Case Report

Adult Onset Still's Disease - Presenting as PUO

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ABSTRACT

Adult onset Still's disease (AOSD) is a Chronic multi-systemic inflammatory disease of unknown etiology, that predominantly affects young adults. The common presentations of the disease are fever of unknown origin, polyarthritis and skin rash. Ambiguity in presentation and lack of serologic markers make diagnosis difficult. Here we describe a 27 year old married female presented with fever, skin rashes and arthralgia for 1 month. On Detailed examination and investigations she was found to be fulfilling Yamaguchi criteria for AOSD[1]. All other causes for acute or chronic infections, haematological malignancies and other rheumatic disorders were excluded by laboratory investigations. Patient was treated with Non-steroidal anti inflammatory drugs and steroids.

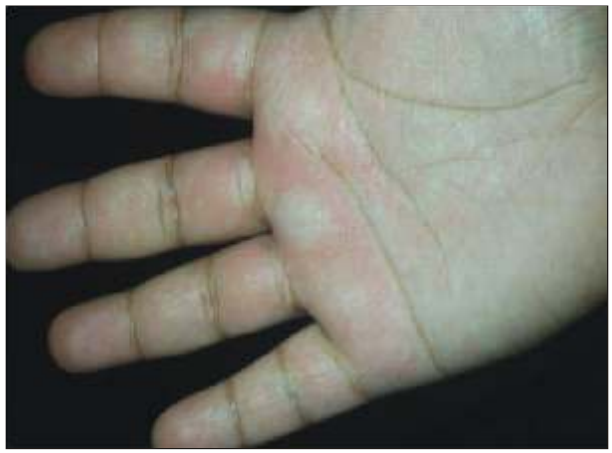
Introduction :

AOSD is characterised by fever, an evanescent skin rash, polyarthralgia, hepatosplenomegaly, leucocytosis and high serum ferritin level. It is a difficult diagnosis to make, as there is no pathognomic test for the disease and it is a great mimicker of other conditions , such as autoimmune disorders and haematological malignancies. AOSD is rare and has a bimodal age distribution in all ethnic groups with peaks at 15- 25 and 36-46 years of age in both sexes with an incidence of 0.16 cases /100000 persons /year. The disease may have a monocyclic (25-30%), polycyclic (25-30%) or chronic course (30-50%)[2]. In our case report, patient went into remission after proper treatment and continues to be symptom free even after stopping treatment.

Case Report :

A 27 year old lady, married, residing at Nalasopara, Mumbai came with chief complaints of fever of 1 month duration and pain in both knee joints since 25 days. Fever was high grade, 2-3 spikes / day, not associated with chills or rigors. Five days after fever he started experiencing pain in right knee joint follwed by pain in left knnee joint a week later. Joint pain was not associated with swelling or any skin discolouration. Waxing and waning of joint pain attacks was there and it also responded to NSAIDS. Patient also developed reddish-pink rash over hands on 7th day of fever which resolved spontaneously over few days later. On quarry there was No history of cough, weight loss, loss of appetite, burning micturition, oral ulcers or miscarriages.

Figure 1 : **Reddish-pink (Salmon pink) rash over palms and hands on 7th day of fever which resolved spontaneously during the course of illness**



On examination she was well built, conscious and oriented with evanescent reddish macular rash over both hands, which disappeared during course of illness. On the day of admission, patient was febrile 103°F with regular heart rate of 98 / min, blood pressure of 110/70 mmHg and normal jugular venous pressure, with no pallor, icterus, clubbing,

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lymphadenopathy. She had both knee joint arthralgia. Examination of chest, abdomen, central and peripheral nervous systems were unremarkable.

In private hospital Patient was worked up extensively for 3 weeks with investigations ranging from complete blood count, fever profile including malaria, leptospirosis, dengue, blood culture, Urine routine and culture, blood for fungal culture, ANA, RA factor, anti-CCP antibody, p-ANCA, c-ANCA, Quantiferon Gold TB test, bone marrow aspirate and biopsy, IgM for brucella, IgM for chikungunya, EBV, HIV, HBs Ag, HCV, CT brain and CT abdomen. All the investigations were within normal limits except the following deviations. CBC showed TLC 10800/mm^3 and raised neutrophils count (88%), ESR was raised (110 mm per hour), ferritin was raised (1529 ng/ml), USG abdomen and pelvis reveal mild hepatosplenomegaly, 2D Echo showed minimal pericardial effusion, CT-Thorax was s/o bilateral minimal pleural effusion, whole body PET scan did not show any other significant abnormality. Patient had received anti malarials and antibiotics like Ceftriaxone (for 5 days), Piperacillin + Tazobactum (for 7 days), Meropenem (for 11days), but fever persisted even after 4 weeks and hence patient was referred to our Sir J. J. Groups of Hospital Mumbai for expert management.

In brief, a 27 year old married female with symptoms of fever, arthralgia, and intermittent rash of 1 month duration; found to have mild Hepato-splenomegaly clinically and investigations showing leucocytosis with neutrophilia and raised ESR, polyserositis,raised ferritin levels with negative ANA and RA-Factor. Our working diagnosis was Antibiotic induced fever / AOSD. We stopped antibiotics soon after the admission but still fever persisted even after 3-4 days. Hence antibiotic induced fever was ruled out and our final diagnosis was AOSD. Patient was started on prednisolone 1mg/kg/day and NSAIDS Diclofenac sodium 50 mg bid. Patient became symptom free after 2-3 days and was discharged with advice of tapering of steroids after 1 month of full dose. Patient followed regularly every month and was symptom free on each visit. Her ESR was also decreased after 2 months.

Discussion :

George F Still, a pathologist, initially described AOSD in 1897. The characteristic features of this illness have subsequently been reported in adults, as detailed by Eric Bywaters in 19713. Pathogenesis of the disease remains unclear; however, roleof genetic, infection, environmental factors and cytokines have been published[4].

Patients with AOSD typically present with fever, rash, sore throat and arthralgia1. The fever normally exceeds 39.0°C and highest temperatures are seen in late afternoon and early evening5 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[1]. Sore throat is one of the features of AOSD and may be associated with odynophagia. 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. Other features of AOSD include lymphadenopathy[1], hepatosplenomegaly[1], pericarditis[1], pleuritis[1] and central nervous system involvement[6].

Laboratory studies show marked ESR elevation and leukocytosis with predominance of neutrophils. Almost 70% of patients have hyperferritinemia[7] that 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[8]. Rheumatoid factor and antinuclear antibody are generally negative1 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 rheumatoid diseases such as systemic vasculitides should be ruled out. Investigations were done to rule out the possible causes before diagnosis was reached in this patient. The Yamaguchi criteria (1992), is the most widely used criteria to diagnose AOSD with a 93.5% sensitivity[1]. 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 leukocytosis > 10,000/mm^3 with > 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 rheumatoid diseases. Our patient fulfilled 4 major and 2 minor criteria (except sore throat and liver dysfunction)

Non-steroidal anti-inflammatory drugs (NSAIDs) or aspirin are recommended as the initial treatment in AOSD, but low response rate has been reported[9]. Prednisolone should be started for patients not responding to NSAIDs or suffering from pericarditis, serositis, persistentanemia or markedly elevated liver enzymes[10]. 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[11]. Sulfasalazine appears to have severe adverse reactions in AOSD and should be avoided[12].

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 with variable prognosis have been described in AOSD[13]. 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[2].

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 rheumatoid diseases.

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