

CASE REPORT

Adult-Onset Still's Disease with Macrophage Activation Syndrome Mimicking Septic Shock During *Clostridioides difficile* Colitis: A Case Report

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Abstract

Background: Adult-onset Still's disease (AOSD) is a rare systemic autoinflammatory disorder characterized by fever, arthritis, and hyperferritinemia. It may be complicated by macrophage activation syndrome (MAS), a life-threatening hyperinflammatory state that can mimic severe sepsis, especially in the presence of concurrent infection. Early recognition is critical but often challenging.

Case Presentation:

We report a 22-year-old previously healthy female who presented with a five-month history of quotidian fever, significant weight loss, and inflammatory polyarthritis. Her clinical course was complicated by septic shock in the setting of confirmed *C. difficile* colitis. Extensive workup excluded infectious, malignant, and autoimmune etiologies. Laboratory findings revealed extreme hyperferritinemia (peaking >33,511 ng/mL), progressive cytopenias, hypertriglyceridemia, hypofibrinogenemia, and elevated soluble IL-2 receptor levels, consistent with MAS/secondary hemophagocytic lymphohistiocytosis. The diagnosis of AOSD was established using Yamaguchi criteria. Despite initial management for sepsis, persistent fevers and worsening laboratory parameters prompted escalation to pulse-dose corticosteroids, anakinra, and intravenous immunoglobulin. The patient demonstrated significant clinical and biochemical improvement, was transitioned to tocilizumab for maintenance therapy, and was discharged in stable condition.

Conclusion:

This case highlights the diagnostic complexity of AOSD complicated by MAS in the setting of concurrent infection. Extreme hyperferritinemia, evolving cytopenias, and lack of response to antimicrobial therapy should prompt consideration of MAS. Early recognition and timely initiation of immunomodulatory therapy are crucial for improving outcomes in this potentially fatal condition.

Keywords: Adult-Onset Still's Disease; Macrophage Activation Syndrome; Hemophagocytic Lymphohistiocytosis;

Clostridioides difficile Colitis; Anakinra; Tocilizumab; Cytokine Storm; Fever of Unknown Origin.

Introduction

Adult-onset Still's disease (AOSD) is an uncommon systemic autoinflammatory disorder with an estimated incidence of 0.1–0.4 per 100,000 persons per year, with a predilection for young adults and particularly women (1,2). It is classically characterized by a triad of quotidian spiking fever, polyarthritis affecting wrists, elbows, and other joints, and a transient salmon-colored rash, frequently accompanied by sore throat, lymphadenopathy, hepatosplenomegaly, and striking elevations of acute-phase reactants and serum ferritin (1–3). Despite the availability of classification criteria, AOSD remains a major diagnostic challenge because its manifestations overlap extensively with severe infections, hematologic malignancies, and other systemic inflammatory diseases, often leading to delays in diagnosis and initiation of appropriate immunomodulatory therapy (1,4,5).

A subset of patients with AOSD develop macrophage activation syndrome (MAS), a form of secondary hemophagocytic lymphohistiocytosis (HLH) that represents one of the most devastating complications of the disease (7–9). The clinical and laboratory picture of MAS frequently mimics severe sepsis, particularly when patients present with shock, organ dysfunction, and markedly elevated inflammatory markers (7–9). This overlap is especially treacherous when a true infection is concurrently documented, as prioritizing sepsis management may dangerously delay the high-dose corticosteroids and cytokine-targeted biologic agents that are essential for reversing the hyperinflammatory cascade (8,9). In this report, we describe a previously healthy young woman who presented with months-long fever of unknown origin, extreme hyperferritinemia, septic shock in the setting of documented *C. difficile* colitis, and progressive cytopenias, and was eventually diagnosed with AOSD complicated by MAS/secondary HLH. The case exemplifies the diagnostic pitfalls encountered when life-threatening hyperinflammation coexists with severe infection, and illustrates how timely escalation to high-dose glucocorticoids, IL-1 blockade, and adjunctive immunomodulation can lead to a favorable outcome.

