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Adult Onset Still's Disease

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ABSTRACT

Adult onset Still's disease(AOSD) is a rare systemic inflammatory disorder of unknown etiopathogenesis , it is characterized by arthritis, fever, evanescent rash and other systemic presentation . This report describes a case of 24 year old female presented with convulsions , fever , evanescent, salmon colored rash , multiple migratory joint pain and hyperferritinemia . She was diagnosed to have AOSD based on Yamaguchi criteria, after exclusion of other potential diagnosis . The patient responded to high dose steroids and was shifted to oral steroids and analgesics on recovery .

INTRODUCTION :

Adult onset stills disease (AOSD) or Wissler Fanconi syndrome is a rare inflammatory disorder of unknown etiology and pathogenesis. Its main features are high spiking fever , evanescent rash , polyarthralgia , lymphadenopathy , hepatosplenomegaly , leukocytosis , increased levels of serum ferritin, liver enzymes, ESR.[1]The first description of an adult patient with signs and symptoms of Still's disease was in 1896[2] .In 1971 Eric Bywaters described 14 adults with similar presentation to that of pediatric Stills disease; hence he used the term AOSD.[3-4]

Case report:

A 24 years female presented in our tertiary care institute with history of convulsions and altered sensorium . On detailed history patient had high grade fever with joint pain and sore throat since 2 weeks .This was preceded by an evanescent nonpruritic salmon coloured macular rash mainly on trunk and extremities. She had joint pain which was migratory in nature involving small and large joints .Further history revealed that she had similar presentation 1 year back with first episode treated with antiflammatory drugs, steriods, antibiotics. She responded to treatment but symptoms reappered on discontinuation of treatment .She had no history of cough with expectoration, abdominal pain, oral ulcers ,blood transfusion, drug abuse .The clinical examination revealed a moderately nourished with 39.8^0 C fever with pallor, inguinal lymphadenopathy (largest $1cm^2$) , pharyngeal congestion and reddish maculopapular rash present over trunk and arm. Her cardiovascular and respiratory system examination was within normal limit per abdomen examination revealed mild splenomegaly 2 cm below costal margin. Patient was in post ictal state regained consciousness on next day. CSF study was not significant. At this stage wbc counts were $18000mm^3$, HB-10.5gm, Platelets-2.8 lacks, ESR- 68 at the end of one hour, C-reactive protein positive. Her thyroid profile, Serum bilirubin, Serum electrolyte within normal limit, Her SGOT-538, SGPT-478. Her infectious disease profile was found to be negative which include (HIV ,HepatatisB,C, VDRL, Dengue , Brucella, weil- felix test, tuberculin, Gamma interferon , PS for Malarial Parasite). Her Auto immune work up was negative for (ANA, DsDNA, Antiphospholipid Anti body, ASO) . Her blood and urine culture were negative, chest x-ray, USG, & cardiac Doppler was normal except mild splenomegaly . Her bone marrow showed mild iron deficiency anemia . MRI brain with venogram suggestive of inflammatory cerebellitis . After the above extensive work up serum ferritin was send with high index of suspicion of AOSD which was 6173.57 supporting diagnosis of AOSD as per Yamaguchi criteria.[33] She was treated with high dose methyl prednisolone , Antibiotics , Anticonvulsant & IV fluid . She had no further convulsion after admission her fever, Rash , Arthralgia , leukocyte counts , ESR , subsided gradually & She was shifted to oral prednisolone , Antibiotic and Analgesics.

DISCUSSION:

AOSD was first described by Eric Bywaters in 1971 .[1] 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 pathogens is of AOSD , including tumor necrosis factor - alpha , 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] Features like splenomegaly[19] , lymphadenopathy[18] were noted in our reported case . Other features of AOSD not noted in this patient include: 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 , malignancies (especially lymphoma) , and other rheumatic diseases such as systemic vasculitis 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] 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 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.[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 responded well on prednisolone and NSAIDs . Sulfasalazine appears to have severe adverse reactions in AOSD and should be avoided.[30]

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 ofAOSD; 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 . The third group show chronic joint problems and are prone to joint destruction.[32] The prevalence of AOSD is estimated to be 1 per 100000[34] .The disease mainly affects young adults and has a bimodal age distribution 15-25 and 35-46 years35 as in patient reported in the case.

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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