Atypical Adult-onset Still's disease with flagellate morphology in a patient with skin of color

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INTRODUCTION

Adult-onset Still's disease (AOSD) is an autoinflammatory disorder that presents with arthralgias, dermatitis, organomegaly, fever, and lymphadenopathy. The dermatitis of AOSD is often described as salmon-colored and evanescent. Atypical cutaneous manifestations of AOSD have been described. Although nearly 30% of AOSD cases are reported in ethnic minorities, there is a scarcity of published images of AOSD in patients with skin of color.[1] Herein, we describe a case of AOSD with flagellate morphology in a patient with skin of color.

CASE REPORT

A 28-year-old African American woman was hospitalized with a 2-month history of polyarthralgia, headaches, recurrent fevers to 103 °F, tachycardia, and pruritic dermatitis. The polyarthralgia involved her wrists, ankles, and knees asymmetrically. She had daily fevers during the week prior to her hospitalization. She was recently treated by an outside hospital for suspected pyelonephritis with levofloxacin and trimethoprim-sulfamethoxazole. Her past medical history was significant for hypertension and a childhood history of atopic dermatitis. She was unable to continue employment due to her symptoms.

Abbreviations used:

ALT:	alanine transaminase
ANA:	antinuclear antibodies
ANCA:	anti-neutrophil cytoplasmic antibodies
AOSD:	Adult-onset Still's disease
ASO:	antistreptolysin O
AST:	aspartate aminotransferase
CK:	creatine kinase
CRP:	C-reactive protein
DRESS:	drug reaction with eosinophilia and systemic symptoms
EBV:	Epstein-Barr virus
ENA:	extractable nuclear antigen
EOS ABS:	absolute eosinophil count
ESR:	erythrocyte sedimentation rate
Hb:	hemoglobin
HIV:	human immunodeficiency virus
IL:	interleukin
IVIG:	intravenous immunoglobulin
NSAIDs:	non-steroidal anti-inflammatory drugs
RF:	rheumatoid factor
RPR:	rapid plasma reagin
TNF:	tumor necrosis factor
WBC:	white blood cells

Dermatology, rheumatology, and infectious disease teams were consulted. Dermatologic exam revealed hyperpigmented plaques with a symmetric distribution on the lateral face, neck, arms, hands, upper back, buttocks, and legs (Figs 1 to 3). Many plaques had linear and flagellate morphology with occasional scale and erythema. Her musculoskeletal

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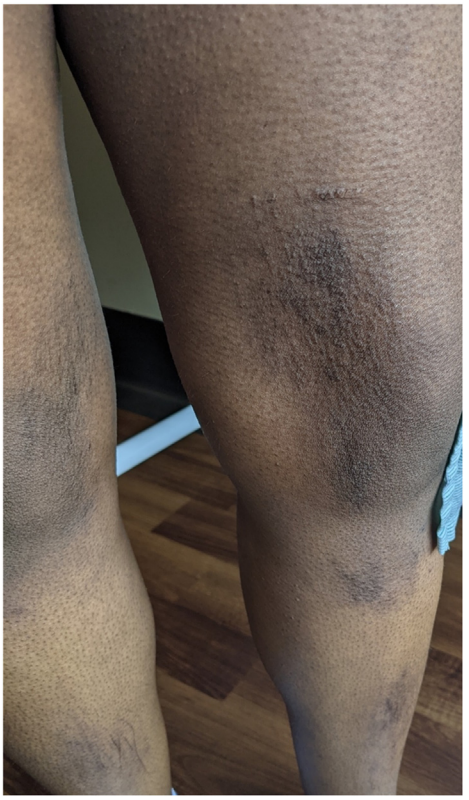

Fig 1. *Dark brown* linear and flagellate plaques on the thighs and legs of a patient with atypical Still's disease.

