

Adult-onset Still's disease with hepatomegaly

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Introduction

Adult-onset Still's Disease (AOSD) is a rare systemic inflammatory disorder with the prevalence estimated to be of one per 100,000 people. It has unknown aetiology. The disease mainly affects young adults and has a bimodal age distribution at 15-25 and 36-46 years of age (1). The main features are evanescent rash, high spiking fever, elevated leucocytes, and elevated liver enzymes (1, 2).

The clinical presentation of AOSD is non-specific and can mimic other infectious, rheumatological, autoinflammatory diseases, and haematological malignancies. Therefore, AOSD is diagnosed by excluding other conditions that may mimic AOSD (2).

We present a case of a middle-aged female who presented with fever for two weeks with arthritis and hepatomegaly. The absence of typical rash and presence of hepatomegaly culminated in a diagnostic dilemma. After extensive set of investigations, a diagnosis of ASOD was made. This case emphasizes the pertinence of considering ASOD as a differential diagnosis for prolonged fever and arthritis as well as highlights the fact that physicians should be hawk-eyed in detecting atypical presentations.

Case presentation

A 59-year-old lady with dyslipidaemia presented with intermittent high-grade fever for two weeks' duration with asymmetrical oligoarticular pattern of large joint involvement. She initially developed

left wrist joint pain without significant swelling or erythema which resolved in three days and subsequently developed pain in right shoulder joint without other inflammatory features. After one week, she developed painful erythematous swelling in the right knee joint that worsened gradually. Later, she developed lower back pain without neck pain or involvement of small joints. She also had myalgia and there were no respiratory or urinary symptoms. She developed right hypochondrial pain after two weeks of the onset of illness without jaundice or vomiting.

She had no travel history and there was no contact history with pets. She had no history of rashes, oral ulcers or hair loss. There was no history of loss of appetite or loss of weight.

On examination, she was febrile and pale. Figure 1 shows her temperature chart. There was no icterus, lymphadenopathy or rash. She was hemodynamically normal with a pulse rate of 92/min with regular normal volume and BP of 130/90 mmHg. There were no murmurs and no evidence of pericardial effusion. She had tender firm hepatomegaly of 1 cm below costal margin without splenomegaly. Her right knee joint was swollen which was tender and warm with evidence of mild effusion and right shoulder joint tenderness was noted. Rest of the examination findings was unremarkable.

She fulfilled the diagnostic criteria for AOSD (Table 2).

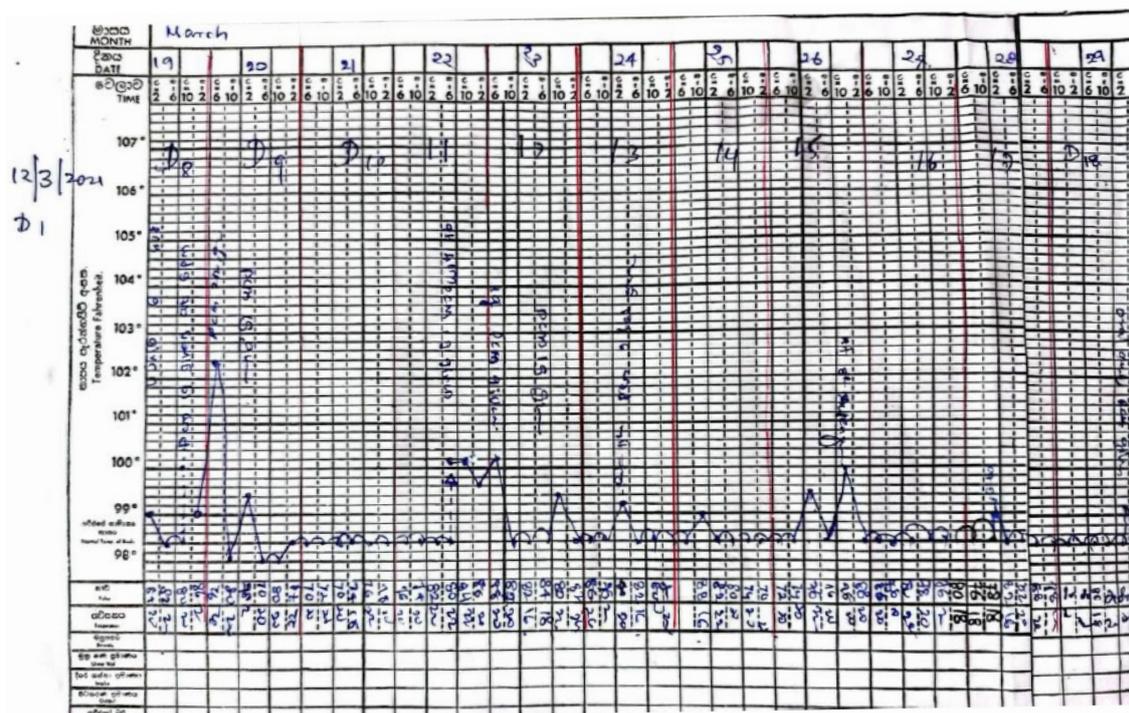


Figure 1: Quarter-hourly temperature plotted against days of illness.

