Evanescent, episodic salmon-colored macules in a young woman

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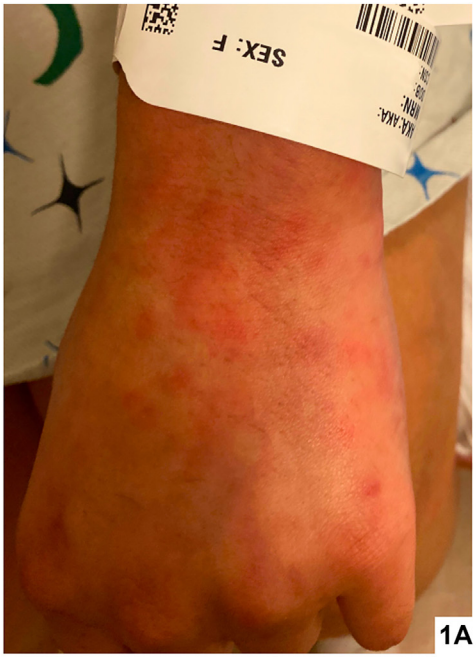
Key words: adult-onset Still's disease; AOSD; autoinflammatory syndromes; fever of unknown origin; Still disease in the adult.



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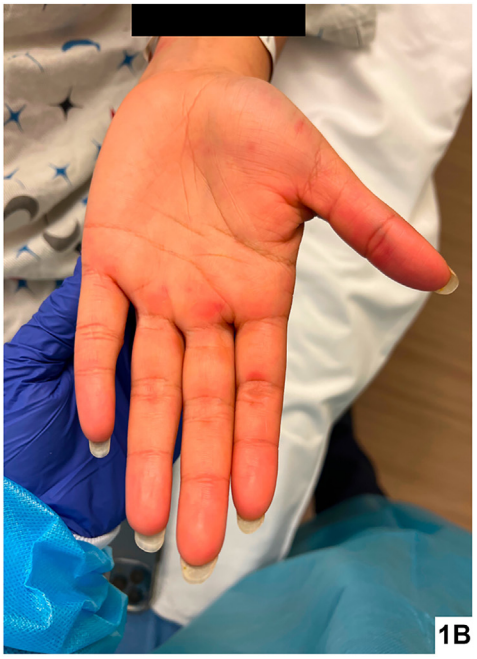

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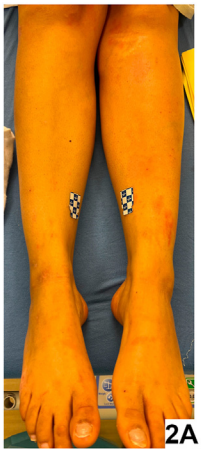

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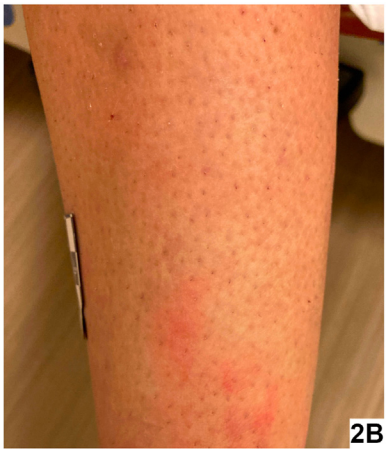

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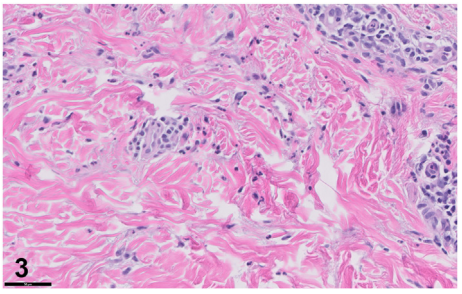

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PRESENTATION

A 29-year-old female presented for an episodic eruption of innumerable erythematous blanchable thin papules and plaques on the back and bilateral extremities. There were erythematous macules on the palms (Figs 1 and 2); the face and oropharynx were spared. She endorsed new-onset joint pain of ankles, elbows, and wrists.

For 1 month preceding these symptoms, she experienced fevers, cough, and sore throat. Histology sections showed dermal edema with sparse perivascular and interstitial infiltrate, consisting of lymphocytes with scattered neutrophils, and the presence of karyorrhectic debris (Fig 3); direct immunofluorescence was negative.

Question 1: What is the appropriate next step?

A. Start oral prednisone 40 mg daily for 3 days

B. Start oral cetirizine and diphenhydramine, refer urgently to allergy

C. Order complete blood count with differential, serum chemistries, and antinuclear antibodies (ANA)

D. Order serum complement C3 and C4, anti-Ro, and anti-La antibodies

E. Start high-dose aspirin and refer to rheumatology

Answer:

A. Start oral prednisone 40 mg daily for 3 days — Incorrect. This patient's systemic symptoms suggest a broad differential requiring further workup.

