Original Research Paper

Volume - 16 | Issue - 01 | January - 2026 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

General Medicine

"ADULT-ONSET STILL'S DISEASE PRESENTING AS FEVER AND RASH: SOUTH INDIAN CASE WITH FOLLOW-UP"

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ABSTRACT Adult-onset Still's disease (AOSD) is a rare multisystem autoinflammatory disorder characterized by high spiking fevers, evanescent salmon-colored rash, arthralgia/arthritis, leukocytosis, and hyperferritinemia. We present a 35-year-old Indian male with persistent fever, evanescent rash, neutrophilic leukocytosis (16,000/mm³, 82% neutrophils), mild hepatosplenomegaly, and ferritin 13,000 ng/mL, fulfilling Yamaguchi criteria after exclusion of infections and malignancies. He responded dramatically to pulse methylprednisolone followed by oral taper, achieving sustained remission at one-year follow-up with normalization of inflammatory markers (ferritin 520 ng/mL), though metabolic comorbidities like obesity BMI 34.34, grade 1 fatty liver, and dyslipidemia emerged. Unlike refractory polycyclic cases requiring biologics, this monophasic presentation underscores steroid efficacy and need for long-term metabolic surveillance.

KEYWORDS : ADULT-ONSET STILL'S DISEASE, HYPERFERRITINEMIA, YAMAGUCHI CRITERI, AUTOINFLAMMATORY SYNDROME, METABOLIC SEQUELAE

INTRODUCTION

Adult-onset Still's disease (AOSD) represents a rare systemic autoinflammatory condition of unknown cause that affects patients over age 16, featuring quotidian spiking fevers, arthralgia or polyarthritis, and an evanescent salmon-coloured maculopapular eruption, typically with intense systemic inflammation and frequently profound hyperferritinemia. [1]AOSD arises from dysregulated innate immunity, where environmental/infectious triggers stimulate Toll-like receptors on macrophages and neutrophils, driving NLRP3 inflammasome hyperactivation and cytokine overproduction (primarily IL-1β, IL-6, IL-18, IFN-γ). Adaptive Th1/Th17 responses sustain inflammation, with profound hyperferritinemia signalling macrophage hyperactivation.[2]

Diagnosis hinges on clinical criteria of Yamaguchi (sensitivity 93.5-96.3%, specificity 92.1-98.5 requiring ≥5 criteria including ≥2 major (fever ≥39°C ≥1 week, arthralgia ≥2 weeks, salmon-pink rash, leukocytosis ≥10,000/mm³ with ≥80% granulocytes) plus ≥3 minor (sore throat, lymphadenopathy/splenomegaly, liver dysfunction, negative ANA/RF) after excluding infections/malignancies.[3] Fautrel criteria (2002) for AOSD diagnosis require ≥4 major criteria (fever ≥39°C, arthralgia, transient erythema, pharyngitis, neutrophils ≥80%, glycosylated ferritin ≤20%) or 3 major + 2 minor (rash, leukocytosis ≥10,000/mm³), offering 80.6% sensitivity/98.5% specificity without exclusions needed. [4]

AOSD manifests as three patterns: monophasic (one-third cases; single episode less than 2 years, best prognosis), polycyclic (one-third; recurrent flares 2+ months apart), and chronic articular (one-third; persistent erosive arthritis needing prolonged immunosuppression). [5] Initial therapy per 2023 EULAR/PReS and 2024 Delphi consensus is glucocorticoids (0.5–1 mg/kg prednisone equivalent) first-line (response 60–80%), escalating to methotrexate/CSF1R inhibitors or IL-1/IL-6 blockers (anakinra 100 mg SC daily, tocilizumab 8 mg/kg) if refractory.[6]

AOSD follow-up requires regular rheumatology monitoring with clinical assessment (fever, rash, arthritis), inflammatory markers (CRP, ESR, ferritin), and complete blood counts every 1-3 months during tapering, then 3-6 months in remission per EULAR/PReS 2024 guidelines.[6]Monophasic cases need surveillance for relapse (20-30% risk year 1) and steroid complications (osteoporosis, metabolic syndrome); polycyclic/chronic require disease activity scoring (Pouchot score) and biologic consideration if relapse.[7]

