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Case Report
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Rare Presentation of Misdiagnosed AOSD in the Absence of Cardinal Symptoms on Presentation

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Abstract

Background: Adult-onset Still's disease (AOSD) is a rare systemic inflammatory disorder characterized by quotidian fevers, evanescent rash, arthritis, and elevated inflammatory markers. Its diagnosis can be challenging due to nonspecific symptoms and overlap with other systemic conditions.

Case Presentation: We report the case of a young male who presented with malaise, peripheral edema, chest pain, fevers, and a productive cough, but without the cardinal symptoms of rash or early joint involvement typically associated with AOSD. Initial evaluations suggested infectious and autoimmune etiologies, leading to treatment with multiple antibiotics, colchicine, and doxycycline. The patient's condition was further complicated by pericardial effusion, persistent systemic inflammation, and delayed onset of arthritis during hospitalization. Extensive laboratory and imaging evaluations excluded malignancy and infectious causes. AOSD was ultimately diagnosed based on clinical features and elevated inflammatory markers. The patient improved with high-dose glucocorticoids and was later transitioned to steroid-sparing therapy with canakinumab.

Discussion: This case underscores the diagnostic challenges of AOSD when cardinal features are absent at presentation. The presence of atypical findings such as peripheral edema, productive cough, and diarrhea, alongside infectious serologies, initially confounded diagnosis. Recognition of evolving clinical features and multidisciplinary collaboration were critical in establishing the diagnosis and initiating effective treatment.

Conclusion: Clinicians should maintain a high index of suspicion for AOSD even in the absence of classic presenting symptoms. Early recognition and appropriate immunosuppressive therapy are essential to prevent complications and improve outcomes.

Keywords: Adult-onset Still's disease, misdiagnosis, atypical presentation, pericarditis, case report

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Introduction

Adult-onset Still's disease (AOSD) is a rare systemic inflammatory disorder characterized by high spiking fevers, evanescent rash, arthritis, and various systemic manifestations. First described by Bywaters in 1971 as the adult counterpart of systemic juvenile idiopathic arthritis, AOSD presents a diagnostic challenge due to its nonspecific symptoms and overlap with other conditions while typically manifesting after the age of 16 [1]. The etiology of AOSD remains unclear, but it is believed to result from a combination of genetic predisposition and environmental triggers, such as infections [2,3]. The estimated incidence remains variable in the literature among different ethnic groups.

The clinical presentation of AOSD is diverse, but three primary patterns characterize its course: monophasic, intermittent, and chronic. All three patterns exist on a continuum and can evolve into one another [3]. Typically, patients experience high spiking fevers exceeding 39°C (102.2°F); however, these are not self-reported in all cases [4,5]. The fever pattern is typically quotidian or double quotidian, peaking in the late afternoon or evening, and returning to normal or subnormal levels between spikes without use of antipyretics [6]. An evanescent, salmon-pink maculopapular rash often accompanies fever spikes, usually appearing on the trunk and proximal limbs and may be exacerbated by heat or mechanical irritation [6-8].

Joint involvement is prominent, with patients experiencing arthralgia or arthritis affecting both large and small joints symmetrically. Chronic arthritis can lead to joint destruction, particularly

in the wrists [4]. A severe sore throat is an early and frequent symptom, characterized by intense pharyngeal discomfort without significant tonsillar exudate [5]. Generalized lymphadenopathy and enlargement of the liver and spleen are common, detectable through physical examination or imaging studies [5]. Generalized muscle pain can be severe and often correlates with fever spikes, contributing to significant patient discomfort [6].

Inflammation of serous membranes can lead to pleuritis and pericarditis, presenting as chest pain and dyspnea. These manifestations require prompt recognition and management [9]. Laboratory abnormalities are significant in AOSD and may commonly include leukocytosis with neutrophil predominance, elevations in inflammatory markers (erythrocyte sedimentation rate [ESR] and C-reactive protein [CRP]), mild to moderate elevations in liver enzymes, and anemia, which is usually normocytic and normochromic [7].