Case Presentation

History of Present Illness

A 22-year-old female with no significant past medical or surgical history presented to the outpatient department for follow-up 10 days post-discharge from a clinical teaching unit (CTU) where she had been evaluated for fever of unknown origin. During the visit, she was found to be febrile and hypotensive, prompting rapid referral to the emergency department.

Her illness course began 5 months prior with constitutional symptoms including daily quotidian fever peaking mainly at night and in the late afternoon, significant unintentional weight loss from 52 kg to 39 kg (13 kg loss), night sweats, poor appetite, and profound malaise. She had been evaluated at multiple hospitals, the last of which was Aseer Hospital where she was admitted for two weeks and discharged against medical advice without an established diagnosis. Her current presenta-

tion was complicated by a 3-day history of watery, foul-smelling, non-bloody diarrhea occurring more than three times per day, and generalized abdominal pain. Review of systems showed persistent nausea and vomiting with febrile spikes, and bilateral inflammatory pain in the wrists and elbows. She mentioned a distant contact history with a tuberculosis-treated grandfather. There was no history of recent skin rash, travel, exposure to fresh or saltwater, contact with house pets or cattle, or substance use. Family history was unremarkable for autoimmunity or malignancy.

Summary of Previous Admission

The patient had been admitted under internal medicine on 23 July 2025 for workup of B symptoms with an initial impression of malignancy. Computed tomography (CT) revealed multiple enlarged supra- and infra-diaphragmatic lymph nodes and mild splenomegaly (13.5 cm). Positron emission tomography (PET) scan demonstrated consistent findings along with diffuse bone marrow uptake. A right inguinal lymph node biopsy on 27 July 2025 showed reactive lymph node with dermatopathic changes, no granulomata, and was negative for malignancy. A repeat axillary lymph node biopsy was taken on 3 August 2025 with a plan to follow up in clinic. During this admission, ferritin was 12,224.0 ng/mL, LDH was elevated (880 U/L initially, declining to 514 U/L on follow-up), and AST trended upward from 136 to a peak of 629 U/L. Platelet count ranged from 318,000 to 547,000/cmm and hemoglobin ranged from 78 to 95 g/L.

An extensive infectious workup during this admission was negative, including blood cultures, urine cultures, tissue culture, hepatitis panel, HIV, syphilis, CMV/EBV serologies, malaria, QuantiFERON-TB Gold/TB PCR, Brucella, Q fever, Parvovirus, Dengue, and Toxoplasmosis. Rheumatology workup was negative for ANA, anti-dsDNA, RF, anti-CCP, ANCA, and cryoglobulins; complement levels were within normal limits. Rheumatology's initial impression favored lymphoproliferative disorder or malignancy over connective tissue disease. The patient was discharged while still febrile and tachycardic to continue follow-up as outpatient.

Physical Examination

On examination, the patient appeared acutely ill (GCS 15/15), lethargic, and cachectic with a current weight of 39 kg, with signs of severe dehydration including dry mucous membranes and delayed capillary refill of more than two seconds. She was hemodynamically unstable with hypotension (SBP 73–93 mmHg, DBP 42–55 mmHg), tachycardia (heart rate 131–141 bpm), and fever (38.4–38.9°C), requiring intensive care admission for inotropic support.

Head and neck examination revealed no palpable lymphadenopathy. Musculoskeletal assessment revealed active synovitis of the bilateral wrists and metacarpophalangeal (MCP) joints, characterized by palpable swelling and tenderness. Skin examination was significant for bilateral hyperpigmentation over the upper extremities and left thigh; the classic evanescent salmon-colored rash was absent. Abdominal examination demonstrated a soft lax abdomen with diffuse generalized tenderness and no evidence of organomegaly on palpation. Cardiovascular examination revealed normal S1 and S2 with no murmurs. Respirat-

ory examination showed equal bilateral air entry with no added sounds. Neurological examination was unremarkable with normal tone, power 5/5 bilaterally, intact sensation, and normal reflexes. There was no lower limb edema or signs of deep vein thrombosis.

