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Case Report

Adult-onset still's disease: a case report and a comprehensive review

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ABSTRACT

Adult-onset still disease (AOSD) is a rare inflammatory disorder affecting young adults, especially women, characterized by fever, arthralgia, skin rash, hyperleukocytosis and increased ferritin levels. It can be monocyclic, polycyclic, or chronic, with chronic cases primarily involving the joints. Ferritin, a protein that stores iron in the body, can be significantly elevated in AOSD due to systemic inflammation and the body's response to it. Treatment typically includes corticosteroids, methotrexate, and biological therapy. Recent treatments like anakinra, tocilizumab, and TNFα-blockers have shown promise. This case report details a 26-year-old woman with a one-month history of fever, arthralgia, and weight loss. She was diagnosed with a new onset AOSD, based on elevated ferritin, liver enzymes, IL-6, and IL-18 levels. Her symptoms improved with systemic corticosteroid therapy, and she was discharged with oral steroids, NSAIDS and regular follow-ups.

Keywords: AOSD, Arthralgia, Fever, Steroids

INTRODUCTION

Adult onset stills disease (AOSD) is a rare, complex, and multisystem disorder characterized by key symptoms such as arthritis, spiking fever, skin rashes, and elevated ferritin levels.[1,2] Initially described in 1971, AOSD typically presents in young adults with spiking fever, arthritis, and evanescent rash, along with other clinical features such as sore throat, hepatomegaly, splenomegaly, lymphadenopathy, and serositis.[1]

The disease is often difficult to diagnose and requires exclusion of autoimmune, infectious, and neoplastic disorders. The clinical progression of AOSD can vary, with a significant number of patients developing a chronic form with frequent flares. The disease's clinical manifestations are often influenced by the absence of specific symptoms and laboratory markers, making it difficult to monitor treatment efficacy.[3]

CASE REPORT

Chief complaints and history of present illness

The patient is a 26-year-old female with no significant past medical or surgical history who presented to our hospital with complaints of fever for one month, headache, nausea, dizziness, and weight loss of 5 kg over the past month from presentation. She initially visited a primary care clinic with these symptoms and was noted to have a temperature of 101°F. A complete blood count taken at the primary care clinic revealed leucocytosis and a significant decrease in hemoglobin count. She was given amoxicillin/clavulanate 625 mg three times daily, and acetaminophen 650mg three times daily as needed and referred to our hospital for further management.

She reported to the hospital two days after visiting the primary care center. By this time, her fever had reportedly

reduced, but she had developed multiple joint pains and abdominal distension in addition to her initial symptoms. Initial vitals were significant for a temperature of 99.2°F, mild tachycardia of 112/min, and tachypnea of 24/min. Further questioning revealed that her fever had been "on and off" for about a month, with the highest recorded temperature being 102.1°F. Her dizziness, headache, and nausea also started around the same time. Interestingly, she noted an unintentional weight loss of approximately 5 kilograms over the past month from presentation. Furthermore, since her visit to the primary care clinic, she had developed multiple joint pains, including bilateral knee pain, bilateral hip pain, and lower lumbar pain.

Physical examination

The patient appeared well-nourished, alert, awake, and oriented to person, place, and time with a normal mood and affect. The skin exam showed good turgor with no rash, unusual bruising, or prominent lesions. Hair had normal texture and distribution, and nails were of normal colour with no deformities. The head was normocephalic and atraumatic with no visible or palpable masses. The neck was supple without lesions, bruits, or adenopathy, and the thyroid is non-enlarged and non-tender. The abdomen had normal bowel sounds with mild hepatomegaly (5 cm below right costal margin), however, no tenderness, masses, or hernia was noted. Cardiovascular examination revealed no cardiomegaly or thrills, with a regular heart rate and rhythm, and both S1 and S2 heart sounds are present. Bilateral air entry was present and equal. Musculoskeletal examination revealed mild tenderness to deep palpation on the bilateral hip and lower lumbar area, as well as mild tenderness to superficial palpation on the bilateral knee area. Lachman test, anterior and posterior drawer tests, and McMurray test were negative. The spine was normal without deformity or tenderness, and there is no costovertebral angle tenderness. Extremities showed no amputations or deformities, cyanosis, edema/varicosities, and peripheral pulses are intact. The patient had a normal gait and station with no misalignment, asymmetry, crepitation, defects, masses, effusions, decreased range of motion, instability, atrophy, or abnormal strength or tone in the head, neck, spine, ribs, pelvis, or extremities. Neurologic examination showed cranial nerves II-XII are normal, sensation to pain, touch, and proprioception was normal, and deep tendon reflexes were normal in the upper and lower extremities with no pathologic reflexes.

