

*Case Report***A Case of Adult-Onset Still's Disease**Singh Yatendra¹, Vivekanand Satyawali², Paramjeet Singh², Makrand Singh²¹Assistant Professor, ²Associate Professor,
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*Received: 03/04/2014**Revised: 23/04/2014**Accepted: 25/04/2014***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 24-year-old female who presented with sore throat, fever, raised liver enzymes and cervical lymphadenopathy. Later on patient developed evanescent skin rash and polyarthritis pointed to a possible rheumatological diagnosis. She was diagnosed to have AOSD based on Yamaguchi criteria after the exclusion of other potential diagnoses. Patient was treated with combinations of NSAID and DMARD leading to remission. So early and aggressive treatment can herald possible fatal deformity and sufferings.

Key-words: Adult-onset Still's disease, Arthritis, fever, Yamaguchi criteria

INTRODUCTION

Adult Onset Still's 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] 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. [2] The disease mainly affects young adults and has a bimodal age distribution at 15-25 and 36-46 years of age. [3] The main features are: evanescent rash, high spiking fever, leukocytosis and elevated liver enzymes.

Because arthritis is typically late onset, patient had already under gone

numerous investigations and courses of antibiotics for presumed infections. 5-6% of patients being evaluated for Pyrexia of unknown origin (PUO) may be diagnosed eventually as Adult onset Still's disease. [4] AOSD remains a clinical diagnosis of exclusion; with typical clinical features, laboratory abnormalities and absence of other explanations. Various diagnostic criteria have been proposed. Among them Yamaguchi criteria has the greatest sensitivity and specificity.

CASE REPORT

The 24 years old non diabetic, normotensive, non-smoker, married female developed fever, which was high grade with maximum temperature of 104oF,

intermittent in nature, associated with chill and rigor, subsided by sweating. She also had throat pain and cervical lymphadenopathy. During that time patient was treated with oral antibiotics Azithromycin and Cefixime; keeping in mind differential diagnosis of pharyngitis and enteric fever. Patient had neutrophilic leucocytosis, high ESR. Blood C/S, urine C/S, throat swab C/S, Malaria Parasite card for Malaria, serology for hepatitis B, Hepatitis C and HIV were negative. With antibiotics fever decreased but without complete remission. About 2 wks of fever, patient developed rash with high swinging temperature. The rash was pink colored, maculo-papular, distributed on back and upper limb. The rash was most noticeable at the height of temperature. At the same time patient also developed arthralgia followed by arthritis involving multiple big joints, e.g. shoulder, hip, wrist, elbow. This pointed to a possible rheumatological diagnosis. The investigations revealed persistent neutrophilic leucocytosis, raised hepatic enzymes with normal bilirubin. All the microbiological tests were again negative. Chest X-ray, ultrasonography of whole abdomen was normal. A lymph node biopsy was done to exclude tuberculosis, it showed chronic non specific lymphadenitis. During that period patient was treated with I/V antibiotics-ceftriaxone, gentamycin, but there was no response. Because of the combinations of high grade fever, arthritis, evanescent rash, sore throat and lymphadenopathy, Adult onset Still's disease was assumed to be a possible diagnosis. Serum rheumatoid factor(RF), anti-Cyclic Citrullinated Peptide antibody(CCP), antinuclear antibody (ANA) were negative, CRP was positive and serum ferritin level was found to be significantly elevated (>2500 ng/dl). Transferrin saturation was normal, which was done to rule out other iron overload conditions. Bone marrow

examination was done to rule out Hemophagocytic syndrome secondary to adult-onset still's disease. Bone marrow examination showed reactive cellular marrow with mild histiocytosis. So with fulfillment of diagnostic criteria (yamaguchi criteria) and exclusion of other causes-a final diagnosis of Adult Onset Still's disease was made. Patient was treated with NSAID and Steroid. Prednisolone 40 mg/daily was given and patient was discharged after one week on prednisolone 40 mg daily with tapering doses of 10 mg weekly .4 wks after starting the treatment, most of the systemic features were improved ,But the arthritis did not subside completely. So DMARD was started and Hydroxy chloroquine was preferred. 4 wks after starting Hydroxy chloroquine 200 mg daily along with Aspirin, the patient had complete clinical & biochemical remission.

DISCUSSION

AOSD was first described by Eric Bywaters in 1971. 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] Laboratory studies show marked ESR elevation and leukocytosis with predominance of neutrophils. Disproportionately elevated ferritin is characteristic of AOSD. ^[18] 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. ^[19,20] Liver enzymes are elevated in almost three quarters of patients. ^[21] Rheumatoid factor and antinuclear antibody are generally negative, ^[22] 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 93.5% sensitivity. ^[23] 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/mm³ 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 4 minor criteria. Non-steroidal anti-inflammatory drugs (NSAIDs) or aspirin are recommended as the initial treatment in AOSD, but low response rate has been reported. ^[24] Prednisolone should be started for patients not responding to NSAIDs or suffering from pericarditis, serositis, persistent anemia or markedly elevated liver enzymes. ^[25] 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. ^[26] The reported patient was started on hydroxychloroquine and responded well. Sulfasalazine appears to have severe adverse reactions in AOSD and should be avoided. ^[27] For patients who do not respond to conventional medications such as corticosteroids and DMARDs, biologic agents should be considered. ^[28]

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. Our patient was require persistent follow up because Bone Marrow examination showed mild histiocytosis and there are few reported cases of hemophagocytic syndrome associated with this disease

Abbreviations

AOSD: Adult Onset Still's Disease, NSAIDs: Non-steroidal anti-inflammatory drugs, DMARDs: Disease modifying anti-rheumatic drugs, C/S: culture & sensitivity, PUO: Pyrexia of unknown origin, CRP: C –reactive protein.

Key message:

We report here, possibly the first documented case of Adult Onset Still's Disease (AOSD) in Kumaon region of Uttarakhand, with geographical diversity from other region. Generally, AOSD has a good prognosis. So early suspicion is must in patients having this type of presentation.

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