Case Report: Adult-onset Still's Disease

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Abstract: Adult-onset Still's disease (AOSD) is an uncommon systemic inflammatory disease of unknown etiology and pathogenesis, characterized by high spiking fever, arthralgia or arthritis, skin rash and other systemic presentation. AOSD, one of the most important causes of fever of unknown origin, is diagnosed after ruling out infection, malignancy, and rheumatologic diseases. This report described a 19-year-old male who presented with, arthritis, fever, sore throat, evanescent rash, raised liver enzyme and hyperferritinemia. He was diagnosed to have AOSD based on Yamaguchi criteria after the exclusion of other potential diagnoses. The patient responded to combined methylprednisolone and methotrexate.

1 INTRODUCTION

Adult-onset Still's disease (AOSD) is a chronic systemic inflammatory disorder of unknown etiology, typically characterized by a clinical triad (daily spiking high fevers, evanescent rash, and arthritis) and a biological triad (hyperferitinemia, hyperleukocytosis with neutrophilia and abnormal liver function test (Bywaters, 1971; Magadur-joly *et al.*, 1995).

AOSD is a rare disorder and has a bimodal age distribution in all ethnic groups with peaks at 15-25 and 36-46 years of age and equal distribution between sexes (Efthimiou, Paik and Bielory, 2006; Chakr *et al.*, 2007).

There are no specific diagnostic test for AOSD. The diagnosis of AOSD remains one of exclusion; with typical clinical features, laboratory abnormalities and absence of other explanations. Several sets of different classification criteria have been proposed for AOSD. Among them Yamaguchi criteria are the most widely used (Bywaters, 1971).

There is no cure for AOSD; however, treatment may offer symptom relief and help to prevent complication. Treatment options include non-steroid anti-inflammatory drugs (NSAIDs) and aspirin, glucocorticoids, and immunomodulating drugs. Most patients require steroids at some point in the course of their AOSD. As it progresses without proper treatment, AOSD may lead to chronic arthritis and other complications. We describe the typical presentations of a patient with AOSD.

2 CASE REPORT

We present a case of 19-year-old male patient, admitted in our hospital with multiple joint pains associated with unresolved fever for two weeks. The patient had also having fever from afternoon until early evening associated with sore throat for the past two weeks. This was preceded by an evanescent, non-pruritic malar rash distributed on upper chest. Patient had been suffering from joint pains involving the shoulder, knee, hip wrist and small joint of the hands , pain was worsening with movement until he could hardly ambulate on his own three days before admission. There were no early morning stiffness, ocular symptoms, orogenital ulcers, gastrointestinal symptoms, urinary symptoms, contact to infected person or major systemic symptoms.

Examination revealed well built, oriented young male with fever of 39^{o}C. There was no lymphadenopathy or splenomegaly. He had synovitis of wrists, elbows, shoulders, ankles, knees and small joints of the hands, the range of movement was limited due to pain. He had reddish evanescent rash on upper chest (figure 1). Other systems were

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unremarkable. Hematological investigations showed leukocytosis of 36,000/uL (93% neutrophils), thrombocytosis of 573,000/uL, elevated liver enzymes (alanine transaminase 303.9 U/L; aspartate transaminase: 67.7 U/L). C reactive protein (CRP) was 6 mg/L and erythrocyte sedimentation rate (ESR) was 110 mm/h. Rheumatoid factor (RF), antinuclear antibody (ANA) and anti-double stranded DNA antibodies were all negative. HbsAg, Anti-HCV, anti-HIV were non-reactive. Renal, coagulation profiles and procalcitonin were normal. Blood and urine cultures revealed no evidence of bacterial or fungal infection. Thorax, thoraco-lumbosacral, pelvic radiograph were normal. Ultrasonography of the whole abdomen was normal. But there was very high ferritin 23,745 ng/mL (normal 15-120 ng/mL).

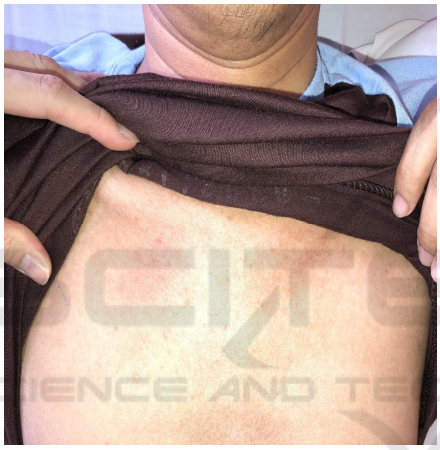

Figure 1. Evanescent rash on upper chest.

