

Adult Onset Stills Disease A Rare Case Presentation

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Abstract

Case Report

Adult onset Still's disease (AOSD) is a rare systemic inflammatory disorder, its etiology remains elusive till date. This disease is typically characterized by a clinical triad of quotidian high-grade fever, evanescent rash and arthritis. The biological triad of hyperferritinemia, leucocytosis with neutrophilia and abnormal liver function test is noted. There are no specific diagnostic tests for AOSD, so the diagnosis of AOSD remains one of exclusion. We present a case of a 16 year female who presented to us with persistent fever since 2 months and other constitutional symptoms she was worked up for the same and was diagnosed to have AOSD based on Yamuguchi criteria after exclusion of other potential diagnosis – she was started on an NSAID, steroid and methotrexate, following which she showed a gradual and sustained response. She is on regular follow up, symptom free.

Keywords: Adult onset Still's disease (AOSD), hyperferritinemia, potential diagnosis.

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INTRODUCTION

AOSD is a rare disorder, first described in children by George Still in 1896, "stills disease" has become the eponymous term for systemic juvenile idiopathic arthritis [1]. In 1971, the term "adult Still's disease" was used to describe a series of adult patients who had features similar to the children with systemic juvenile idiopathic arthritis and did not fulfill criteria for classic rheumatoid arthritis (RA) [2].

Adult Still's disease is very uncommon. A retrospective French study estimated the annual incidence of adult Still's disease (ASD) to be 0.16 cases per 100,000 people, with an equal distribution between the sexes [3].

There is a bimodal age distribution, with one peak between the ages of 15 and 25 and the second between the ages of 36 and 46. However, patients older than age 70 have been reported [4].

The etiology of adult Still's disease (ASD) is unknown; both genetic factors and a variety of infectious triggers have been suggested as important, but there has been no proof of an infectious etiology, and the evidence supporting a role for genetic factors

has been mixed. It is uncertain whether all patients with ASD share the same etiopathogenic factors.

There are no specific diagnostic tests for AOSD. The diagnosis of AOSD remains one of exclusion and the differential diagnosis may be lengthy. Infectious, neoplastic, autoimmune diseases or drug hypersensitivity reactions can mimic the clinical manifestation of AOSD. Therefore, several sets of different classification criteria have been proposed for AOSD [5, 6]. The classification criteria proposed by Yamaguchi et al published in 1992 are the most widely used [7].

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 ASD; the usual prednisone dose is 0.5-1.0 mg/kg/day. Responses to steroid therapy range from 76% to 95% [8, 9].

CASE REPORT

A 16-year old female presented with multiple joint pains associated with unresolved fever for two months. The patient had been having daily spiking fevers for the past two months. This was preceded by an

evanescent, non-pruritic macular rash mainly over the trunk and extremities. According to her, she had been suffering from joint pains involving the wrist and small joints of the hands associated with joint stiffness (metacarpophalangeal and interphalangeal joints). Further history revealed that he had similar presentation 6 months back for which she took pain killers and continued with her daily routine. Patient came to our OPD with worsening of symptoms. On examination she was febrile but vitally stable on per abdominal examination she mild splenomegaly.

Hematological investigations showed leucocytosis of 15200 (80% were neutrophils), elevated liver enzymes. Both the acute phase reactants were high with C-reactive protein (33.6 mg/L) and erythrocyte sedimentation rate (ESR: 62 mm/hr). There were markedly elevated levels of serum ferritin (>10,000 ug/L). Anti-cyclic citrullinated peptide, antinuclear antibody (ANA) and rheumatoid factor (RF) were all negative. Renal and coagulation profiles were normal. Blood cultures revealed no evidence of bacterial, fungal or viral infection.

Investigations =

| | |
|--------------------------|---|
| 1. Hb | 6.9 g/dl |
| 2. Total leucocyte count | 15200 |
| 3. Platelet | 1.13 lakhs/cumm |
| 4. LDH | 1439 (Normal <247 U/L) |
| 5. Ferritin | 10,000 ng/ml (Normal female 11-306.8 ng/ml) |
| 6. RAF | 6.2 IU/ml (Normal <14IU/ml) |
| 7. HsCRP | 33.6 mg/dl (Normal <5 mg/dl) |
| 8. ESR | 62 mm/hrs (Normal 0-20 mm/hrs) |

Prednisolone 0.5 mg/kg/day and methotrexate was then started, and great response to therapy was shown, with total resolution of the clinical manifestations.

DISCUSSION

Patients with AOSD typically present with fever, rash, sore throat and arthralgia [10]. The fever normally exceeds 39.0°C and highest temperatures are seen in late afternoon and early evening [11], as presented in this patient. The typical rash in AOSD is asymptomatic and is described as salmon-pink, maculopapular eruptions mainly affecting the trunk, extremities and tends to occur with the fever and disappear during afebrile periods [12, 13]. 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 [14, 15]. Carpal joints are the target of most destructive arthritis in AOSD [16]. Other features of AOSD not noted in this patient include: lymphadenopathy [17], hepatosplenomegaly [18], pericarditis, pleuritis and central nervous system involvement [19].

Laboratory studies show marked ESR elevation and leukocytosis with predominance of neutrophils. Disproportionately elevated ferritin is characteristic of AOSD [20]. Almost 70% of patients have hyperferritinemia [14], Rheumatoid factor and antinuclear antibody are generally negative, 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 vasculitis should be ruled out.

The diagnosis is clinical, not based upon serology. At least seven sets of diagnostic criteria have been devised, however the Yamaguchi criteria have the highest sensitivity. Diagnosis requires at least five features, with at least two of these being major diagnostic criteria.

| Major criteria | Minor criteria |
|---|---|
| Fever of at least 39 °C for at least one week | Sore throat |
| Arthralgias or arthritis for at least two weeks | Lymphadenopathy |
| Nonpruritic salmon-colored rash (usually over trunk or extremities while febrile) | Hepatomegaly or splenomegaly |
| Leukocytosis (10,000/microL or greater), with granulocyte predominance | Abnormal liver function tests |
| | Negative tests for antinuclear antibody and rheumatoid factor |

Initial therapeutic decisions depend upon the degree of disease activity, including the extent and

severity of organ system involvement. Subsequent treatment decisions depend upon the clinical response

to initial therapies. Most patients present with mild to moderate disease, while a significantly smaller number present with severe disease. These groups can be distinguished as follows:

Mild Disease: Patients with mild disease may present with fevers and rash, as well as with arthralgias or mild arthritis. Some patients with mild disease will respond to nonsteroidal anti-inflammatory drugs (NSAIDs) alone, but the majority of such patients require at least low-dose glucocorticoid therapy for control of the inflammatory response and the signs and symptoms of disease.

Moderate Disease: Patients with moderate disease may experience high fevers, debilitating joint symptoms, or evidence of internal organ involvement that is not life-threatening or severe. Initial treatment of such patients generally requires glucocorticoids to control the inflammatory response and disease manifestations. Nonbiologic or biologic disease-modifying antirheumatic drugs (DMARDs) may be needed for long-term management, prevention of joint and other organ injury, and treatment of refractory inflammatory manifestations. Our patient fitted in this category.

Severe Disease: Severe disease is defined by the presence of life-threatening organ involvement and/or conditions, such as severe hepatic involvement, cardiac tamponade, and/or disseminated intravascular coagulation. Such patients require high-dose or pulse glucocorticoid therapy and should receive early intervention with a biologic agent, such as an interleukin (IL)-1 or IL-6 inhibitor.

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