Post-remission metabolic derangements (obesity, NAFLD, dyslipidemia) in our obese sedentary patient mirror emerging data underrepresented in acute reports, emphasizing holistic follow-up. This South Indian case adds to sparse regional literature, where AOSD mimics tropical fevers (dengue, scrub typhus) excluded here

CASE REPORT

A 35-year-old male presented with a history of persistent fever and an erythematous rash over the chest, back, and upper limbs for two weeks. He had no associated sore throat, arthralgia, lymphadenopathy, or weight loss. There was no preceding drug intake, recent travel, or exposure to pets. On examination, he was afebrile and hemodynamically stable. Systemic examination, including cardiovascular, respiratory, abdominal, and neurological systems, was unremarkable.

Baseline laboratory investigations revealed haemoglobin of 12.6 g/dL, total leukocyte count of 16,000/mm³ (neutrophils 82%, lymphocytes 14%), and platelet count within normal limits. Renal function tests demonstrated urea 24 mg/dL and creatinine 0.9 mg/dL with normal electrolytes. Liver function tests showed mild transaminitis (SGPT 50 U/L, ALP 130 U/L). Inflammatory markers were markedly elevated with ESR 60 mm/hr and CRP 62 mg/L. Serum ferritin was notably elevated at 13,000 ng/mL.

ECG revealed normal sinus rhythm, and chest radiography and echocardiography were unremarkable. Ultrasonography of the abdomen showed mild hepatosplenomegaly.

Comprehensive infective evaluation including malarial parasite QBC, dengue serology, scrub typhus IgM, leptospira IgM, HIV, Epstein–Barr virus, hepatitis B and C serology, blood and urine cultures were all negative. Autoimmune workup revealed negative antinuclear antibody (ANA), anti-dsDNA, rheumatoid factor, and anti-CCP antibody.

Considering the constellation of quotidian fever, evanescent rash, leukocytosis, elevated inflammatory markers, hyperferritinemia, and exclusion of infections and autoimmune diseases, a diagnosis of Adult-onset Still's Disease (AOSD) was established as per Yamaguchi criteria. The patient was initiated on pulse corticosteroids followed by a tapering course of oral steroids with symptomatic improvement and was discharged in stable condition.

At one-year follow-up, the patient presented with mild pain in the thighs and knees for three weeks. He had discontinued steroid therapy four months prior. There was no joint swelling, fever, or rash. He was obese (BMI 34.3 kg/m²), hemodynamically stable, and systemic examination was unremarkable.

Repeat laboratory evaluation revealed haemoglobin 15.2 g/dL, total leukocyte counts 8190/mm³ (N 52%, L 37%), and platelet count 3.38 x 10 /mm³. ESR was 7 mm/hr, and CRP was 8 mg/L. Renal and hepatic parameters were within normal limits except for a mildly elevated gamma-glutamyl transferase (GGTP) level of 62 U/L. Serum ferritin was 520 ng/mL. Lipid profile showed dyslipidaemia (LDL 137 mg/dL, HDL 37 mg/dL, triglycerides 152 mg/dL). HbA1c and thyroid

function were normal.

Ultrasonography of the abdomen revealed Grade I fatty liver with focal fat sparing and a small sub centimetric simple cyst in the right hepatic lobe. Serum vitamin D levels were marginally low at 21.2 ng/mL. He was advised lifestyle modification including a low-fat diet and regular exercise, along with hepatoprotective agents and vitamin D supplementation.

He remained clinically stable on follow-up with no recurrence of systemic symptoms or biochemical evidence of disease reactivation.

