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Adult Onset Still's Disease as Differential Diagnosis of PUO: A Case Report

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Abstract
Adult onset Still's disease AOSD) is chronic multi-system inflammatory disorder of unknown etiology. It is characterized by high spiking fever, ploy arthralgia and skin rash. Lymphadenopathy is another prominent feature of adult onset Still's disease. The rarity of this diease has been associated with low index of suspicion[3] among physicians and hence delayed diagnosis in patients suffering from it. We reported a 23 years old female presented with fever, myelgia, skin rashes and polyarthritis for 1.6 months, Examination revealed fever, typical skin rash, and polyarthritis for 1.6 months Examination revealed fever, typical skin rash and polyarthritis. On investigation there were neutrophilic leukocytosis, high ESR, high ferritin level, but RA test and ANA test, CPK and Jo-1 were negative. All of her history, clinical examinations and laboratory findings fulfill the diagnostic Yamaguchi criteria for AOSD. With proper treatment, now she is completely symptoms free and leaving a healthy life.
Keyworks: *Fever, skin rash, polyarthritis, Adult onset Still's disease and CPK.*

Introduction

Adult onset Still's disease (AOSD) is a chronic systemic inflammatory disorder of unknown etiology and its major clinical manifestations include high spiking fever, sore throat, muscle pain, polyarthralgia, salmon colored evanescent rash, hepatosplenomegaly, lymphadenopathy and netrophilic leukocytosis[1,2]. AOSD is rare but potentially serious disease and its rarity make the suspicion index for it low, among physicians[3]. It has bimodal age distribution in all ethnic groups with peaks at 15-25 and 36-46 years of age in both sexes with an incidence of 0.16 cases/100000 persons/year[2]. There is no cure for adult Still's disease; however, treatment may offer symptom relief for adult Still's disease and help to prevent complication. As it progresses, adult Still's disease may lead to chronic arthritis and other complications. We have diagnosed a case of AOSD in our hospital, who became complete symptoms free with proper treatment, though it is non curable.

Case Report

23 years old Women who is normotensive, non diabetic admitted at department of Medicine, in

rural tertiary care institution Tanda Medical College Kangra at Tanda with complaints of fever, multiple joint pain and skin rashes over whole body for last 1½ months. Fever was high grade continuous in nature. Generalized macular rashes especially in upper limbs and chest with symmetrical polyarthritis involving wrist, proximal interphalangeal joints (PIP), metacarpophalangeal joints (MCP), knees and ankles. She also gave history of sore throat for last month. There were no early morning stiffness, ocular symptoms, orogenital ulcers, urinary symptoms, photophobia and contact to inflected person or major systemic symptoms. On examination she revealed well built, orientation with macular rashes over upper limbs and chest and there was no rash over her finger knuckles. The patient was febrile 100^0-103^0 F with regular heart rate 96/min, blood pressure of 112/70 mmHg and normal jugular venous pressur. She had acute synovitis of ankles, wrists and PIP joints, mainly of ring fingers with full range of movements of all locomotor system and no promimal or distal muscular weakness. Deep tendon reflexes were normal. Examination of chest, abdomen, Central and peripheral nervous systems were unremarkable.

Investigations revealed haemoglobin 8.5 gm/dl, erythrocyte sedimentation rate (ESR) 77 mm in 1st hour, total white blood cell count 22.17 x 10/L, neutrophil 81%, lymphocyte 16% peripheral blood film suggestive of anaemia of chronic disorder with neutrophilic leukocytosis. Urine routine examination was normal, no growth in urine culture. Liver fuction test was normal, RA test negative, anti CCP, ANA negative, LDH, serum CPK and serum CK-MB within normal limit. Ultrasonography of the whole abdomen was normal, but there was very high ferritin>2000 ng/ml (normal 15-120ng/ml).

Finally AOSD diagnosis was made according to Yamaguachi Criteria (she is having 4 major features and 3 minor features) and she was started on prednisolone 40mg daily, Methotrexate 10 mg once a week and NSAID (Diclofenac sodium 100mg daily) after which she became afebrile for the first time in last 1.6/months after onset of illness. The patient showed considerable improvement and was discharged.

