Faridpur Med. Coll. J. 2016;11(2):86-89

Case Report

Adult Onset Still's Disease

MMSU Islam[1], MN Sarker[2], MI Hossain[3], MI Hossain[4], M Kamruzzaman[5]

Abstract:

Adult Still's disease is rare disease presented with high spiking fever, joint pain, rash, organomegaly and serositis. It is difficult to diagnose as it closely mimics with many systemic diseases, so it can be diagnosed after exclusion of them. There are lots of diagnostic criteria, of them Yamaguchi's criteria is well established. Treatment consists of NSAIDS, corticosteroids & other immunosuppressive drugs. Course of the disease is unpredictable with relapse & remission in many cases. Here we present a 25 years old lady with Adult Onset Still's Disease.

Key words: Adult Onset Still's Disease, Yamaguchi's Criteria.

Introduction:

Still's disease is named after English physician Sir George Frederic Still (1861-1941)[1]. Adult-onset Still's disease (AOSD) is a rare systemic inflammatory disease characterized by the classic triad of persistent high spiking fevers, joint pain and a distinctive salmon-colored bumpy rash[2]. Although some features are similar, AOSD is different than Still's in children. In children, Still's disease is considered a form of juvenile rheumatoid arthritis and referred to as systemic-onset juvenile rheumatoid arthritis[3].

AOSD has been described all over the world. The number of new cases of AOSD per year is estimated to be 0.16 new cases per 100,000 population[2]. There is a bimodal age distribution with one peak incidence between ages 15-25 and a second peak between ages of 36-46 years[4]. It affects women more often than men[5].

1. Dr. M. M. Shahin-Ul- Islam, MBBS, FCPS (Medicine), MD (Gastroenterology), Assistant Professor, Department of Gastroenterology, Faridpur Medical College, Faridpur.

2. Dr. Mst. Naznin Sarker, MBBS, FCPS (Paediatrics), Junior Consultant, UHC, Goalunda, Rajbari.

3. Dr. Md. Iqbal Hossain, MBBS, Registrar, Department of Gastroenterology, Faridpur Medical College, Faridpur.

4. Dr. Mohammad Iqbal Hossain, MBBS, FCPS (Medicine), Assistant Professor, Department of Medicine, Faridpur Medical College, Faridpur.

5. Dr. Muhammad Kamruzzaman, MBBS, FCPS (Hematology), Assistant Professor (CC), Department of Medicine, Faridpur Medical College, Faridpur.

Address of correspondence :
Dr. M. M. Shahin-Ul-Islam, MBBS, FCPS (Medicine), MD (Gastroenterology), Assistant Professor, Department of Gastroenterology, Faridpur Medical College, Faridpur.
Phone: +88-01711986290, Email: shahin52dmc@gmail.com

Cause, risk factors & pathophysiology:

The cause of AOSD is unknown & no risk factors for the disease have been identified[5]. Some researchers suspect the condition might be triggered by a viral or bacterial infection[6]. Age is the main risk factor for adult Still's disease, with incidence peaking twice: One from 15 to 25 years and again from 36 to 46 years[6]. Exact pathophysiology is still unknown but it presumably involves interleukin-1 (IL-1), since medications that block the action of IL-1β are effective treatments. Interleukin-18 is expressed at high levels[7,8].

Signs and Symptoms:

The disease typically presents with joint pain, high fevers, a salmon-pink rash, enlargement of the liver and spleen, swollen lymph nodes, and an increased white blood cell count in the blood[2]. Daily fever of at least 102^0 F (38.9^0C) for a week or longer, fever usually peaks in the late afternoon or early evening. There might have two fever spikes daily, with temperature returning to normal in between. A salmon-pink rash might come and go with the fever. The rash usually appears on trunk, arms or legs. Sore throat may be one of the first symptoms of adult Still's disease. The lymph nodes might become swollen and tender. Joints especially knees and wrists might be stiff, painful and inflamed. Ankles, elbows, hands and shoulders might be involved. The joint discomfort usually lasts at least two weeks. Muscular pain usually ebbs and flows with the fever, but the pain can be severe enough to disrupt daily activities. Signs and symptoms of this disorder

can mimic those of other conditions, including lupus, lyme disease, crohn's disease and lymphoma[6]. Patients experiencing a flare-up from AOSD usually report extreme fatigue, swelling of the lymph nodes and, less commonly with pleural & pericardial effusion. In rare cases, AOSD can cause aseptic meningitis and sensorineural hearing loss[2].

Laboratory tests[3]:

It can be difficult to diagnose AOSD. That's because Still's has some similarities to other diseases, such as Lyme disease, Crohn's disease, and certain infections. Before confirming diagnosis, it requires rule out other problems. A medical history and physical exam are often the first steps. Variety of blood tests may need to check for inflammation, changes in blood cell counts, iron levels and liver enzymes. Imaging tests check for inflammation or enlargement of certain organs.

