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Adult-Onset Still's Disease – Still a Diagnostic Dilemma: A Case Report

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Case Report

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Abstract

Background

Adult-onset Still's disease (AOSD) is a rare autoinflammatory disorder which is characterized by fever, arthritis, rash, and marked hyperferritinemia. This poses a diagnostic challenge due to overlapping with infectious, malignant, and autoimmune conditions. This case contributes to scientific literature by demonstrating the importance of an early diagnosis of AOSD and the need to quickly escalate treatment to biologic therapy. It is especially unique due to the challenges presented by extreme hyperferritinemia (>16,000 ng/mL), a prolonged pyrexia of unknown origin, and the diagnostic quandary of intersecting presentations of an inflammatory and infectious nature.

Case Presentation

we report a case of a 31-year-old Pakistani male who presented with prolonged high-grade fever, a sore throat, polyarthritis, and systemic inflammation. Laboratory studies showed extreme hyperferritinemia (>16,000 ng/mL) and analysis of the blood revealed leukocytosis with neutrophilic predominance, and inflammatory markers that were all increased. Extensive evaluation for infection, malignancy, and autoimmune disease was all negative. The patient met the Yamaguchi criteria for AOSD and received initial treatment with corticosteroids specifically intravenous methylprednisolone 1 mg/kg daily for 5 days, followed by escalation to Tocilizumab 162 mg subcutaneously once weekly due to persistent disease activity, who then resulted with a significant clinical and biochemical improvement.

Conclusion

This case highlights the importance of considering AOSD in patients with fever of unknown origin and extreme hyperferritinemia. Early recognition and timely initiation of targeted therapy are essential to improve outcomes and prevent complications such as macrophage activation syndrome.

This case highlights the critical need to consider AOSD in patients presenting with fever with no clear cause and very high ferritin levels. Recognizing it early and timely initiation of appropriate therapy is important to increase patient outcomes and to prevent serious complications such as macrophage activation syndrome.

Introduction

AOSD is a rare systemic inflammatory condition that affects the whole body. It is characterized by three main signs: very high fevers that come and go, a fleeting salmon-colored rash, and joint pain or arthritis, with occasional lymphadenopathy. The disease tends to appear most often in two age groups, young adults between 15–25 years old and in people between 36–46 years[1], and a slightly higher prevalence in females. Even though doctors don't fully understand what causes AOSD, it is thought to be linked to involve dysregulation of the innate immune system. This leads to the body producing too many

proinflammatory cytokines (interleukin (IL)-1, IL-6, IL-18, and tumor necrosis factor-α). These cytokines play a big role in the symptoms people experience. For example, IL-1 and IL-6 are responsible for fevers and general inflammation, while TNF-α contributes to synovial inflammation, and IL-18 activates certain immune cells called macrophages. The rash usually appears with fever spikes and is a sign of cytokine-mediated temporary dermal inflammation. One important lab found in AOSD is very high levels of ferritin, a protein that stores iron. This high ferritin level reflects both the widespread inflammation in the body and the activation of macrophages.[1,2]

Diagnosis remains challenging due to the lack of a definitive diagnostic test and the significant overlap with infectious, malignant, and other rheumatologic conditions. The Yamaguchi criteria is the most used classification system and incorporates clinical and laboratory findings alongside the exclusion of alternative diagnoses.

The absence of a definitive diagnostic test, combined with the heterogeneous clinical presentation of adult-onset Still's disease, often results in delayed recognition, thus making it a clinical diagnostic challenge. Marked hyperferritinemia, although not specific, may provide an important diagnostic clue in the appropriate clinical context.[1,4]

Patient Information

De-identified Patient Information

A 31-year-old previously healthy Emirati male presented with a three-week history of spiking fever, persistent sore throat, back pain, and progressive polyarticular joint pain.

Primary Concerns and Symptoms

Joint symptoms started in the right elbow, then spread to the right shoulder, and later involved both knees, the finger joints metacarpophalangeal (MCP), proximal interphalangeal (PIP) and both wrists. Severe back pain made it very difficult for the patient to move around.

The fever was high-grade and kept coming back, with only short-lived relief from fever-reducing medications like paracetamol and ibuprofen. The patient also experienced unintentional weight loss of approximately 4 kilograms over three weeks.

Medical, Family, and Psychosocial History

The patient was previously healthy and had no notable history. There was no associated chest pain, dyspnea, abdominal pain, or other cardiopulmonary symptoms. No relevant family or genetic history was identified.

Relevant Past Interventions and Outcomes

Relevant Past Interventions and Outcomes
The patient initially used antipyretics including paracetamol and ibuprofen, which produced only transient relief without sustained improvement.