Table 1: Significant laboratory exam.

Variables	Results	Interpretation
Complete blood count (CBC)		
Hemoglobin	7	Low. AOSD is known to cause anemia of chronic disease due to the underlying chronic inflammation.[5]
WBC	18200	Elevated. Leukocytosis, with predominance of neutrophils, is a typical finding in AOSD.[6]
MCV	69.12	Low. AOSD is known to cause anemia of chronic disease due to the underlying chronic inflammation.[5]
Platelet count	82000	Low. Although uncommon, AOSD can cause thrombocytopenia. This is often seen in severe cases or as a complication, especially when associated with conditions such as macrophage activation syndrome. [5]
MCH	24.02	Low
Comprehensive metabolic panel (CMP)		
SGOT	66	Elevated-could be due to autoimmune cell injury and inflammation of liver cells secondary to AOSD.[4]
SGPT	102	Elevated-could be due to autoimmune cell injury and inflammation of liver cells secondary to AOSD.[4]
Alkaline phosphatase	510	Elevated-known to be elevated in AOSD due to inflammation of bone and liver. [4]
Total protein	7.99	Within normal limits
Albumin	2	Low
Potassium	4.2	Normal
Serum electrolytes	140	Normal
Iron studies		
Iron level	85	Normal
Ferritin	12694	Significantly elevated: Ferritin levels are often elevated in cases of AOSD. [4]
Transferrin saturation	51	Normal
TIBC	149	Normal
Inflammatory markers		
ESR	78	Elevated. Inflammatory markers such as ESR is also shown to be elevated in AOSD.[6]
CRP	94	Elevated-Inflammatory markers such as CRP is also shown to be elevated in AOSD. [6]

Continued.

Variables	Results
Miscellaneous tests	
HBsAG	Negative
HCV	Negative
HIV	Negative
ANA	Negative
Gene Xpert	Negative
Anti CCP	Negative

Table 2: Laboratory exam and imaging studies.

Lab test	Result	Interpretation
SGOT	66	Elevated-could be due to autoimmune cell injury and inflammation of liver cells secondary to AOSD (14)
SGPT	102	Elevated-could be due to autoimmune cell injury and inflammation of liver cells secondary to AOSD (14)
Alkaline phosphatase	510	Elevated-known to be elevated in AOSD due to inflammation of bone and liver (14)
Total protein	7.99	Within normal limits
Albumin	2	Low
Serum electrolytes	140	Normal
Potassium	4.2	Normal
Transferrin saturation	51	Normal
Ferritin	12694	Significantly elevated: Ferritin levels are often elevated in cases of AOSD (19)
Iron level	85	Normal
TIBC	149	Normal
Hemoglobin	7	Low. AOSD is known to cause anemia of chronic disease due to the underlying chronic inflammation (20)
WBC	18200	Elevated. Leukocytosis, with predominance of neutrophils, is a typical finding in AOSD (21)
ESR	78	Elevated. Inflammatory markers such as ESR is also shown to be elevated in AOSD (21)
CRP	94	Elevated-Inflammatory markers such as CRP is also shown to be elevated in AOSD (21)
MCV	69.12	Low. AOSD is known to cause anemia of chronic disease due to the underlying chronic inflammation (20)
Platelet count	82000	Low. Although uncommon, AOSD can cause thrombocytopenia. This is often seen in severe cases or as a complication, especially when associated with conditions such as macrophage activation syndrome (20)
MCH	24.02	Low
HBsAG	Negative	
HCV	Negative	
HIV	Negative	
ANA	Negative	
Gene Xpert	Negative	
Anti CCP	Negative	

