ADULT ONSET STILL'S DISEASE

Ranjeet Kaur[1], Gurinder Mohan[2]

HOW TO CITE THIS ARTICLE:
Ranjeet Kaur, Gurinder Mohan. "Adult onset still's disease". Journal of Evolution of Medical and Dental Sciences 2013; Vol2, Issue 49, December 09; Page: 9606-9610.

ABSTRACT: Adult onset Still's disease is an uncommon autoimmune inflammatory disease, most often seen in young adults. It presents as a combination of systemic manifestations typically including spiking fevers, short – lived rashes, and joint symptoms ranging from arthralgia to aggressive arthritis. No specific diagnostic test is available and clinical diagnosis is based on pattern recognition and exclusion. Disease remits in a third of patients, whereas debilitating disease course is seen in those with root joint involvement. We report a case of Adult – onset Still's disease presenting with manifestations of fever, sore throat and arthritis.

INTRODUCTION: In 1896, George Frederic Still first reported a form of joint disease in children, distinct from Rheumatoid Arthritis with occurrence of periods of fever, lymphadenopathy, splenomegaly and pericardial adhesions. The term Adult Onset Still's Disease (AOSD) was introduced by Bywaters in 1971 as occurrence of seronegative polyarthritis, rash, fever and raised ESR in females in their 3rd decade of life.

CASE: A 35 year old female presented with complaints of sore throat for past 2 months along with pain, swelling and stiffness in right knee joint. Eight days after the presentation, she developed pain, swelling and stiffness of left knee joint with subsequent involvement of both shoulders, elbows and wrists over next 15 days. There were minimal complaints in small joints of hand and feet. Early morning stiffness was lasting for 15 minutes. During this interval, she was managed initially with three courses of antibiotics for sore throat and analgesics for joint symptoms. 20 days later, she started having fever which was high grade (104-105^{0}F), 1-2 spikes per day, with minimal response to antipyretics. There was no complaint of body rash. At presentation, patient had pallor with mild icterus. Abdominal examination revealed hepatomegaly. There was no splenomegaly and lymphadenopathy. Musculoskeletal examination revealed tenderness in both knees, shoulders, elbows, wrists, ankles and small joints of hands and feet. Swelling was present in both knee joints.

Laboratory diagnosis: She was anemic with hemoglobin of 8.0 gm/dl, her total count was 16,200/cu mm (N-86%, L-10%, M-02%, E-02%), platelet count was 5.9 lacs. PBF picture was suggestive of normocytic normochromic anemia. Her ESR was 120 mm/hr and CRP was 10mg/l. her serum bilirubin was 1.6 mg/dl, SGOT – 79 IU/L, SGPT – 67 IU/L. Her viral markers (Hbs Ag, Anti-HCV and HIV) were non- reactive. Immunological profile as Rheumatoid factor (RF), ANA, Anti-CCP were negative. Her thyroid profile was also normal and ASO titer was 172 IU/ml. Urine examination did not reveal any abnormality. On clinical suspicion of Adult Onset Still's Disease, serum ferritin was done which was 1123 ng/ml (normal value 13-150 ng/ml). Diagnosis of AOSD was made as per Yamaguchi criteria and patient was put on oral corticosteroids. She responded well to treatment with relief of fever and joint symptoms within 24 hours. On day 5, hemoglobin improved to 9.3 gm/dl, total cell count was 14,400/cu mm (N-85, P-10, M-02, E-03) and platelet count was 2.3 lacs.

Her LFTs also improved and inflammatory markers, ESR was reduced to 70mm/hour and CRP reduced to 6mg/l.

DISCUSSION: There is no universally agreed upon diagnostic test for AOSD. Therefore, the clinical diagnosis is based on the recognition of a specific disease pattern together with the exclusion of other causes of chronic inflammation, such as infection and malignancy. The more sensitive criteria of Yamaguchi and colleagues requires long list of diseases to be excluded, while more specific criteria of Fantrel and associates require not readily available measurement of glycosylated ferritin.

Yamaguchi et al (1992)[2]

Major fever ≥39^{0}C for more than 1 week

Arthralgia > 2 weeks

Maculopapular non pruritic salmon pink rash

Leukocytosis ≥ 10,000 / cu mm with ≥ 80% neutrophils

Minor pharyngitis or sore throat

Lymphadenopathy and / or splenomegaly

Abnormal aminotransferases

Negative RF or ANA assay

Diagnosis requires at least 5 criteria, including 2 major criteria with exclusion of infections, malignancies and vasculitides.