DISCUSSION

AOSD, the adult counterpart of systemic juvenile idiopathic arthritis, is a rare entity with incidence 0.16–0.4/100,000, showing bimodal peaks at 16–25 and 36–46 years—precisely matching our 35-year-old patient's demographic, unlike the female predominance (4:1 F:M) in some cohorts. [8] This case epitomizes classic AOSD presentation with quotidian fever, evanescent salmon-pink rash, extreme neutrophilic leukocytosis (82%), hepatosplenomegaly, and hyperferritinemia (13,000 ng/mL), fulfilling Yamaguchi criteria after exclusion of mimics, closely mirroring a 2024 Cureus report of a 26-year-old female with ferritin >2000 ng/mL, similar multiorgan involvement, and steroid response but contrasting our sustained monophasic remission versus her polycyclic trajectory. [9]

Adult-onset Still's disease (AOSD) represents a classic diagnosis of exclusion, necessitating comprehensive exclusion of infections, malignancies, and rheumatologic disorders before confirmation via Yamaguchi criteria.[10] In South India's tropical setting, our broad serological panel (negative scrub typhus, dengue, leptospirosis) was essential, as endemic infections frequently mimic AOSD presentations requiring differentiation through targeted testing.[11] Regional Indian studies confirm AOSD constitutes 5-10% of fever of unknown origin (FUO) cases among young adults, underscoring its underdiagnosis amid prevalent tropical fevers like tuberculosis, brucellosis, and enteric fever.[12]

Recent 2025 research established that ferritin elevations >3,000-5,000 ng/mL strongly support AOSD diagnosis within the proper clinical scenario, setting it apart from non-variable markers given our patient's negative infectious evaluations.[13] Ferritin concentrations exceeding 10,000 ng/mL demonstrated strong diagnostic specificity for AOSD compared to other conditions (positive predictive value 77-90%), supported by 2022 findings where 15 out of 17 individuals with ferritin >10,000 ng/mL were confirmed to have AOSD (sensitivity 85.71%, specificity 81% using a >1,757 ng/mL cutoff).[14] In our patient, the marked reduction in serum ferritin from 13,000 ng/mL to 520 ng/mL precisely correlated with clinical and inflammatory remission, demonstrating ferritin's utility as a dynamic biomarker of AOSD activity.[15]

Recent 2025 BMJ Case Reports documented atypical AOSD presentations failing Yamaguchi criteria (e.g., absent leukocytosis) where hyperferritinemia nonetheless guided diagnosis, illustrating ferritin's diagnostic utility in non-classic scenarios.[16] Unlike pruritic plaque or monocytosis variants reported in 2025 literature, our patient's typical non-pruritic evanescent rash and classic neutrophilia (82%) upheld Yamaguchi criteria robustness while affirming AOSD's diagnostic heterogeneity.[17]

Our patient's monophasic disease pattern corresponds to roughly one-third of AOSD cases exhibiting optimal outcomes, consistent with findings from Pouchot's landmark 1991 study involving 62 patients .[18] In contrast, recurrent polycyclic forms , approximately 20%, marked by flares spaced more than two months apart and chronic articular forms around 50% causing destructive erosive arthritis typically demand extended immunomodulatory therapy, whereas a 2015 Chinese cohort documented 45.3% relapse incidence mainly during corticosteroid tapering.[19]

The EULAR/PReS 2023 guidelines recommend glucocorticoids as first-line therapy for AOSD, reporting 60-80% response rates and 70% complete remission at one month, consistent with our patient's successful steroid monotherapy achieving glucocorticoid-free remission.[20] The 2024 Delphi consensus similarly advocates reserving DMARDs or biologic agents for cases with adverse prognostic indicators such as macrophage activation syndrome or recurrent flares-features not present in our monophasic presentation-validating the selected initial high-dose steroid approach.[21]

A 2025 UAE case report described a 49-year-old female requiring anakinra after glucocorticoid failure,[22] while a 2024 JDDT fever of unknown origin case necessitated escalation to tocilizumab for adequate control.[23] In a 2022 multicentre cohort of 136 patients, methotrexate achieved complete remission in 70% and steroid discontinuation in 39%, though biologics proved superior for significantly reducing Pouchot systemic scores in refractory disease.[24] Our avoidance of therapeutic escalation-required in 40-45% of glucocorticoid-resistant cases-highlights favourable monophasic prognostic factors including younger age, male gender, and lower systemic involvement score.[25]

Follow-up revealed obesity-associated metabolic syndrome (BMI 34.34 kg/m², grade 1 NAFLD with focal fat sparing, dyslipidaemia: HDL 37 mg/dL, LDL 137 mg/dL, TG 152 mg/dL, vitamin D 21.2 ng/mL)-manifestations not evident during the acute phase [26] A 2024 IJRMS comprehensive review highlighted that NSAIDs and glucocorticoids can unmask NAFLD risks in AOSD patients mirroring the hepatic changes observed in our steroid-treated patient.[26]

The 2025 non-classical complications study associated higher systemic severity scores and lymphadenopathy, absent in our case , with chronic disease progression and extended steroid requirements.[27] Reduced physical activity intensified dyslipidaemia, aligning with Cleveland Clinic observations of lifestyle-exacerbated metabolic disturbances following AOSD remission.[28].

