Adult Onset Still's Disease: A Case Report

Fayaz A Wani1, Waseem Raja2, Muzaffar Maqbool1, Rakesh K Koul1, Parvaiz A Shah3
1Assistant Professor, Department of Medicine, Government Medical College, Srinagar, Jammu and Kashmir, India, 2Registrar, Department of Medicine, Government Medical College, Srinagar, Jammu and Kashmir, India, 3Professor and Head, Department of Medicine, Government Medical College, Srinagar, Jammu and Kashmir, India

Adult onset Still’s disease (AOSD) is a rare inflammatory disorder of unknown etiology. Because of lack of a defined diagnostic test the diagnosis of AOSD can only be made after excluding infectious, malignant, and autoimmune diseases. A 21-year-old female patient was admitted in our hospital with intermittent high-grade fever, polyarthritis and rash. On further history, examination and laboratory investigation she was found to be fulfilling all the Yamaguchi criteria for AOSD. All other causes consisting of acute or chronic infections, hematological malignancies, and other rheumatic disorders were excluded by laboratory investigations. Patient was treated as AOSD with non-steroidal anti-inflammatory drugs and steroids and is completely free of symptoms.

Keywords: Adult onset still’s disease, Fever, Polyarthritis, Skin rash

INTRODUCTION

Adult onset still’s disease (AOSD) is a rare inflammatory disorder of unknown etiology characterized by high spiking fever, evanescent rash, arthritis, and multi-organ involvement.1 In 1896, the first case of an adult patient with signs and symptoms of AOSD was published. Subsequently, in 1971 Bywaters described 14 adults with similar presentations.2 Because of the lack of a defined diagnostic test the diagnosis of AOSD can be made after exclusion of several differential diagnoses in particular infectious, malignant, and autoimmune origin.3 The disease may have a monocyclic (25-30%), polycyclic (25-30%) or chronic course (30-50%). In those with the monocyclic course, the disease remits within a year, never to appear again.4 Recently, we diagnosed a patient as AOSD, with the monocyclic course, who went into remission after proper treatment and continues to be symptom-free even after stopping treatment.

CASE REPORT

A 21-year-old female, normotensive, non-diabetic, non-smoker, unmarried, admitted at Department of Medicine, Government Medical College, Srinagar with the complaints of fever and polyarthritis for last 1 month. Fever was high grade with a maximum temperature of 103°F, intermittent in nature, associated with chills and rigors. Fever occurred mostly at evening, persisted for 2-5 h and then subsided. Two weeks after fever patient developed polyarthritis involving the wrist, knee, ankle, proximal interphalangeal, and metacarpophalangeal joints. There was no history of morning stiffness, ocular symptoms, orogenital ulcers, urinary symptoms, photophobia and contact with infected persons or other systemic symptoms. In the hospital, the patient was found to have a rash on her body. The rash was pink colored, macular, non-pruritic, most noticeable at the height of temperature, distributed on the upper chest, back, and proximal parts of lower limbs. Examination revealed fair, well built, hemodynamically stable lady with fever (102°F). She had a pink macular rash over the chest, lower back, upper limb, and there was no rash over finger knuckles. Examination of the chest was unremarkable. Examination of the abdomen reveals moderate splenomegaly. Examination of central and peripheral nervous systems was unremarkable. There was no proximal or distal muscle weakness. Deep tendon reflexes were normal. Her ears, nose, and throat examination was normal. Investigations revealed hemoglobin of 10.7 g/dl, erythrocyte sedimentation rate (ESR) 110 mm in 1st h, persistent neutrophilic leukocytosis, total leukocyte count = 18.90 × 10^9/L, differential leukocyte count, neutrophils 82%, lymphocytes 12%, mixed 6%, peripheral blood film suggestive of anemia of chronic disorder with neutrophilic leukocytosis. Abnormal liver function test with hypoalbuminemia 2.65 mg/dl, elevated liver enzymes...
aspartate transaminase 100 U/L, alanine aminotransferase 38 U/L with normal bilirubin level, and slightly high creatine phosphokinase 378 U/L, and high lactate dehydrogenase 1439 U/L. The investigations such as blood sugar (F&PP), serum electrolytes, Kidney function test, serum calcium, phosphorous, magnesium, coagulation profile, thyroid function test were all normal. Urine routine examination was normal. Investigations for her pyrexia revealed blood culture, urine culture, throat swab culture were sterile. Sputum was negative for acid fast bacilli in three samples. Bone marrow examination was suggestive of anemia of chronic disease, bone marrow polymerase chain reaction for *Mycobacterium tuberculosis* was negative. Ultrasonography (USG) abdomen showed splenomegaly, contrast-enhanced computed tomography chest, and abdomen was normal except splenomegaly. Serological tests for typhoid, brucella were all negative. Other serological studies showed marked acute phase reactants with high C-reactive protein 32 mg/dl (NR 0-0.5 mg/dl) and hyperferritinemia 2074.25 ng/ml (NR 4.63-204). Antinuclear antibody (ANA), anti-ds-DNA, rheumatoid factor, and anti-cyclic citrullinated peptide antibodies were negative with normal arterial blood gas, electrocardiogram, echocardiogram and chest X-ray. USG abdomen revealed splenomegaly, the rest was normal. Based on her history, clinical examination and review of the laboratory evaluations diagnosis of AOSD was made using the Yamaguchi criteria. She was started on prednisolone 40 mg daily and non-steroidal anti-inflammatory drugs (NSAIDs) (aceclofenac 100 mg twice daily) after which she became afebrile for the first time in last 1 month after onset of illness. The patient showed considerable improvement was discharged home after 1 week on prednisolone 40 mg daily with tapering dose of 5 mg weekly. With proper treatment, now she is completely symptom-free and living a healthy life.