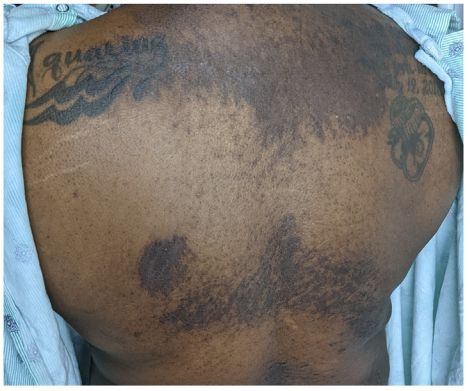

Fig 2. *Grey-brown* papules and plaques distributed bilaterally on the back of a patient with atypical Still's disease.

exam was notable for diffuse joint tenderness without synovitis. Strength was 5/5 in the upper and lower extremities. The initial differential diagnosis included drug reaction with eosinophilia and systemic symptoms (DRESS), dermatomyositis, a photosensitive eczematous eruption, and viral exanthem.

Initial labs showed leukocytosis with eosinophilia (WBC 16.5 $\times$ 10^9/L, EOS ABS 2.26 $\times$ 10^9/L), anemia (Hb 7.4 g/dL), normal platelets, increased

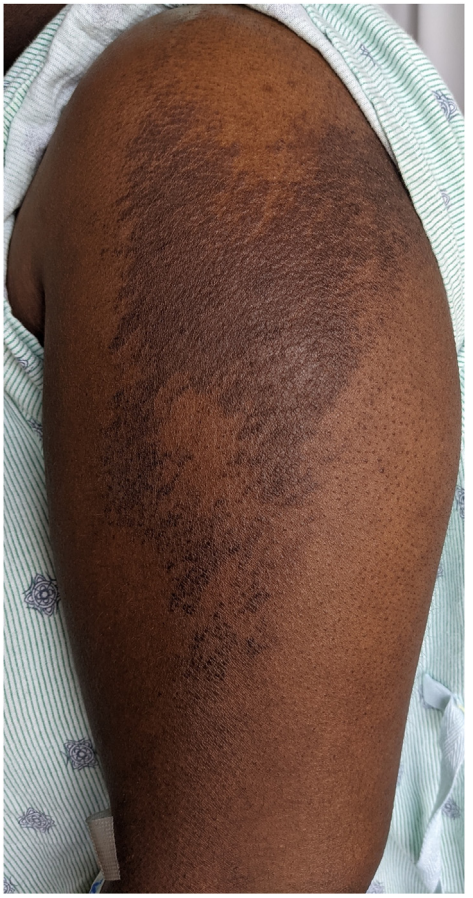

Fig 3. Hyperpigmented plaque on the *left upper arm* of a patient with atypical Still's disease.

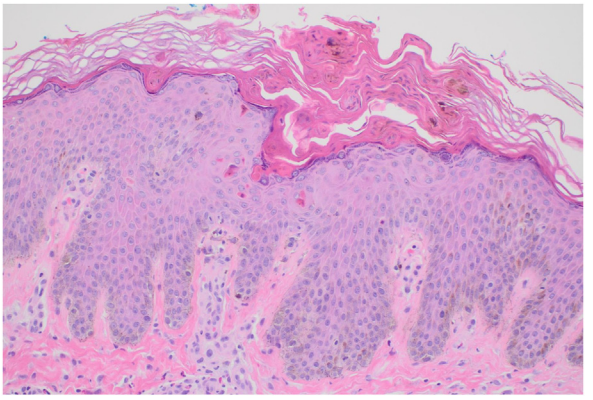

Fig 4. Hyperkeratosis and parakeratosis overlying an acanthotic epidermis with dyskeratotic keratinocytes. Within the dermis, an inflammatory infiltrate is present with eosinophils. These findings were consistent with the eruption of atypical Still's disease.

inflammatory markers (ESR > 130 mm/hr, CRP 23.7 mg/L), hyperferritinemia (13,660 mcg/L), and slight elevation of transaminases (AST/ALT 150s units/L). Her CK was 77 U/L and aldolase was mildly

elevated 14.3 U/L. Further work-up including ANA, ENA, ANCA, RF, parvovirus, blood and urine cultures, hepatitis, HIV, RPR, gonorrhea, chlamydia, monospot, respiratory viral panel, and COVID tests were negative. Her chest X-ray and abdominal ultrasound were unremarkable. Pelvic and lumbar spine X-rays showed mild sclerotic changes of the bilateral sacroiliac joints and lower lumbar spine.

