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Recurrent high-grade fever and joint symptoms in a 19-year-old: A diagnostic challenge of adult-onset Still's disease

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Abstract

Adult-Onset Still's Disease (AOSD) is a rare systemic inflammatory disorder characterized by spiking fevers, arthritis, and a salmon-colored rash. Its diagnosis is mainly clinical which mainly depends on excluding all the other potential causes. We report the case of a 19-year-old female presenting with intermittent high-grade fever (up to 103.5°F) for one month, accompanied by chills, rigors, arthralgia, and subjective weakness. Examination revealed tenderness in the Metacarpophalangeal (MCP) joints, swollen wrists with restricted motion, and a malar-like rash. Laboratory investigations showed leukocytosis ($16.3\times10^3/\mu L$), elevated ferritin (>1650 ng/mL), and ESR (120 mm/hr), with negative rheumatoid factor and anti-CCP antibodies. Blood cultures were sterile, and no evidence of infection was found. The diagnosis of AOSD was confirmed since the patient satisfied the Yamaguchi criteria. Her condition significantly improved after receiving supportive care, analgesics, and corticosteroids. This case highlights the importance of identifying the distinguishing features of AOSD and using diagnostic criteria to distinguish it from illnesses that mimic it. Early diagnosis and treatment can lead to favorable outcomes.

Keywords: Adult-onset still's disease; AOSD; Diagnostic challenges; Fever; Joint symptoms.

Background

Adult-Onset Still's Disease (AOSD) is a rare inflammatory disorder characterized by high-spiking fever, arthritis, and a salmon-pink rash, often with elevated inflammatory markers. It primarily affects young adults, though cases in older patients are increasingly reported. Elevated liver enzymes, lymphadenopathy, hepatosplenomegaly, and serositis are also commonly seen symptoms that support the diagnosis [1]. Additionally, people with AOSD may encounter many potentially fatal consequences [1,2]. First described by Eric Bywaters in 1971, AOSD is considered an adult counterpart of systemic-onset juvenile idiopathic arthritis. There isn't a single clinical, biochemical, histological, or radiological characteristic of the illness, nevertheless, as has long been disputed [3]. Early disease, especially when patients present as Fever of Unknown Origin (FUO), can be easily mistaken for other conditions such as malignant lymphoma or chronic infections [2]. One must take AOSD into consideration more frequently when patients present with fever of unknown origin [4]. Despite the lack of clarity surrounding the disease's precise pathogenic pathways, significant progress has been made in favor of the idea of a Still's disease spectrum [5]. The origin of this condition has been attributed to a number of factors, including infections (from bacterial and viral pathogens), a dysregulated immune system, and genetics (associated with Human Leukocyte Antigen [HLA] DRB1*1201 and 1501,

B35, DR2 and DR5). A genetic background would confer susceptibility to the development of autoinflammatory reactions to environmental triggers [6]. Macrophage and neutrophil activation are a hallmark of AOSD which can lead to a reactive hemophagocytic lymphohistiocytosis. The cytotoxic function of natural killer cells is diminished in patients with active AOSD, just like in the latter condition. Two proinflammatory cytokines involved in the pathophysiology of AOSD are IL-18 and IL-1β, which are processed by the inflammasome machinery and result in the release of IL-6 and Th1 cytokines as well as NK cell dysregulation that activates macrophages [7]. Diagnosis is mainly clinical, with Yamaguchi's criteria being one of the most widely used. It requires exclusion of infectious, neoplastic, and other autoimmune diseases. Laboratory tests are non-specific and reflects heightened immunological activity [8]. In this report, we present an atypical case of AOSD in a 19-year-old female, who was initially misdiagnosed and treated for malaria. She was ultimately diagnosed with AOSD based on supportive test results, prolonged high-grade fever, polyarthritis, and a distinctive rash. The case emphasizes the difficulties in detecting AOSD and the significance of taking it into account when making a differential diagnosis in young adults who have unexplained fever and systemic inflammatory signs.

