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Adult-onset Stills Disease from Dermatological Perspective: A Case with Atypical Cutaneous Manifestation

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Abstract

Still's disease is a rare and complex systemic autoinflammatory disorder. Characterized by high fevers, salmon-colored rash, and joint involvement, this condition can be a challenging diagnosis due to its overlapping symptoms with other illnesses [1,2]. First described by British physician Sir George Still in 1897, the disease manifests in both systemic juvenile idiopathic arthritis (sJIA) and adult-onset Still's disease (AOSD), each carrying its own set of clinical nuances and implications [3,4]. Epidemiological data on AOSD are characterized by a prevalence estimated at 0.73 to 6.77 per 100,000 individuals, a bimodal age distribution with two peaks of onset (the age groups of 16–25 years and 36–46 years), a mean age of approximately 38 years and without sex predilection [5-7]. Recent advancements in medical research have shed light on the pathophysiology of Still's disease, emphasizing the role of genetics and immune system components such as cytokines and infectious agents [7,8]. Otherwise, the exact etiology is still unknown. Diagnosing AOSD is challenging due to the absence of pathognomonic clinical signs or serologic markers. Here we present a patient with atypical cutaneous manifestations associated with adult-onset Still disease.

Keywords: Stills disease; Immune system; Autoinflammatory disorder; High fevers; Joint; Systemic juvenile idiopathic arthritis

Introduction

Still's disease is a rare and complex systemic autoinflammatory disorder. Characterized by high fevers, salmon-colored rash, and joint involvement, this condition can be a challenging diagnosis due to its overlapping symptoms with other illnesses [1,2]. First described by British physician Sir George Still in 1897, the disease manifests in both systemic juvenile idiopathic arthritis (sJIA) and adult-onset Still's disease (AOSD), each carrying its own set of clinical nuances and implications [3,4]. Epidemiological data on AOSD are characterized by a prevalence estimated at 0.73 to 6.77 per 100,000 individuals, a bimodal age distribution with two peaks of onset (the age groups of 16–25 years and 36–46 years), a mean age of approximately 38 years and without sex predilection [5-7]. Recent advancements in medical research have shed light on the pathophysiology of Still's disease, emphasizing the role of genetics and immune system components such as cytokines and infectious agents [7,8]. Otherwise, the exact etiology is still unknown. Diagnosing AOSD is challenging due to the absence of pathognomonic clinical signs or serologic markers. Here we present a patient

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with atypical cutaneous manifestations associated with adult-onset Still disease.

Case Presentation

A 45-year-old male presented to the Infectious Disease Service with complaints of persistent fever for approximately three months. He also reported a pruritic rash involving the superior trunk and extremities, present for at least one month. Additional symptoms included spiking fevers (≥39°C), cough, myalgias, arthralgias, fatigue, muscle weakness, excessive sweating, and dysphagia.

Initial laboratory findings revealed several abnormalities, including leukocytosis (32.9 × 10^3/µL, reference range: 4–10.5 × 10^3/µL) with granulocytosis (30.3 × 10^3/µL, reference range: 1.6–7.56 × 10^3/µL), anemia (RBC 2.55 × 10^6/µL, Hemoglobin 6.9 g/dL, Hematocrit 20.4%), thrombocytosis (172 × 10^3/µL, reference range: 150–400 × 10^3/µL), elevated inflammatory markers (CRP 12.4 mg/dL, reference range: <0.3 mg/dL), renal dysfunction (uremia 179 mg/dL, reference range: 19.1–44.1 mg/dL; creatinine 3.37 mg/dL, reference range: 0.72–1.25 mg/dL), and significantly elevated ferritin levels (8232.2 ng/mL, reference range: 22–275 ng/mL). Autoimmune markers, including ANA and RF, were negative. Extensive infectious disease evaluation was also negative. Radiologic imaging did not reveal lymphadenopathy or organomegaly (Figure 1,2).