Key Investigations

The initial hematological laboratory investigations for the current presentation were remarkable for severe microcytic hypochromic anemia demonstrated by 8.3 g/dL hemoglobin, mean corpuscular volume (MCV) of 68.2 fL, and a mean corpuscular hemoglobin (MCH) of 22.6 pg. Additionally, there was marked leukocytosis ($20.9 \times 10^9/L$) with neutrophilia measured as $18.81 \times 10^9/L$ and lymphopenia at $0.84 \times 10^9/L$ (Table 1a). Inflammatory markers showed extreme hyperferritinemia (17,347.7 ng/mL), an elevated C-reactive protein (CRP) of 104.80 mg/L, erythrocyte sedimentation rate (ESR) of 64 mm/hr, and procalcitonin (PCT) of 0.78 ng/mL (Table 1b).

Table 1a. Hematology Results

Parameter	Patient Value	Reference Range
Hemoglobin	8.3 g/dL	12–16 g/dL
Hematocrit	24.3%	36–46%
RBC	$3.56 \times 10^6/mm^3$	$3.5–6.0 \times 10^6/mm^3$
MCV	68.2 fL	80–100 fL
MCH	22.6 pg	27–32 pg
MCHC	33.1 g/dL	30–35 g/dL
RDW	20.6%	11.5–14.5%
Total Leukocytic Count	20,900/cmm	4,000–11,000/cmm
Neutrophils	18,810 cells/mm ³	2,000–7,500 cells/mm ³
Lymphocytes	840 cells/mm ³	1,500–4,500 cells/mm ³
Monocytes	630 cells/mm ³	200–800 cells/mm ³
Eosinophils	210 cells/mm ³	40–400 cells/mm ³
Platelets	495,000/cmm	150,000–450,000/cmm

Table 1b. Biochemical and Inflammatory Markers

Parameter	Patient Value	Reference Range
Ferritin	17,347.7 ng/mL	20–250 ng/mL
CRP	104.80 mg/L	<5.0 mg/L
ESR	64 mm/hr	0–20 mm/hr
PCT	0.78 ng/mL	<0.5 ng/mL
Iron	1.70 μ mol/L	11–30 μ mol/L
TIBC	18.6 μ mol/L	45–81 μ mol/L
LDH	880 U/L	125–220 U/L
Total Bilirubin	5.2 μ mol/L	<17 μ mol/L
AST	46 U/L	<40 U/L
ALT	14 U/L	<41 U/L

Parameter	Patient Value	Reference Range
ALP	119 U/L	40–130 U/L
Albumin	31 g/L	35–50 g/L
Total Protein	65 g/L	60–80 g/L
INR	1.13	0.8–1.2
PT	13.00 s	11–13.5 s
PTT	27.90 s	25–35 s

The arterial blood gas revealed respiratory alkalosis with pH 7.49, PCO₂ 29 mmHg, and relatively normal bicarbonate (HCO₃) of 22.1 mmol/L. Oxygenation markers showed a PaO₂ of 61 mmHg, oxygen saturation of 91.3%, and O₂Hb of 88.4%. The renal and electrolyte profile showed mild electrolyte imbalances, specifically hyponatremia and borderline hypokalemia (Table 2).

Table 2. Kidney Function and Electrolyte Profile

Parameter	Patient Value	Reference Range
Creatinine	44 μ mol/L	60–110 μ mol/L
BUN	2.7 mmol/L	2.5–7.1 mmol/L
eGFR	166 mL/min	>90 mL/min
Sodium	133 mmol/L	135–145 mmol/L
Potassium	3.5 mmol/L	3.5–5.2 mmol/L
Chloride	103 mmol/L	98–107 mmol/L
Calcium	2.09 mmol/L	2.12–2.62 mmol/L
Magnesium	0.73 mmol/L	0.85–1.10 mmol/L
AGAP	16 mEq/L	6–12 mEq/L
Uric Acid	269 μ mol/L	155–357 μ mol/L
Phosphorus	1.03 mmol/L	0.81–1.45 mmol/L

