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Adult-Onset Still's Disease: A Case Report

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Abstract

Adult-onset Still's disease (AOSD) is a rare clinical entity with unknown etiology, characterized by arthritis, fever, evanescent rash and other systemic presentations. This report described a 45-year-old male who presented with sore throat, fever, arthritis, evanescent rash, raised liver enzymes and hyperferritinemia. He was diagnosed to have AOSD based on Yamuguchi criteria after the exclusion of other potential diagnoses. The patient partially responded to combined celecoxib and prednisolone. He was also prescribed methotrexate and his symptoms improved.

Keywords: Adult-onset Still's disease; Arthritis; Fever; Evanescent rash; Methotrexate.

Introduction

Adult Onset Still Disease (AOSD) is a rare systemic inflammatory disorder with unknown etiology. The prevalence of AOSD is estimated to be one per 100,000 people.[1] The disease mainly affects young adults and has a bimodal age distribution at 15-25 and 36-46 years of age.[2] The main features are: evanescent rash, high spiking fever, leukocytosis and elevated liver enzymes. In 1896, the first case of an adult patient with signs and symptoms of AOSD was published. Subsequently, Bywaters described 14 adults with similar presentations and the term AOSD was used in 1971.[3] We describe the typical presentations of a patient with AOSD.

Case Report

A 45-year old Malay male presented with multiple joint pains associated with unresolved fever for two weeks. The patient had also been having spiking fevers, especially in the evening associated with severe sore throat for the past two weeks. This was preceded by an evanescent, non-pruritic macular rash mainly over the trunk and extremities. According to him, he had been suffering from joint pains involving the shoulder, knee, hip, wrist and small joints of the hands until he could hardly ambulate on his own. Further history revealed that he had two similar presentations with a one year gap for the past two years. During the first presentation; the patient was treated as Rheumatoid arthritis and given Methotrexate, but the patient defaulted follow up after the pain had resolved. The second presentation resolved spontaneously with just painkillers he bought over the counter.

Examination revealed a well built male with fever of 39.0°C. There was no lymphadenopathy or splenomegaly. He had acute synovitis of wrists, elbows, ankles, knees and the small joints of the hands. His throat was mildly congested, however other systems were unremarkable. Hematological investigations showed leucocytosis of 23.9 × 10^9/L (93.0% neutrophils), elevated liver enzymes (alanine transaminase: 157 U/L; aspartate transaminase: 92 U/L). Both the acute phase reactants were high with C-reactive protein (265.4 mg/L) and erythrocyte sedimentation rate (ESR: 101 mm/hr). There were markedly elevated levels of serum ferritin (>10,000 ug/L). Anti-cyclic citrullinated peptide, antinuclear antibody (ANA) and rheumatoid factor (RF) were all negative. Renal and coagulation profiles were normal. Blood and urine cultures revealed no evidence of bacterial, fungal or viral infection. Computerized tomographic scan of the thorax and abdomen were normal.

Based on his clinical features and review of the laboratory evaluations, he was diagnosed to have AOSD using the Yamaguchi criteria.[4] He was started on Celecoxib 200 mg/bd and prednisolone 30 mg/daily. Over the next few days, the patient became afebrile. The arthralgia improved and he was able to ambulate himself after two weeks of needing assistance. The patient was discharged after one week on prednisolone 30 mg daily with tapering doses of 5 mg weekly. Besides, he was also given Cap Celecoxib 200 mg/od, rocaltrol 0.25 mg/od and calcium lactate 300 mg/bd. Two days after discharge, the patient presented back with multiple pruritic papules over the chest wall and upper limbs. This was different from the evanescent rashes from his initial presentation. In view of this; we attributed this new skin lesion as being allergic to either rocaltrol or calcium lactate which he was given, and both medications were stopped. Eight days later, the patient was readmitted to the ward for generalized body weakness with polyuria and polydipsia. Random blood sugar was high at 27.1 mmol/l, with no history of diabetes mellitus. The HBA1c charted 10.5% with significant glycosuria. His joint pain slightly improved and the pruritic rashes resolved, but he remained afebrile. He was then started on insulin and the blood sugar was controlled. The prednisolone was decreased to 10 mg with celecoxib 200 mg taken as needed. Since joint pain just partially improved; methotrexate 7.5 mg/weekly was initiated after the liver enzymes had normalized. During follow up; the steroids were tapered off and the symptoms improved.