Blood Tests

A high white blood cell count and low red blood cell count, high C-reactive protein, high erythrocyte sedimentation rate (ESR), negative antinuclear antibodies, negative rheumatoid factor, high liver enzymes, high ferritin and fibrinogen.

Imaging Tests

Sometimes more than one imaging test, such as abdominal ultrasound or CT, or X-rays of joints, chest, or abdomen are required. These tests may check for the following: pericarditis, pleural effusion, an enlarged spleen, liver, or lymph nodes, joint inflammation or damage, joint inflammation or damage.

Diagnostic criteria:

There are a number of diagnostic criteria of AOSD of which Yamaguchi's criteria is well known.

Yamaguchi's criteria[9]
Five or more criteria are required, of whom two or more must be major

Major criteria

1. Fever >39°C, lasting 1 week or longer
2. Arthralgia or arthritis, lasting 2 weeks or longer
3. Typical rash
4. Leukocytosis >10,000/mm^3 with >80% polymorphonuclear cells

Minor criteria

1. Sore throat
2. Recent development of significant lymphadenopathy
3. Hepatomegaly or splenomegaly
4. Abnormal liver function tests
5. Negative tests for antinuclear antibody (IF) and rheumatoid factor (IgM)

Exclusion criteria

1. Infections
2. Malignancies (mainly malignant lymphoma)
3. Other rheumatic disease (mainly systemic vasculitides)

Treatment:

It isn't yet possible to prevent Still's disease, and there is no cure. After diagnosis has been made, the goal is to control symptoms and the course of the disease. This can help prevent or lessen any complications.

Early treatment for AOSD disease is aimed at controlling symptoms of arthritis with nonsteroidal anti-inflammatory drugs (NSAIDs) includes ibuprofen, naproxen, and high-dose aspirin. These may begin even before diagnosis has been confirmed.

With a firm diagnosis of AOSD & if disease is severe or doesn't respond to NSAIDs corticosteroids, such as prednisone may be required. Because of potential serious side effects steroids can't be used for a very long time.

In chronic case of Still's; medications which suppress the immune system to control arthritis and other symptoms may be needed like Methotrexate, Sulfasalazine, Hydroxychloroquine, Azathioprine, Cyclophosphamide, Cyclosporine, Anakinra, Adalimumab, Etanercept, Infliximab. More than one medication at the same time may need to take for long time[3].

Complications:

Most complications from AOSD arise from chronic inflammation of organs and joints. Like joint destruction (knees and wrists, neck, foot, finger and hip joints also may be affected, but much less frequently), pericarditis, myocarditis, pleural effusion etc. Macrophage activation syndrome, another rare but potentially fatal complication of AOSD, can cause low blood cell counts, very high triglyceride levels and abnormal liver function[6].

Prognosis:

The course of the disease is difficult to predict. But these statistics may give some idea of what may

happen. About 1 in 5 people have symptoms that go away and never come back. About 1 in 3 has symptoms that go away but come back several times over several years. These relapses are often less severe and shorter than the first episode. About 1 in 2 people have symptoms that last a long time, with the disease sometimes affecting vital organs[3].

Case Report:

Mrs. Runa, a 23 years of lady presented to us with the complaints of high fever (104-105^{0}F) and multiple joint pain for about 3 weeks. Her fever persists all over the day but sharply rises mainly at afternoon. She had sore throat & headache but gives no history of cough, scalding micturition, loose motion, vomiting, and photophobia. She gives no history of travel to malaria endemic zone. Along with fever she also noticed joint pain; which starts at right knee then right elbow, left knee and both wrists joints. Joint pain was associated with joint swelling and right knee became so swollen that she could not straight her leg to full extent & could not walk or go to toilet. She gives no history of skin rash. On examination she was toxic, restless at the time of high fever with a flushed appearance, she was anaemic, with swollen different joints and deformed and semi-flexed right knee. There was cervical lymphadenopathy and just palpable spleen. She was a dark coloured lady and no rash could be identified at the time of high fever. There were no signs of meningeal irritation and examination of other system were normal. When we received her, she was on broad spectrum combination antibiotics (Ceftriaxone 4 gm/day & Tetracycline 2gm/day) and Antimalarial (Artemether & Lumefantrine), we continued those medication with Indomethacine 150mg/day for arthritis. We transfused two unit of whole blood to correct her anaemia. Her condition was not improving. She gave same type of attack about 8 months back with lots of antibiotics & 3 units of blood transfusion at that time. We searched for previous papers and found that she had severe anaemia, very high WBC count, raised CRP, negative RA & ANA. At that time she was improved with empirical corticosteroid (Prednisolone). We repeated few investigations at this time and we think that, this young lady may be suffering from AOSD. We advised for serum ferritin and it turns to be very high. We stopped antibiotics & started Prednisolone 60mg/day and patient responded very quickly, she became afebrile on next day and joint swelling & deformity improved within one week. We labeled her as AOSD & discharged her with 60mg Prednisolone for one month then taper over another month. We requested her to come for follow up after one month. She came to us 2 & ½ months later and stated that after about 1 month of discharge she developed right sided hemiparesis and consulted with a neurosurgeon. She underwent MRI of brain and diagnosed as acute ischemic stroke and was treated accordingly but stopped prednisolone. Her hemiparesis is now improved but again she develops fever and arthritis. We advised for a bone marrow study to exclude subleukaemic or alekae micleulaemia. After exclusion of that we started Prednisolone 30mg/day, Aspirin 75mg/day, Methotrexate 7.5mg/week and Folic acid 5mg/week. We are now hoping for her best.