This criteria has a sensitivity of 96% and specificity of 92%

Fantrel et al (2002)[3]

Major criteria

- Spiking fever ≥ 39^o C
- Arthralgias
- Transient erythema
- Pharyngitis
- Neutrophils > 80%
- Glycosylated ferritin fraction <20%

Minor criteria

- Typical rash
- Leukocytosis ≥ 10,000/cu mm

Diagnosis requires 4 major criteria or 3 major and 2 minor criteria with no exclusion criteria. Sensitivity of criteria is 81% and specificity 98%.

The three predominant clinical features are spiking high fever, arthritis and transitory rash. High fever (>39^{o}C) is the presenting symptom in >95% of AOSD patients with 1-2 daily spikes, more often occurring late during the day and receding within hours.[4] Musculo-skeletal pain is present at onset and often worsens during fever spikes. Arthritis is more often polyarticular and symmetrical affecting knees, wrists, fingers and ankles, but asymmetric oligoarticular and monoarticular presentations have also been described.[5,6] The classic skin manifestation is often maculo-papular rash consisting of flat salmon pink skin areas that have small confluent lumps. Rash is predominantly seen on trunk and proximal extremities and often evanescent (i.e. pronounced during febrile periods and disappearing almost completely in between).

Sore throat is present in 50-80% of cases. Diffuse pharyngeal erythema can be seen in 50% of these patients while circumscript mucosal lesions as aphthae or ulcers are uncommon.[7] Lymphadenopathy is usually mild with moderately enlarged non –tender nodes detected clinically in 40-60% of patients.[8] Hepatosplenomegaly occurs mainly in the presence of abnormal level of liver enzymes and is seldom severe. Pleuritis and/or pericarditis is seen in upto 30% of patients, whereas serous peritonitis occurs more seldom. Other less common findings include uveitis, aseptic meningitis and encephalitis, seizures, cerebrovascular ischemia, pulmonary fibrosis, myocarditis, interstitial nephritis, collapsing glomerulopathy, isolated renal and liver failure as well as multiple organ failure.[9]

Patients with active AOSD display increased serum levels of CRP and fibrinogen/ESR together with reductions in hemoglobin and albumin levels. Serum ferritin may reach disproportionately high levels in excess of 10,000 ng/ml. Ferritin increases more than 5 times the normal upper level for increased specificity for AOSD over 80% and, when associated with decrease in proportion of glycosylated ferritin, is the single most discriminative test for AOSD.[10]

AOSD is a benign disease, however fatality rate upto 12% with 5 year survival of 93% have been described. Macrophage activation syndrome have been reported in 5-10% of AOSD patients with very high ferritin levels together with rapidly progressive cytopenias. MAS seems more responsible for early deaths.[11]

Three distinctive patterns are recognized in the disease course of AOSD. In about one third of cases, AOSD is a monocyclic disease with remissions within 1 year of onset, although drug weaning may take longer. A remitting-relapsing pattern is seen in 20-40% of patients. In 30-50% of patients, AOSD evolves into a chronic disease in which progressive inflammatory joint destruction becomes the main concern. Baseline risk factors for the development of chronic disease include polyarthritis, root joint (shoulder/hip) involvement, absence of HLA-BW 35, moderately elevated serum ferritin levels, high ferritin/CRP ratios and elevated levels of ICAM-1 AND IL-8.[12,13]

NSAID's are considered the first-line agents for AOSD and will suffice as monotherapy in about 25% of the patients. Early administration of systemic corticosteroids (0.5-1 mg/kg/day of prednisolone) provides rapid control of symptoms. In patients with life threatening disease (pericardial tamponade, myocarditis, diffuse intravascular coagulation), corticosteroids are given as intravenous pulse therapy with control of acute disease (clinical and biochemical remission), gradual tapering of corticosteroids is done over period of 6-12 months. All patients do not achieve remission with corticosteroid therapy and require methotrexate as corticosteroid sparing agent. Chloroquine gives similar disease control as methotrexate, whereas cyclosporine is used as third line agent.[15] Encouraging results have been reported with the use of Anti-TNF agents (Infliximab, Etanercept), IL-1 receptor antagonist (Anakinra) and anti-IL-6 receptor (Tocilizumab).[16] Recurrent disease activity after initial remission is classified as relapsing disease and treatment follows same strategy as initial presentations. Relapses are less severe and managed less aggressively. Persistent disease activity or recurrent disease activity beyond 1 year of disease is generally classified as chronic disease.[18] Chronic disease relates primarily to the development of articular complications because more internal organ complications remit with treatment. Carpal ankylosis was seen after 1.5-3.5 years of the disease with progressive joint space narrowing and only mild osseous erosions, seen in 67% of the patients after 5 years of disease.[19] It is reasonable to manage such patients in

more aggressive manner in an effort to prevent damage development and subsequent loss of function.