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Discussion

AOSD was first described by Eric Bywaters in 1971.[3] Pathogenesis of the disease remains unclear; however, observations suggesting the role of genetic, infectious and environmental factors have been published.[5-7] There is a correlation between several cytokines in the pathogenesis of AOSD, including Tumor necrosis factor-alpha (TNF-α), interleukin (IL)-6 and IL-18. The levels of these cytokines are highly elevated in active AOSD.[8]

Patients with AOSD typically present with fever, rash, sore throat and arthralgia.[9] The fever normally exceeds 39.0°C and highest temperatures are seen in late afternoon and early evening,[10] as presented in this patient. The typical rash in AOSD is asymptomatic and is described as salmon-pink, maculopapular eruptions mainly affecting the trunk and extremities.[11-13] Sore throat is one of the major signs of AOSD and may be associated with odynophagia.[14] Arthralgia and arthritis mainly involving the knees, wrists, ankles and elbows have also been noted. The flare up of joint symptoms occurs during the febrile spikes.[15,16] Carpal joints are the target of most destructive arthritis in AOSD.[17] Other features of AOSD not noted in this patient include: lymphadenopathy,[18] hepatosplenomegaly,[19] pericarditis, pleuritis and central nervous system involvement.[20]

Laboratory studies show marked ESR elevation and leukocytosis with predominance of neutrophils. Disproportionately elevated ferritin is characteristic of AOSD.[21] Almost 70% of patients have hyperferritinemia,[14] which was thought to be due to cytokine secretion induced by the reticuloendothelial system or hepatic damage. In most cases however; the ferritin levels increased without obvious liver damage.[22,23] Liver enzymes are elevated in almost three quarters of patients.[24] Rheumatoid factor and antinuclear antibody are generally negative,[25] as seen in our patient.

In the early stages of the disease, diagnosis of AOSD is difficult. Before making a diagnosis of AOSD, other diagnoses including infections such as infectious mononucleosis, malignancies (especially lymphoma), and other rheumatic diseases such as systemic vasculitides should be ruled out. Investigations were done to rule out the possible causes before this patient's diagnosis was reached.

The Yamaguchi criteria (1992), is the most widely used criteria to diagnose AOSD with a 93.5% sensitivity.[26] In this criteria, there are 4 major and 4 minor criteria with 3 exclusion criteria. The 4 major criteria include: arthralgia more than two weeks, fever more than 39°C for more than 1 week, typical rash and leucocytosis for more than 10,000/mm^3 including more than 80% granulocytes. While the 4 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, including 2 or more major criteria, after excluding infections, malignancies or rheumatic diseases. The patient in this report fulfilled 4 major and 3 minor criteria.

Non-steroidal anti-inflammatory drugs (NSAIDs) or aspirin are recommended as the initial treatment in AOSD, but low response rate ahs been reported.[27] Prednisolone should be started for patients not responding to NSAIDs or suffering from pericarditis, serositis, persistent anemia or markedly elevated liver enzymes.[28] Disease modifying anti-rheumatic drugs (DMARDs) such as methotrexate have been used to control the acute symptoms, and it is suggested that at least 6 months of therapy should be given to allow ample time for the assessment of the therapeutic effect.[29] The reported patient was started on methotrexate and responded well. Sulfasalazine appears to have severe adverse reactions in AOSD and should be avoided.[30]

For patients who do not respond to conventional medications such as corticosteroids and DMARDs, biologic agents should be considered. Since cytokines such as TNF-alpha, IL1 and IL6 involved are implicated in the pathogenesis of AOSD; biologic agents targeting these cytokines have proven to be effective in treating AOSD. Three different patterns have been described in AOSD,[31] and the prognosis is variable. The first category of patients tends to have monocyclic or self-limited pattern with complete remission within a year. The second group have intermittent or polycyclic pattern with recurrence of systemic and articular flares separated by periods of remission as shown in our patient. The final group show chronic joint problems and are prone to joint destruction.[32]

Conclusion

AOSD is a rare disease with unknown etiology and pathogenesis. It should be considered in patients presenting with rash, arthritis and fever after excluding other possible diagnoses such as malignancies, infections and rheumatic diseases.

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