

Case Report

Adult-Onset Still's Disease: An Unusual Cause of Fever

Sombo Fwoloshi, Sally Trollip, Owen Ngalamika

Department of Internal Medicine, University Teaching Hospital, University of Zambia School of Medicine, Lusaka, Zambia

ABSTRACT

Adult-onset Still's disease (AOSD) is a rare auto-inflammatory syndrome. In Zambia, like most parts of Africa, fever is usually caused by infections (e.g., tuberculosis) and infestations (e.g., malaria). AOSD represents one of the few febrile conditions that are not due to microbial infections or parasitic infestations. It therefore cannot be managed with antibiotics or antihelminthics. Generally, patients are <35-year-old, febrile, have arthralgias, and an evanescent maculopapular rash. Treatment of AOSD requires the use of immunosuppressant drugs. This is the first report of a patient with AOSD in Zambia. It is one of the very few cases to be reported in Africa.

Keywords: Adult-onset Still's disease, auto-inflammatory syndrome, fever, microbial infections, parasitic infestations

INTRODUCTION

Adult-onset Still's disease (AOSD) is a rarely encountered systemic inflammatory condition of unknown etiology. It's characterized by spiking fever, an evanescent salmon-colored maculopapular rash, and arthritis of large and small joints.^[1] The color description of the rash may be difficult to notice in dark-skinned populations. Other associated features include sorethroat, fatigue, night sweats, lymphadenopathy, serositis, hepatosplenomegaly, raised acute phase proteins, and neutrophilic leukocytosis. Pathogenesis of AOSD is presumed to be cytokine-driven, predominantly interleukin-1 (IL-1), which is increased in sera and target tissues. IL-1 promotes bone and cartilage destruction, pyrexia, exanthems, and anorexia. IL-6 is also overproduced and promotes the synthesis of acute phase proteins (e.g., ferritin). There is also increased expression of IL-18 in the liver, which promotes inflammation leading to elevated transaminases.

Prognosis is usually favorable, and most patients respond well to immunosuppressant drugs. However, it's very important to recognize AOSD early to prevent complications and improve patient's quality of life. In this report, we present a case of AOSD that was initially treated as severe malaria and sepsis.

CASE REPORT

A 30-year-old female was referred from a Primary Health Care Centre to the University Teaching Hospital (UTH) for suspected severe malaria. She presented with a 2 week history of joint pains, daily fevers-predominantly nocturnal, and a rash. She also gave a history of poor appetite, a sore throat, fatigue, headache, and night sweats. She was referred because her symptoms were worsening despite receiving antimalarials and intravenous antibiotics for 1-week. Her family history was unremarkable. At about the age of 9-11 years, she had recurrent joint pains and presumed to have had sickle cell disease until laboratory tests proved otherwise.

On admission, she was febrile (39.2°C), had an urticarial rash (on thighs, arms, and face), with tender fingers, knees, and elbows. No joint deformity was noted. Her Pulse was 88 bpm and blood pressure was 111/77 mmHg. The rest of the examination was unremarkable. An impression of febrile illness was made, Ceftriaxone and paracetamol

Access this article online	
Quick Response Code:	Website: www.ssajm.org
	DOI: 10.4103/2384-5147.157433

Address for correspondence: Dr. Owen Ngalamika, Department of Internal Medicine, University Teaching Hospital, University of Zambia School of Medicine, Lusaka, Zambia. E-mail: owen_ngalamika@yahoo.com

Received: 02-01-15,

Accepted: 12-03-15

were commenced. She was then investigated for malaria, pulmonary tuberculosis, sepsis, and rheumatoid arthritis. The table below shows the laboratory results of the initially ordered investigations [Table 1].

The laboratory results, a poor response to antibiotics, and the patient's symptoms and signs led to the suspicion of AOSD as the most plausible diagnosis for this patient. Serum ferritin was immediately ordered (1759 ng/ml - very high), antibiotics were stopped, and a moderate Prednisolone dose (40 mg/day) was commenced. Low-dose Methotrexate (5 mg/week) was also commenced as a steroid-sparing agent. The patient's symptoms waned and she was discharged 3 days later. The patient returned for a follow-up visit 2 weeks later and was asymptomatic. The methotrexate dose was then raised to 10 mg/week and a tapering of Prednisolone was begun. Six weeks later, the patient was still asymptomatic, and her serum ferritin dropped to 50 ng/ml. She continues to be followed up at UTH.

DISCUSSION

Adult-onset Still's disease is one of the principle disorders considered under auto-inflammatory syndromes. There is only a handful of documented cases in Africa. Though there can be new onset in adults, it mostly occurs in children.^[2] Our patient gave a history of having an undiagnosed joint disorder in childhood. Our assumption is that the childhood condition was most probably juvenile idiopathic arthritis.

During her admission, the patient had a fluctuating course of feeling better in the morning while her

symptoms worsened at night. An infectious etiology was ruled out after administering antimalarials and trying several antibiotics with insignificant effect. A notable observation was the concurrent onset of symptoms. Even though the joint pains were almost always present at any time of the day, they worsened at night and were associated with the onset of fever and the itchy rash.

Both anti-nuclear antibody test and rheumatoid factor were negative. A negative rheumatoid factor excluded rheumatoid arthritis as a cause of the polyarthritis. Autoinflammatory syndromes like AOSD lack significant autoantibodies.^[3] Our patient also had a neutrophilic leukocytosis.