Case presentation

A 19-year-old female patient, presented to the outpatient department at Lady-Reading-Hospital in Peshawar, complaining of a high-grade fever that had been coming on and off for the past month along with chills and rigors. There were three to four episodes of fever per day, with a maximum temperature of 103.5°F. On arrival, her vital signs, showed a heart rate of 125 beats per minute and a blood pressure of 110/70 mmHg. Additionally, the patient reported subjective weakness and intermittent spasticity episodes.

Examination findings: The patient showed notable musculoskeletal signs during physical examination. The Metacarpophalangeal (MCP) joints were painful, but there was no erythema or apparent effusion. Both wrist joints were enlarged, had a restricted range of motion, and were resistant to passive and dynamic motion. Multiple tender points were identified throughout her body. She also had a pink, erythematous rash that was consistent with a malar-like spread over her nose and cheeks. The remainder of the physical examination was unremarkable.

Laboratory investigations: To investigate possible explanations, extensive laboratory studies were carried out.

Complete Blood Count (CBC): With a white blood cell count of 16.3×10³/µL, primarily neutrophils (85%) and 12% lymphocytes, her complete blood count revealed leukocytosis. A mean corpuscular volume of 91.8 fL and hemoglobin levels of 9.29 g/dL indicated mild anemia.

Serum electrolytes: Hyponatremia (sodium 131 mmol/L) and hypokalemia (potassium 2.89 mmol/L) were found in her electrolyte panel. At 110 U/L, alkaline phosphatase was within the normal range.

Iron studies and inflammatory markers: Ferritin levels above 1650 ng/mL and an Erythrocyte Sedimentation Rate (ESR) of 120 mm/hr were both significantly high in the inflammatory marker profile.

Autoimmune profile: Anti-cyclic citrullinated peptide (anti-CCP) and rheumatoid factor antibody testing came out negative.

Blood culture: After five days, blood cultures indicated no development.

Urine-RE: A high-power field of urine showed four to six pus cells containing calcium oxalate.

Clinical course and follow-up investigations: The woman was initially misdiagnosed with malaria and treated accordingly but her symptoms persisted, necessitating further evaluation. Malaria, dengue fever, Rheumatoid Arthritis (RA), Systemic Lupus Erythematosus (SLE) and Adult-Onset Still's Disease (AOSD) were among the differential diagnoses considered due to her presentation of high-grade intermittent fevers, arthritis-like symptoms, a distinctive rash, and elevated inflammatory markers.

Table 1: Hematology and clinical chemistry report.

Test	Result	Unit	Reference range
WBC	16.3	x10³/µL	4.0-11.0
Neutrophils	85	%	40-75
Lymphocytes	12	%	20-45
Hemoglobin (Hb)	9.29	g/dL	11.5-16.5
MCV	91.8	fL	80-100
Sodium	131	mmol/L	135-145
Potassium	2.89	mmol/L	3.5-5.1
Alkaline Phosphatase	110	U/L	40-150
Ferritin	>1650	ng/mL	13-150
Blood Culture	No Growth	after 5 days	-
Rheumatoid Factor	<3.5	IU/mL	<14
Anti-CCP	<0.5	IU/mL	Negative: <17

`The Yamaguchi criteria for AOSD were satisfied by the patient's clinical presentation and laboratory results, which strongly supported the diagnosis with a score of 5.

Management: Corticosteroids, supportive antibiotics, and analgesics were used to treat the patient. She showed significant improvement and was discharged with a prescription for omeprazole 40 mg daily for 14 days, crotamiton sulfur lotion once daily for 5 days, desloratadine 5 mg twice daily for 14 days, and ibuprofen 200 mg twice daily for 10 days. Follow up was advised to opd for ongoing monitoring and symptoms management.

