Clinical report of five adult-onset Still's disease cases and discussion on early intervention strategies

Sir,

Adult-onset Still's disease (AOSD) is an uncommon systemic autoinflammatory condition with an unknown cause. It typically presents with high-spiking fevers, evanescent rash, sore throat, lymphadenopathy, and increased peripheral neutrophil counts. Diagnosis relies on excluding other conditions and is often delayed due to the wide variability in clinical presentation. The Yamaguchi criteria, known for their high sensitivity and specificity, are the most widely accepted standard for classification and were used in this case series (1). Recently, there has been growing interest in using hematologic biomarkers like the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) as accessible tools to assess systemic inflammation in a variety of diseases (2, 3). These biomarkers, derived from routine complete blood counts, have been used as prognostic indicators in cancer, cardiovascular diseases, and infections. However, their relevance and clinical utility in AOSD, particularly in predicting disease progression and complications such as macrophage activation syndrome (MAS), have yet to be fully explored.

We retrospectively reviewed five AOSD cases treated at the Emergency Centre of the First Affiliated Hospital of Xinjiang Medical University between January and December 2024. The study was approved by the Ethics Committee of the Huashan Hospital Fudan University and First Affiliated Hospital of Xinjiang Medical University and written informed consent was provided by all patients prior to the study start. All procedures were performed in accordance with the ethical standards of the Institutional Review Board and The Declaration of Helsinki, and its later amendments or comparable ethical standards.

All patients met the Yamaguchi diagnostic criteria, and infectious, malignant, and other autoimmune conditions were systematically ruled out. We recorded each patient's clinical features, laboratory results with an emphasis on NLR and PLR, treatment regimens, and clinical outcomes. Three of the five patients developed MAS, a life-threatening hyperinflammatory syndrome associated with AOSD. Notably, patients in cases 3 through 5 exhibited significant dynamic changes in NLR and PLR before clinical worsening. These observations suggest that temporal trends in these ratios may reflect disease activity and act as early indicators of complications such as MAS. This could be particularly valuable during the diagnostic window when AOSD is strongly suspected but not yet confirmed. In case 3, laboratory abnormalities, including hepatic dysfunction and coagulopathy, led to suspicion of MAS. A marked drop in PLR and NLR was observed before the clinical picture deteriorated. Timely immunosuppressive treatment with glucocorticoids, cyclosporine A, tocilizumab, and intravenous immunoglobulin (IVIG) facilitated recovery. Similarly, case 4 showed improved outcomes following the introduction of biologics in response to increasing inflammatory indices. In contrast, case 5, who had multiple chronic comorbidities and a prolonged disease course, received delayed intervention and ultimately succumbed to multiorgan failure despite aggressive supportive care.

Previous studies have highlighted the diagnostic utility of NLR. For example, Seo *et al*. (4) reported that NLR had greater sensitivity than traditional markers such as ESR, CRP, and ferritin in patients with AOSD. Furthermore, a prospective study by Daghor Abbaci *et al*. (5) demonstrated that an NLR threshold of 4 yielded a sensitivity of 93.8% for diagnosing AOSD. In other inflammatory diseases, including COVID-19, dynamic NLR and PLR patterns have been found to correlate with disease severity and prognosis (6). Given the accessibility of these markers through standard laboratory panels, we propose that NLR and PLR be incorporated into the diagnostic workup for suspected AOSD, particularly in emer-

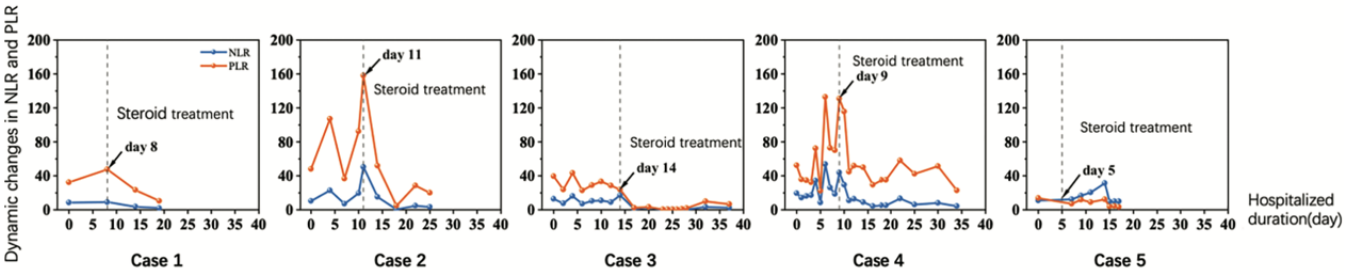

Fig. 1. Dynamic changes in neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) during hospitalisation in the five patients. The dashed line indicates the initiation of hormone therapy after admission.