Based on his clinical features and review of laboratory evaluations, he was diagnosed to have AOSD using the Yamaguchi criteria (Yamaguchi *et al.*, 1992). He was started on methylprednisolone 125mg intravenously for 3 days and was followed by 0.5mg/kg prednisone, methotrexate 10 mg/weekly and folic acid 5 mg/weekly. Over the next few days, the patient became afebrile. Polyarthritis improved and he was able to ambulate himself. The patient was discharged after one week on methylprednisolone 24 mg daily with tapering doses of 4 mg weekly. Besides, he was also given lansoprazole 30 mg/od, methotrexate 10mg/weekly, folic acid 5mg/weekly. During follow up; the steroids were tapered off , the symptoms improved and decreased of ferritin to 1,254 ng/mL, leucocyte to 12,804/uL (72.1% neutrophils), ESR to 18 mm/h and CRP to 2.4 mg/L.

3 DISCUSSION

Still's disease is named after an English doctor name George Still, who described the condition in children in 1897. Still's disease is now knows as systemic onset juvenile rheumatoid arthritis (JRA). Adult-onset Still's disease was used to describe adults who had a condition similar to systemic onset JRA. It was firs described by Eric Bywaters in 1971(Bywaters, 1971). Although cause and pathogenesis of AOSD remains unclear, the condition may be triggered by infection, and also there are role of genetic and environmental factors (Daibata and Taguchi, 2002; Youm *et al.*, 2007).

Most common clinical features of AOSD are arthritis or arthralgia, fever, myalgia, rash, sore throat (Pouchot *et al.*, 1991). Fever is an early feature, usually quotidian (a daily recurring fever) or double-quotidian (two fever spikes per day) in pattern with rise of temperature in early morning/late afternoon and normally exceeds 39ºC, 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 (Phillips *et al.*, 1994).

Serum ferritin is considered to be specific diagnostic criteria for AOSD (Cagatay *et al.*, 2009). Elevated serum ferritin levels 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 ASD (Van Reeth *et al.*, 1994). Hyperferritinemia was thought to be due to cytokine secretion induced by the reticuloendothelial system or hepatic damage. Elevated ferritin levels may be observed as an acute phase reactant in rheumatological disease, although levels in these disease are not elevated high as in AOSD. Our patient had a serum ferritin level higher than 190 times the upper limit of normal. Liver enzymes are elevated in almost three quarters of patients (Motoo *et al.*, 1991). Rheumatoid factor and antinuclear antibody are generally negative (Pouchot *et al.*, 1991), as seen in our patient.

According to the Yamaguchi criteria, its diagnosis first requires ruling out infectious, malignant (especially lymphoma), and rheumatological diseases, followed by the presence of at least five features, with at least two of these being major diagnostic criteria (Yamaguchi *et al.*, 1992). Yamaguchi criteria are shown in Table 1. Investigations were done to rule out the possible cause before this patient's diagnosis was reached. Our patient was considered to have AOSD, since his symptoms and signs met three major and three

minor criteria of the Yamaguchi criteria are given below: Our patient had fever, arthritis, and neutrophilic leukocytosis from major criteria, and sore throat, liver dysfunction and RF and ANA negativity from minor criteria.

Table 1: Yamaguchi Criteria.

Major criteria	**Minor criteria**
Fever > 39ºC	Sore throat
Arthralgia/arthritis>2 weeks	Lymphadenopathy
Typical rash	Hepatomegaly or Splenomegaly
Neutrophilic leukocytosis	Hepatic dysfunction
	RF/ANA negative

Treatment for AOSD may include NSAIDS, aspirin, corticosteroids, and immune-modulating drugs, depending on disease severity and organ involvement. Presence of high fever attacks, severe articular symptoms, or internal organ involvement may justify corticosteroid. In patient with severe disease, such as life-threatening organ involvement and/or conditions such as severe hepatic involvement, cardiac tamponade, and/or disseminated intravascular coagulation, treatment with high-dose intravenous (IV) pulse glucocorticoid, followed by high-dose oral glucocorticoid. Methotrexate has been used successfully in a small series of people to treat AOSD. It may also be used as "steroid-sparing agent," meaning that if one gives methotrexate, smaller dose of corticosteroid may be sufficient to control disease (Ebrahim *et al.*, 2006). As seen in our patient had hepatic involvement and very high serum ferritin level we treated with intravenous high dose methylprednisolone for 3 days followed by 0.5 mg/kg prednisone. This was combined with methotrexate tablets, 10 mg weekly and folic acid 5mg weekly.

It is difficult to predict the course of AOSD, even with treatment. Three different patterns have been described in AOSD (Fautrel, 2008), and the prognosis is variable. The first category of patients tend to have monocyclic or self-limited pattern with complete remission within a year. Two other groups are have intermittent or polycyclic pattern and chronic joint problems. About one-third of people with the disorder may fall into each of the above patterns. Even if the patient symptoms free sometime they need to continue medications to control inflammation and prevent complications, at least 6 months of treatment (Ebrahim *et al.*, 2006).

4 CONCLUSION

AOSD is a rare disease with unclear etiology and pathogenesis. It should be considered in patients presenting with fever, arthritis and rash after excluding other possible diagnoses. We present this case is a typical presentation AOSD which was consistent with Yamaguchi criteria and responded well to methylprednisolone and methotrexate.

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