CASE REPORT

Adult-onset Still's disease in a Nigerian woman

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SUMMARY

Adult-onset Still's disease (AOSD) is an uncommon systemic inflammatory disorder of unknown aetiology. Although there have been reports and series elsewhere, there have been very few such reports on black Africans. The rarity of the reporting of this disease has been associated with a low index of suspicion and hence delayed diagnosis in patients suffering from it. We report a case of a 28-year-old woman, a teacher, who had been repeatedly treated for malarial fever over a 2-month period. She was also briefly managed elsewhere for systemic lupus erythematosus due to a persistent fever with associated polyarthralgia, sore throat, rash and high erythrocyte sedimentation rate. On presentation to our facility, she fulfilled the Yamaguchi criteria for AOSD and had a markedly elevated serum ferritin level. She was successfully managed with etanercept and methotrexate. This is the first report of AOSD from Nigeria.

BACKGROUND

Adult-onset Still's disease (AOSD) is a systemic inflammatory disorder of unknown aetiology characterised by fever, rash, arthralgia, leucocytosis and negative immunological study.¹ It is a rare but potentially serious disease, and its rarity often makes the index of suspicion for it low among physicians.^{2–3} There have been very few reports of AOSD from Africa,^{4–6} and none previously reported from Nigeria. Initially described in 1971, AOSD is considered a multigenic syndrome that requires a background genetic susceptibility for the development of spontaneous autoinflammatory reactions following exposure to environmental triggers. Macrophage and neutrophil activation, the hallmark of AOSD, can lead to a reactive haemophagocytic lymphohistiocytosis.⁷ We report a case of AOSD in a Nigerian woman.

CASE PRESENTATION

A 28-year-old Nigerian woman, a teacher, was referred to our facility with a 2-month history of fever, polyarthralgia and rash. The fever was high grade, intermittent with daily peaks around late evening. The patient had previously been treated for malarial fever, but the current fever persisted even after blood film for malarial parasite was negative. There were associated periodic pleuritic chest pains and a sore throat, which had lasted 2 weeks before presentation. On examination, there were tender swellings of the knees, wrists and elbow, and also tenderness in the metacarpophalangeal joints, shoulders and the left ankle. The patient had reddish maculopapular rashes on the trunk and arms (figures 1 and 2). These rashes

Figure 1 Salmon-pink rash on right arm. Rash fades daily as fever subsides.

usually faded away by late morning and reappeared with the fever towards evening. There were no skin changes on the face and no oral or genital ulcers. She had no ocular symptoms. On examination, there were palpably enlarged, discrete lymph nodes

Figure 2 Salmon-pink rash on right arm. Rash fades daily as fever subsides.

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in the left axilla and the liver was enlarged down to 4 cm below the right subcostal margin. The diagnosis of AOSD was made based on the Yamaguchi criteria.⁸ The patient had been on prednisolone and diclofenac for weeks at the referring hospital for supposed systemic lupus erythematosus, without improvement. This was because of an elevated erythrocyte sedimentation rate, however, antinuclear antibody and anti-double stranded DNA were both negative.

INVESTIGATIONS

Full blood count showed leucocytosis (total white cell count was $13.6 \times 10^9/L$) with absolute neutrophilia. Serum ferritin was 1417 ng/mL (reference: 22–112 ng/mL), C reactive protein was 57.5 mg/L (reference: <5) and erythrocyte sedimentation rate was 42 mm/h. Rheumatoid factor, anticyclic citrullinated peptide, antinuclear and anti-double stranded DNA antibodies were all negative. The patient's alanine aminotransferase was 123 IU/L, while her aspartate aminotransferase was 108 IU/L.

DIFFERENTIAL DIAGNOSIS

Systemic lupus erythematosus was excluded in the absence of antinuclear antibody and failure to meet the American College of Rheumatology criteria. Rheumatoid arthritis was also excluded in the absence of rheumatoid factor, anticyclic citrullinated peptide or fulfilment of the 2010 American College of Rheumatology/European League Against Rheumatism classification criteria. Septic work up was negative.