B. Start oral cetirizine and diphenhydramine, refer urgently to allergy — Incorrect. Although the histology could be consistent with urticaria, extensive systemic symptoms warrant further workup before presumptive treatment with antihistamines.

C. Order complete blood count with differential, serum chemistries, and ANA — Correct. This patient likely has adult-onset Still's disease (AOSD). The majority of AOSD patients experience an episodic evanescent eruption of discrete salmon-colored macules which are asymptomatic and may exhibit the isomorphic response.[1] Typically the eruption comes and goes with spiking and remitting fevers.[2] The trunk is most often affected, with some cases involving the extremities, palms, and soles.[1-3] AOSD is diagnosed with Yamaguchi's criteria, which has a sensitivity of 96.3%, specificity of 98.9%, and positive and negative predictive values of 94.5% and 99.3%, respectively.[4] Diagnosis requires 5 criteria, at least 2 of which must be major. Major criteria include intermittent fever (≥1 week), arthralgia (≥2 weeks), characteristic skin eruption, and serum white blood cell count over 10,000 (≥80% polymorphonuclear cells). Minor criteria include pharyngitis, lymphadenopathy, hepatomegaly or splenomegaly, transaminitis, and negative ANA and rheumatoid factor. Diagnosis remains challenging; many conditions present with features seen in AOSD.

D. Order serum complement C3 and C4, anti-Ro, and anti-La antibodies — Incorrect. Serum complement is useful for characterizing urticarial vasculitis (UV); however, histology was inconsistent with UV. UV can be a sign of Sjogren's syndrome, which also usually has anti-Ro antibodies, but this patient lacks xerostomia and keratoconjunctivitis. If connective tissue disease is suspected, ANA and rheumatoid factor should be checked first.

E. Start high-dose aspirin and refer to rheumatology — Incorrect. There has been no evaluation for rheumatic disease, which should be done prior to considering referral to rheumatology.

Question 2: What is the most appropriate treatment for this patient?

A. Oral prednisone

B. Methotrexate

C. Low-dose aspirin

D. Interleukin-1 blockade

E. Ultrapotent topical corticosteroids

Answer:

A. Oral prednisone — Correct. The majority of AOSD patients require oral prednisone 40 to 60 mg

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daily, usually tapered after 4 to 6 weeks. Forty-five percent of these patients become chronically steroid dependent.[2]

B. Methotrexate — Incorrect. If relapse occurs upon tapering prednisone, methotrexate is a common second-line option.[3]

C. Low-dose aspirin — Incorrect. Patients with AOSD may respond to high-dose aspirin or nonsteroidal anti-inflammatory drugs, such as naproxen.[2]

D. Interleukin-1 blockade — Incorrect. Case series report utility in AOSD that has been refractory to treatment with other medications, including glucocorticoids and methotrexate, but it is not a first-line treatment.

E. Ultrapotent topical corticosteroids — Incorrect. This patient has AOSD, and oral corticosteroids are first-line treatment.

Question 3: What is the most frequent fatal complication of AOSD?

A. Fulminant hepatitis

B. Disseminated intravascular coagulopathy

C. Multiple organ failure

D. Cardiac tamponade

E. Macrophage activation syndrome

Answer:

A. Fulminant hepatitis — Incorrect. This is a life-threatening complication of AOSD but not the most common cause of death. Liver abnormalities, including hepatomegaly and transaminitis, are observed in AOSD and may lead to acute liver failure. These changes are generally related to the disease, rather than treating medications, as they typically improve as the disease remits and predate the start of nonsteroidal anti-inflammatory drugs.[5]

B. Disseminated intravascular coagulopathy — Incorrect. This is a life-threatening complication of AOSD but not the most common cause of death.

C. Multiple organ failure — Incorrect. This is a life-threatening complication of AOSD but not the most common cause of death.

D. Cardiac tamponade — Incorrect. This is a life-threatening complication of AOSD but not the most common cause of death. Other cardiac complications include pericarditis and myocarditis, leading to arrhythmias and heart failure.[2,6] Affected patients may present with cough, chest pain, or dyspnea. Pleuritis and acute respiratory distress syndrome may occur with AOSD but are more likely to present with macrophage activation syndrome (MAS).[6]

E. Macrophage activation syndrome — Correct. MAS occurs in up to 15% of AOSD patients and is the most frequent fatal complication, with mortality ranging 10% to 41%. MAS typically presents with an unremitting fever, abdominal pain, hepatosplenomegaly, neurologic findings, cytopenia, and hemophagocytosis in the bone marrow, spleen, or lymph node.[2] Serum ferritin is a useful indicator of AOSD disease activity; levels 5 times normal may herald MAS.[2] The percentage of the ferritin that is glycosylated in AOSD tends to be lower than that in other rheumatic diseases and may remain low during the active phase and remission.[7]

Abbreviations used:

ANA: antinuclear antibodies
AOSD: adult-onset Still disease
MAS: macrophage activation syndrome
UV: urticarial vasculitis

Conflicts of interest

None disclosed.

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