Clinical Findings

On examination, the patient was alert and oriented (GCS 15/15). Vital signs showed a temperature of 38.9°C, pulse 118 bpm, and blood pressure 135/87 mmHg. Respiratory examination was normal, with no cyanosis, jaundice, or digital clubbing.

Musculoskeletal examination revealed swelling and tenderness of the right wrist and right elbow, with tenderness along the lower dorsal spine. On day four of hospitalization, a generalized non-pruritic maculopapular rash appeared over the chest, neck, and abdomen.

Timeline

Timeline	Clinical Event
Week 1	High-grade fever, sore throat, and back pain started.
Week 2	Joint pain progressed from the right elbow to the right shoulder and later involved both knees, MCP, PIP joints, and wrists bilaterally.
Week 3	The patient reported persistent high-grade recurrent fever, severe back pain, impaired mobility, and approximately 4 kg unintentional weight loss.
Hospital Day 1	Initial clinical evaluation and laboratory investigations were performed. Infectious, autoimmune, and radiological workup was initiated.
Hospital Day 4	A generalized non-pruritic maculopapular rash appeared over the chest, neck, and abdomen.
During Hospitalization	CRP peaked at 361.6 mg/L, leukocyte count reached 30 ×10⁹/L with 93% neutrophils, and serum ferritin was markedly elevated at > 16,000 ng/mL.
Diagnostic Conclusion	Infectious, malignant, and autoimmune causes were excluded, and the patient fulfilled the Yamaguchi criteria for adult-onset Still’s disease.
Initial Treatment	Systemic corticosteroids were initiated, resulting in partial clinical improvement.
Escalation of Therapy	Due to persistent disease activity and recurrence of fever, therapy was escalated to Tocilizumab.
Follow-up	Following biologic therapy, the patient demonstrated marked clinical and biochemical improvement.

Diagnostic Assessment

Diagnostic Methods

Initial laboratory investigations revealed haemoglobin of 12.3 g/dL, leucocytosis with neutrophilic predominance, and markedly elevated inflammatory markers. During hospitalization, CRP peaked at 361.6 mg/L and leukocyte count reached 30 ×10⁹/L with 93% neutrophils. Serum ferritin was markedly elevated at > 16,000 ng/mL.

Autoimmune serologic testing including antinuclear antibodies (ANA), rheumatoid factor (RF), and anti-CCP antibodies were negative.

An extensive infectious workup including blood cultures, urine cultures, viral serologies, hepatitis panel, tuberculosis screening, malaria smear, and Brucella serology was negative, as shown in Table 1.

Table 1
Diagnostic workup for infectious etiologies

Test	Result
Blood cultures	No growth
Urine cultures	No growth
Viral serologic testing (EBV, CMV, COVID-19, Influenza A/B)	Negative
Hepatitis panel	Negative
Tuberculosis screening	Negative
Malaria smear	Negative
Brucella serology (Brucella abortus, Brucella melitensis)	Negative
Anti-streptolysin O (ASO) titer	Negative

Radiological investigations were largely unremarkable. MRI of the dorsal and lumbar spine showed only mild degenerative disc changes. Echocardiography showed no vegetation or valvular abnormality.

Diagnostic Challenges

The major challenge was differentiating AOSD from infectious, malignant, and autoimmune causes of fever of unknown origin due to overlapping systemic inflammatory features.

Diagnosis

Based on the clinical presentation and laboratory findings, the patient fulfilled the Yamaguchi criteria for the diagnosis of adult-onset Still's disease.

Differential Diagnoses Considered

Infectious diseases, autoimmune disorders, malignancy, tuberculosis, viral infections, brucellosis, and bacterial endocarditis were considered and excluded.

Therapeutic Intervention

Types of Therapeutic Intervention

Pharmacologic intervention included systemic corticosteroids followed by biologic therapy.

Administration of Therapeutic Intervention

The patient was initially treated with systemic corticosteroids, specifically intravenous methylprednisolone 1 mg/kg daily for 5 days, which resulted in partial clinical improvement. Due to persistent disease activity and recurrence of fever, therapy was escalated to tocilizumab 162 mg subcutaneously once weekly, an interleukin-6 inhibitor. The patient responded very well and was subsequently discharged on the same dose, with advice to follow up in the outpatient department.

Changes in Therapeutic Intervention

Corticosteroid therapy alone was insufficient to achieve sustained remission; therefore, escalation to Tocilizumab was performed to achieve better disease control.

Follow-up and Outcomes

Clinician- and Patient-Assessed Outcomes

Following initiation of biologic therapy, the patient demonstrated marked clinical improvement with reduction in fever, improvement in joint symptoms, and better mobility.