CONCLUSION

AOSD requires vigilance for fever/rash/hyperferritinemia post-exclusions; this monophasic South Indian case affirms steroid efficacy, Yamaguchi utility, and post-remission metabolic monitoring per latest guidelines. Early intervention yields durable remission, avoiding biologics in about 60% cases.

DECLARATION

Funding: NONE

Conflict Of Interest: NONE

Ethical Approval: NOT REQUIRED

REFERENCES

1. Gerfaud-Valentin M, Jamilloux Y, Iwaz J, Seve P. Adult-onset still's disease. *Autoimmun Rev*. 2014;13(7):708-22. doi: 10.1016/j.autrev.2014.02.005.
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. Immunologic research. 2015 Feb;61(1):53-62.
3. Yamaguchi M, Ohta A, Tsunematsu TO, Kasukawa RE, Mizushima YU, Kashiwagi HE, Kashiwazaki SA, Tanimoto KI, Matsumoto YO, Ota TO. Preliminary criteria for classification of adult Still's disease. J Rheumatol. 1992 Mar 1;19(3):424-30.
4. Fautrel B, Zing E, Golmard JL, Le Moel G, Bissery A, Rioux C, Rozenberg S, Piette JC, Bourgeois P. Proposal for a new set of classification criteria for adult-onset still disease. Medicine. 2002 May 1;81(3):194-200.
5. Wang MY, Jia JC, Yang CD, Hu QY. Pathogenesis, disease course, and prognosis of adult-onset Still's disease: an update and review. Chinese medical journal. 2019 Dec 5;132(23):2856-64.
6. Fautrel B, Mitrovic S, De Matteis A, Bindoli S, Anton J, Belot A, Bracaglia C, Constantin T, Dagna L, de Bartolo A, Feist E. EULAR/PreS Recommendations for the Diagnosis and Management of Systemic Juvenile Idiopathic Arthritis (sJIA) and Adult Onset Still's Disease (AOSD). InAnnals of the Rheumatic Diseases 2024 Nov 14 (Vol. 83, No. 12, pp. 1614-1627). Leeds
7. Akritidis N, Papadopoulos A, Pappas G. Longterm followup of patients with adult onset Still's disease. Scandinavian journal of rheumatology. 2006 Jan 1;35(5):395-7.
8. Magadur-Joly G, Billaud E, Barrier JH, Pennec YL, Masson C, Renou P, Prost A. Epidemiology of adult Still's disease: estimate of the incidence by a retrospective study in west France. Annals of the rheumatic diseases. 1995 Jul 1;54(7):587-90.
9. Mathews A, Prazad A, Neville B. Adult-onset still's disease: a case report and a comprehensive review. *Int J Res Med Sci*. 2024;12(12):4749-4753. doi: 10.18203/2320-6012.ijrms20243738.
10. Anderson CW, Shah PA, Roberts JR. Adult-Onset still's disease: is this truly a diagnosis of exclusion?. Hawai'i Journal of Medicine & Public Health. 2017 Nov;76(11 Suppl 2):3.
11. Pannu AK, Singla V, Suri V, Kumar R, Mathur Y, Mohindra R, Jain S. Adult-onset Still's disease and fever of unknown origin in India. Clinical and Experimental Medicine. 2023 Sep;23(5):1659-66.
12. Gopalarathinam R, Orlowsky E, Kesavalu R, Yelaminchili S. Adult onset Still's disease: a review on diagnostic workup and treatment options. Case reports in rheumatology. 2016;2016(1):6502373.
13. Laurent C, Foeldvari I, et al. Beyond Hyperferritinemia: Evaluating Ferritin as a Predictor of Advanced Therapy in Adult-Onset Still's Disease. *Diagnostics (Basel)*. 2025;15(20):2585. doi: 10.3390/diagnostics15202585.
14. Fukunaga T, Inden Y, Kato T, et al. Adult-Onset Still's Disease With Severe Hyperferritinemia and the Role of Glycosylated Ferritin. *Intern Med*. 2022;61(19):2901-2906. doi: 10.2169/internalmedicine.9764-22.
15. Srinivas V, Chandra Mouli SV, Sravan Kumar S. Adult-onset Still's disease. J Med Sci Res. 2015;3(3):126-9.
16. Kelleher AC, Samuels J. Atypical adult-onset Still's disease that fails to meet Yamaguchi

