Case Report

Still's Disease in Adult: A Case Report

Nabi G[1], Rahman NMW[2], Miah MB[3], Asha NN[4], Bonik M[5]

Abstract:
Still's disease in adult or Adult onset Still's disease (AOSD) is a rare systemic inflammatory disease of unknown etiology and pathogenesis. Some people have just one episode of adult Still's disease. In other people, the condition persists or recurs. AOSD is characterized by the classic triad of persistent high spiking fever, arthralgia and salmon colored skin rash. This inflammation can destroy affected joints, particularly the wrists. 5 to 10% of AOSD patients have fever of unknown origin (FUO) accompanied by systemic manifestations. However, diagnosing AOSD is often difficult due to the presence of several nonspecific symptoms and the absence of characteristic serological biomarkers. Definitive diagnosis of AOSD should be made only after excluding infections, granulomatous diseases, malignancy and other connective tissue diseases as the signs and symptoms of this disorder can mimic those of other conditions. Timely diagnosis and treatment of the disease with corticosteroids followed by maintenance therapy with disease modifying anti rheumatic drugs (DMARDs) or biologic drugs such as tumor necrosis factor alpha (TNF-α) agents or interleukin (IL-1) antagonists can prevent complications and lead to a favorable prognosis. Here we report an interesting case of a 20-year-old Bangladeshi male who presented in ZH Sikdar Womens Medical College Hospital (ZHSWMCH) with one-month duration of FUO along with skin rash, sore throat and arthralgia. After extensive workup, potential differential diagnoses were ruled out and the patient was diagnosed with AOSD based on the Yamaguchi criteria. High dose prednisolone (60 mg PO daily) was started and the patient was improved with significant relieve of fever, skin rash and joint pain. Then he was discharged in a stable condition with outpatient follow up instructions. At the OPD visit after 2 weeks, his problems were subsided completely and steroid dose was tapered appropriately. Then methotrexate 20 mg once weekly was started.

Keywords: Arthralgia, Fever, Rash, Prednisolone

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Introduction:
Adult onset Still's disease (AOSD) is a rare systemic inflammatory disease of unknown etiology and pathogenesis that presents in 5 to 10% of patients as fever of unknown origin (FUO) accompanied by systemic manifestations [1]. Only one episode of adult Still's disease can occur in some patients whereas in other patients the condition may persists or recurs. Due to the presence of several nonspecific symptoms and the absence of characteristic serological biomarkers, the diagnosis of AOSD is often difficult [2].

AOSD is typically considered as a diagnosis of exclusion and a definitive diagnosis should be made based only after excluding infections, granulomatous diseases, malignancy and other connective tissue diseases. The signs and symptoms of this disorder can mimic those of other conditions, including lupus and lymphoma. Timely diagnosis and treatment of the disease with corticosteroids followed by maintenance therapy with disease modifying anti rheumatic drugs (DMARDs) or biologic drugs such as tumor necrosis factor alpha (TNF-α) agents or interleukin (IL-1) antagonists can prevent complications and lead to a favorable prognosis [3].

We report an interesting case of a 20-year-old Bangladeshi male who presented in ZH Sikdar Womens Medical College Hospital (ZHSWMCH) with one-month duration of FUO along with skin rash, sore throat, and arthralgia. After extensive workup, potential differential diagnoses were ruled out and the patient was diagnosed with AOSD based on the Yamaguchi criteria. The case history, incidence, pathogenesis, clinical manifestations, differential diagnoses, diagnostic workup, treatment modalities and prognosis of AOSD are discussed in this case report.

Case report:
A 20 years old Bangladeshi male presented to the outpatient department (OPD) of ZHSWMCH with a four weeks history of high-grade fever, sore throat and dry cough. His fever was accompanied by non-pruritic macular skin rash on his trunk, arthralgia of bilateral ankles and knees, myalgia and night sweats and severe anaemia.

[1] Dr. Golam Nabi, Assistant Professor, Department of Medicine, ZHSWMCH, Dhaka, Bangladesh.
[2] Dr. NM Wahidur Rahman, Associate Professor, Department of Microbiology, ZHSWMC, Dhaka, Bangladesh.
[3] Dr. Md. Babul Miah, Senior Medical Officer, Department of Cardiology, BIRDEM, Dhaka, Bangladesh.
[4] Dr. Nazmun Nahar Asha, Medical Officer, Department of Medicine, ZHSWMC, Dhaka, Bangladesh.
[5] Dr. Mousumi Bonik, Intern Doctor, Department of Medicine, ZHSWMC, Dhaka, Bangladesh.