Less commonly, patients may exhibit neurological symptoms like aseptic meningitis or cardiac involvement, such as myocarditis. Pulmonary manifestations, including interstitial lung disease, though rare, represent serious complications [8].

Diagnosing AOSD is primarily based on clinical criteria after excluding other potential causes. The most often used criterion, the Yamaguchi Criteria, require five or more criteria (with at least two being major criteria) from a combination of major and minor clinical features [9]. The major criteria include fever of at least 39°C lasting one week or more, arthralgia or arthritis lasting two weeks or more, non-pruritic maculopapular rash during fever spikes, and leukocytosis of at least 10,000/mm^3 with 80% or more neutrophils. The minor criteria consist of sore throat, lymphadenopathy and/or splenomegaly, abnormal liver function tests, and negative antinuclear antibody (ANA) and rheumatoid factor (RF) [10-12].

Case Presentation

Patient information/Presenting complaints/Medical history/Clinical findings

Patient with a past medical history of attention deficit hyperactive disorder with no known allergies presented to the emergency department with complaints of malaise, peripheral edema, productive cough, chest pain, and fevers for approximately 1 week. Additionally, he reported bilateral upper and lower extremity edema with generalized pain but denied joint pain. He reported an ongoing productive cough for approximately 7 days with a sore throat that had already resolved. He also reported diarrhea onset 1 week prior with 3–4 watery bowel movements per day that had resolved upon admission to the hospital.

While the patient denied a history of joint pain, outside records showed he had complained of headaches, clavicular pain, hand pain, and knee pain during a previous emergency department visit following a mechanical ground-level fall. Fevers were occurring daily, but primarily at night. Upon further conversation, the patient reported a history of fevers for the last 2–3 months for which he could not identify a clear pattern. Patient denied having a rash. Notably, the patient was admitted for a brief time at an outside facility but left on his own volition due to frustration with his medical care. From this hospitalization, the patient was noted to have leukocytosis, markedly elevated inflammatory markers with associated pleural and pericardial effusions concerning for infectious versus autoimmune etiology.

The patient was started on vancomycin and cefepime for 2 days, which were ultimately discontinued after no growth from his blood cultures for 48 hours. TTE revealed a small pericardial effusion. In the setting of pleuritic chest pain, the patient was treated for potential pericarditis with colchicine. He was also treated with doxycycline due to concerns of a tick-borne illness. Mild elevation of AST and ALT were noted. The patient ultimately elected to undergo a patient-directed discharge with multiple labs pending. He was discharged with a 14-day course of doxycycline and 3-month course of colchicine, but shortly returned to the emergency department with persisting symptoms.

A comprehensive evaluation was conducted during his subsequent hospitalization. CT chest with IV contrast revealed enlarged pulmonary veins and shadowing consistent with pericarditis with no overt infectious findings. A peripheral blood smear was not concerning for malignancy or other hematologic disorders. Notably, the patient was found to have a positive Hepatitis-B antigen with a low hepatitis-B antibody level. Epstein–Barr virus (EBV) IgG was elevated with an elevation of EBV nuclear antigen as well. Prior to his discharge from the previous hospitalization, SPEP with an IgM spike was noted with a normal kappa-lambda ratio. Transthoracic echocardiogram revealed a moderate posterior pericardial effusion measuring 1.5 cm.

Rheumatoid factor, anti-CCP, ANA, anti-Smith, RNP, double-stranded DNA, chromatin, SSA, SSB, anti-PR3, and anti-MPO were all within normal limits. During the admission, several subspecialties were consulted, including infectious disease, hematology & oncology, rheumatology, cardiology, gastroenterology, and pulmonology. While admitted, the patient developed swelling and tenderness in his distal interphalangeal joints, proximal interphalangeal joints, and metacarpophalangeal joints bilaterally that was constant and refractory to all opioids and acetaminophen. Topical diclofenac gel was able to minimize the patient's pain.

During the admission, the patient experienced worsening chest pain and shortness of breath, which was attributed to a pericardial effusion with associated pericarditis.