A comprehensive multiplex PCR stool panel tested positive for *C. difficile* toxin A/B, Enteroaggregative *E. coli* (EAEC), and Enteropathogenic *E. coli* (EPEC), while ruling out a wide array of other gastrointestinal pathogens including *Campylobacter*, *Salmonella*, *Shigella*, *Vibrio*, *Cryptosporidium*, *Giardia*, and numerous enteric viruses (Norovirus, Rotavirus, Adenovirus, Astrovirus, Sapovirus). A comprehensive respiratory panel was completely negative for all tested viral and bacterial targets, including SARS-CoV-2, Influenza A/B, RSV, Parainfluenza 1–4, *Mycoplasma pneumoniae*, *Bordetella pertussis*, *Chlamydo-phila pneumoniae*, and MERS-CoV. All blood cultures drawn as part of the septic screen remained persistently negative throughout the hospital course.

Immunological workup, including antinuclear antibody (ANA), anti-dsDNA, rheumatoid factor (RF), anti-CCP, anti-SS-A, anti-SS-B, MPO-ANCA, PR3-ANCA, and cryoglobulins, was negative. Notably, the repeated anti-dsDNA (ELISA) returned a value of 51.56, which was below the positive threshold but in the borderline range, compared with a clearly negative result on the initial admission. Complement C3 was within normal limits (0.735 g/L); however, C4 was low at 0.06 g/L (reference 0.10–0.40 g/L), which may reflect complement consumption in the setting of systemic inflammation. Despite the borderline anti-

dsDNA value and the low C4, systemic lupus erythematosus (SLE) was not pursued further because the patient did not meet any other 2019 EULAR/ACR SLE classification criteria: there was no mucocutaneous, renal, serosal, hematologic (autoimmune), or neuropsychiatric involvement attributable to SLE; ANA was negative; and the clinical phenotype was dominated by quotidian fever, polyarthritis of the wrists and MCPs, extreme hyperferritinemia, and progression to MAS, which is far more consistent with AOSD. The isolated low C4 was interpreted as complement consumption in the context of systemic hyperinflammation rather than evidence of an underlying connective tissue disease. These findings further supported the clinical diagnosis by excluding connective tissue diseases.

Imaging

A portable anteroposterior thoracic radiograph revealed diffuse, bilateral interstitial opacities and prominent reticular markings throughout both lung fields, without obvious large focal consolidations, large pleural effusions, or pneumothoraces. The cardiomedastinal silhouette appeared generally within normal limits. Multiple external ECG leads and wires were seen overlying the patient's chest. ECG demonstrated sinus tachycardia. CT abdomen was unremarkable for ileus or megacolon.

Hospital Course and Management

The patient was admitted to the ICU for inotropic support and started on empirical broad-spectrum antibiotics, alongside oral vancomycin and IV metronidazole for fulminant *C. difficile* colitis. CT abdomen was unremarkable for ileus or megacolon. She was shifted back to the floor after two days of hemodynamic stabilization. Hematology was consulted and the patient was scheduled for bone marrow biopsy. She continued to spike high-grade fevers throughout.

Gastroenterology was consulted for persistent watery diarrhea and hyperpigmentation; upper endoscopy (EGD) was performed to rule out Whipple's disease, with unremarkable scope findings and biopsy. The oral vancomycin course was extended to 14 days for ongoing diarrhea. During this period, the patient developed features of preseptal cellulitis versus dacryoadenitis, confirmed by orbital CT and ophthalmology assessment.

She subsequently became hypotensive again, requiring a second ICU admission with an impression of sepsis/hypovolemia. She was started on inotropic support and empirical meropenem, to which she responded well. Relevant investigations during this period showed CRP 105.50 mg/L (rising from 104.80), PCT 0.17 (declining from 0.78 on initial presentation), ferritin declining to 8,692.8 ng/mL, hemoglobin 89 g/L, WBC $19.20 \times$

$10^9/L$, platelets 549,000/cmm, AST 51 U/L, ALT 8 U/L, ALP 224 U/L, albumin 28 g/L, and INR 1.19.