Her fever and symptoms did not respond to broad spectrum IV antibiotics. A skin biopsy of the patient's right hip showed acanthosis, hyperkeratosis, and dyskeratotic keratinocytes predominantly in the upper levels of the epidermis, including the cornified layer (Fig 4). A sparse infiltrate of lymphocytes, neutrophils, and eosinophils was present in the dermis. This histopathologic pattern was consistent with the atypical eruption of Adult-onset Still's disease (AOSD).

The patient was treated with anakinra 100 mg subcutaneously daily and triamcinolone 0.1% ointment BID. She experienced resolution of all symptoms after the first anakinra dose. Due to lack of insurance, she was switched to prednisone upon discharge. While she was taking prednisone, she experienced 2 flares over 4 months. The first was associated with a new diagnosis of COVID pneumonia. Once she obtained financial assistance, anakinra was re-started. As she developed injection site reactions, headaches, and nausea, she was later switched to tocilizumab infusions every 4 weeks. At the time of this writing, she had not had a documented flare for 9 months.

DISCUSSION

AOSD is an autoinflammatory disorder with various clinical features including fever, dermatitis, polyarthralgia, pharyngitis, leukocytosis, transaminase elevation, and hyperferritinemia. The estimated incidence is 0.16 per 100,000 from a retrospective study in France on this rare condition.[2] Diagnosis of AOSD is often made based on criteria by Yamaguchi or Fautrel.[3,4] Shared criteria include fever, arthralgia, rash, leukocytosis, and pharyngitis.

There are key features that give rise to the clinical presentation of atypical AOSD compared to typical AOSD. The typical dermatologic manifestation of AOSD is a confluent, evanescent eruption that is nonpruritic. Documented cases of atypical AOSD have detailed the presence of pruritic urticarial eruptions, flagellate morphology, and hyperpigmented linear plaques that may persist when the patient is afebrile. Atypical eruptions have been associated with a more severe disease course.[5] Other causes of flagellate dermatitis include bleomycin-induced drug eruptions, mechanical, zebra-like dermatomyositis, shiitake mushroom dermatitis, and jellyfish stings.[6]

Skin biopsy findings in typical AOSD include a sparse, superficial inflammatory infiltrate with neutrophils and an uninvolved epidermis. In comparison, the presence of dyskeratotic keratinocytes confined to the upper layers of the epidermis is a feature of atypical AOSD.[7] Maeda–Aoyama et al. proposed that the dyskeratotic cells are apoptotic and may be a negative prognostic factor of AOSD.[7] Additional epidermal features observed in this case that are usually absent in typical eruptions of AOSD included acanthosis with hyperkeratosis and parakeratosis. The presence of eosinophils in the dermal infiltrate in our case is another distinguishing factor from typical AOSD.[8] Recommended serological work-up includes CBC, renal and liver function tests, ferritin, ESR, and CRP. Ruling out autoimmune and infectious etiologies may also be clinically indicated by checking ANA, RF, EBV, and ASO titers. Therapies include NSAIDs, systemic steroids, methotrexate, IVIG, TNF-alpha, IL-1, and IL-6 inhibitors.

Solid organ and hematologic malignancies have been reported in patients with both typical and atypical AOSD. Sun et al. found that a malignancy diagnosis did not precede or immediately follow AOSD symptoms in 42% of cases.[9] Screening for malignancies can be considered at the time of AOSD diagnosis in patients with suspicious symptoms or risk factors such as atypical dermatological features and older age.[10] Patients with AOSD should be followed longitudinally as delayed onset malignancies have been described.

Images of skin conditions in patients with skin of color are underrepresented in medical literature. Our patient's presentation was notable due to the color of her eruption, flagellate morphology, and persistence when afebrile. Recognizing inflammation in skin of color, such as violaceous erythema and brown discoloration, is important to minimize diagnostic delays and misdiagnoses. Optimizing lighting, dampening overlying dry skin with an alcohol pad or moist towel, and comparing involved to uninvolved skin can make inflammation more visible during dermatologic exams of patients with skin of color. Dermatologists should be aware of the spectrum of atypical AOSD and recognize clinical features in patients with skin of color.

Conflicts of interest

None disclosed.

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