**DISCUSSION**

Still’s disease is named after an English doctor George Still, who described the condition in children in 1897. Bywaters in 1971 used the term “adult Still’s disease” to describe adults who had a condition similar to systemic onset JRA.³

Prevalence of AOSD is estimated to be 1.5 cases per 100,000-1,000,000. The diseases are slightly more common in women than men.²

The etiology of the disease is not complete understood. Observations supporting the role of genetic, infectious and environmental factors have been published.²

The diagnosis of adult Still’s disease is possible only by recognizing the striking constellation of clinical and laboratory abnormalities.⁶ AOSD is a diagnosis of exclusion. One needs to exclude infections and other rheumatological or blood disorders before arriving at the diagnosis of Adult’s Still’s disease.⁷ The infective, rheumatological, and blood disorders like a lymphoproliferative disorder or multiple myeloma were ruled in our patient.

Our patient was a 21 years female, who shared most of the features as laid down for diagnosis of AOSD by Yamaguchi (Table 1).

Most common clinical features of AOSD are: Arthralgia (98-100%), fever >39°C (83-100%), myalgia (84-90%), rash (87-90%), and sore throat (50-92%).⁴ Fever is an early feature, quotidian or di quotidian in pattern with rise of temperature in early morning/late afternoon.⁴

In the differential diagnosis of a patient with fever of unknown origin, AOSD should be considered and maculopapular rashes, arthralgia, and sore throat should raise the suspicion of AOSD.⁷ Febrile spikes are often accompanied by exacerbation of other symptoms like rash, fatigue, and arthralgia. The classic rash is an evanescent, Salmon-pink, maculopapular eruption, which frequently appears during febrile attacks and is predominantly in the proximal limbs and trunk with rare involvement of the face.⁶

Arthritis is often late onset and overshadowed by systemic features. This may be responsible for the disease being often categorized as pyrexia of unknown origin. The joints most commonly involved in decreasing frequency are wrist, knee, ankle and elbows. Erosion and fusion of the carpal bones (50%), tarsal bones (20%), and cervical spine (10%) may also be seen. A destructive arthritis is seen in up to 20-25% cases.⁴ Our patient developed a skin rash and arthritis 2 weeks after the onset of fever and was characterized by large and small joint polyarthritis.

Other clinical features include - Lymphadenopathy (48-74%), splenomegaly (45-55%), hepatomegaly (29-44%), pleuritis (23-53%), and pericarditis (24-37%). Patients may present with complications such as acute hepatic failure, aseptic meningitis, disseminated intravascular coagulation, etc. The characteristic findings in investigations are - Elevated ESR >50 (90-100%), neutrophil leukocytosis

