SKIN

BRIEF ARTICLE

Adult-Onset Still's Disease with an Atypical Cutaneous Manifestation

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ABSTRACT

Adult-onset Still's disease (AOSD) is a rare systemic inflammatory disorder, characterized by daily fevers, arthralgias, and rash without evidence of infection. Recently there has been a growing number of cases reported with atypical cutaneous manifestations. We present a 37-year-old type VI Fitzpatrick skin type female who was seen in the hospital for a pruritic rash on her chest, back, and legs. Skin examination was significant for hyperpigmented papules coalescing into plaques on the chest, and hyperpigmented linear patches and excoriated plaques on the back and legs. Punch biopsy showed acanthosis and numerous apoptotic keratinocytes in the upper layers of the epidermis, which was characteristic of AOSD. As of recently, there is a growing body of evidence describing an atypical eruption of persistent, pruritic papules and plaques with typical histologic findings of AOSD. Further, these atypical features may be associated with more severe symptoms, higher incidence of macrophage activation syndrome, and possible delayed malignancy. Due to the scarcity of atypical cutaneous manifestations reported in the literature, these eruptions have not been included in the diagnostic criteria and can therefore be overlooked and misdiagnosed. Prompt recognition of these atypical eruptions is imperative to prevent a worsening prognosis and serious adverse effects.

INTRODUCTION

Adult-onset Still's disease (AOSD) is a rare systemic inflammatory disorder that is characterized by daily fevers, arthralgias, and rash without evidence of infection. AOSD can present itself in various ways, making the diagnosis a difficult one to make. More recently, there has been an increasing number of cases reported with atypical cutaneous presentations. Herein, we describe a case of AOSD with an atypical cutaneous presentation in a black female to add to the growing body of literature.

CASE PRESENTATION

A 37-year-old skin type Fitzpatrick VI female with past medical history significant for obesity, solitary kidney, and paranoid personality disorder presented to the hospital with complaints of subjective fevers, cough, and lower extremity pain following a motor vehicle accident which occurred 15 days prior

to presentation. Within a few days of admission, she developed a pruritic rash that involved the face, chest, abdomen, legs, and hands. Dermatology was consulted.

Skin examination was significant for hyperpigmented papules coalescing into plaques on the chest in a V-shaped distribution **(Figure 1**). On the back and legs there were hyperpigmented linear patches intermixed with linear excoriations (**Figure 2**). Additional clinical findings included cyclical fevers, diffuse lymphadenopathy, elevated ferritin, pericardial effusion and pulmonary infiltrates. Laboratory evaluation revealed an elevated ferritin of 16,580 ng/mL, an elevated erythrocyte sedimentation rate (ESR) of >130 mm/h, and an elevated c-reactive protein (CRP) of 19.25 mg/L. All infectious etiologies were ruled out. A punch biopsy of the chest showed skin with acanthosis and numerous apoptotic keratinocytes predominantly located in the upper layers of the epidermis. Within the dermis, there is a superficial perivascular inflammatory infiltrate composed of lymphocytes, neutrophils and scattered melanophages. No interface changes were identified.

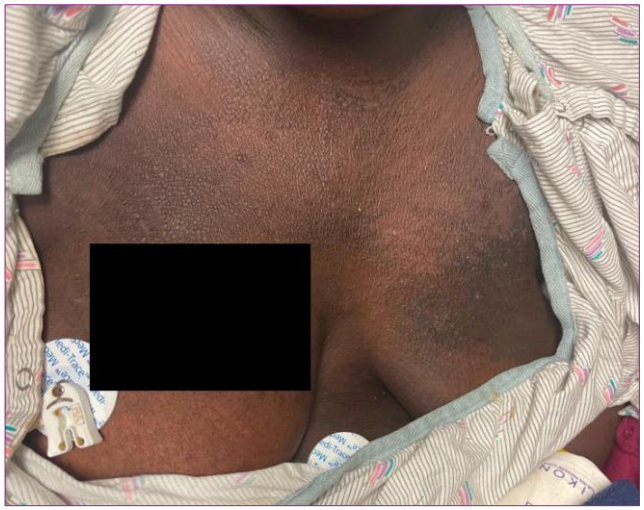

Figure 1. Hyperpigmented papules coalescing into plaques in a V-shaped distribution