A multidisciplinary team diagnosed AOSD based on Yamaguchi's criteria. The patient was started on methylprednisolone 80 mg/day along with renal supportive therapy. Due to worsening renal function, oliguria, and the development of acute kidney injury, hemodialysis was initiated (Figure 3).

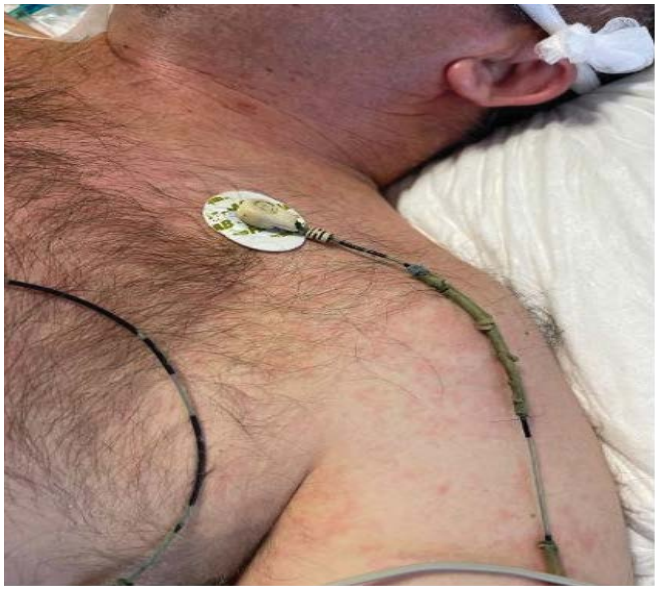

Figure 1: Irregular erythematous confluent plaques over the arm.

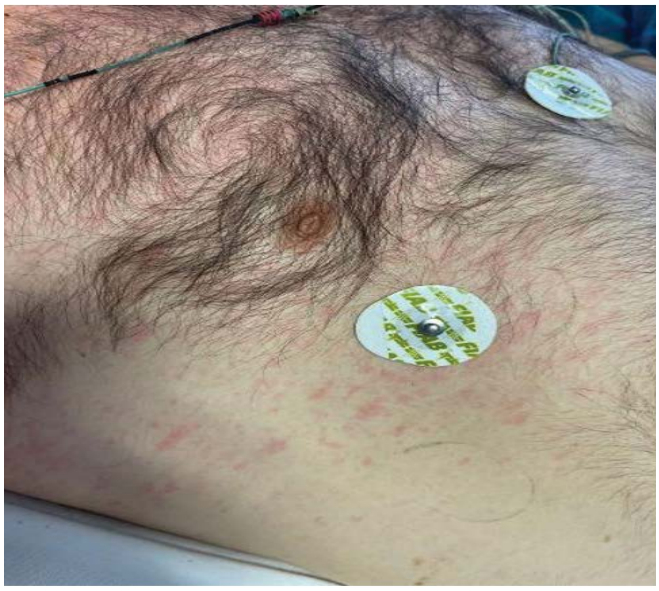

Figure 2: Persistent pruritic erythematous plaques in the trunk.

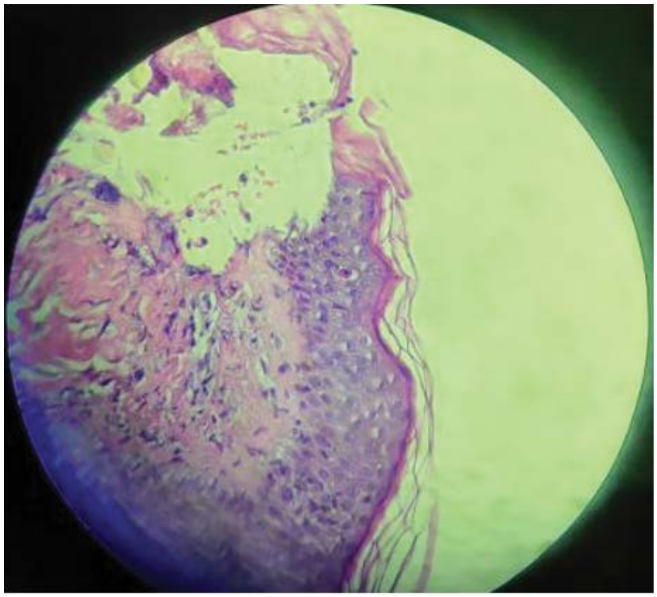

Figure 3: Dyskeratosis with necrotic keratinocytes and irregular acanthosis.