Address of Correspondence: Dr. Golam Nabi, Assistant Professor, Department of Medicine, ZH Sikder Womens Medical College & Hospital (ZHSWMCH), Dhaka, Bangladesh. Mobile: +8801819229570, Email: lotus_pharma75@yahoo.com

He denied the presence of joint stiffness in the mornings, blurry vision, eye pain, oral ulcers, headache, back pain, burning urination, recent travel, sick contacts, decreased appetite, or weight loss.

The rest of the review of the systems was negative. He had no significant past medical history, was not taking any medications previously, and had no significant family history. He had no known allergies. On physical examination, the patient was febrile with a temperature of 39°C, tachycardic with a heart rate of 110 beats per minute, tachypneic with a respiratory rate of 22 breaths per minute and a blood pressure of 120/70 mmHg. Patient had a maculopapular skin rash on the chest, abdomen and back. He also had inflamed throat without any exudates or cervical lymphadenopathy.

Musculoskeletal exam showed minimal tenderness in bilateral ankles and knees with normal active and passive range of motion. There were no signs of active synovitis in any of his joints. Abdominal examination showed mild hepatosplenomegaly. Cardiovascular, respiratory and neurological examination were unremarkable.

He was admitted to the hospital and his initial workup revealed elevated acute phase reactants [Erythrocyte sedimentation rate (ESR): 118 mm/hr, C-reactive protein (CRP): 80 mg/L and ferritin 41082 ng/ml], Hb% 7.9 gm/dl, mildly elevated liver function tests (aspartate transaminase: 67 U/L, alanine transaminase: 87 U/L, and alkaline phosphatase: 90 IU/L), normocytic anemia with normal white cell count with neutrophilic predominance (89%) and normal platelet count.

Rapid strep throat test, HIV, hepatitis panel, blood cultures, throat cultures and urine analysis were all negative. Anti-nuclear antibody (ANA), rheumatoid factor (RF) and cyclic citrullinated peptide antibody (Anti-CCP) were negative too. Chest X-ray showed no acute infiltrates. The patient received a course of antibiotic (cefuroxime + clavulanic acid) during hospitalization which did not resolve his symptoms.

A few days following admission, the patient experienced nausea, vomiting and left upper quadrant abdominal pain without diarrhea. An abdominal and pelvic CT scan was done which was normal except for a borderline hepato-splenomegaly. Hematological conditions such as leukemias, lymphomas and hemophagocytic lymphohistiocytosis were ruled out due to the absence of physical and laboratory findings. An anti-neutrophil cytoplasmic antibody (ANCA) panel, Lyme disease serology and HLA-B27 tests were done and the results came back negative.

After ruling out tuberculosis and other infectious causes, a diagnosis of adult onset Still's disease was made based on the Yamaguchi criteria. Subsequently, the patient was started initially on high dose prednisolone 60 mg PO daily. Since then, the patient was improved and the intensity of his fever, skin rash and ankle and knee pain came down significantly. The patient was discharged home in a stable condition with outpatient follow up instructions. During the next OPD visit after 2 weeks, his fever, rash and arthralgia subsided completely and his steroid dose was tapered appropriately. Then methotrexate 20 mg once weekly PO was started.

Discussion:

AOSD is a rare systemic inflammatory disease of unknown etiology. It was initially described by Bywaters in 1971 as a distinct clinical entity in adults that is quite similar to the one observed in children known as systemic juvenile idiopathic arthritis (sJIA) [1]. It has an estimated prevalence of 1.5 cases per 1,00,000 to 10,00,000 people. It has been described all over the world and has a bimodal age distribution with 2 peaks, the first peak affecting people within 15–25 years of age and the second peak affecting people within 36–46 years of age [2]. Although it usually affects the younger adult population, it can also affect elderly people [3]. The disease affects predominantly females as compared to males [4].

The exact pathogenesis of AOSD is unknown. Several factors such as genetics, infectious (bacterial and viral) agents and environmental factors have been thought to play a causative role [5]. An important step in the pathogenesis of AOSD is interleukin-18 (IL-18) mediated macrophage and neutrophil activation (evidenced by upregulation of CD 64 in patients with active disease) [6]. The pathogenesis of AOSD involves the interplay of numerous activated cytokines. There is increased serum levels of tumor necrosis factor alpha (TNF-α), IL-1, IL-6, IL-18, Interferon gamma IFN-γ, IL-8 and soluble interleukin-2 receptor.

