Salmon-pink skin rashes in adult-onset Still's disease

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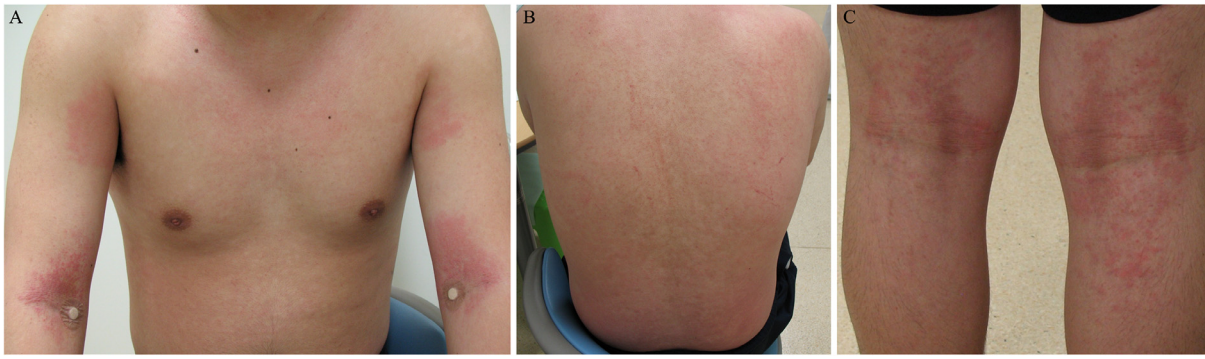

FIG. 1.

CASE PRESENTATION

An otherwise healthy 21-year-old man visited a neighborhood clinic for evaluation of pharyngeal pain, arthralgia, and nocturnal fever that had begun the previous day. The arthralgia and pharyngeal pain had appeared in conjunction with the fever. The symptoms remained after administration of levofloxacin and cefditoren pivoxil. One week later, he was hospitalized because the symptoms did not improve. Two weeks after hospitalization, he had developed left inguinal pain, salmon-pink skin rashes, and >10-kg weight loss. His family history and allergic history, including atopic dermatitis, were unremarkable. Physical examination revealed facial redness, stomatitis, and salmon-pink skin rashes from the trunk to the limbs (Figs. 1A–C). The skin rashes were characterized by pruritus, diurnal variation, and no Köbner phenomenon but showed nocturnal expansion along with the fever. The patient had mild liver dysfunction, hyperferritinemia (2097.6 ng/mL; reference range, 21.0–282.0 ng/mL), and leukocytosis (10,820 cells/mm^3; reference range, 4000–9000 cells/mm^3) with a neutrophil count of <80%; however, serum virus, autoimmune antibody, blood culture, bone marrow puncture, and fundus examinations were negative or nonspecific. Pathological findings of a skin biopsy from the salmon-pink skin rashes on his trunk were also nonspecific. The patient fulfilled three major criteria (fever, arthralgia, and skin rash) and three minor criteria (sore throat, abnormal liver function, and negative rheumatoid factor and antinuclear antibody) in the Yamaguchi classification of adult-onset Still's disease (AOSD).[1] Oral prednisolone (40 mg/day) was initiated in accordance with the clinical practice guideline for AOSD.[2] Two weeks later, the patient recovered with a decreased ferritin level (235.5 ng/mL). After tapering of prednisolone, the patient was discharged. However, he subsequently experienced several episodes of recurrence. After adjustment of the prednisolone dosage for more than 5 years, the patient was finally diagnosed with AOSD. He thereafter experienced no episodes of recurrence and required no prednisolone.

The lack of specific diagnostic tests, specific features, and robust diagnostic criteria makes correct diagnosis of AOSD challenging for physicians.[3] AOSD is diagnosed by excluding specific diseases that cause symptoms similar to those of AOSD. When diagnosing AOSD, the clinician's rounds should be based on the patient's fever pattern because skin rash and arthralgia are often missed if the internist makes only morning rounds. Although the clinical manifestations of AOSD are diverse, the major clinical presentations include daily recurring fever, salmon-pink skin rashes that are synchronous with disease activity, and arthritis. Patients can have myalgia, pharyngitis, lymphadenopathy, and splenomegaly. Elevated ferritin levels, liver enzyme levels, and leukocyte counts can be helpful for diagnosis of AOSD.[3]

Because AOSD is a diagnosis of exclusion, the differential diagnoses include a wide variety of diseases such as malignant neoplasms, infectious diseases, and systemic autoimmune diseases as well as adverse events of medications. Malignancies such as non-Hodgkin lymphoma, which manifests with fever, lymphadenopathy, and leukocytosis, can trigger diagnostic confusion. A

lymph node biopsy can help to distinguish AOSD from malignant lymphoma. Bacterial and viral infections can also cause fever, leukocytosis, and rashes. However, laboratory findings or blood cultures are usually specific for infectious diseases. Autoimmune or rheumatologic arthritis can clinically resemble AOSD, but unlike AOSD, autoantibodies such as anti-double-stranded DNA or rheumatoid factor antibodies are positive. Hyperferritinemia (serum ferritin level of ≥2500 μg/L) is highly specific for AOSD, and when combined with the Yamaguchi criteria, its sensitivity is 43.0% and specificity is 99.9%.[4] However, hyperferritinemia is also seen in macrophage activation syndrome, catastrophic antiphospholipid syndrome, and septic shock.[5] Compared with AOSD, macrophage activation syndrome tends to show a lower erythrocyte sedimentation rate with lower white blood cell counts and an elevated C-reactive protein level. In addition, both catastrophic antiphospholipid syndrome and septic shock are involved in infection or trauma.[5] Furthermore, drug-induced hypersensitivity syndrome can mimic the manifestations of the cutaneous lesions in AOSD.[6]

Salmon-pink skin rashes that typically appear with fever spikes, extreme elevation of serum ferritin levels, careful follow-up, and confirmation of response to corticosteroid therapy are clues to the diagnosis of AOSD.[3]

CONFLICTS OF INTEREST

None.

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