Discussion

Still's disease is named after an English doctor named George Still, who described the condition in children 1897. George Still published his monograph, "On a Form of Chronic Joint Disease in Children[4.] Still's disease is now known as systemic onset juvenile rheumatoid arthritis (JRA[2]). By waters in 1971, the term "adult Still's disease" was used to describe adults who had a condition similar to systemic onset JRA. Although cause of AOSD is unknown, the condition may be triggered by a viral or bacterial infection.

High sensitivity classification criteria have been proposed, since there is no single test to establish the diagnosis (Table1)[2].

Table 1: Classification criteria for adult-onset Still's disease proposed by Yamaguchi et al[2]

Major criteria	Minor criteria
Temperature of >39^0C for >1 WK.	Sore throat
Leukocytosis>10000 /cu mm and Including 80	Lymph node enlargement
More of granulocytes	Splenomegaly
	Liver dysfunction
Typical rash	(high ALT)
Negative ANA, Arthraglias>2wk	RF

After excluding infections, malignancies and other rheumatic diseases, adult Still's should be considered if 5 criteria (2 of which being major ones) are present. ANA= antinuclear antibody; RF=rheumatoid factor. (Yamaguchi criteria 1992: specificity 92% and sensitivity 96%)

A salmon-pink bumpy or flat rash (87% cases) may come and go with the fever. The rash usually appears on trunk, arms or legs[5,6.] Physical contact such as rubbing of skin may provoke the rash to appear. In 90% cases symmetrical or

asymmetrical polyarthralgia or arthritis present, which usually involves knees, wrists, ankles, elbows, hands, shoulders joints and cervical spines[5,6]. ANA= antinuclear antibody; RF=rheumatoid factor. (Yamaguchi criteria 1992, specificity 92% and sensitivity 96%).

Usually, the joint discomfort lasts at least two weeks. Lymphadenopathy is a prominent feature of AOSD seen in about 65% of patients and must do a biopsy to rule out lymphoma. Life threatening conditions such as hepatic involvement, cardiac tamponade, disseminated intravascular coagulation (DIC) respiratory distress syndrome or pancytopenia were occasionally developed in the course of diseases and some cases were often associated with hemophagocytic syndrome (HS)[7]. Laboratory features of the disease are increase serum levels of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), leukocytosis, liver dysfunction, negative results for both rheumatoid factor and antinuclear antibodies and an increased incidence of hyperferritinemia[5]. Increased serum ferritin level is a nonspecific finding and should not be regarded as a diagnostic test. That ferritin may be helpful for monitoring disease activity during treatment[6].

Symptoms free sometimes they need to continue medications to control inflammation and prevent complications. So, patient needs at least 6 months of treatment. Our patient had been receiving empirical treatment for pyrexia and joint pain for last 1½ months before the eventual diagnosis of AOSD was made. For this reason, different studies have recommended that AOSD be considered in patients with fever of unknown origin[8]. The absence of a diagnostic test and the fact that infectious, haematological, immunological and malignant diseases must first be ruled out. It is polygenic autoinflammatory disorder[9]. This has mainly been deduced from demonstration of the pivotal role of innate immune pathways, mostly those involved in the processing of two cytokines of the interleukin (IL)-1 family (namely IL-1B and IL-18). Other cytokines, such as IL-6 and to a lesser extent tumour necrosis factor a (TNF-a) are also involved in the pathogenesis of AOSD and data from genetic and immuno-logical studies, together with the dramatic effect of biological treatments, have confirmed the major role of these cytokines. Two broad phenotypes of AOSD are being recognized one with profound systemic manifestations and the other with mainly articular features[10]. Our patient was with systemic features and achieve significant improvement with non steroidal anti-infammatory drugs, glucocorticoides and etanercept, a TNF-a inhibitor.

Conclusion

AOSD is an important cause of pyrexia of unknown origin (PUO). It needs proper documentation of fever, exclusion of other diseases and observation for at least 6-8 weeks to diagnose the disease. But a definite diagnosis and proper managements can make the prognosis better.

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