Important Follow-up Diagnostic Results

Following initiation of biologic therapy, the patient demonstrated marked clinical improvement with gradual normalization of inflammatory markers, as shown in Table 2.

Table 2
Laboratory trends and treatment response in Adult-Onset Still's disease

Category	Parameter	Reference Range	Admission	Peak / Worst	Post-treatment
Inflammatory Markers	CRP (mg/L)	< 5 mg/L	195.8 mg/L	361.6 mg/L	112 mg/L
	ESR (mm/hr)	< 20 mm/hr	—	86 mm/hr	
	Procalcitonin		—	2.69	—
	Ferritin (ng/mL)	30–400 ng/mL	—	> 16000 ng/mL	—
Hematological Profile	Hemoglobin (g/dL)	13–17 g/dL	12.3 g/dL	10.1 g/dL	11.3 g/dL
	WBC (± Neutrophils %)	4–11	17.26(90%)	30(93%)	26.82(88%)
	Platelets (×10⁹/L)	150–400×10⁹/L	200×10⁹/L	434×10⁹/L	434×10⁹/L
	Vitamin B12 (pg/mL)	200–900	—	565	—
	Serum Iron (μg/dL)	60–170	—	30.93	—
Key Immunologic Tests	ANA	Negative	Negative	—	—
	RF	Negative	Negative	—	—
	Anti-CCP-IgG	Negative	Negative	—	—
Liver Function Tests	ALT	10–40 U/L	54	55	—
	AST	10–40 U/L	43	58	—
	ALP	44–147 U/L	90	115	—
	LDH	40–280 U/L	377	377	—

Intervention Adherence and Tolerability

Treatment response was assessed through serial inflammatory markers, clinical symptoms, and physician follow-up. Tocilizumab was well tolerated.

Adverse and Unanticipated Events

No major adverse events were observed during treatment. Although macrophage activation syndrome was suspected because of marked hyperferritinemia, the patient did not demonstrate cytopenia, coagulopathy, or organ dysfunction suggestive of MAS.

Discussion

Adult-onset Still's disease is a rare systemic inflammatory disorder that frequently presents as pyrexia of unknown origin, making early diagnosis challenging. The disease is characterized by high-grade spiking fever, arthralgia or arthritis, evanescent rash, leukocytosis with neutrophilic predominance, and marked hyperferritinemia.

In the absence of a definitive diagnostic test, diagnosis is primarily clinical and supported by classification systems such as the Yamaguchi criteria, which remain the most widely used criteria in clinical practice.[3] These criteria require the presence of at least five features, including two or more major criteria, following exclusion of infectious, malignant, and other autoimmune conditions. The Yamaguchi criteria exhibit excellent diagnostic performance, with reported sensitivity and specificity of 96.3% and 92.1%, respectively after excluding the other possible causes.[5]

A notable feature in this case was extreme hyperferritinemia (> 16,000 ng/mL). Ferritin levels more than 10,000 ng/mL strongly support the diagnosis in the appropriate clinical context and correlate with disease activity.[4]

Another noteworthy finding was the elevated procalcitonin level. Even though procalcitonin is typically considered a marker of bacterial infection, high levels have also been seen in adult-onset Still's disease and may reflect the intense cytokine-mediated inflammatory response rather than true infection.[6]

The successful response to Tocilizumab supports the role of cytokine-targeted therapy in refractory AOSD cases. This is consistent with recent EULAR recommendations supporting early initiation of IL-1 or IL-6 inhibitors.[7,8]. In this patient, corticosteroid therapy initially resulted in partial clinical improvement but was not enough to achieve sustained remission. Therefore, escalation to Tocilizumab, an IL-6 receptor antagonist, resulted in marked clinical and biochemical improvement[7], consistent with previously reported outcomes.

Strengths and Limitations

This case report provides a detailed account of Adult-Onset Still's Disease with extreme hyperferritinemia, highlighting a rare but clinically significant presentation. The comprehensive diagnostic workup and clear documentation of laboratory trends and treatment response strengthen the clinical relevance.

As a single case report, the findings cannot be generalized to all patients with AOSD. Long-term follow-up data are limited, and some advanced biomarkers were not measured.

Conclusion

Adult-onset Still's disease remains a diagnostic challenge due to its nonspecific presentation and overlap with infectious and autoimmune conditions. This case highlights the importance of considering AOSD in patients presenting with prolonged fever, polyarthritis, and markedly elevated inflammatory markers after exclusion of infectious and malignant aetiologies.

