Adult Onset Still’s Disease

Ankur Dalal

Abstract

Adult onset Still’s disease (AOSD) is a rare systemic inflammatory disorder of unknown aetiology, characterised by daily spiking high fevers accompanied by rash, arthritis, and systemic manifestations. There are no specific diagnostic tests for AOSD. To establish the diagnosis of AOSD one should require the fulfilment of proposed major and minor criteria as well as exclusion of other diseases. This report described a 35-year-old female who was presented with fever, pruritus, arthritis, sore throat, leukocytosis and hyperferritinemia. She was diagnosed to have AOSD based on Yamaguchi et al. criteria after the exclusion of other possible conditions.

Introduction

Adult onset Still’s disease (AOSD) is a rare systemic inflammatory disorder of unknown aetiology. It may be responsible for a significant proportion of cases of fever of unknown origin (FUO) and can also have serious musculoskeletal sequelae. It occurs worldwide and characteristically affects younger people with slight female predominance. The name was derived from Sir George Frederick Still who in 1897 described 22 children with so called Still’s disease (currently known as systemic onset juvenile idiopathic arthritis), however, AOSD was established as a disease entity by Eric Bywater in 1971, when he described 14 adults who had symptoms similar to those seen in paediatric Still’s disease and did not meet the criteria for rheumatoid arthritis (RA).

Case Report

A 35-year-old female patient was presented with H/O high grade fever with chills for 15 days mostly in afternoon and associated with mild pruritus over limbs, soreness of throat for 15 days, low back pain associated with bilateral thigh and leg pain for 7 days, bilateral knee joints pain with swelling and difficulty in walking for 7 days, loose stools 2-3 per day and vomiting after food for 5 days while abdominal pain for 3 days. Patient had P/H/O fever on and off associated with arthralgia especially of lower limbs in last 5-6 months. On general examination skin colour of patient was dark with bilateral mild pedal oedema. Systemic examination was normal. Musculoskeletal examination showed muscle tenderness around hip girdle and evidence of synovitis at both knee joints.

Patient was investigated in view of recurrent FUO (old reports in last 5-6 month were inconclusive regarding aetiology) with significant musculoskeletal system involvement. Investigation results showed: Her urine examination showed albumin +1 and 10-12 pus cells/ h.p.f. Her random blood sugar was 124 mg/dl. Her haemogram showed haemoglobin-10 gm%, total count- (TC)-72400/c.mm (Neutrophils-96%) on admission and 26400/c.mm (Neutrophils-90%) after five days while platelets count- 3.15 lacs/c.mm. Her peripheral blood smear showed normochromic normocytic picture without abnormal cells. Her renal function test showed blood urea- 23 mg/dl, serum creatinine- 1.4 mg/dl, serum sodium- 129 mEq/L and serum potassium- 3.5 mEq/L. Her liver function test showed serum bilirubin-1.7 mg/dl (D-1.0, L- 0.7), SGPT- 38 IU/L, SGOT- 30 IU/L, S.Alk. P- 154 U/L and serum protein- 5.8 g/dL (albumin- 2.7 g/dL). Her ESR and CRP were 40 mm/hour and164 Mg/L. Her HIV/ HBsAg/ HCV were negative. Her S. Procalcitonin was 16.33 ng/ml on admission and was 40.07 ng/ml after five days. Her urine and blood culture were negative. Her serum amylase, serum lipase and CPK were 62 U/L, 122 U/L and 27 U/L respectively. Her rheumatoid factor was 6.0 IU/ML by turbidometric and ANA by IIF was negative. Her serum ferritin was advised, which was turn back to very high at 58375 ng/mL. Her Chest x-ray was normal, x-ray both knee was normal. Her USG abdomen showed small right kidney, USG thorax showed mild bilateral pleural effusion, and MSK USG both knee showed mild effusion in infrapatellar region. Her 2D echo was normal. Her MRI L-S spine with pelvis showed diffuse soft tissue and muscle hyperintensity/ oedema with minimal bilateral hip joint effusion.

