Case report

Adult onset still's disease; a rare disease in Nigeria?

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Abstract

Adult Onset Still's Disease (AOSD) is an inflammatory disease of unknown aetiology. Its global prevalence is estimated at 1 case per 100,000. Because of its pattern of presentation which mimics many inflammatory and malignant conditions, the diagnosis requires high index of suspicion. Few cases have been reported from Africa. The first case in Nigeria was reported in July 2015. We hereby report two more cases diagnosed in the same rheumatology clinic of Lagos State University Teaching Hospital within six months of the first reported case. This is to highlight the fact that the disease while rare, requires a high index of suspicion for diagnosis.

Both patients were males. The ages of the patients were 19 and 62 years. Both patients had high grade fever, symmetrical inflammatory polyarthritis and weight loss. The first patient had sore throat. On examination, both were found to be febrile. The second was emaciated and pale.

Both patients had marked leukocytosis with neutrophil predominance, thrombocytosis, elevated liver enzymes and elevated acute phase rectants. Rheumatoid factor, anti-CCP, anti-nuclear antibody and extractable nuclear antigen were negative in both patients. Serum ferritin was markedly elevated in both. Retroviral screening, anti-HCV and HBsAg were negative in both. Septic work up and direct Coomb's test were negative in them. Peripheral blood film was normal and bone marrow aspirate was suggestive of chronic inflammatory condition in the second patient. The first patient was treated with steroid, hydroxychloroquine and azathioprine. The second patient was treated with steroid and methotrexate. Both made good clinical recovery.

Introduction

Adult Onset Still's Disease (AOSD) first described by Bywaters in 1971[1,2] is an inflammatory disease of unknown aetiology[3]. Its global prevalence is estimated at 1 case per 100,000[4]. Because of its pattern of presentation which mimics many inflammatory and malignant conditions, the diagnosis requires high index of suspicion. Few cases have been reported from Africa. The first case in Nigeria was reported in July 2015[4]. We hereby report two more cases diagnosed in the same rheumatology clinic of Lagos State University Teaching Hospital within six months of the first reported case. This is to highlight the fact that the disease while rare, requires a high index of suspicion for diagnosis.

Case 1

A 19 year old undergraduate had presented to the Lagos State University Teaching Hospital, Ikeja, Lagos State with complaints of fever of 2 months duration described as a high grade fever, intermittent and is worse during the evenings. Fever was associated with a history of weight loss and fatigue. He also complained of polyarthritis involving the wrist, knees, ankles and small joints of the hand for the same duration. There was a 2 weeks history of sore throat. He however did not have a history of skin rash. Examination had revealed a febrile patient at presentation with normal respiratory rate, pulse rate and a blood pressure of 120/80 mmHg. There were no lymphadenopathy or splenomegaly on examination.

Investigations had revealed a leukocytosis (23,290 cells/mm^3) with a neutrophilia of 84.9%, elevated liver enzymes, negative rheumatoid factor and anti-nuclear factor, C-reactive protein was 162.7ng/ml (<5), Erythrocyte Sedimentation Rate (ESR) was 112mm/hour (1-20, Westergreen method). X-rays of the hands were normal. Serum ferritin was 23,002ng/ml. He was negative for HIV, Hepatitis B and C, connective tissue disease screen, anti-cyclic citrullinated peptide (anti-CCP) and direct Coomb's test. Peripheral blood film and bone marrow cytology were normal.

Differentials of Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA) were excluded based on the negative results of anti-nuclear antibody, rheumatoid factor and anti –cyclic citrullinated peptide. American College of Rheumatology (ACR) criteria and ACR/EULAR 2010 criteria were not fulfilled for either. Haematologic malignancy was also excluded.

Based on the Yamaguchi criteria, a diagnosis of AOSD was made. He was commenced on azathioprine (AZA) 50mg twice daily, prednisolone 10mg twice daily and hydroxychloroquine (HCQ) 200mg twice daily.