<table>
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<tr>
<th>Table 1: Diagnostic criteria for AOSD (Yamaguchi)⁷</th>
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<td>Major criteria</td>
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<td>Fever &gt;39°C, &gt;1 week</td>
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<td>Arthralgia/arthritis &gt;2 weeks</td>
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<td>Typical rash</td>
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<td>WBC&gt;10,000 with &gt;80% PMNs</td>
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Exclusion: Infections, malignancy, rheumatologic diseases. Five criteria with at least two major criteria. AOSD: Adult onset still's disease. WBC: White blood cell, ANA: Antinuclear antibody, RF: Rheumatoid factor, PMN: Polymorphonuclear
(71-97%), anemia (59-92%), hypoalbuminemia (44-85%), thrombocytosis (52-62%), negative rheumatoid factor, and ANA (90-100%). An extremely elevated serum ferritin level is suggestive of AOSD. Although ferritin level may rise in other diseases and patient with AOSD may also have a normal ferritin level. A value of >1000 ng/dl in proper clinical setting being confirmatory of the diagnosis; specially if associated with low glycosylated ferritin level. \(^4\) Our patient had most of the clinical and almost all biochemical features of AOSD. Our patient had a serum ferritin level of more than 2000.

There is no single diagnostic test for AOSD. Before considering AOSD, many other diagnoses should be ruled out. Acute or chronic infections such as brucellosis, tuberculosis, and bacterial endocarditis infections; malignant diseases, especially lymphoma; and autoimmune disorders like systemic lupus erythematosus and systemic vasculitides are among the most important differential diagnosis.\(^5\)

Several diagnostic criteria have been proposed for the diagnosis of AOSD. Among them, Yamaguchi criteria and Cush criteria are most popular. The Yamaguchi criteria (1992), is most widely used to diagnose AOSD with 93.5% sensitivity. In this criteria, there are four major and four minor criteria with three exclusion criteria. The four major criteria include arthralgia more than 2 weeks, fever more than 39°C for more than 1 week, typical rash, and leukocytosis for more than 10,000/mm³ including more than 80% granulocytes. While the four minor criteria include sore throat, lymphadenopathy or splenomegaly, liver dysfunction, negative RF and ANA. Five or more criteria must be met in order to make a diagnosis of AOSD, excluding two or more major criteria, after excluding infections, malignancies or rheumatic diseases.\(^6\) The patient in this report was diagnosed as AOSD, as she fulfilled four major and three minor criteria, and all other diagnoses were excluded by doing all relevant investigations.

Because the disease is an inflammatory one, treatment is anti-inflammatory drugs. Aspirin or NSAIDs are recommended as the initial treatment in AOSD, but the response rate is reported to be as low as 20-25%.\(^8\) Liver enzymes should be closely monitored in patients in whom NSAIDs are used. Since the response to NSAID monotherapy is not enough, most patients are treated with corticosteroids in the course of their disease, with an efficacy of up to 95%. Prednisolone should be used for the patients who do not respond to NSAIDs and also to patients suffering from persistent anemia, pericarditis, serositis and marked elevation of liver enzyme.\(^10\)

Disease-modifying anti-rheumatic drugs - Methotrexate and hydroxychloroquine are required if there are persistent articular features. Tumor necrosis factors-α receptor blockers etanercept, infliximab are the recent advances in therapy, but costly and not available everywhere. Resistant cases may be treated with I/V gamma globulin/interferon-g, plus cyclophosphamide, a cyclosporine, mycophenolate mofetil.\(^4\)

Prognosis of AOSD is variable. Even with treatment, it’s difficult to predict the course of adults Still’s disease. Three different patterns have been described in AOSD. The first category of patients tends to have monocyclic or self-limited pattern with complete remission after treatment. The second group have intermittent or polycyclic pattern with recurrence of systemic and articular flares separated by periods of remission. The final group show chronic joint problems and are prone to joint destruction.\(^8\)

The patient under discussion was started on NSAIDs (aceclofenac), but did not show much improvement, so prednisolone 1 mg/kg body weight/day was added to which she responded very well. Once she responded, the dose of prednisolone was reduced to a minimum of 10 mg/day and continued for 6 months and then tapered and stopped. The patient is on follow-up and is doing well without any relapse. Our patient possibly has a monocyclic pattern and is in complete remission after treatment.

**CONCLUSION**

A diagnosis of AOSD should be kept in mind, if a patient in the age group of 15-25 or 36-46 years presents with high-grade intermittent fever, polyarthritis and skin rash of more than 2 weeks duration. However, the patient should be extensively evaluated to rule out other differentials of AOSD like acute or chronic infections, autoimmune disorders, vasculitis and malignant disorders.

**REFERENCES**


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