Multidisciplinary approach, imaging studies, and outcome

Initially, the patient was suspected to have systemic lupus erythematosus. However, since the ANA test was negative, expert consultations in rheumatology and hematology were obtained. The hematologist suggested a bone marrow study for the anemia, which showed cellular marrow with trilineage hematopoiesis. Both AFB and gram stain tests were negative. The rheumatologist recommended a PET CT, which showed no evidence of metabolically active disease. Furter imaging and studies included: An ultrasound of the abdomen revealed mild hepatomegaly. The echocardiogram (Echo) showed a left ventricular ejection fraction (LVEF) of 69%, pericardial thickening, and normal bi-ventricular function. An ECG indicated sinus tachycardia. A chest X-ray revealed a mild right-sided infiltrate and normal bronchopulmonary markings. The peripheral smear showed low red blood cell count with dimorphic characteristics. Direct coombs test was positive.

The multidisciplinary team agreed on starting the patient on intravenous (IV) steroid injection (Inj) methylprednisolone, IV fluids with ringer lactate 500 ml

over 3 hours, and IV ceftriaxone 2 gm based on the presumed diagnosis of AOSD. The patient's fever spikes resolved after the initiation of this treatment. The patient was medically stable to be discharged with per oral (PO) prednisolone 40 mg daily for two weeks, tetrafol Plus, acetaminophen 650 mg three times daily as needed, and pantoprazole 40 mg twice daily for two weeks. Follow-up with the primary care doctor, hematologist, and rheumatologist was recommended. She followed up at the outpatient departments after two weeks and is advised to continue her medications. Complete blood count, liver function tests, lactate dehydrogenase, serum ferritin (SF) and CRP were monitored regularly on each follow-up.

DISCUSSION

AOSD is a complex immune disorder with an unclear etiology. It affects both innate and adaptive immunity, with a higher interferon gamma-producing TH cell population in active patients.[7] AOSD is often triggered by bacteria or viruses, such as rubella, measles, mumps, Epstein bar wires, hepatitis A/B/C, HIV, CMV, parvovirus 19, adenovirus, influenza, coxsackie virus, *Campylobacter jejuni*, *Chlamydia trachomatis*, *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, and *Borrelia burgdorferi*.[8] Symptoms include high spiking fever, maculopapular evanescent salmon pink skin rash, sore throat, polyarthralgia, lymphadenopathy, hepatosplenomegaly, serositis, as well as elevated liver enzymes, leucocytosis with neutrophilic predominance, erythrocyte sedimentation rate (ESR), C-reactive proteins (CRP), and SF.[2] Arthralgia, often polyarthritis involving small joints, can be severe enough to show osteodestructive features like ankyloses.[9] Pharyngitis, myalgia, pleuritis, and abdominal pain can also be other concomitant symptoms.[10] There are three main patterns of clinical courses: Self-limiting or monocyclic systemic course which is single episode followed by sustained remission throughout the follow-up period. Intermittent or polycyclic systemic course which causes recurrent systemic flares with remissions in between the flares. And chronic articular course which is characterized by at least one episode of persistent symptoms.[2]

Laboratory findings of AOSD include elevated ferritin levels, ESR, CRP, ANA, RF, and other markers. Elevated ferritin levels indicate the disease with 80% sensitivity and 46% specificity, which increases to 93% when glycosylated ferritin is below 20%. Inflammatory markers such as ESR and CRP are typically elevated, and hematological abnormalities include leucocytosis, normocytic normochromic anemia, and thrombocytosis.[7,11]