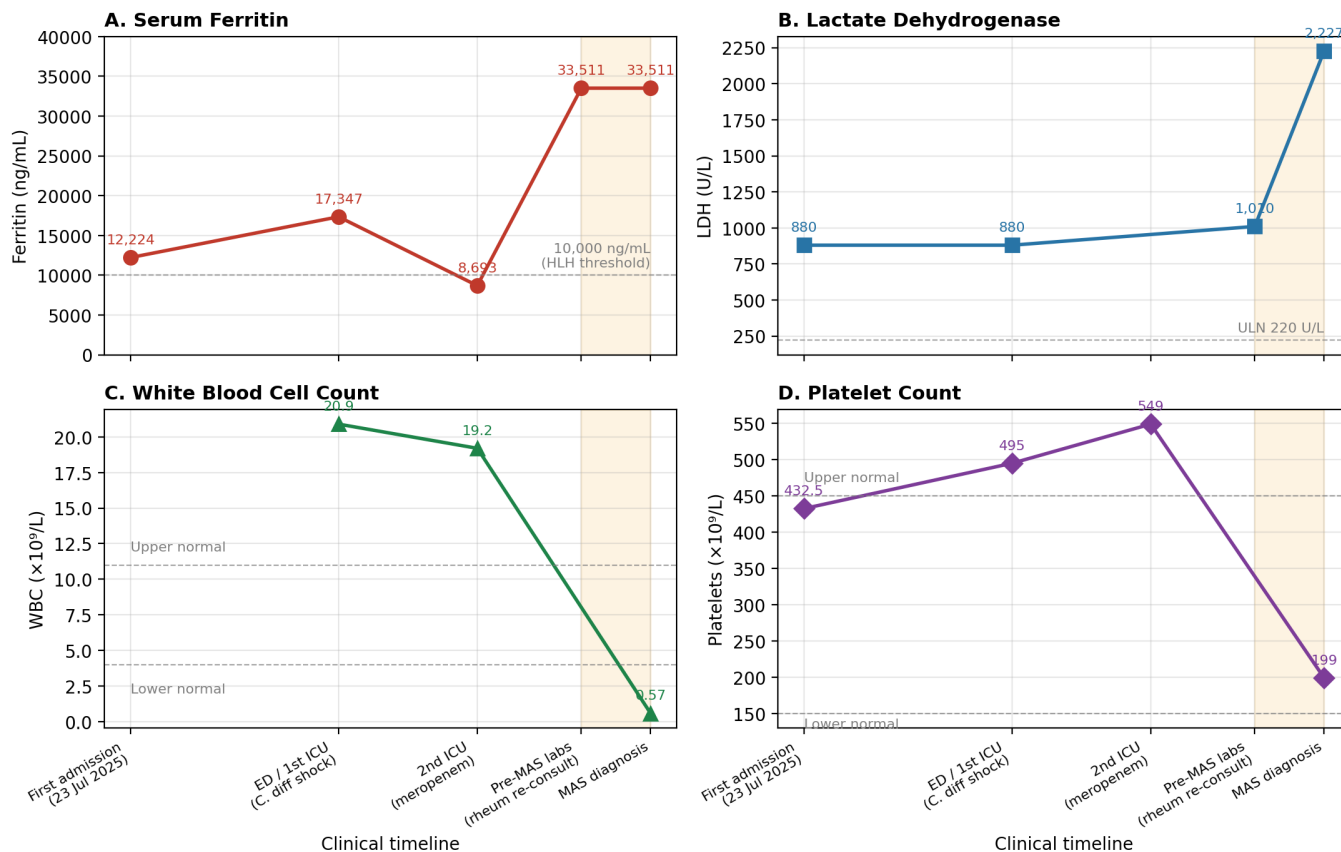
Bone marrow biopsy from the unilateral posterior iliac crest (aspirate smears, clot section, trephine biopsy, and peripheral blood) returned the following: normocellular bone marrow with increased granulopoiesis, megakaryopoiesis, and normal erythropoiesis; no immunomorphological evidence of hematology-lymphoid malignancy in the provided sample. Hemophagocytosis was not confirmed on the reviewed bone marrow specimen.

