CASE REPORT

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Adult-Onset Still's Disease: Persistent Pruritic Erythematous Plaques and Papules

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ABSTRACT We present a case of a 24 year-old woman with high fever, pruritic erythematous plaques and papules on the trunk and extremities, inflammatory peripheral joint symptoms and sore throat for two weeks. The patient had neutrophilic leucocytosis, elevated acute phase proteins (erythrocyte sedimentation rate, C-reactive protein and ferritin) and increased liver enzymes. Abdominal ultrasonography revealed mild splenomegaly. After the exclusion of infection, malignancy and other rheumatic inflammatory diseases, the patient was diagnosed with adult-onset Still's disease (AOSD) meeting to Yamaguchi criteria. Clinical symptoms and abnormal laboratory tests rapidly improved within days of starting glucocorticoid treatment. The presence of typical evanescent skin rash (salmon-pink) is one of the major criteria of disease, however different skin lesions such as persistent pruritic erythematous plaques and papules have been occasionally reported in association with AOSD on trunk and extremities, which may be confused with other diseases. Therefore, the recognition of the atypical skin lesions with AOSD is necessary for diagnosis and choice treatment of disease.

Keywords: Still's disease, adult-onset; pruritus; erythema

Adult-onset Still's disease (AOSD) was first described in adult patients with features similar to the systemic form of juvenile idiopathic arthritis (sJIA) by Bywaters in 1971.[1] It is a rare, acute-onset, systemic inflammatory disease with unknown etiology that is responsible for a significant proportion of cases of fever of unknown orgin. Its pathogenesis is unknown, infectious agents as initiators of the disease have implicated but a definitive agent has been revealed.[2] Current opinion that increased cytokine production such as IL-1, IL-6, IL-18, TNF-α and IFNγ plays an important pathophysiological role in AOSD.[3]

AOSD is characterised by intermittent high fever, arthralgia/arthritis, sore throat, the well-described typical evanescent rash, lymphadenopathy, splenomegaly and liver dysfunction. Other manifestations rarely seen are serositis, myopericarditis, interstitial pulmonary disease. The presence of neutrophilic leucocytosis and increased serum ferritin level are significant laboratory markers in establishing the diagnosis. Diagnosis is usually made using Yamaguchi criteria. Major criteria are high fever for >1 week, arthralgias for 2 weeks, neutrophilic leukocytosis (>10.000 mm^3 with >80% of neutrophils), and the typical evanescent rash. Minor criteria include sore throat, lympadenopathy and /or splenomegaly, liver dysfunction, and the absence of rheumatoid factor and antinuclear antibody. A minimum of 5 criteria, including at least 2 major criteria, were

required for diagnosis after exclusion of other diseases accompanied by similar symptoms such as infection, malignancy and various systemic inflammatory rheumatic diseases.[4]

The "Still"s rash' is consists of a transient "salmon pink" usually nonpruritic macular , maculopapular eruptions localised on trunk and upper extremities, may be mildly pruritic. It is usually observed with the fever spike. Various atypical cutaneous manifestations have been reported among AOSD patients, persistent pruritic eruptions such as urticarial erythema, flagellate erythema, erythematous papules, and/or plaques on trunk and extremities may occur in some patients.[5-9] The recognition of this clinical variant is necessary for diagnosis.

Herein we present a young female patient with acute-onset high fever, persistent erythematous skin eruptions with prurity and polyarthralgia and polyarthritis for two weeks, who was diagnosed as adult Still's disease and a favorable response was observed with glucocorticoid treatment within a short time.

CASE REPORT

A 24-year-old woman who presented with high fever, sore throat, articular symptoms, and pruritic rash on her extremities and trunk for two weeks. She had no significant medical history and family history, was not taking any medication. Clinical findings at admission were temperature (39 C°), polyarthralgia, arthritis of the knees, elbows and proximal interphalangeal joints of both hands, and she had pruritic erythematous plaques and papules on the chest , back, abdomen and bilateral extremities (Figures 1, 2).

Laboratory investigations disclosed normocytic normochromic anemia (hemoglobin 12.0 g/l, hematocrit 35.1%), leucocytosis with neutrophil (15.800x10^3/uL, 80.9 %), normal eosinophil count, elevated sedimentation rate (ESR) 103 mm/h, CRP 89.6 mg /dl (<5), ferritin 9837 ng/ml (10-204), ALT 111 U/L (5-34) and AST 150 U/L (7-36). Most of viral antibodies (Anti-CMV IgM, Anti- HAV IgM, Anti-Hbc IgM, Anti-HBe Ag, Anti HCV) and HBsAg were negative and anti-HBs was positive. Bacterial cultures were unremarkable, bacterial serology showed negative for brucella and salmonella agglutination. Rheumatoid factor, antinuclear antibody screening test, specific nuclear antibodies and anti-cyclic citrillunated peptid were negative. Serum complement 3 and 4, immunoglobulin values were within normal limits. Abdominal ultrasonography revealed hepatosteatosis and splenomegaly (15.5 cm).