Bone marrow biopsies may show granulocytic hyperplasia and hemophagocytosis. Elevated hepatic transaminases and aldolase levels are also common. Less than 10% of patients may show low-titre ANA and RF. Synovial fluid usually exhibits findings significant for inflammation, reflecting the systemic nature of AOSD. Additional tests needed for diagnosis include CBC with differentials and platelet count, autoantibody testing, ANA, RF, anti-citrullinated peptide (anti-CCP) antibodies, blood cultures, liver enzymes, bilirubin, aminotransferase, alkaline phosphatase, serum albumin, serologic testing, renal function tests, blood urea nitrogen (BUN), creatinine, urinary analysis, microscopic examination, and uterine culture.[1]

Therapeutic objectives for AOSD include managing symptoms, controlling physical signs, and preventing end-organ damage. Treatment approaches include NSAIDs, low-dose glucocorticoids, and medications like Anakinra or methotrexate. These strategies are based on observational studies and clinical experience, tailored to disease activity and patient response.[12] Treatment regimen can also include immunosuppressive drugs such as leflunomide, gold, azathioprine, ciclosporin A, and cyclophosphamide. IV gammaglobulin is also used in some cases. [12] Recent biological agents like anti-tumor necrosis factor, anti-IL1, and anti-IL6 have been successfully applied, often in combination with traditional immunosuppressive drugs. [12]

Differential diagnosis of AOSD

The differential diagnosis of AOSD includes a variety of infections, malignancies, and systemic diseases. Infections that need to be considered are tuberculosis, toxoplasmosis, brucellosis, yersiniosis, HIV, Epstein-Barr virus, cytomegalovirus, hepatitis, herpes simplex, influenza, parvovirus B19, measles, and rubella. Laboratory and physical findings in our patient led diagnosis away from infectious causes through various tests and clinical evaluations. Laboratory testing revealed negative HBsAG, HCV, and HIV. Epstein-Barr virus, cytomegalovirus, measles, and rubella were deemed less likely due to the lack of adenopathy upon physical examination. Herpes simplex likely would present with vesicular lesions, influenza with myalgias, and parvovirus B19 with resolution of fever within three days. Lack of cough and night sweats (tuberculosis), lack of immunosuppression (toxoplasmosis), and lack of gastrointestinal symptoms (yersiniosis) helped to further narrow the diagnosis.[13]

Malignancies such as lymphoma, castleman disease, myeloproliferative disorders, melanoma, and cancers of the colon, breast, lung, kidney, and thyroid are also part of the differential diagnosis. In pediatric cases, leukemia should also be considered. However, the lack of evidence of malignancy on PET CT and lack of constitutional symptoms made malignant causes less likely.

Systemic diseases that could present similarly include systemic lupus erythematosus, idiopathic inflammatory myopathies, vasculitis, hereditary autoinflammatory syndromes, neutrophilic dermatosis, sweet syndrome, reactive arthritis, sarcoidosis, Schnitzler syndrome, and Kikuchi-Fujimoto disease. Ferritin values below 3000 ng/mL generally are not associated with rheumatic

diseases. [13] Further, ANA and anti CCP resulted negative. The lack of muscular pain, skin lesions, and lymphadenopathy help lead the diagnosis away from inflammatory myopathies, vasculopathies, sweet syndrome, Schnitzler syndrome, and Kikuchi-Fujimoto disease. [13]

CONCLUSION

In conclusion, AOSD remains a difficult and multifactorial disorder that primarily affects young adults. We reviewed a 26-year-old young woman with a one-month history of fever, arthralgia, and weight loss who was diagnosed and treated successfully for AOSD. This case report underlines the effectiveness of systemic corticosteroid therapy in managing AOSD symptoms, providing further evidence for this treatment approach. This case report also highlights the diagnostic work-up to AOSD, which involves a combination of clinical symptoms, laboratory findings, and exclusion of other conditions, reinforcing the importance of a comprehensive evaluation. Although a good prognosis is common for most patients, a subset of potentially severe complications, including macrophage activation syndrome, may mandate watchful monitoring and prompt intervention. As our understanding of AOSD evolves, so too will our ability to provide targeted and effective treatments that improve outcomes for individuals affected by this disorder.

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