Atypical cutaneous and histological presentation of adult-onset Still's disease

Madeeha Mian, BA^a, Connie Tran Fiore, MD^b, and Elizabeth Wilder, MD^b

^aTexas A&M College of Medicine, Bryan, Texas; ^bDivision of Dermatology, Department of Internal Medicine, Baylor University Medical Center, Dallas, Texas

ABSTRACT

Adult-onset Still's disease (AOSD), the adult variant of systemic juvenile idiopathic arthritis, is a rare auto-inflammatory condition that presents with characteristic skin findings. There is no specific test available; diagnosis is usually based on the symptoms and evanescent rash found in patients. More recently, however, descriptions of atypical cutaneous and histological manifestations of AOSD have been published. We describe a case of atypical AOSD and discuss recent literature on this different cutaneous and histological presentation. Our results add to the growing discussion on atypical AOSD and suggest that this presentation may have been underreported and more common than previously thought.

KEYWORDS Adult-onset Still's disease; auto-inflammatory; pathology; rash

Adult-onset Still's disease (AOSD), the adult variant of systemic juvenile idiopathic arthritis, is a rare auto-inflammatory condition that presents with characteristic skin findings in nearly 90% of cases.¹ The typical rash is evanescent and salmon pink or urticarial.¹ Typical histology is characterized by a perivascular mixed inflammatory infiltrate containing neutrophils.² More recently, descriptions of atypical cutaneous manifestations of AOSD have been published. We describe a case of AOSD with an unusual cutaneous and histological presentation.

CASE DESCRIPTION

A 32-year-old black woman presented to the emergency department with a pruritic rash that had been present for several weeks. She first noticed the rash a day after starting sulfamethoxazole/trimethoprim for upper respiratory infection symptoms and subsequently stopped the drug 3 days after noticing the rash. The patient's history included a sore throat, arthralgias, subjective fevers, and prior "hives" on both of her upper extremities. She denied a personal or family history of any other skin conditions.

On exam, she had a fever of 101°F. Skin examination revealed lichenified, pink, and hyperpigmented papules coalescing into plaques with isolated linear areas on the

face, scalp, neck, back, chest, shoulders, and right forearm (*Figure 1*). There was no involvement of the oral mucosa. No urticarial papules or plaques were noted. The patient had significant right-sided cervical lymphadenopathy that was tender to palpation.

Her ferritin level was 15,203 ng/mL; erythrocyte sedimentation rate, 104 mm/h; rheumatoid factor, 17 IU/mL; lactate dehydrogenase, 870 units/L; and leukocytes, 13,900/μL. Viral serology and polymerase chain reaction results were negative for HIV; antiphospholipid and antinuclear antibody screens, rapid Streptococcus A, and syphilis screens were negative. Fine needle aspiration of an enlarged cervical lymph node was consistent with reactive hyperplasia.

A punch biopsy was performed from a lesion on the patient's back. Histology revealed intracorneal pustules, parakeratosis, single necrotic keratinocytes scattered from the stratum spinosum to the stratum corneum without involvement of the basal layer, and a dermal perivascular mixed inflammatory infiltrate with neutrophils and eosinophils (*Figure 2*). Notably, there was no vacuolar interface.

The patient was treated with triamcinolone 0.1% ointment and hydrocortisone 2.5% ointment for the eruptions on her body and face, respectively, and was initiated on Zyrtec and Benadryl for itching. Over the next few days, her rash improved.

Corresponding author: Madeeha Mian, BS, Texas A&M College of Medicine, 8447 Bryan Rd., Bryan, TX 77807 (e-mail: madeehamian@yahoo.com)

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Figure 1. Atypical cutaneous presentation of adult-onset Still's disease with erythematous and hyperpigmented lichenified papules coalescing into plaques with some areas forming a linear pattern.