Case 2

A 62 year old man presented with one year history of recurrent high grade intermittent fever, weight loss and inflammatory polyarthritis involving the shoulders, elbows, hips, wrists, ankles and small joints of the hands and feet. Fever was associated with chills and rigors and he had lost 12kg body weight at presentation. There was no rash and he did not have sore throat. He had visited several hospitals for treatment to no avail. At presentation he was emaciated, febrile with temperature of 39.2°C, pale but with no peripheral lymphadenopathy. Systemic examination was unremarkable.

He had leukocytosis (24,000 cells/mm^3) with neutrophilia (90.2%), microcytic hypochromic anaemia (haematocrit of 14%), thrombocytosis (878,000 cells/mm^3), elevated ES (>150mm/Hour), high serum ferritin (4000 ng/ml) and elevated liver enzymes. RF, anti-CCP and connective tissue disease screening were negative. Serum uric acid was normal. Hepatitis B and C and HIV were negative. Chest X-ray, abdominal ultrasound scan and mantoux were normal. Septic work yielded no bacterial growth. Bone marrow aspiration cytology was in keeping with chronic inflammatory reaction. Based on the Yamaguchi criteria, a diagnosis of AOSD was made. Treatment was with intravenous pulse methylprednisolone 500mg daily for three days, oral prednisolone and weekly methotrexate. He was transfused with two units of sedimented red cells. His improvement was remarkable and both platelet and white cell counts normalized after two months.

Discussion

AOSD is a chronic inflammatory disorder of unknown aetiology[3]. Its pathogenesis remains poorly understood and due to its rarity, there is no approved treatment guideline for clinical use.

Various infectious agents have been postulated to be involved in the aetiology of AOSD[1,5]. These include Epstein-Barr virus, erythrovirus B19, parvovirus, cytomegalovirus, human immunodeficiency virus, rubella, hepatitis A,B,C and chlamydia pneumonia. It has been reported to occur as a paraneoplastic syndrome[6] and also as an association with Miller-Fisher syndrome[2].

In the past decade, it has come to be classified as a polygenic autoinflammatory disease[7] because of the recognition that its pathogenesis involves mainly the innate immune system. The hallmark of the disease is neutrophil and macrophage activation mediated by cytokines, mainly tumour necrosis factor alpha (TNF-α), interleukin (IL) 1, IL-6, IL-8 and IL-18[1,7,8]. Helper T cells may also be involved in the pathogenesis[1,9]. No familial trend has been described[1].

Most patients present with fever[1,3,10-12]. Polyarthritis involving synovial joints, sore throat, rash and weight loss are other symptoms[1,3,5,10-12]. Lymphadenopathy, hepatomegaly, splenomegaly and pyrexia >38.8°C are frequently seen.

Anaemia of chronic disease is often present. Leukocytosis with marked neutrophilia, thrombocytosis, elevated serum ferritin but normal glycosylated ferritin levels are seen[11,13]. Liver enzymes may be elevated. ESR is usually raised. Pro-inflammatory cytokines are elevated. Cytokine level and serum ferritin fluctuate with disease[11]. X-ray of affected joints may show erosions and joint space narrowing but carpal ankylosis is highly specific to AOSD[10,11]. Diagnosis of AOSD is by way of diagnostic criteria of which the Yamaguchi criteria[5] is the most validated and widely accepted. It has a sensitivity and specificity of 0.96 and 0.92. Exclusion of malignancy, infections and other inflammatory diseases are required.

Patients with AOSD have been treated successfully with non-steroidal anti-inflammatory drugs, corticosteroids and combination of disease modifying anti-rheumatic drugs[3,4,10-12]. Resistant and complicated cases have been treated with biologics like anti-IL 1 (anankira), anti IL-6 (tocilizumab), anti TNF α (eternacept) and abatacept[1,8,9,13-16]. Ciclosporin A, intravenous immunoglobulin have also been used[1,13].

Complications of AOSD include reactive hemophagocytic lymphohistiocytosis, disseminated intravascular coagulopathy, alveolar haemorrhage, liver failure, myocarditis and thrombotic thrombocytopenic purpura[1,7,14,16].

Conclusion

AOSD is a rare inflammatory disorder of unknown aetiology. The diagnosis requires high index of suspicion. This case report highlights AOSD as an important differential diagnosis of inflammatory polyarthritis.

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