During her hospitalisation, we evaluated the patient other potential differantial diagnosis. In the patient with high fever, persistent pruritic skin rash and arthritis laboratory profile revealed systemic inflammation with neutrophilic leucocytosis,increased CRP and ferritin as acute phase reactants. Viral and bacterial infection markers and autoimmune tests such as antinuclear antibody, rheumatoid factor and others indicating systemic autoimmune diseases were negative. Neoplastic disorders such as leukemia, lymphoma were excluded with atypical rash and the haematological profile. After on extensive work up, the patient was diagnosed with AOSD based on Yamaguchi criteria for the diagnosis of AOSD and also a very high ferritin level.[2]

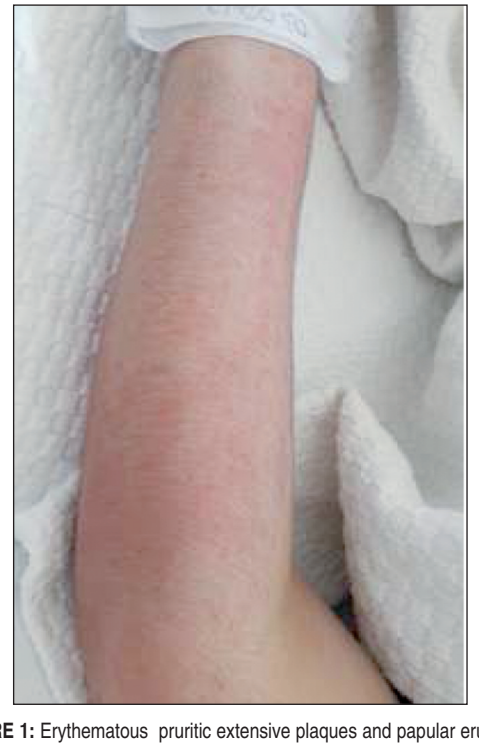

FIGURE 1: Erythematous pruritic extensive plaques and papular eruptions on upper extremity.

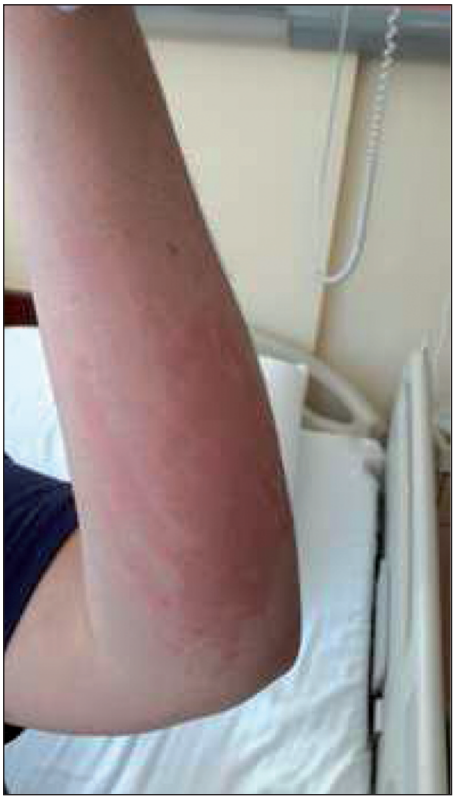

FIGURE 2: Erythematous pruritic extensive plaques and papular eruptions on forearm.

We initiated treatment with 1 mg/kg/day of prednisone and observed a succesfully response to the treatment within days. Her fever, skin and joint symptoms and elevated laboratory values largely regressed. The dose of corticosteroid was tapered gradually each week. After one month, all clinical findings were disappeared and abnormal laboratory tests were normalized (leucocyte 10.43x10^3/uL, neutrophil 53.14% hemoglobin 13.2 g/L, hematocrit 40.9%, ESR 16 mm/h, CRP 0.01 mg/L, ferritin 102 ng/ml, ALT 24 U/L and AST 34 U/L).

Informed consent: Verbal informed constent was obtained from the patient who presented in this study.

DISCUSSION

AOSD is a febril disorder, fever spiking once a day usually in the evening or night, often accompanied typical evanescent skin rash and the majority of patients have arthralgia and arthritis. Her high fever did'nt return to a normal level until the begining of treatment, which was accompanied with persistent pruritic rash on trunk and extremities and inflammatory articular findings. She had also an aseptic non exudative pharyngitis which is common presentation for AOSD. Typical salmon pink skin rash of AOSD is one of the major criteria of AOSD according Yamagushi's criteria.[4] Her skin manifestation was non-classic, non-evanescent and pruritic plaques and papules. An extensive infectious serological workup and autoimmune serology were negative. The different cutaneous features such as pruritic eruptions associated with AOSD have been reported as case report or case series.[5-9] The prevalance of atypical cutaneous features among AOSD patients was 14% in a review.[6] Nagai et al. reported that five of 80 patients (29%) with AOSD revealed atypical skin rash.[7] Persistent pruritic rash of histopathological findings show dyskeratosis confined to the upper epidermis and superficial dermal infiltrate containing scattered neutrophils.[7-9] Skin biopsy was not obtained from the patient. Laboratory findings in AOSD are similar to those in other inflammatory events including leucocytosis (mostly neutrophils), anemia, acute phase proteins (CRP, ESR, liver enzymes and ferritin), which were present in our patient. Hyperferritinemia is often used for screning, although it is non-specific, particularly prevalent in AOSD which is thought to be related to cytokines release.[10] In most studies, serum ferritin levels of 1000 ng/ml (five times the upper limits of normal, 40-200 ng/ml) has been used to suggest AOSD, our patient had very high level of ferritin. Serum ferritin levels correlate with disease activity and often normalise at the remission time.[11] She showed a significant decrease from initial high ferritin value (9837 ng/ml) to normal value (102. 6 ng/ml) within four weeks, which accompanied with other abnormal laboratory findings and a remarkable clinical improvement under corticosteroid treatment. In AOSD, non-steroidal antiinflammatory drugs, corticosteroids are first-line agents, hydroxycholoroquin may be added to this regime.

Comment: AOSD is a rare disease, therefore, its well-recognition is require for early diagnosis

and appropriate treatment of the disease. It may be diffucult to diagnose AOSD in the patients presenting atypical skin semptoms. Clinical suspicion is very important, the presentation AOSD with different skin manifestations should be remembered after exclusion of other diagnoses.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

All authors contributed equally while this study preparing.

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