Clinically, the most classic manifestations of AOSD are fever, rash, sore throat and arthralgia with fever and arthralgia being the most common among them [7]. The fever is usually a high spiking quotidian fever (≥39°C) that occurs in the evening with return of normal temperature in the next day morning. The fever is often accompanied by other symptoms or could present as PUO (pyrexia of unknown origin) alone [8]. In our patient, his high-grade fever occurred mostly during the evenings and was accompanied by pharyngitis and maculopapular skin rash.

Nonsuppurative pharyngitis is one of the common earlier findings in AOSD and can either precede the

development of fever or can occur along with other symptoms. The pharyngitis in AOSD patients is proposed to be from underlying cricothyroid perichondritis [9]. The characteristic rash in Still's disease is a transient, nonpruritic, salmon colored, macular or maculopapular lesion often observed during febrile episodes. The most common locations of the rash include the trunk and proximal extremities.

Another common finding in many AOSD patients is an exaggerated urticarial response to cutaneous stimuli (i.e., the scratch test) which is referred to as dermatographism [10]. Intense arthralgia is ubiquitously seen in all AOSD patients. The most commonly involved joints are the knees, wrists, ankles and elbows. AOSD often involves the distal interphalangeal joints of the hand, which are commonly spared in inflammatory joint disease of the young adults (e.g., SLE and rheumatoid arthritis) with the exception of psoriatic arthritis. Hepatosplenomegaly can be a common manifestation in the early phase of the disease. Less commonly, pericarditis or pleuritis may occur.

The laboratory tests in AOSD show features suggestive of an inflammatory process. The most common laboratory abnormalities include:

(i) Elevated erythrocyte sedimentation rate (ESR)
(ii) Leukocytosis (in most cases within 15,000 – 30,000, mainly neutrophils)
(iii) Thrombocytosis >4,00,000
(iv) Elevated ferritin levels

Elevated ferritin level is a nonspecific but common finding and a helpful feature for diagnosing AOSD [11]. The ferritin levels are often higher (>2000 mg/mL) but normal levels of serum ferritin should not rule out the diagnosis of AOSD. Serum albumin < 3.5 gm/dL, anemia of chronic disease and elevated hepatic transaminase levels. Rheumatoid factor and antinuclear antibody tests are usually negative. Synovial and serosal fluids are inflammatory type with neutrophilic predominance.

Diagnosing AOSD is often difficult due to the presence of several nonspecific symptoms and the absence of characteristic serological biomarkers. The Yamaguchi criteria are the most widely cited criteria and are shown to be the most sensitive ones (93%) [12]. The major and the minor criteria of the Yamaguchi criteria are shown below.

Major Yamaguchi criteria are as follows:
i. Fever of at least 39°C for at least a week.
ii. Arthralgia or arthritis for at least 2 weeks.
iii. Nonpruritic salmon colored rash on trunk/ extremities.
iv. Granulocytic leukocytosis (10,000/ microL or greater).

Minor Yamaguchi criteria are as follows:
i. Sore throat.
ii. Lymphadenopathy.
iii. Hepatomegaly or splenomegaly.
iv. Abnormal liver function tests.
v. Negative tests for RF and ANA.

Diagnosis requires at least 5 features, with at least 2 of these being major diagnostic criteria. Our patient had all 4 of the major criteria and all of the minor criteria except lymphadenopathy.

The disease pattern of patients with AOSD can be divided into 3 distinct types:

i) Monocyclic or self-limiting pattern: has a single episode of systemic disease of variable duration followed by complete remission.

ii) Polycyclic or intermittent pattern: has two or more episodes of systemic disease separated by symptom-free remission period lasting for a minimum of 2 months.

iii) Chronic articular pattern: characterized by the severe articular manifestations causing joint destruction.

The patient presented here is suffering from monocyclic pattern of AOSD.

Corticosteroids remain the first-line treatment for AOSD, regardless of the clinical presentation. Usually, prednisolone is preferred among steroids. Steroids control symptoms in about 60% of AOSD patients. Intra-articular steroid injection can be used in the treatment of chronic articular pattern of AOSD [13]. Disease modifying anti-rheumatic drugs (DMARDs), such as methotrexate (MTX), azathioprine, cyclosporine and cyclophosphamide, are often used for maintenance therapy of the disease. Since several cytokines such as TNF-alpha, IL-1, and IL-6 are implicated in the pathogenesis of AOSD, biologic agents can be used in refractory AOSD patients [14,15].

Conclusion:
AOSD is treatable, though there is no complete cure for it. Treatment will help to manage inflammation if symptoms recur. Chronic arthritis with joint symptoms persisting for years may develop in a small number of patients with AOSD. However, medications as well as self-care can help these patients. So, the best option for AOSD patient is the regular doctor's consultation for effective treatment and management of specific AOSD symptoms.

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