Other documented manifestations of AOSD are deep vein thrombosis,^[4] neurological disorders, atypical cutaneous features,^[5] and acute respiratory distress syndrome. Three patterns of disease are described; monocyclic (self-limited pattern with complete remission within 2-4 weeks), Polycyclic/intermittent (symptomatic flares separated by periods of remission ranging from 2 weeks to 2 years), and a chronic polyarthritis pattern.^[6] The monocyclic and polycyclic phenotypes are highly symptomatic while the chronic subtype has an indolent course with paucity of systemic symptoms.^[7]

Adult-onset Still's disease is a diagnosis of exclusion. Yamaguchi criteria are the most widely used in diagnosing AOSD. Our patient met all the four major plus three minor criteria. Ferritin is a marker of inflammation that is markedly raised but not specific for AOSD. Other conditions with hyperferritinemia include septic shock, antiphospholipid syndrome, and macrophage activation syndrome.^[8] Serum ferritin levels are directly associated with AOSD disease activity.^[9] In the acute phase, our patient had serum ferritin levels more than 10 times the upper limit of normal. As expected, the serum ferritin levels dropped drastically and fell within the normal range upon responding to treatment.

Our patient went into remission after a few weeks of corticosteroid and methotrexate, which are considered the first-line drugs in the treatment of moderate to severe AOSD.^[10] Methotrexate is also useful in preventing destructive arthritis.^[10] In patients who are refractory to corticosteroids and other steroid sparing immunosuppressive agents, other options of proven efficacy include anakinra (IL-1 receptor antagonist) and tocilizumab (IL-6 inhibitor).

This case report illustrates an unusual cause of fever in a region of the world where fever is common and mostly due to the high burden of infectious diseases. Therefore, it is not surprising that microbial infections were the conditions initially sought for in this patient.

Table 1: Laboratory results of investigations ordered upon admission of the patient

Test	Result	Reference range
Haemoglobin (g/dl)	13.0	12.1-16.3
Platelets	221×10 ⁹ /l	178-400
White cell count	13.72×10 ⁹ /l	4.00-10.00
Neutrophils (%)	11.32×10 ⁹ /l (82.5)	0.96-6.40
HIV	Negative	
Malaria parasite slide	No malaria parasites seen	
Blood culture	No growth	
Serum ferritin (ng/ml)	Baseline-1759 10 weeks later-50	15-160
CRP (mg/l)	21.9	0.0-8.0
RPR	Negative	
ANA	Negative	
RF	Negative	
Transaminases (U/l)	AST-40 ALT-28	0-37 0-41
Renal function tests	Normal	
Chest X-ray	Normal	

HIV = Human immunodeficiency virus, CRP = C-reactive protein, RPR = Rapid plasma reagin, ANA = Anti-nuclear antibody, RF = Rheumatoid factor, AST = Aspartate aminotransferase, ALT = Alanine aminotransferase

Nevertheless, she presented with the typical cluster of symptomatology and laboratory findings of AOSD. Despite AOSD being a rare condition, clinicians are advised to have a high index of suspicion in patients presenting with spiking fever, joint pains, and an evanescent rash.

REFERENCES

1. Cozzi A, Papagrigoriaki A, Biasi D, Colato C, Girolomoni G. Cutaneous manifestations of adult-onset Still's disease: A case report and review of literature. *Clin Rheumatol* 2014. [Epub ahead of print].
2. Cush JJ. Autoinflammatory syndromes. *Dermatol Clin* 2013;31:471-80.
3. Efthimiou P, Flavell RA, Furlan A, Gasbarrini G, Gava A, Koné-Paut I, *et al.* Autoinflammatory syndromes and infections: Pathogenetic and clinical implications. *Clin Exp Rheumatol* 2008;26:S53-61.
4. Morita H, Nishiwaki H, Nagayama Y, Yoshimura A. Portal vein thrombosis in adult-onset Still's disease: A case report and literature review. *Rheumatol Int* 2009;29:1515-8.
5. Affleck AG, Littlewood SM. Adult-onset Still's disease with atypical cutaneous features. *J Eur Acad Dermatol Venereol* 2005;19:360-3.
6. Pouchot J, Vinceneux P. Diagnosis, progression and prognosis, aetiology and treatment of adult-onset Still's disease. *Presse Med* 2004;33:1019-26.
7. Gerfaud-Valentin M, Jamilloux Y, Iwaz J, Sève P. Adult-onset Still's disease. *Autoimmun Rev* 2014;13:708-22.
8. Rosário C, Zandman-Goddard G, Meyron-Holtz EG, D'Cruz DP, Shoenfeld Y. The hyperferritinemic syndrome: Macrophage activation syndrome, Still's disease, septic shock and catastrophic antiphospholipid syndrome. *BMC Med* 2013; 11:185.
9. Mehta B, Efthimiou P. Ferritin in adult-onset Still's disease: Just a useful innocent bystander? *Int J Inflam* 2012;2012:298405.
10. Manger B, Rech J, Schett G. Use of methotrexate in adult-onset Still's disease. *Clin Exp Rheumatol* 2010;28 Suppl 61:S168-71.

How to cite this article: Fwoloshi S, Trollip S, Ngalamika O. Adult-Onset Still's Disease: An Unusual Cause of Fever. *Sub-Saharan Afr J Med* 2015;2:93-5.

Source of Support: Nil, **Conflict of Interest:** None declared.

Staying in touch with the journal

1) Table of Contents (TOC) email alert

Receive an email alert containing the TOC when a new complete issue of the journal is made available online. To register for TOC alerts go to www.ssajm.org/signup.asp.

2) RSS feeds

Really Simple Syndication (RSS) helps you to get alerts on new publication right on your desktop without going to the journal's website. You need a software (e.g. RSSReader, Feed Demon, FeedReader, My Yahoo!, NewsGator and NewzCrawler) to get advantage of this tool. RSS feeds can also be read through FireFox or Microsoft Outlook 2007. Once any of these small (and mostly free) software is installed, add www.ssajm.org/rssfeed.asp as one of the feeds.