After stabilization and discharge from the ICU on meropenem, oral vancomycin, and resumed IV metronidazole, the patient continued to spike high-grade fevers with persistently negative cultures. Rheumatology was contacted again; their impression initially favored a lymphoproliferative disorder versus infection, as ferritin was declining without immunosuppressive therapy. However, repeated laboratory workup was notable for: ferritin $>33,511$ ng/mL, LDH 1,010 U/L, triglycerides 5.88 mmol/L, fibrinogen 1.44 g/L (low), CRP 50.60 mg/L (rising to 102.90), PCT 0.48 (rising to 3.25), ESR 33 mm/hr, AST 107 U/L, INR 1.22, and PT 13.50 seconds.

She was subsequently transferred to rheumatology's care as a case of Still's disease and was started on methylprednisolone 100 mg BID. Repeated labs two days afterward showed dramatic worsening with pancytopenia: WBC crashed to $0.57 \times 10^9/L$ (neutrophils $0.23 \times 10^9/L$, lymphocytes $0.24 \times 10^9/L$), hemoglobin 78 g/L, platelets 199,000/cmm, ferritin $>33,511$ ng/mL, LDH surging to 2,227 U/L, AST 318 U/L (rising from 181 U/L), ALT 126 U/L (improving to 17), triglycerides 5.66 mmol/L, fibrinogen 1.18 g/L, and soluble IL-2 receptor (sCD25) 2,202 U/mL. These findings were consistent with the progression to macrophage activation syndrome (MAS)/secondary HLH. The evolution of ferritin, LDH, WBC, and platelet count across the clinical course is summarized in Figure 1.

Hematology consultation concluded that AOSD was progressing into MAS/HLH. The patient was escalated to pulse-dose methylprednisolone, anakinra, and 4 doses of intravenous immunoglobulin (IVIG). The diagnosis of AOSD was established by fulfillment of the Yamaguchi criteria (11): three major criteria — quotidian fever $>39^\circ\text{C}$ for more than one week, arthralgia/arthritis lasting more than two weeks (bilateral wrist and MCP synovitis), and leukocytosis $>10,000/\text{mm}^3$ with $>80\%$ granulocytes (WBC 20,900 with 90% neutrophils) — and two minor criteria — lymphadenopathy and/or splenomegaly (radiologically confirmed) and a negative ANA and RF. The classical evanescent rash, which constitutes the fourth major criterion, was absent.

Figure 1. Trajectory of key laboratory parameters during the clinical course



Shaded band indicates the MAS recognition window. Subsequent clinical and biochemical improvement on pulse steroids, anakinra, IVIG, and tocilizumab is described in the text; individual post-treatment laboratory values are not plotted.

Figure 1. Trajectory of key laboratory parameters during the clinical course. (A) Serum ferritin, (B) lactate dehydrogenase (LDH), (C) white blood cell count, and (D) platelet count at successive clinical milestones, plotted using values reported in the case narrative. The shaded band indicates the recognition window for MAS. Subsequent improvement on pulse-dose corticosteroids, anakinra, IVIG, and tocilizumab was clinical and biochemical; individual post-treatment laboratory values are not plotted.

Follow-up

On the targeted regimen, she demonstrated gradual improvement over one month. She was discharged from the hospital in stable condition and transitioned to tocilizumab therapy. Her outpatient care plan involves continued follow-up with the rheumatology department to manage her condition and monitor her ongoing response to treatment.

Timeline

Date	Clinical Status and Milestones
Early 2025	Onset of constitutional symptoms (fever, weight loss 52–39 kg, night sweats). Seen at multiple hospitals including Aseer Hospital (discharged AMA, no diagnosis).
23 Jul 2025	First admission (FUO workup): CT showed supra/infra-diaphragmatic lymphadenopathy and mild splenomegaly (13.5 cm); PET showed diffuse BM uptake; ferritin 12,224 ng/mL; LDH 880 U/L.
27 Jul 2025	Right inguinal lymph node biopsy: reactive with dermatopathic changes. No granuloma. Negative for malignancy.
3 Aug 2025	Axillary lymph node biopsy taken. Patient discharged while still febrile for OPD follow-up.