Outcome and follow up: Following the recommended course of corticosteroids and supportive drugs, the patient showed a noticeable improvement. Her symptoms, which included rash, joint discomfort, and fever, were almost completely resolved during the follow-up. Her joint assessment revealed full range of motion with no swelling or pain, and she did not disclose any new complaints. The patient was counseled on the significance of monitoring for any recurrence of symptoms and was encouraged to maintain follow-up appointments in order to manage any possible relapses of Adult-Onset Still's Disease.

Discussion

Adult-onset Still's Disease (AOSD) is an uncommon systemic

inflammatory disease that manifests as a salmon-colored rash, arthritis or arthralgia, and high-spiking fevers. Its symptoms coincide with those of other autoimmune, neoplastic, and infectious diseases, making diagnosis difficult. It has been noted clinical diagnosis of AOSD is typically made by exclusion while working up for a patient who has a fever of unknown origin [9]. The difficulty of identifying and treating AOSD is demonstrated by this case of a 19-year-old girl who presented atypically, particularly when the disease's early symptoms resemble those of more prevalent diseases.

Diagnostic challenges: Given our patient's history of recurring high-grade fever, joint pain, and an erythematous rash, infectious etiologies including dengue or malaria were initially considered. Due to their common presentation and endemicity in many areas, many illnesses are frequently misdiagnosed at first. The necessity of reevaluating instances of Fever of Unknown Origin (FUO) when first-line treatment fails was highlighted by the persistence of symptoms despite proper antimalarial therapy, which required further investigations. The Yamaguchi criteria, which call for the presence of both major and minor clinical symptoms as well as the elimination of other possible causes, were finally used to support the diagnosis of AOSD. Five criteria were met by our patient: increased ferritin, leukocytosis with neutrophilia, arthralgia, a characteristic rash, and a fever >39°C that lasted longer than a week. Given that hyperserotonemia is a defining feature of AOSD and frequently correlates with disease activity, her noticeably increased ferritin levels (>1650 ng/mL) are especially noteworthy. The diagnosis was further confirmed by the lack of anti-CCP and rheumatoid factor antibodies, which also served to distinguish AOSD from other autoimmune diseases including rheumatoid arthritis.

Management and outcomes: Immunosuppressive drugs and anti-inflammatory drugs are the cornerstones of AOSD treatment. Intravenous Immunoglobulin (IVIG) and biological agents (e.g. anti-TNFα, anti-IL-1 and anti-IL-6) have been successfully used in refractory cases [10]. On follow-up, our patient's symptoms were completely resolved since she responded effectively to corticosteroids and Nonsteroidal Anti-Inflammatory Medicines (NSAIDs). This result emphasizes how well early steroid medication works to reduce systemic inflammation and stop the course of the disease. The possible adverse effects of corticosteroid use, however, highlight the necessity of close observation and the evaluation of steroid-sparing medications in long-term situations. Biologics are recommended over traditional treatment. The function of IL-1 and IL-6 blocking medications are considered to be significant in the treatment of adult-onset still disease [11].

Clinical implications and learning points: This case highlights several important aspects of AOSD management.

High suspicion for AOSD: Patients with persistent fever, arthralgia, and hyperferritinemia should raise the suspicion of AOSD in clinicians, particularly if the results of autoimmune and infectious workups are unclear.

Use of yamaguchi criteria: The Yamaguchi criteria is a useful diagnostic tool for AOSD because they let clinicians assess the constellation of symptoms in a systematic way.

Timely and appropriate treatment: As this instance illustrates, early corticosteroid administration is essential to reduce systemic inflammation and enhance results.

Conclusion

Diagnostic delays may result from adult-onset Still's Disease's unique presentation, which might mimic more common diseases. It is crucial to understand the clinical criteria and employ a systematic strategy to rule out alternative causes. This example illustrates the value of reevaluating differential diagnosis in cases of chronic fever and shows effectiveness of steroid medication to reduce symptoms. Continued follow-up is necessary to monitor for recurrence and manage long-term disease activity.

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