Table I: Investigations

Investigations	Results
Hb	6 gm/dl
ESR	150 mm in 1st hour
Total Count of WBC	22.45 x 10^9/L
Total Count of RBC	2.98 x 10^{12}/L
Total Count of Platelet	753 x 10^9/L
Neutrophil	84%
Lymphocytes	11%
PBF	Microcytic hypochromic Anaemia with Neutrophilia with Thrombocytosis
Serum Creatinine	1.1 mg/dl
Urine RME	Normal (RBC – nil, Protein-nil, Pus cell 2-4/HPF)
CRP	48.0 mg/L (Normal <6 mg/L)
ALT	190 U/L
RA	Negative
ANA	Negative
Anti ds-DNA	Negative
Blood Culture	No growth
Urine Culture	No growth
Serum Ferritin	93,090.00 ng/ml (Normal 18-160ng/ml)
Chest X-ray	Normal
USG of Whole Abdomen	Splenomegaly
Bone Marrow Study	Cellularity- Normal, M:E ratio- Increased, Erythropoiesis- Depressed & Normoblastic, Granulopoiesis- Hyperactive & Maturing into segmented form, Megakaryocyte-Increased.

Discussion:

AOSD is a rare systemic inflammatory disease characterized by the classic triad of persistent high spiking fevers, joint pain and a distinctive salmon-colored bumpy rash[2]. Along with these there may be enlargement of the liver and spleen, swollen lymph nodes, and an increased white blood cell count in the blood[2]. There is a bimodal age distribution with one peak incidence between ages 15-25 and a second peak between ages of 36-46 years[4]. It affects women more often than men[5]. Our patient was a 23 years old female started the disease at about 22 years of age (1st attack) and had high fever and inflammation of multiple joints. She also had cervical lymphadenopathy, splenomegaly and very high WBC count. Our patient had no skin rash; this may not be found as she was a black beautiful lady. Sore throat may be one of the first symptoms of adult Still's disease[6]. Our patient had sore throat also.

A high white blood cell count, low red blood cell count, high C-reactive protein, high ESR, negative antinuclear antibodies, negative rheumatoid factor, high liver enzymes, high ferritin and fibrinogen is typical of ASOD[3]. Our patient had most of these findings; we did not perform fibrinogen level so we can't comment on this.

Our patient responded well with oral prednisolone, majority of AOSD patients respond with corticosteroids. She had an attack of ischemic stroke; this may be due to very high platelet count.

Conclusion:

Adult Onset Still's Disease is a rare disease. Careful history, thorough physical examination & relevant investigations will establish the diagnosis & will exclude other mimicking diseases. With appropriate treatment disease can be controlled & patient may lead a reasonably normal life.

References :

1. Wikipedia http://en.m.wikipedia.org>wiki>Adult-onset Still's disease.

2. Akkara VBM, Yee AH, Warrington KJ, Aksamit AJ Jr, Mason TG. Aseptic meningitis in adult onset Still's disease. Rheumatol Int. 2012; 32 (12): 4031-4.

3. WebMD Medical Reference. http://www.webmd.com/arthritis/adult-onset-stills-disease.

4. Owlia MB, Mehrpoor G. Adult - onset Still's disease: a review. Indian J Med Sci. 2009; 63 (5): 207-21.

5. Adult Still's disease: MedlinePlus Medical Encyclopediamedlineplus.gov › Medical Encyclopediahttp: //medlineplus.gov>ency>article.

6. Overview - Adult Still's disease - Mayo Clinicwww.mayoclinic.org/diseases-conditions/adult-stills.../ovc-20190876.

7. Serena C, Roberta P, Cristiano A, Carlo P, Monica P, Giovanna P, et al. IL-18 Serum Level in Adult Onset Still's Disease: A Marker of Disease Activity. International Journal of Inflammation. 2012:1-6.

8. Sugiura T, Kawaguchi Y, Harigai M, Terajima-Ichida H, Kitamura Y, Furuya T, et al. Association between adult-onset Still's disease and interleukin-18 gene polymorphisms. Genes and immunity 2002; 3(7):394-9.

9. Yamaguchi M, Ohta A, Tsunematsu T, kasukawa R, Mizushima Y, Kashiwagi H, et al. Preliminary criteria for classification of adult stills disease . J Rheumatol. 1992; 19:424-30.