Table I. Baseline information at admission.

	Case 1	Case 2	Case 3	Case 4	Case 5
Gender	Male	Female	Male	Male	Male
Age	48	54	56	28	71
Fever	Recurrent fever for 3 weeks	Recurrent fever for over 3 weeks	Recurrent fever for over 1 month	Recurrent fever for 1 month	Recurrent fever for 6 months
Rash	No	Yes	Yes	Yes	No
Sore throat	No	Yes	No	No	Yes
Hepatosplenomegaly	Yes	No	No	Yes	No
Lymphadenopathy	Yes	No	No	Yes	Yes
Neutrophil ratio (%; median)	78.75	81.30	68.45	88.90	89.70
Lymphocyte ratio (%; median)	13.95	8.20	22.55	6.70	7.75
Platelet count (median)	369.50	425	153.50	354	39.50
Ferritin	625.02	> 2000	> 2000	> 2000	> 2000
AST	35.78	62.28	162.2	81.16	100.12
Fibrinogen	2.01	2.30	1.45	1.76	2.09
Triglycerides	2.08	1.46	2.20	1.98	2.06
Hypertension	Yes	No	No	No	Yes
Diabetes	No	No	No	No	Yes
Renal insufficiency	No	No	No	No	Yes

Table II. Diagnostic criteria, MAS complication, and treatment of the five AOSD patients.

Patient number	Yamaguchi diagnostic criteria	MAS occurrence	Treatment
1	Recurrent fever >1 week, leucocytosis ≥10×10^9/L, neutrophils ≥80%, superficial lymphadenopathy, splenomegaly	No	GC+MTX
2	Recurrent fever >1 week, leucocytosis ≥10×10^9/L, neutrophils ≥80%, arthralgia, sore throat, typical rash	No	GC+MTX+TCZ
3	Recurrent fever >1 week, leucocytosis ≥10×10^9/L, neutrophils ≥80%, typical rash, abnormal liver function, ANA positive	Yes	GC+IVIG+TCZ+CsA
4	Recurrent fever >1 week, leucocytosis ≥10×10^9/L, neutrophils ≥80%, typical rash, lymphadenopathy, splenomegaly	Yes	GC+IVIG+TCZ+MTX
5	Recurrent fever >1 week, leucocytosis ≥10×10^9/L, neutrophils ≥80%, sore throat, lymphadenopathy, abnormal liver function	Yes	GC+LEF

CsA: cyclosporine A; GC: glucocorticoid therapy; IVIG: intravenous immunoglobulin; LEF: leflunomide; MAS: macrophage activation syndrome; MTX: methotrexate; TCZ: tocilizumab.

Table III. HS score of the five AOSD patients (total score >169 indicates high suspicion of MAS).

HS score	Case 1	Case 2	Case 3	Case 4	Case 5
Known underlying immunosuppression	0	0	0	0	18
Temperature	49	49	49	49	49
Hepatosplenomegaly	23	0	0	23	0
Cytopenia	0	0	24	24	0
Ferritin	0	35	35	35	35
Triglycerides	44	44	44	44	44
Fibrinogen	0	0	30	30	30
Serum AST	0	19	19	19	0
Evidence of hemophagocytosis on bone marrow aspiration	0	0	0	0	0
Total score	95	147	201	224	176

gency departments where rapid decision-making is vital. When used in conjunction with tools like the HScore (7), these ratios may help identify high-risk patients and prompt earlier therapeutic intervention. Although this case series is limited by its small sample size and retrospective design, our findings reinforce the potential value of monitoring NLR and PLR over time. Future multicentre prospective studies are needed to determine validated thresholds and assess the predictive performance of these biomarkers in larger populations.

Future integration of artificial intelligence with dynamic biomarker data may allow for real-time risk modelling in suspected AOSD, potentially transforming diagnostic and therapeutic paradigms. Early identification of inflammatory trajectories could enable pre-emptive treatment, improving outcomes in this often-elusive disorder.

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