Figure 2. (a) Low-power hematoxylin-eosin stain showing intracorneal pustules and mixed perivascular infiltrate in the superficial dermis. (b) High-power hematoxylin-eosin stain showing parakeratosis, single necrotic keratinocytes scattered from the stratum spinosum to the stratum corneum layers, and a mixed perivascular infiltrate with neutrophils and eosinophils.

After ruling out malignancy and infection, AOSD was diagnosed. The patient was initiated on systemic prednisone and discharged with a plan to follow up with rheumatology.

DISCUSSION

AOSD, first described by Eric Baywaters in 1971, is a potentially fatal auto-inflammatory systemic disease.³ The disease is characterized by arthralgias, recurring fevers, a skin rash, and lab abnormalities including hyperferritinemia and leukocytosis.¹ The histology of the typical evanescent eruption is characterized by a sparse perivascular mixed inflammatory infiltrate with neutrophils.²

Diagnosis is based on Yamaguchi et al's criteria of 1992.² Major diagnostic criteria include a fever >1 week in duration, arthralgia >2 weeks in duration, leukocytosis ($\geq 10,000/\mu\text{L}$), and an evanescent salmon pink or urticarial skin eruption. Sore throat, lymphadenopathy, hepatomegaly, splenomegaly, transaminitis, and negative antinuclear antibody and rheumatoid factor are considered minor diagnostic criteria; five or more criteria, with at least two major features, are required for diagnosis. In 2002, Fautrel et al further proposed increased ferritin levels as one of the major diagnostic criteria.⁴ An atypical rash may therefore pose a diagnostic challenge, leading to delayed diagnosis and potentially worsening disease outcome and complications.

With elevated ferritin, leukocytosis, fever, history of recent migratory arthralgias, and possible hives, AOSD was on the differential. However, our patient's eruption with lichenified, hyperpigmented papules and plaques was atypical for AOSD, and urticaria was not present on exam. Moreover, histological findings were different from the typical histology of AOSD. In fact, the case was initially read as a possible allergic drug reaction due to the amount of dyskeratosis and eosinophils. However, in a drug reaction, vacuolar interface and involvement of the basal layer with necrotic keratinocytes—findings not present in our patient's histology—are usually seen.⁵

Our case is consistent with atypical presentations of AOSD found in more recent studies. Lee et al found that a distinct lichenoid eruption of papules and plaques was commonly observed in their study of 11 patients with AOSD.⁶ These lesions were characterized histologically by multiple individual necrotic keratinocytes in the upper epidermis and a dermal infiltrate of neutrophils.⁶ Moreover, their patients with persistent papules and plaques also exhibited linear lesions like our patient. They noted that these linear arrays revealed the same characteristic changes on histology as the papules and plaques. Thus, they were not excoriation marks but rather represented Koebner's phenomenon,⁶ which is the appearance of a skin condition on lines of trauma. In addition, in a retrospective review of atypical AOSD with 81 cases reports, Garcia et al found that persistent pruritic papules and/or plaques were the most common atypical cutaneous manifestation.⁷ These lesions had a distinct histological pattern characterized by singly or aggregated necrotic keratinocytes in the upper layers of the epidermis and a perivascular inflammatory infiltrate in the upper and mid dermis; the inflammatory infiltrate consisted of lymphocytes and neutrophils with an occasional presence of eosinophils.⁷ These atypical papules and plaques often presented in addition to the typical evanescent rash but sometimes were the

only cutaneous manifestation.^{6,7} Another retrospective review of 36 patients diagnosed with AOSD found that although 86% of patients presented with the typical evanescent rash, 78% of patients had pruritic, papular eruptions.⁸

Santa et al's report of AOSD concluded that this atypical presentation may have been underrecognized in the past.¹ Given the prevalence of this atypical rash and histology in recent studies,^{7,8} this cutaneous presentation may be underreported, making it important for clinicians to recognize this variant of AOSD.

ORCID

Elizabeth Wilder <http://orcid.org/0000-0002-9175-7871>

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