Date	Clinical Status and Milestones
Late Aug 2025	ER/ICU admission: hypotensive shock, <i>C. difficile</i> colitis, ferritin 17,347 ng/mL. Started on oral vancomycin, IV metronidazole, broad-spectrum antibiotics.
Hospital course	Second ICU admission for recurrent hypotension; meropenem started. Bone marrow biopsy: normocellular, no malignancy. EGD to rule out Whipple's: unremarkable. Ferritin declined to 8,693 then surged to >33,511 ng/mL.
Early Sep 2025	Transferred to Rheumatology. Diagnosis of AOSD confirmed. Labs showed pancytopenia (WBC 0.57), LDH 2,227, fibrinogen 1.18, triglycerides 5.66, sCD25 2,202 – consistent with MAS/HLH.
Mid Sep 2025	Escalation to pulse steroids, anakinra, and 4 doses of IVIG.
Discharge	Significant recovery over 1 month; discharged on tocilizumab.

Discussion

Adult-onset Still's disease (AOSD) is a rare systemic autoinflammatory disorder with an estimated annual incidence of 0.1–0.4 per 100,000 (1,2). The Yamaguchi classification criteria remain the most widely used diagnostic tool, with a reported

sensitivity of 96.2% and specificity of 92.1% (11). The 2024 EULAR/PReS recommendations have recognized that systemic juvenile idiopathic arthritis and AOSD represent a single disease entity now termed “Still's disease” and endorse the early use of IL-1 or IL-6 inhibitors combined with short-duration glucocorticoids as the optimal therapeutic strategy (12).

Our patient's illness evolved over five months with quotidian fevers, 13 kg weight loss, bilateral wrist and elbow synovitis, marked leukocytosis with neutrophilia, and extreme hyperferritinemia that escalated from 12,224 ng/mL to 17,347 ng/mL and ultimately to >33,511 ng/mL, fulfilling the Yamaguchi criteria (three major and two minor) (11). The absence of the classic salmon-colored rash is consistent with reports that the rash may be absent in a substantial proportion of AOSD patients without precluding the diagnosis (3,5). The exhaustive negative infectious and malignancy workups including negative cultures, viral serologies, two reactive lymph node biopsies, and a bone marrow biopsy showing no malignancy were crucial in establishing AOSD as a diagnosis of exclusion (13).

Markedly elevated serum ferritin exceeding five times the upper limit of normal is a hallmark of AOSD, with a reported sensitivity of approximately 80% and specificity of 41% when used alone; combining this with glycosylated ferritin $\leq 20\%$ increases specificity to 93% (14). Ferritin levels exceeding 10,000 ng/mL demonstrate 90% sensitivity and 96% specificity for HLH (15). In our case, the ferritin trajectory from 12,224 to >33,511 ng/mL served as both a diagnostic and prognostic marker, heralding the evolution into MAS.

MAS, occurring in approximately 12–17% of AOSD patients with a mortality exceeding 20% (2,7), was diagnosed in our patient based on the dramatic development of pancytopenia (WBC $0.57 \times 10^9/L$, Hgb 78 g/L, platelets 199,000/cmm), hyperferritinemia >33,511 ng/mL, elevated LDH (2,227 U/L), hypertriglyceridemia (5.66 mmol/L), hypofibrinogenemia (1.18 g/L), elevated sCD25 (2,202 U/mL), and hepatic dysfunction (AST 318 U/L). These findings are consistent with the 2022 EULAR/ACR points to consider for HLH/MAS, which emphasize the importance of monitoring the evolution of laboratory parameters over time rather than relying on any single abnormality (16). A critically challenging feature of this case was the concurrent *C. difficile* colitis with septic shock. The overlap between MAS/HLH and severe sepsis poses one of the most difficult diagnostic dilemmas in critical care, as both conditions share features of fever, organ dysfunction, and elevated inflammatory markers (17). However, extreme hyperferritinemia (>10,000 ng/mL), progressive multilineage cytopenias, and persistence of high fevers despite appropriate antimicrobial therapy are features that favor MAS/HLH over isolated sepsis (17). Importantly, infections can serve as triggers for MAS in patients with underlying autoinflammatory conditions, and the two processes may coexist (7,18). In our patient, *C. difficile* colitis likely served as a secondary trigger that precipitated fulminant MAS in the setting of already dysregulated immunity. Management followed a stepwise escalation aligned with current recommendations. After initial stabilization with antibiotics and targeted *C. difficile* treatment, recognition of AOSD led to methylprednisolone. The development of MAS

