplasmic antibodies – ANCA) was negative. Features of EGPA were absent (no asthma or sinusitis; ANCA-negative)[6].

Clonal (neoplastic) causes were excluded: serum tryptase and vitamin B12 levels were normal, and peripheral smear revealed no blasts, dysplasia or left shift. Molecular testing for FIP1L1–PDGFRA and other rearrangements was deferred, but the dramatic steroid response made a clonal variant less likely, supporting idiopathic HES as the working diagnosis[6].

Thrombocytopenia aetiologies were excluded: heparin-induced thrombocytopenia (HIT) antibodies were negative, ADAMTS13 activity was normal and no schistocytes were present, excluding HIT and thrombotic thrombocytopenic purpura.

The patient met NCCN/WHO/ICC criteria for idiopathic hypereosinophilic syndrome, with multi-organ involvement (probable EM and secondary watershed infarctions) and exclusion of secondary and clonal causes[6].

Aspirin was started empirically, along with a course of heparin, which was subsequently stopped upon recognition of thrombocytopenia. High-dose IV methylprednisolone (1 g/day for three consecutive days) was started on hospital day seven. The intervention led to quick resolution of eosinophilia, troponin T levels and platelet counts *(Fig. 3)*, making it highly suggestive of an eosinophil-mediated acute disease that was responsive to steroids.

There was a temporary discontinuation of corticosteroid medication for a period of two days during transfer from the coronary care unit to the medical intensive care unit, while completing the diagnostic workup to exclude secondary or clonal causes of eosinophilia. Methylprednisolone was continued at 1 mg/kg/day for seven days, followed by a gradual prednisone taper via a gastrostomy tube.

However, despite haematologic and cardiac recovery, the patient required supportive care, including a collar tracheostomy with minimal mechanical ventilation and a gastrostomy tube. He was subsequently transferred to a long-term acute care facility due to persistent severe neurologic deficits. This scenario shows that established

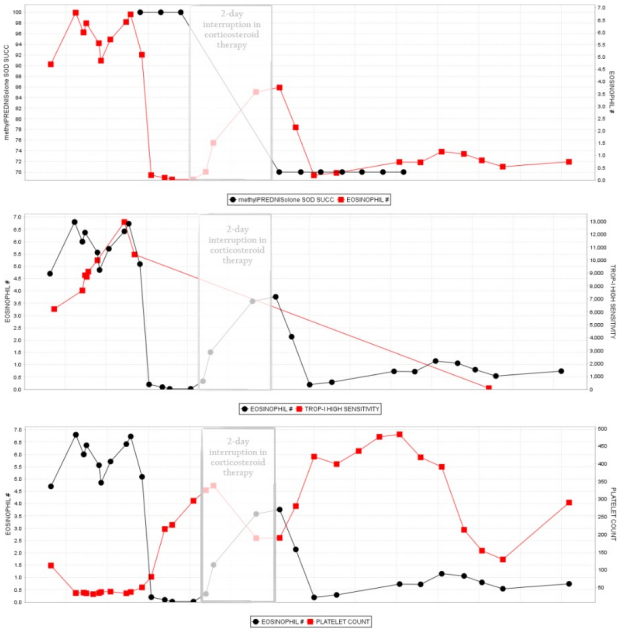


Figure 3. Timeline of eosinophil count, troponin and platelet trend relative to steroid therapy.

ischaemic damage can be non-reversible despite early treatment[5].

Molecular testing for clonal HES variants (PDGFRA, PDGFRB, FGFR1, FIP1L1–PDGFRA) was deferred during acute hospitalisation, as the steroid response made clonal aetiology less likely, supporting the working diagnosis of idiopathic HES[6].

DISCUSSION

Idiopathic hypereosinophilic syndrome is a unique immunologic condition that is characterised by sustained eosinophilia and multi-organ damage in the absence of identifiable secondary or clonal causes. Eosinophil-mediated injury is driven by cytotoxic granule proteins (major basic protein, eosinophil cationic protein and eosinophil peroxidase) which promote endothelial dysfunction, microvascular thrombosis and tissue necrosis. These mechanisms underlie the cardiac, neurologic and haematologic manifestations observed in this case.

Although secondary and clonal markers were negative, the patient demonstrated a hallmark steroid-responsive course; definitive exclusion of all clonal variants requires molecular testing, which was deferred[6].

EM is a potentially fatal complication of HES[3]. It typically progresses from an acute necrotic phase – driven by eosinophil degranulation and direct myocyte injury – to a thrombotic phase, which can be complicated by mural thrombi and embolic events, and finally to a fibrotic phase, resulting in endomyocardial fibrosis and restrictive cardiomyopathy[3].

In this case, troponin T peaked at 12,952 ng/l coinciding with peak eosinophilia, while echocardiography remained normal; the rapid decline of troponin following corticosteroid therapy supports early-stage EM. Endomyocardial biopsy, the gold standard for diagnosis, was deferred due to critical illness, and cardiac MRI, the preferred non-invasive modality, was not available. Therefore, the diagnosis of probable EM relies on clinical evidence of myocardial injury concurrent with peak eosinophilia and its rapid steroid-responsive resolution[3].

The patient's bilateral watershed infarcts likely reflect eosinophil-mediated endothelial injury, microvascular thrombosis and haemodynamic instability[4]. An MRI revealed acute and subacute infarcts in bilateral watershed territories, while magnetic resonance angiography excluded large-vessel occlusion, supporting microvascular/hypoperfusion aetiology. Despite rapid normalisation of eosinophils neurologic deficits persisted, highlighting that ischaemic injury may be irreversible once established[4].

Although amphetamines are not recognised causes of HES, their effects on endothelial function, vasospasm and cardiovascular stress may have acted as a 'second hit', exacerbating microvascular hypoperfusion and contributing to the watershed infarcts in a patient predisposed to eosinophilic activation[7].

Severe thrombocytopenia tracked closely with eosinophilia and resolved promptly after corticosteroid therapy *(Fig. 3)*, suggesting reactive marrow suppression or consumption rather than primary immune-mediated destruction[5]. Laboratory testing and peripheral smear excluded HIT and thrombotic thrombocytopenic purpura.

High-dose corticosteroids remain the cornerstone of therapy for acute, organ-threatening HES, often producing rapid clinical and laboratory improvement[6]. While dramatic steroid responsiveness reduces the likelihood of a clonal variant, molecular testing remains important for prognosis and guiding future therapy, especially if the patient becomes steroid-dependent or refractory.

For steroid-refractory or dependent disease, options include targeted biologics (anti–IL-5 agents: mepolizumab, reslizumab; anti–IL-5R: benralizumab) and cytoreductive agents or tyrosine kinase inhibitors in PDGFRA-positive disease[6]. Given its multi-organ nature, multidisciplinary management is essential[6].

CONCLUSION

This case represents a potentially life-threatening multi-organ presentation of idiopathic HES involving EM, bilateral watershed strokes and secondary thrombocytopenia. The rapid diagnostic workup and the prompt start of high-dose corticosteroids reversed acute eosinophil-mediated injury to the heart and bone marrow. However, persistent severe neurologic deficits underscore the urgency of timely therapeutic measures preventing fixed neuronal damage. HES should remain a strong consideration in the clinical differential diagnosis of adults with unexplained hypereosinophilia and acute multisystem dysfunction.

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