and Fautrel criteria. BMJ Case Reports CP. 2025 Jul 1;18(7):e267006.
17. Mehta B, Kim J, Park Y. Persistent pruritic plaques in adult-onset Still's disease: a case report. *The Rheumatologist*. 2025 Mar.
18. POUCHOT J, SAMPALIS JS, BEAUDET F, CARETTE S, DÉCARY F, Salusinsky-Sternbach MA, HILL RO, GUTKOWSKI A, HARTH M, MYHAL D, SENÉCAL JL. Adult Still's disease: manifestations, disease course, and outcome in 62 patients. Medicine. 1991 Mar 1;70(2):118-36.
19. Liu Z, Lv X, Tang G. Clinical features and prognosis of adult-onset Still's disease: 75 cases from China. International journal of clinical and experimental medicine. 2015 Sep 15;8(9):16634.
20. Fautrel B, Mitrovic S, De Matteis A, Bindoli S, Antón J, Belot A, Bracaglia C, Constantin T, Dagna L, Di Bartolo A, Feist E. EULAR/PReS recommendations for the diagnosis and management of Still's disease, comprising systemic juvenile idiopathic arthritis and adult-onset Still's disease. Annals of the rheumatic diseases. 2024 Dec 1;83(12):1614-27.
21. Leavis HL, van Daele PL, Mulders-Manders C, Michels R, Rutgers A, Legger E, Bijl M, Hak EA, Lam-Tse WK, Bonte-Mineur F, Fretter P. Management of adult-onset Still's disease: evidence-and consensus-based recommendations by experts. Rheumatology. 2024 Jun 1;63(6):1656-63.
22. Ali S, Khan M, Al-Mansoori A, et al. Adult-Onset Still's Disease in a 49-Year-Old Female in the UAE: A Case Report. *Cureus*. 2025;17(7):e87858. doi: 10.7759/cureus.87858.
23. Fukunaga T, Ohta R, Yamane F, Sano C. Adult-onset Still's disease with severe hyperferritinemia and the Asian salmon-pink rash: a case report. Cureus. 2022 Jun 23;14(6).
24. Galozzi P, Bindoli S, Doria A, Sfriso P. Progress in biological therapies for adult-onset Still's disease. Biologics: Targets and Therapy. 2022 Apr 21:21-34.
25. Li R, Liu X, Chen G, Tang G, Chen X, Liu X, Wang J, Lu L. Clinical phenotypes and prognostic factors of adult-onset Still's disease: data from a large inpatient cohort. Arthritis research & therapy. 2021 Dec 8;23(1):300.
26. Mathews A, Prazad A, Neville B. Adult-onset still's disease: a case report and comprehensive review. *Int J Res Med Sci*. 2024;12(12):4749-4753. doi: 10.18203/2320-6012.ijrms20243738.
27. Narváez J, Palacios-Olid J, García de Yebenes MJ, Holgado S, Olivé A, Casafont-Solé I, Castañeda S, Valero-Martínez C, Martín-López M, Carreira PE, Mora-Limiñana M. Non-Classical Complications of Adult-Onset Still's Disease: A Multicenter Spanish Study. Journal of clinical medicine. 2025 Jan 6;14(1):285.
28. Cleveland Clinic. Adult-onset Still's disease (AOSD) [Internet]. Cleveland (OH): Cleveland Clinic; 2025 [updated 2025 Jun 1; cited 2025 Dec 23].