This patient's initial exam findings were significant for elevated temperature of 38.9°C, tachycardia with HR of 101, and hypertension with a blood pressure of 142/69. He was also found to have 3+ pitting edema in bilateral lower extremities, as well as trace edema in bilateral upper extremities. His cardiac and pulmonary evaluation were unremarkable with the exception of diminished breath sounds over the bilateral lung bases. The patient eventually developed pain, edema, and decreased range of motion in multiple interphalangeal joints bilaterally on the second day of hospitalization.

Based on the constellation of findings from the history/physical examination and the presence of several laboratory abnormalities (leukocytosis, elevated liver enzymes, ferritin level, and inflammatory markers), the diagnosis of AOSD was felt to be the most likely etiology for the patient's clinical presentation. Signs and symptoms included pleuritic chest pain, arthralgia, joint swelling, fevers, and sore throat. Additionally, the patient gradually improved with high-dose steroids, which suggested a probable autoinflammatory etiology. The patient underwent extensive malignancy/infectious laboratory evaluations that did not yield results consistent with a systemic process that could better explain his presentation.

Ultimately, the multidisciplinary team involved in this patient's

care reached a common conclusion and felt that high-dose glucocorticoid therapy was the most appropriate treatment option in the acute setting, with the addition of an IL-1 inhibitor at the time of discharge.

Treatment and management

Treatment options for AOSD are guided by disease activity and severity. Patients with mild disease can trial NSAIDs, although NSAIDs alone are not effective in approximately 75% of cases. Most patients require immunosuppressive therapy with glucocorticoids for acute flares. Chronic management usually involves the use of steroid-sparing agents including methotrexate, anti-IL-1, or anti-IL-6 medications. For refractory disease, anti-TNF agents or cyclosporin A can be used if other therapy is not effective [13].

The patient in this case was treated with high-dose IV steroids and subsequently transitioned to oral steroids at the time of discharge with plans to gradually taper after initiation of a steroid-sparing agent.

At the patient's initial outpatient visit with Rheumatology, his steroid dose was 40 mg of oral methylprednisolone daily. The patient reported significant improvement in signs and symptoms of joint pain, chest pain, joint swelling, and fevers. In addition to subjective improvement, laboratory results also improved. His leukocyte count, ESR, and CRP were mildly elevated but had decreased compared to discharge labs. His ferritin and liver enzymes returned to normal levels. He did report side effects consistent with glucocorticoid use, including weight gain, acne, and facial swelling.

Canakinumab was initiated at this visit at a dose of 300 mg every 4 weeks. After starting Canakinumab, the patient was instructed to begin tapering steroids with a dose reduction of 8 milligrams every 10 days. He was advised to return in 1–2 months for follow-up.

Discussion

In the presented case, the patient exhibited several atypical features when compared to the classic clinical presentation of adult-onset Still's disease (AOSD). Notably, the patient denied having the characteristic evanescent, salmon-pink rash that often accompanies fever spikes in AOSD. Additionally, while joint pain and arthritis are prominent early features in AOSD, affecting both large and small joints symmetrically, the patient initially denied joint pain. It was only during the admission that he developed swelling and tenderness in the distal interphalangeal, proximal interphalangeal, and metacarpophalangeal joints bilaterally. This delayed onset of joint symptoms differs from the typical presentation where arthritis is an early and persistent symptom.

Furthermore, the patient presented with peripheral edema and a productive cough, symptoms not commonly associated with AOSD. While serositis manifesting as pleuritis and pericarditis is a recognized feature of AOSD, the presence of significant peripheral edema and respiratory symptoms like productive cough may suggest alternative or additional diagnoses. The patient's positive Hepatitis B antigen and elevated Epstein–Barr virus antibodies introduced potential infectious etiologies not characteristic of AOSD. Moreover, the history of diarrhea and the detection of an immunoglobulin M (IgM) spike on serum protein electrophoresis are not typical findings in AOSD. These discrepancies highlight that the patient's presentation differs from the classic manifestations of AOSD, emphasizing the need for a comprehensive evaluation to rule out other conditions.

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