Two days later, the patient's condition deteriorated further with a drop in SpO_2 to 82.85%, necessitating transfer to the intensive care unit (ICU). Consequently, methylprednisolone was increased to 100 mg/day to control systemic inflammation (Figure 4).

On physical examination, persistent erythematous plaques and irregular confluent erythema were noted. Dermatology consultation was obtained, and a skin biopsy was performed from a lesion on the lateral trunk. Histopathological findings included dyskeratosis with necrotic keratinocytes, irregular acanthosis, basal zone vacuolization, and perivascular

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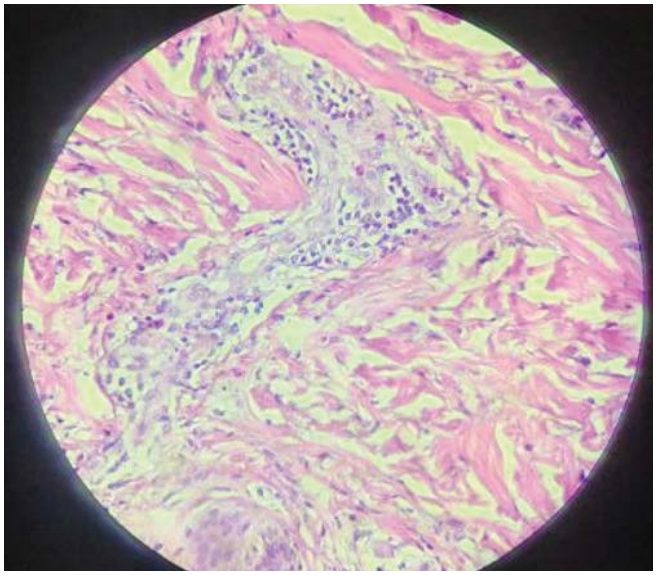

Figure 4: Periadnexal mixed infiltrate with lymphocytes and neutrophils.

mixed inflammatory infiltrate composed of neutrophils and lymphocytes. These findings were consistent with the persistent papules and plaques variant of AOSD, and drug eruption was ruled out (Figure 5).

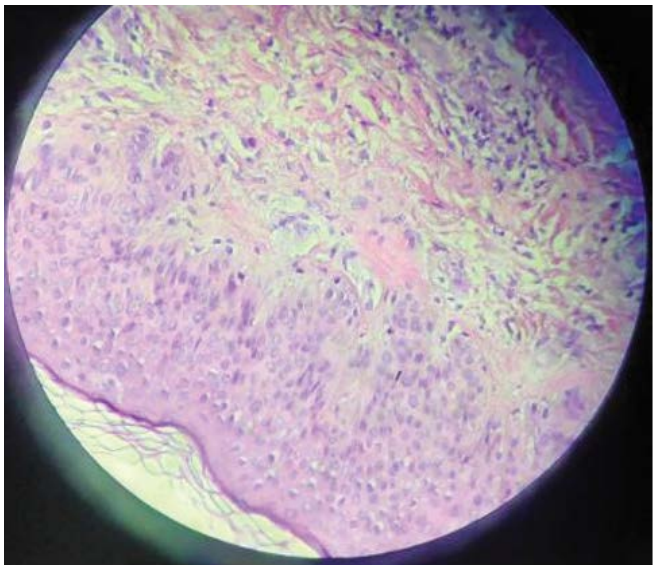

Figure 5: Basal zone vacuolization and perivascular mixed infiltrate.