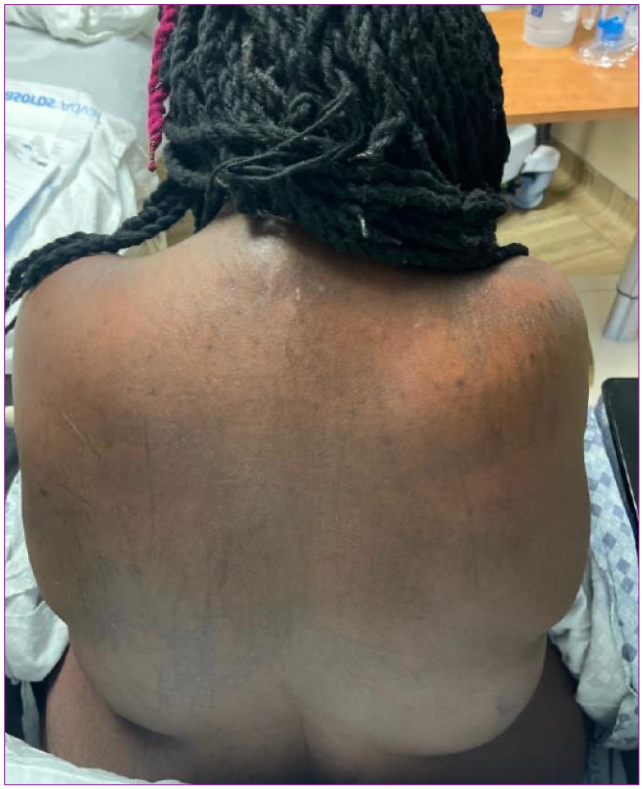

Figure 2. Hyperpigmented linear patches and linear excoriations

In the setting of fever, polyarthralgia, pericardial effusion, elevated ESR, CRP, and ferritin, rash, and characteristic biopsy findings, she was diagnosed with AOSD. She was treated with a prednisone taper, colchicine 0.6mg twice daily, as well as triamcinolone 0.5% twice daily as needed for her pruritic rash. Prednisone taper consisted of 50mg twice daily for 10 days, then 60mg daily decreased by 10mg each week until she reached 20mg, where it was then tapered by 5mg weekly. She showed very mild improvement of the pruritus and rash in the hospital. On outpatient rheumatology follow up, she had no recurrent flares of the rash, and her inflammatory markers were trending down. At this time, her prednisone taper was being decreased by 5mg weekly, and during follow up she was taking 15mg daily with complete resolution of her rash. Systemic therapy, such as anakinra, may be needed in

Table 1. Yamaguchi criteria for the diagnosis of AOSD[1]

Major Criteria	**Fever 39° for ≥ 1 week**
	Arthralgia or arthritis ≥ 2 weeks
	Typical nonpruritic salmon-colored rash
	Leukocytosis ≥ 10,000/mm^3
Minor Criteria	Pharyngitis
	Lymphadenopathy
	Hepatomegaly and/or splenomegaly
	Liver dysfunction
	Negative rheumatoid factor and antinuclear antibody
Exclusion Criteria	Infection, malignancy, or other rheumatic diseases

Diagnosis is made with ≥ 5 criteria present, ≥ 2 being major criteria with no exclusion criteria present

the future if she is unable to taper off the steroids.

DISCUSSION

AOSD is a rare, multisystem inflammatory condition with an unknown etiology. Due to its uncommon occurrence and variable presentation, diagnosis of AOSD may be delayed. There is a broad differential diagnosis for patients with overlapping features of AOSD, including infection, autoimmune disease, autoinflammatory disease, and malignancy. The proposed Yamaguchi major criteria for AOSD, summarized in **Table 1**, consists of fever, arthralgias, typical rash, and leukocytosis, while the minor criteria include pharyngitis, lymphadenopathy and/or splenomegaly, liver dysfunction, and the absence of rheumatoid factor and antinuclear antibody.[1] The typical rash of AOSD is characterized by nonpruritic, salmon-pink macules, papules, and plaques that coincide with fever spikes.

As of recently, more cases of AOSD have been reported in the literature with atypical cutaneous presentations. There is a growing body of evidence describing the atypical eruption of persistent, pruritic papules and plaques in patients with AOSD.[2-8] These persistent lesions have characteristic findings on histology, including dyskeratotic cells in the upper epidermis and a lymphocytic infiltrate in the papillary dermis.[2] In patients who develop linear lesions with the appearance of excoriations, as seen in our patient, histology remains consistent, and this therefore represents Koebner's phenomenon.[9] Skin findings differ from the typical rash in both morphology and time course, leading to further difficulty making the diagnosis of AOSD.

Moreover, these atypical features may be associated with more severe symptoms and are theorized to be a negative prognostic factor for disease.[10-12] A cohort study including 150 patients with AOSD found that those with atypical persistent pruritic eruptions had higher levels of lactate dehydrogenase and ferritin and a higher rate of macrophage activation syndrome than patients with the typical evanescent rash.[10] Dyskeratotic cells on histology in persistent pruritic eruptions have been linked to an increase in IL-18 and subsequently a worse prognosis.[11] Further, AOSD has been increasingly associated with delayed malignancies, commonly breast cancer and lymphoma.[13] In a review of 19 patients with atypical presentations of AOSD, diagnostic workup for malignancy showed hepatosplenomegaly in 26%, lymphadenopathy in 11%, and pleural and pericardial effusion in 5%.[13]

CONCLUSION

Early recognition of AOSD is important as to not delay treatment in patients with diffuse systemic disease. Due to the scarcity of atypical cutaneous manifestations reported in the literature, these eruptions have not been included in the diagnostic criteria and can therefore be overlooked and misdiagnosed. Prompt recognition of these atypical eruptions is imperative to prevent a worsening prognosis and serious adverse effects such as macrophage activation syndrome or delayed recognition of malignancy.

Conflict of Interest Disclosures: Dr. Correa is a consultant for Accutec Blades and a consultant and a researcher for Novartis Pharmaceutical.

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