TREATMENT

The patient was treated with intravenous pulse methylprednisolone 500 mg daily for 3 days followed by subcutaneous etanercept 50 mg weekly. This was combined with methotrexate tablets, 10 mg weekly.

OUTCOME AND FOLLOW-UP

The fever, rash, arthralgia and joint pain resolved rapidly, and the patient did not need non-steroidal anti-inflammatory drugs again. She is still being followed up.

DISCUSSION

Our patient had the well-characterised reddish evanescent rash of AOSD, which was hard to find on first contact. This initial contact was in the afternoon during an afebrile period. This rash, however, appeared again with spiking fever the same night while the patient was still being investigated, and she exhibited the typical Koebner phenomenon along sites where her clothing made tight contact with her skin. The diagnosis of our patient was based on the fulfilment of the Yamaguchi criteria.⁸

There are no specific diagnostic tests for AOSD. Several sets of different classification criteria have been proposed, among which are the Yamaguchi criteria and the Fautrel criteria.^{8,9} The classification criteria proposed by the former, published in 1992, however, are the most widely used.¹⁰

AOSD is uncommon, with an estimated prevalence of less than 1 case/100 000 people.¹¹ Being uncommon, actual knowledge about this disease is based on isolated descriptions or very small series. There are no specific guidelines, but diagnostic criteria have improved in recent years, as have the insights into pathophysiology and therapeutic resources.¹² There have been very few reports of this disease in Africa. Two cases have been reported at different times in black Senegalese Africans,^{4,13} while four cases have been reported from Gabon.⁶ There have been no previous reports of AOSD among Nigerians. A systematic review of 20 cases of AOSD from two hospitals in Chile by

Carreno *et al*¹⁴ in 2009 showed that 80% of patients had a prior different diagnosis. This underscores the high rate of misdiagnosis and sometimes wrong treatment over a long period. Our patient had been receiving treatment for systemic lupus erythematosus 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.^{1,14} The manifestations of AOSD are diverse, but the most typical are fever, evanescent skin rash and arthralgia.¹² The absence of a diagnostic test and the fact that infectious, haematological, immunological and malignant diseases must first be ruled out can also make the diagnosis difficult. Accordingly, patients' financial limitations may often prevent the diagnosis of the condition in sub-Saharan Africa.⁶

It was only over the last decade that AOSD was reclassified as a polygenic autoinflammatory disorder.^{15,16} 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-1 β and IL-18). Other cytokines, such as IL-6 and to a lesser extent tumour necrosis factor α (TNF- α), are also involved in the pathogenesis of AOSD, and data from genetic and immunological studies, together with the dramatic effect of biological treatments, have confirmed the major role of these cytokines.¹⁷

It is known that serum ferritin is markedly elevated in as many as 70% of patients with AOSD, and the elevations correlate with disease activity.¹⁸ Elevated serum ferritin levels, higher than five times the upper limits of normal, may suggest the presence of the disease with 80% sensitivity and 46% specificity. However, when it is combined with a decrease in the proportion of glycosylated ferritin (<20%), the specificity rises to 93%.¹⁹ Levels between 3000 and 30 000 are not uncommon, and levels greater than 250 000 have been reported.²⁰ Our patient had a serum ferritin level higher than 12 times the upper limit of normal, but the proportion of glycosylated ferritin could not be tested as the facility for testing is not available in our setting.

Two broad phenotypes of AOSD are being recognised, one with profound systemic manifestations and the other with mainly articular features.¹⁷ The presentation of our patient was with marked systemic features, and failure to achieve significant improvement with non-steroidal anti-inflammatory drugs or glucocorticoids necessitated the use of etanercept, a TNF- α inhibitor. With further research, it is possible that targeted biological therapies will be favoured for earlier use in AOSD, as they seem to have a dramatic effect when given as first-line treatment in systemic-onset juvenile idiopathic arthritis, a condition that has been described as juvenile Still's disease.¹⁷

Learning points

- ▶ Adult-onset Still's disease (AOSD) occurs in Nigerians, though rarely.
- ▶ A high index of suspicion is needed to recognise a case of AOSD
- ▶ The clinical course of AOSD can be unpredictable

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Competing interests None declared.

Patient consent Obtained.

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