According to the fact that S. Procalcitonin is less than a perfect marker, which may sometimes be increased in non-infectious conditions or may even remain low in infection and therefore, the diagnosis of bacterial infections is still requiring a critical clinical awareness, careful patient history, dedicated physical examination, and appropriate cultures. Even though S. Procalcitonin was high on first day in this patient, it was significantly reduced after five days without change in patient’s clinical condition and TC. Patient’s urine and blood culture were also came negative and no obvious focus of infection was found. So after careful analysis of history and investigation results, the bacterial infection was excluded in this patient. Possibility of malignancy and connective tissue diseases (CTD) was also excluded after careful analysis of history and investigations. Patient was suspected as having Adult onset Still’s disease due to presence of recurrent fever with mild pruritic rash, oligoarthropathy, myopathy, sore throat, mild bilateral pleural effusion, low albumin with raised ESR and CRP, leukocytosis with predominant neutrophils, normochromic normocytic anaemia, mild raised bilirubin, very high serum ferritin level, negative RF and negative ANA test. Typical rash of AOSD seen in approximately 73% of patients was not obvious in this patient may be due to dark coloured
At present there is no consensus on the systemic inflammation and no finding which is specific for AOSD. The ESR and CRP may be found to be raised. Common haematological abnormalities include leucocytosis, which is the result of a striking neutrophilia that is probably secondary to bone marrow granulocyte hyperplasia.1,5,6 Unlike other systemic rheumatic diseases, it is not associated with RF or ANA positivity, and this fact has been used in various sets of criteria used to define the disease.1 Recently, serum ferritin and glycosylated ferritin have received a lot of attention as diagnostic and disease activity markers. Ferritin, an acute phase reactant, is intimately involved in inflammatory processes and is associated with increased production by the histiocyte-macrophage system and/or increased release from damaged hepatocytes.1 In most studies, a threshold for serum ferritin levels of 1000 ng/ml, five times the upper limits of normal (40–200 ng/ml), has been used to suggest AOSD, however very high levels ranging from 4000 ng/ml to 30 000 ng/ml or more are not uncommon.1 The usefulness of serum ferritin is limited by the fact that very high levels can also be seen in other diseases such as liver disease, infections, malignancies and especially the haemophagocytic syndrome.1 A more specific diagnostic marker than ferritin may be its glycosylated fraction; in AOSD, where the glycosylation of ferritin is often <20%,1 it is not readily available.

Several different sets of classification criteria have been proposed. In comparison, the classification criteria proposed by Yamaguchi et al. (Table 1) provided the highest sensitivity (93.5%).1 A new set of classification criteria proposed by Fautrel et al.6 (Table 1) does not contain exclusion criteria, and includes the glycosylated fraction of serum ferritin. This set of classification criteria provided 80.6% sensitivity and 98.5% specificity in a retrospective study.1,6

The clinical course of AOSD can be divided into three main patterns with different prognoses: self-limiting or monophasic pattern, intermittent or polycyclic systemic pattern, and a chronic articular pattern with poor prognosis.1,4,5 There are no randomised, controlled, clinical trials assessing efficacy of treatment in AOSD.
Treatment may include NSAIDs and aspirin, glucocorticoids, and immunomodulating drugs. NSAIDs, including aspirin, are generally used as fist-line therapy for musculoskeletal symptoms and fever however; most patients require steroids at some point in the course of their diseases. The use of immunomodulating drugs should be reserved for cases that are refractory to NSAIDs and steroids, or when a reduction in the dose of steroids is required. Biological therapy can be added in the form of Anti-IL1 or Anti-TNF (Infliximab > Etanercept) in refractory patients not responding to immunomodulating drugs (such as Methotrexate) and low dose steroids ± NSAIDS.

References