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A Case Of Adult Onset Still's Disease

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ABSTRACT: Adult Onset Still's disease (AOSD) is a systemic inflammatory disorder of unknown etiology, typically characterized by a clinical triad of high fever, evanescent rash, and arthritis. This report described a 15-year-old female who presented with these symptoms along with raised liver enzymes and hyperferritinemia. After ruling out systemic infections, localized infections, malignancies and other rheumatological diseases, Adult onset Still's disease diagnosis was made according to Yamaguchi criteria (having 4 major features and 3 minor features). In patients with prolonged fever combined with musculoskeletal symptoms and macular rash, the differential diagnosis should include AOSD. Timely diagnosis and treatment of the disease can prevent complications and lead to a favorable prognosis**.**

Keywords:- Adult onset still's disease, Arthritis, Evanescent rash , Fever

I. BACKGROUND

Adult-onset Still disease (AOSD) is a rare systemic inflammatory disorder of unknown etiology. Its prevalence is less than 1/100,000 and it affects predominantly young people [1]. AOSD typically presents with high-grade fever, evanescent rash, sore throat, arthromyalgia, arthritis, serositis, discrete lymphadenopathy, hepatosplenomegaly, neutrophilic leukocytosis, hepatic cytolysis, and high serum ferritin [2, 3].

The pathogenesis of AOSD is not clear. Several factors have been suggested to contribute to the disease occurrence, including genetics, viral and bacterial infections, and immune dysfunction [4-7]. A number of studies reported an important role for interleukins (IL-1, IL-6, and IL-18), macrophage colony stimulating factor, interferon gamma (INF-g), and tumor necrosis factor alpha (TNF-a) in AOSD pathogenesis [8-11]. In a recent study performed in South Korea, serum levels of CXCL10 and CXCL13 in 39 patients with active AOSD were significantly higher than in patients with rheumatoid arthritis and healthy people [12].

In this paper, we aimed to report a case that presented with sore throat, fever, macular rash, and arthralgia and was subsequently diagnosed as AOSD.

CASE PRESENTATION

A 15 year old lady was admitted with the complaints of unresolved intermittent fever for more than 2 weeks with maculo - papular rash all over the body , multiple joint pain , throat pain , headache and body aches. According to her, she had been suffering from multiple joint pains involving the shoulder, knee, hip, wrist and small joints of the hands until she could hardly ambulate on her own but not associated with morning stiffness. Her past and family history was insignificant. Patient took cefpodoxime 200mg in the first week from a nearby community health center , but since the fever was not relieved ,she was started on amoxicillin clavulanate 625 mg for 5 days but symptoms persisted , after which she was admitted.

At the time of admission , she was conscious , oriented and her vitals were as follows :- blood pressure- 100/66 mm Hg, pulse rate- 104 bpm, and body temperature: 39.8°C. On physical examination, the pharynx was hyperemic and bilateral tonsils were hypertrophic but no lymphadenopathy. A diffuse maculo-papular rash that blanched on pressure was noted, which was more diffuse on the trunk, arms, and legs (Figure 1). Bilateral knee and elbow joints were swollen and tender upon palpation. There was no hepatomegaly or splenomegaly. Cardiovascular, respiratory and neurological examinations were normal . During hospitalization, the patient experienced intermittent high fevers (>39.4^{o}C) and her rashes would reappear with the fever.

Laboratory results were as follows: erythrocyte sedimentation rate: 110 mm/hour, C-reactive protein Positive, white blood cell count: 17,000/mm3, hemoglobin: 10.4 gr/dL, total protein: 6.3 gr/dL, albumin: 2.8 gr/dL, AST: 118 U/L, ALT: 48 U/L, ALP: 489 U/L, CK: 30 U/L, GGT: 250 U/L, ferritin: 3278 ng/mL, iron: 32 ug/dL, iron-binding capacity: 206 ug/dL, and transferrin saturation: 15.5%. Examination of the peripheral smear revealed neutrophils with a left shift. Rheumatoid factor (RF), anti-CCP (anti-cyclic citrullinated peptide), anti-nuclear antibody (ANA), anti-neutrophilic cytoplasmic antibody (ANCA), and anti-double-stranded DNA (anti

ds-DNA) were normal. Liver function tests were elevated; however, autoimmune and viral hepatitis serology was negative. Throat, blood, and urine cultures were sterile. Abdominal ultrasonography (USG) was normal.

We started prednisolone (60 mg once a day) for the patient. Subsequently, her joint pain began to improve. However, she continued experiencing fever (102.2°F, 39°C). In light of the available examinations and tests, the patient was diagnosed to have AOSD and was started on Non-steroidal anti-inflammatory drugs (NSAIDs) and steroid (prednisolone) . She was then discharged and called for a follow-up appointment 1 month later.

II. DISCUSSION

It is a systemic inflammatory disease with unknown etiology and pathogenesis. AOSD is characterized by fever, rash, and articular manifestations. It has no pathognomonic findings. According to the Yamaguchi criteria (1992), its diagnosis first requires ruling out infectious, malignant, and rheumatological diseases, followed by the presence of at least five features, with at least two of these being major diagnostic criteria[13] Yamaguchi criteria are given in Table 1. Our patient was considered to have AOSD, since her symptoms and signs met four major and three minor criteria. Patients with AOSD typically present with fever, rash, sore throat and arthralgia.[14]The fever normally exceeds 39°C and highest temperatures are seen in late afternoon and early evening,[15] 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.[16-18] Sore throat is one of the major signs of AOSD and may be associated with odynophagia.[19] Other features of AOSD not noted in this patient include: lymphadenopathy,[20] hepatosplenomegaly,[21] pericarditis, pleuritis and central nervous system involvement.[22]