Extreme hyperferritinemia may serve as a valuable diagnostic clue and indicator of disease activity. Early recognition and timely initiation of appropriate therapy, including biologic agents in refractory cases, are essential to improve outcomes and prevent serious complications such as macrophage activation syndrome.

Abbreviations

ANA
Antinuclear antibodies
AOSD
Adult-onset Still's disease
ASO
Anti-streptolysin O
ALT
Alanine aminotransferase
AST
Aspartate aminotransferase
ALP
Alkaline phosphatase
CCP
Cyclic citrullinated peptide
CMV
Cytomegalovirus
CRP
C-reactive protein
EBV
Epstein–Barr virus
ESR
Erythrocyte sedimentation rate
GCS
Glasgow Coma Scale
IL
Interleukin
LDH
Lactate dehydrogenase
MAS

Macrophage activation syndrome
MCP
Metacarpophalangeal
MRI
Magnetic resonance imaging
PIP
Proximal interphalangeal
RF
Rheumatoid factor
TNF
Tumor necrosis factor
WBC
White blood cell.

Declarations

Patient Perspective

The patient described the period before diagnosis as physically exhausting and emotionally stressful because of persistent high-grade fever, severe joint pain, back pain, weight loss, and uncertainty about the cause of his illness. He reported that the repeated investigations and lack of an early clear diagnosis caused considerable anxiety for him and his family.

After the diagnosis was explained and treatment was initiated, the patient felt reassured and more confident about his recovery. Following escalation to biologic therapy, he noticed meaningful improvement in fever, joint pain, mobility, and overall daily functioning. He expressed relief that a clear diagnosis had been reached and appreciated the multidisciplinary care provided during his hospitalization.

Ethics and Consent to Participate

Not applicable.

Informed Consent

Written informed consent was obtained from the patient for publication of this case report and any potentially identifiable data included in this article. A copy of the written consent is available for review by the Editor-in-Chief if requested.

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Declaration of AI-Assisted Technologies

AI-assisted tools were used solely for language and clarity improvement. All scientific content was critically reviewed and approved by the authors.

Author contributions

SSS: Writing – original draft, Writing – review & editing, Visualization.

AD: Conceptualization, Visualization.

AA: Writing – review & editing.

HE: Writing – review & editing.

JA: Writing – review & editing.

NAA: Conceptualization, Supervision, Validation, Visualization.

MAN: Writing – review & editing.

MAY: Investigation, Writing – review & editing.

ACT: Writing – review & editing.

RAE: Supervision, Validation, Writing – review & editing.

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Availability of data and materials

All relevant data supporting the findings of this case report are included within the article. No additional datasets were generated.

Competing interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

1. Bhargava J, Panginikkod S. Still disease [Internet]. StatPearls. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2026 Mar 26]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538345/
2. Jamilloux Y, Gerfaud-Valentin M, Martinon F, Belot A, Henry T, Sève P. Pathogenesis of adult-onset Still's disease: new insights from the juvenile counterpart. Immunol Res. 2014;61(1–2):53–62. doi:10.1007/s12026-014-8561-9
3. Yamaguchi M, Ohta A, Tsunematsu T, Kasukawa R, Mizushima Y, Kashiwagi H, et al. Preliminary criteria for classification of adult Still's disease. J Rheumatol. 1992;19(3):424–30.
4. Ali NM, Ibrahim MO, Mohamed OM. Adult-onset Still's disease in a 49-year-old female in the UAE: a case report and literature review. Cureus. 2025 Jul 13;17(7):e87858. Available from: https://www.cureus.com/articles/385183-adult-onset-stills-disease-in-a-49-year-old-female-in-the-uae-a-case-report-and-literature-review#!/
5. Fautrel B, Zing E, Golmard JL, Le Moël G, Bissery A, Rioux C, et al. Proposal for a new set of classification criteria for adult-onset Still disease. Medicine (Baltimore). 2002;81(3):194–200. doi:10.1097/00005792-200205000-00003
6. Scirè CA, Cavagna L, Perotti C, et al. Diagnostic value of procalcitonin measurements in patients with systemic inflammatory diseases. Clin Exp Rheumatol. 2006;24(2):123–8.
7. Kaneko Y, Takeuchi T. Interleukin-6 inhibition: a therapeutic strategy for the management of adult-onset Still's disease. Expert Opin Biol Ther. 2021;22(1):79–85. doi:10.1080/14712598.2022.1977266
8. Bindoli S, De Matteis A, Mitrovic S, et al. Efficacy and safety of therapies for the treatment of adult-onset Still's disease (AOSD) and systemic juvenile idiopathic arthritis (sJIA): a systematic review informing the EULAR/PReS guidelines. RMD Open. 2024.