Table 1: Summary of investigations on admission and during hospital stay

Investigations	Results
Full blood count	WBC - 11,900 /mm ³ (N - 81%, L - 16%)
	Hb - 9.9 g/dL
	MCV - 85 fl
	PLT - 383,000/μl
Erythrocyte sedimentation rate	138 mm/ hour → 100 mm/hour
C reactive protein	300 mg/L → 50 mg/L
Renal functions	Na ⁺ - 140 mmol/L, K ⁺ - 4.3 mmol/L
	S.Cr - 0.8 mg/dL
Liver functions	ALP - 355 U/L
	ALT - 238 → 162 U/L
	AST - 126 → 76 U/L
	Gamma GT - 462 U/L
	Albumin - 3.5 g/dL, globulin- 3.5 g/dL, Total bilirubin - 0.4 mg/dL
Serum ferritin	2252 μg/L
Lactate dehydrogenase	267 U/L (120 - 225)
Creatinine phosphokinase	27 U/L
Uric acid	2 mg/dL (2.6 - 6.1)

Investigations	Results
3 sets of blood cultures and urine cultures	No growth
Hepatitis B surface antigen and Hep C IgM antibody	Negative
Anti streptolysin O titre	Negative
Brucella antibody	Negative
Retroviral 1 & 2 antibodies	Negative
Cervical and vaginal gonococcal smear	Negative
Ultrasound scan of abdomen	Normal
Contrast enhance CT chest abdomen pelvis	
Anti-nuclear antibody	Negative
Double stranded DNA	
Anti-Cyclic citrullinated peptide antibody and Rheumatoid factor	
2D echo cardiogram & Trans oesophageal Echocardiogram (TOE)	No TOE evidence of infective endocarditis. Ejection fraction- 60%
Chest X ray	Normal
Mantoux test	Negative

WBC - White cell count, N - neutrophil percentage, L - lymphocyte percentage, Hb - Haemoglobin, PLT - platelet count, Na⁺ - Serum sodium, K⁺ - serum potassium, S.Cr. - serum creatinine, AST - aspartate aminotransferase, ALT - alanine aminotransferase, ALP - alkaline phosphatase

Table 2: Yamaguchi diagnostic criteria for AOSD

Major criteria	Fever 39°C for > 1 week Arthralgia or arthritis for > 2 weeks Typical non-pruritic salmon-colored rash Leukocytosis > 10,000/mm ³ with predominant granulocytes 80%
Minor criteria	Sore throat Lymphadenopathy Splenomegaly Abnormal liver function test Antinuclear antibody and rheumatoid factor negativity
Exclusion criteria	Infection Malignancy Rheumatological disease

Criteria for diagnosis - more than 5 criteria are present and more than 2 being major criteria without exclusion criteria.

After liaising with rheumatology team, she was started on naproxen 500 mg twice daily for 2 weeks. Her joint symptoms initially improved with analgesics. However, in the follow up visit she complained of persistent low grade joint symptoms which warranted treatment with methotrexate 15 mg weekly and prednisolone 20 mg daily after liaising with consultant rheumatologist. Our plan was to tail off steroids in 2 months while escalating methotrexate to 25 mg weekly.

Discussion

Adult-onset Still's disease (AOSD) is a rare inflammatory disorder, a subset of juvenile idiopathic arthritis which begins in patients' ≥ 16 years of age (1).

Patients with AOSD typically present with fever, rash, sore throat, and arthralgia. The fever of AOSD usually has quotidian or double-quotidian pattern (Figure 1). The characteristic rash in AOSD is described as salmon-pink, maculopapular evanescent eruption mainly affecting the trunk and extremities. Arthralgia and arthritis mainly involving large joints have also been noted. ASOD can cause lymphadenopathy, hepatosplenomegaly, serositis with central nervous system involvement in the form of seizure, aseptic meningitis, encephalitis or posterior reversible encephalopathy. Laboratory studies reveal elevated inflammatory markers and leukocytosis with neutrophil predominance and disproportionately elevated ferritin which is characteristic of AOSD. Liver transaminases are elevated in most of patients (1,2).

ASOD can have atypical presentations which might lead to diagnostic dilemmas, like in our case the patient was investigated extensively for pyrexia of unknown origin with arthritis as this was not a straightforward case and the typical rash was absent. But there were cases where Still's disease has presented with fever, arthralgia, and myalgia without rash (3). Hepatomegaly is reported in a minority of patients; the frequency in different studies ranges from 12 - 45% whereas elevations of transaminases seem to be common. Rarely liver failure can occur in Still's disease and hepatic involvement can be a presenting feature as well (1,4).

The Yamaguchi criteria (1992) are the most widely used criteria to diagnose AOSD with 93.5% sensitivity. There are 4 major and 4 minor criteria with 3 exclusion criteria. Five or more criteria must be met to make a diagnosis of AOSD, including 2 or more major criteria, after excluding infections, malignancies, or rheumatic diseases (5).

Our patient had a total score of 5 with 3 major criteria including fever lasting for more than one week, arthritis lasting for more than two weeks and leukocytosis with neutrophil predominance. She also had fulfilled 2 minor criteria which are negative immunological markers and abnormal liver function test. Infection, malignancy and other rheumatological diseases were excluded.

AOSD can follow 3 courses: monophasic, intermittent, and chronic; each group containing approximately one third of the patients affected. First two forms can progress into the chronic articular pattern (1). Our patient had chronic articular pattern requiring immune suppressive medications.

Informed written consent was obtained from the patient to publish this case report with relevant photographs.

Conclusions

AOSD is a rare disease with unknown etiology which should be considered in the differential diagnosis for pyrexia of unknown origin and arthritis with or without rash. Medical practitioners need to be vigilant of the atypical presentations of ASOD.

References

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