Laboratory studies show marked ESR elevation and leukocytosis with predominance of neutrophils. Disproportionately elevated ferritin is characteristic of AOSD.[23] Almost 70% of patients have hyperferritinemia, 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.[24,25] Liver enzymes are elevated in almost three quarters of patients.[26] Rheumatoid factor and antinuclear antibody are generally negative,[27] as seen in our patient. Serum ferritin and glycosylated ferritin levels are considered to be specific diagnostic criteria for AOSD. A ferritin level 5-fold greater than the upper limit of normal has been reported to have a sensitivity of 80% and specificity of 46% for the diagnosis of AOSD [28]. ANA and RF negativity is important with respect to the differential diagnosis of AOSD from other connective tissue disorders. Elevated ferritin levels may be observed as an acute phase reactant in rheumatological diseases, although levels in these diseases are not elevated as high as in AOSD. Thus, it has been recommended to measure serum ferritin levels absolutely in cases with fever of unknown etiology, especially when rheumatological signs are also present. Excess elevation in ferritin level combined with elevated CRP and sedimentation rate supports the diagnosis of AOSD.

It is important to exclude the presence of any infection, malignancy or other rheumatic disorder as it precludes the diagnosis of AOSD. Our patient fulfilled 4 major and 3 minor criteria required for the diagnosis of AOSD, namely the exclusion of other disorders. An extensive investigation was drawn to exclude infectious aetiologies. Nevertheless, an unidentified microorganism could be responsible for these manifestations and empirical antibiotic therapy could have eradicated it. Although some clinical features attenuated during antibiotherapy, others, such as arthritis , so we considered that an infectious agent was unlikely and started corticosteroids.

Treatment protocols may include NSAIDs, aspirin, corticosteroids, and immune-modulating drugs, depending on disease severity and organ involvement. NSAIDs and acetylsalicylic acid should be given as first-line treatment in cases with musculoskeletal symptoms and fever [29] While 20% of cases respond to this therapy, adequate control of both arthritis and systemic signs requires modified antirheumatic drugs (DMARD) alone or combined with aggressive steroid treatment in the remaining 80% [30]. Presence of high fever attacks, severe articular symptoms, or internal organ involvement may justify corticosteroid (usually prednisolone) use at a dose of 1 mg/kg [31]. We began prednisolone 1 mg/kg/day, since our case had intermittent spikes of high fever combined with severe articular involvement.

Hematological abnormalities in AOSD vanish with remission or effective treatment of the disease [32]. Control laboratory tests in our patient revealed normalized hematological (white blood cell count) and biochemical parameters (AST, ALT, ALP, GGT, ferritin) after combined NSAID and steroid therapy.

III. FIGURES AND TABLES

TABLE 1: YAMAGUCHI CRITERIA.

Major criteria	Minor Criteria
Fever of at least 39°C lasting at least one week	Sore throat
Arthralgia or arthritis lasting two weeks or longer	Lymphadenopathy
Characteristic skin rash (nonpruritic macular or maculopapular salmon-colour) over the trunk or extremities during febrile episodes	Hepatomegaly or splenomegaly
Leucocytosis (10,000/mL or greater) with at least 80% granulocytes	Elevation in liver enzymes concentrations - ALT, AST, LDH
	RF and ANA negative

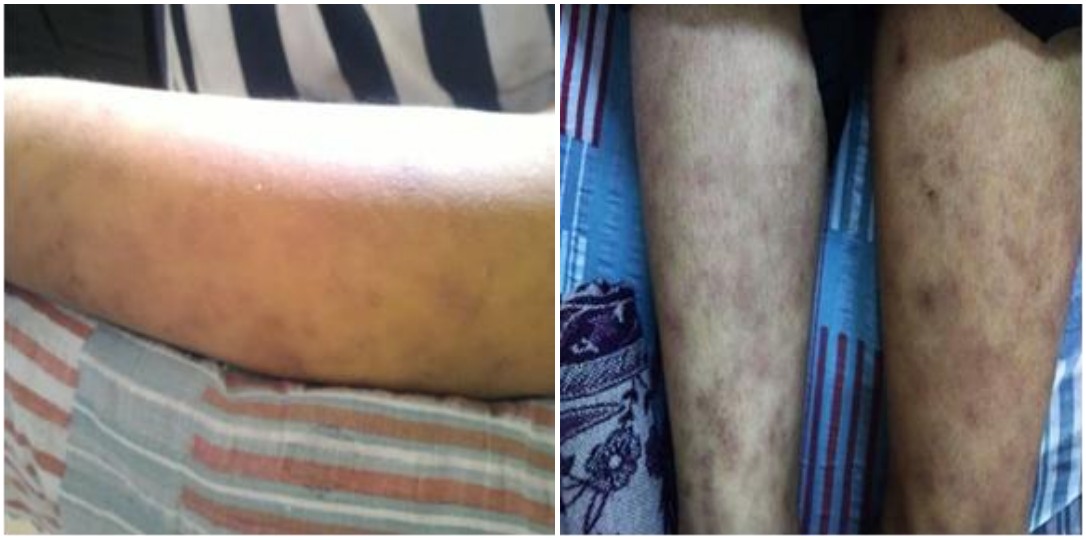

Figure 1: Macular rash over the arms and legs

IV. CONCLUSION

In patients with prolonged fever combined with musculoskeletal symptoms and macular rash, the differential diagnosis should include AOSD. Timely diagnosis and treatment of the disease can prevent complications and lead to a favourable prognosis.

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