Discussion

The diagnosis of AOSD is largely clinical and requires the exclusion of other conditions such as infections, malignancies (particularly lymphomas), and autoimmune diseases [7]. The Yamaguchi criteria are the most widely recognized diagnostic tool for AOSD diagnosis [9]. According to these criteria, a diagnosis is made if at least five features are present, including two major criteria. The major criteria include fever of at least 39°C lasting at least one week, arthralgias or arthritis lasting two weeks or longer, a transient salmon-colored rash, and leukocytosis (≥10,000/mm³) with at least 80% granulocytes. Minor criteria include sore throat, lymphadenopathy and/or splenomegaly, liver dysfunction, and negative RF and ANA tests. Our patient fulfilled three major criteria (high fever, arthralgia, leukocytosis with predominant granulocytes) and minor criteria such as sore throat, ANA, and RF negative. Common laboratory findings in AOSD reflect an ongoing inflammatory process. These include an ESR and CRP, high white blood cell count with neutrophilia, hypoalbuminemia, elevated liver enzymes, anemia, thrombocytosis, and significantly increased serum ferritin levels. Although high ferritin levels are not specific to AOSD, a dramatic increase (often more than five times the normal value) strongly supports the diagnosis. Continuous long-term follow-up is often necessary, as life-threatening systemic complications can appear over time [2,7,10].

The presence of a typical salmon-pink maculopapular rash is a key component of the major diagnostic criteria for AOSD. It is usually asymptomatic, coincides with fever, and fades as the fever subsides [7]. Despite this, recent studies have increasingly reported atypical eruptions in AOSD patients. They have been reported in 29-78% of AOSD patients and include urticarial papules, lichenoid papules, dermographism-like lesions, vesiculopustular eruptions, a widespread peau d'orange appearance of the skin, dermatomyositis-like lesions, prurigo pigmentosa-like lesions, and lichen amyloidosis-like lesions that could be markers of disease severity, potentially necessitating more aggressive treatment [11-13]. Lee et al. [13] propose that these may represent stages of a single evolving process and note a seasonal presentation pattern [11]. We presented a case of an AOSD patient with an atypical, persistent rash that was not fever-related. It manifested as persistent, itchy, erythematous plaques, and irregular confluent erythema located in the upper superior extremities and trunk. The initial cutaneous features were overlooked and mistakenly presumed to be the typical rash associated with AOSD. However, a thorough dermatological examination, supported by biopsy, revealed otherwise.

Histopathological findings are distinctive for typical and atypical skin eruptions. Persistent pruritic AOSD skin lesions involving the upper layers of the epidermis are characterized by dyskeratotic cells. The nature of dyskeratotic cells in AOSD remains unclear, whether these cells are necrotic or apoptotic. AOSD with an evanescent rash showed no dyskeratotic cells [14,15]. In our patient, dyskeratosis with necrotic cells in the epidermis and dermal inflammatory cells are the main findings, as reported in other studies. In a retrospective study,

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the presence of dyskeratosis was significantly associated with elevated serum IL-18 levels, suggesting that it may serve as a negative prognostic indicator [15]. These findings align with the outcome observed in our patient who experienced a complicated clinical course.

There are no internationally recognized guidelines for the management of AOSD. The first-line treatment is systemic glucocorticoids, and in refractory or dependent cases, methotrexate or biologics can be alternative options [7,15]. In our case, methylprednisolone therapy was initiated on the first day of AOSD diagnosis. If the atypical rash had been identified earlier, a higher dose of glucocorticoids might have been administered, given the association of atypical rashes with a more severe clinical course in such cases.

Conclusions

Adul-onset Still disease is an inflammatory disease that can be life-threatening because of systemic complications. Although not very specific, atypical cutaneous features should be considered in the diagnosis and management of ASDO patients. They can be an early valuable predictor of the patient's prognosis. This case underscores the importance of early dermatological consultation and thorough evaluation of atypical rashes in AOSD, which can indicate a more severe clinical course and necessitate more aggressive treatment.

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