prompted escalation to pulse steroids, anakinra, and IVIG. The 2024 EULAR/PReS recommendations endorse high-dose glucocorticoids as the foundation of MAS therapy, with anakinra, cyclosporine, and/or interferon- γ inhibitors as part of initial therapy (12). Meta-analytic data demonstrate complete remission rates of approximately 73% with anakinra and 80% with tocilizumab in AOSD (19). Following acute stabilization, the transition to tocilizumab for maintenance therapy represents a rational strategy addressing both the immediate cytokine storm and long-term disease control (12,19).

Limitations

This report has several limitations. First, it describes a single patient, and therefore the diagnostic and therapeutic conclusions cannot be generalized. Second, hemophagocytosis was not confirmed on the reviewed bone marrow specimen; while this does not preclude the diagnosis of MAS/secondary HLH given the otherwise classical clinical and laboratory profile, its absence weakens histopathological confirmation. Third, the HScore could not be reliably reconstructed retrospectively, as the maximum recorded temperature during the MAS phase and other component variables required for the score were not all systematically documented at the same time point. Fourth, follow-up under tocilizumab maintenance therapy was limited to the immediate post-discharge period, and longer-term outcomes regarding sustained remission, relapse, and steroid tapering are not yet available. Finally, the temporal association between *C. difficile* colitis and the onset of fulminant MAS is suggestive but does not establish causation; whether the infection acted as a true trigger or as a coincident process cannot be determined from a single case.

Clinical Pearls

- In a febrile young adult with negative infectious and malignancy workup, extreme hyperferritinemia (>10,000 ng/mL) should immediately raise suspicion for AOSD and its hyperinflammatory complication, MAS/secondary HLH.
- Persistent high-grade fever and rising inflammatory markers despite appropriate, source-controlled antimicrobial therapy in a patient with documented infection should prompt re-evaluation for an underlying hyperinflammatory syndrome rather than escalation of antibiotics alone.
- Trends matter more than isolated values: a falling ferritin or platelet count from a markedly abnormal baseline can paradoxically herald progression to MAS rather than recovery.
- Concurrent infection does not exclude MAS; infections frequently act as triggers in patients with underlying autoinflammatory predisposition, and the two processes can require simultaneous management.
- Early multidisciplinary collaboration (rheumatology, hematology, critical care, and infectious diseases) and timely escalation to high-dose glucocorticoids, IL-1 blockade, and adjunctive immunomodulation are essential for survival.

Conclusion

This case underscores the diagnostic and therapeutic challenges of adult-onset Still's disease complicated by macrophage activation syndrome, particularly when it coexists with severe

infection such as *C. difficile* colitis. The significant overlap between MAS/HLH and septic shock can delay recognition of the underlying hyperinflammatory state, with potentially life-threatening consequences. In our patient, extreme hyperferritinemia, progressive cytopenias, and persistent fever despite appropriate antimicrobial therapy were key features that guided the diagnosis.

Importantly, this case highlights the need for a high index of suspicion for MAS in patients with unexplained systemic inflammation and rapidly evolving laboratory abnormalities. The prompt escalation to high-dose corticosteroids, IL-1 blockade, and adjunctive immunomodulatory therapy resulted in a favorable outcome, emphasizing the importance of early and aggressive treatment.

Clinicians should remain vigilant for the coexistence of infection and hyperinflammatory syndromes, recognizing that infections may act as triggers rather than sole explanations for clinical deterioration. Early multidisciplinary collaboration and timely initiation of targeted therapy are essential to improving survival in this complex and potentially fatal condition.

Declarations

Conflicts of Interest: The authors declare no conflicts of interest.

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Ethical Approval: Not required for case reports in accordance with institutional policy.

Consent for Publication: Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Author Contributions: All authors contributed to the conception, drafting, and revision of the manuscript and approved the final version.

Data Availability: Data sharing is not applicable as no datasets were generated or analyzed.

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