BIBLIOGRAPHY:

1. Bywaters EG. Still's disease in the adult. Ann Rheum Dis 1971; 30: 121-133.
2. Vamaguchi M, Ohta A, Tsunematsu T, et al. Preliminary criteria for classification of Adult Onset Still's Disease. J Rheumatol 1992; 19:424-30.
3. Fantrel B, Zing E, Golmard JL, et al. Proposal for a new set of classification criteria for adult onset Still's diease. Medicine (Baltimore) 2002; 81: 194-200.
4. Mert A, Ozaras R, Tabak F, et al. Fever of unknown origin: a review of 20 patients with adult onset Still's Disease. Clin Rheumatol 2003; 22: 89-93.
5. Cagatay Y, Gul A, Cagatay A, et al. Adult onset Still's disease. Int J Clin Pract 2009; 63: 1050-55.
6. Wouters JM, Van de Putte LB. Adult onset Still's disease; clinical and laboratory features, treatment and progress of 45 cases. QJ Med 1986; 61: 1055-65.
7. Caln DY, Lan HH, Hsieh TY et al. Crico-thyroid perichondritis leading to sore throat in patients with active adult onset Still's disease. Ann Rheum Dis 2007; 66: 1264-66.
8. Jeon YK, Paik JH, Park SS, et al. Spectrum of lymph node pathology in adult onset Still's disease; analysis of 12 patients with one follow up biopsy. J Clin Pathol 2004; 57: 1052-56.
9. Efthimiou P, Paik BK, Bielory L. Diagnosis and management of adult onset Still's disese. Ann Rheum Dis 2006; 65: 564-72.
10. Fantrel B, Le Moel G, Saint-Marcoux B, et al. Diagnostic value of ferritin and glycosylated ferritin in adult onset Still's disease. J Rheumatol 2001; 28:322-29.
11. Fukaya S, Yasuda S, Hashimoto T, et al. Clinical features of haemophagocytic syndrome in patients with systemic autoimmune diseases, analysis of 30 cases. Rheumatology (oxford) 2008; 47: 1686-91.
12. Wouters JM, Reekers P, Van de Putte LB. Adult onset Still's disease: disease course and HLA associations. Arthritis Rheum 1986; 29: 415-18.
13. Evensen KJ, Swaak TJ, Nossent JC. Increased ferritin response in adult Still's disease: specificity and relationship to outcome. Scand J Rheumatol 2007; 36:107-10.
14. Efthimiou P, Kontzias A, Ward CM, et al. Adult onset Still's disease : can recent advances in our understanding of its pathogenesis lead to targeted therapy? Nat Clin Pract Rheumatol 2007; 3: 328-35.
15. Fautrel B, Borget C, Rozenberg S, et al. Corticosteroid sparing effect of low dose methotrexate treatment in adult Still's disease. J Rheumatol 1999; 26: 373-8.
16. Fautrel B. Adult onset Still's disease. Best Pract Res Clin Rheumatol 2008; 22: 773-92.
17. Zeng T, Zou YQ, Wu MF, et al. Clinical features and prognosis of adult onset Still's disease: 61 cases from china. J Rheumatol 2009; 36: 1026-31.
18. Cush JJ, Medsger TA Jr, Christy WC, et al. Adult onset still's disease: clinical course and outcome. Arthritis Rheum 1987; 30: 186-94.
19. Appenzeller S, Castro GR, Costallat LT, et al. Adult onset still's disease in southeast Brazil. J Clin Rheumatol 2005; 11: 76-80.

CASE REPORT

AUTHORS:

1. Ranjeet Kaur
2. Gurinder Mohan

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of General Medicine, Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar.
2. Professor, Department of General Medicine, Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar.

NAME ADRRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Ranjeet Kaur,
Simran Hospital,P.O. Rayan 2,
Silk Mills, Opp. Old Octroi,
Chheharta, Amritsar.
Email – ranjeet10101@gmail.com

Date of Submission: 25/11/2013.
Date of Peer Review: 26/11/2013.
Date of Acceptance: 30/11/2013.
Date of Publishing: 04/12/2013