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Adult-Onset Still's Disease: Case Report

Erişkin Still Hastalığı: Olgu Sunumu

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ABSTRACT

Introduction: Adult-onset Still's disease (ASD) is a systemic inflammatory disease of unknown etiology and pathogenesis. ASD, one of the most important causes of fever of unknown origin, is diagnosed after ruling out infection, malignancy, and rheumatologic diseases. It may also present with fever alone, without typical skin rash and articular manifestations.

Case Report: There are no pathognomonic laboratory findings in ASD. In this paper, we report a case that presented to the emergency department with fever, malaise, and joint pain for 5 days and was subsequently diagnosed with ASD.

Conclusion: In patients with prolonged fever combined with musculoskeletal symptoms and macular rash, the differential diagnosis should include ASD. Timely diagnosis and treatment of the disease can prevent complications and lead to a favorable prognosis

ÖZET

Giriş: Erişkin Still hastalığı (ESH), etiyolojisi ve patogenezi bilinmeyen sistemik inflamatuvar bir hastalıktır. Nedeni bilinmeyen ateşin önemli nedenlerinden birisi olan ESH'nın tanısı infeksiyon, malignite ve romatolojik hastalıkların dışlanmasıyla konur. Hastalık, tipik deri döküntüleri ve eklem bulguları olmaksızın tek başına yüksek ateşle de karşımıza çıkabilmektedir.

Olgu Sunumu: Erişkin Still hastalığının patogonomik bir laboratuvar bulgusu yoktur. Bu yazımızda beş gündür devam eden ateş, halsizlik, eklem ağrısı ve vücudunda yaygın maküler döküntü şikâyetleriyle acil servise başvuran ve yapılan tetkiklerde ESH tanısı konulan bir olgu sunuldu.

Sonuç: Uzun süren ateş ile birlikte, kas-eklem şikâyetleri ve maküler döküntüleri olan hastalarda ayırıcı tanıda ESH düşünülmelidir. Hastalığın erken tanı ve tedavisi ile komplikasyon gelişimi önlenerek prognoza olumlu katkı sağlanabilir.

Keywords: Adult-onset Still's disease, fever, macular rash

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Introduction

Adult-onset Still's disease (ASD) is a systemic inflammatory disease with the same clinical and laboratory properties as the acute systemic form of juvenile chronic arthritis (1). One study reported its incidence as 0.16 per 100,000 (2). The disease has a bimodal age distribution. The first peak is between 15-25 years of age, and the second is between 36-46 years of age. Forty-nine percent of cases are men, and 51% are women (3). Infectious and genetic factors are held responsible in its etiology, although the exact etiologic factors remain unknown (2). A "Quotidian" type fever (body temperature reaching 39°C to 40°C once or twice a day, usually at morning and evening, and decreasing to normal or subnormal levels at least once a day), articular manifestations, maculo-papular skin rash, sore throat, and systemic organ involvement are the main clinical signs and symptoms. The majority of patients has sore throat or other signs of a viral syndrome. Severe myalgia, arthralgia, anorexia, nausea, and rapid weight loss may also be observed (4).

In this paper, we aimed to report a case that presented to the emergency department with sore throat, fever, macular rash, and arthralgia and was subsequently diagnosed with ASD.

Case Report

A 40-year-old woman presented to the emergency department with a 5-day history of malaise, loss of appetite, sore throat, fever, arm and knee pain, and rash all over the body with redness and burning sensation. Her skin rash was vanishing

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after the fever had subsided. She had joint pain involving all joints, particularly both knee joints. She had limitation of movement in both knees but no morning stiffness. Her past and family history was insignificant. She had been given amoxicillin+clavulanic acid for 2 days at an outside clinic. She was admitted to our emergency department because of persistence of her symptoms without any improvement. Her vital signs were as follows: blood pressure: 100/75 mm Hg, pulse rate: 108 bpm, and body temperature: 39.8°C. In her physical examination, the pharynx was hyperemic and the bilateral tonsils were hypertrophic. There were 2-3 painless, soft, mobile lymphadenopathies of less than 1 cm in size in the submandibular region. A diffuse maculo-papular rash that blanched on pressure was also noted, which was more diffuse on the trunk, arms, and legs (Figure 1). The spleen was smooth and painless and was palpated 2-3 cm below the point where the left mid-clavicular line intersected the rib curve. There was no hepatomegaly. Both knee joints were swollen and tender upon palpation. Laboratory results were as follows: erythrocyte sedimentation rate: 102/hour, C-reactive protein 22 mg/dL, white blood cell count: 21,000/mm^3, hemoglobin: 12.4 gr/dL, thrombocyte count: 346,000/mm^3, neutrophil count: 19,800/mm^3, lymphocyte count: 780/mm^3, total protein: 6.5 gr/dL, albumin: 2.5 gr/dL, AST: 76 U/L, ALT: 83 U/L, ALP: 177 U/L, LDH: 551 U/L, CK: 346 U/L, GGT: 472 U/L, ferritin: 9283 ng/mL, iron: 32 ug/dL, iron-binding capacity: 206 ug/dL, and transferrin saturation: 15.5%. Examination of the peripheral smear revealed neutrophils with a left shift. TORCH (toxoplasma, rubella, cytomegalovirus, herpes simplex virus) and EBV (Epstei-Barr virus) panels were both negative. Salmonella and Brucella tube agglutination and Rose-Bengal tests were all negative. Rheumatoid factor (RF), anti-CCP (anti-cyclic citrullinated peptide), anti-nuclear antibody (ANA), anti-neutrophilic cytoplasmic antibody (ANCA), and anti-double-stranded DNA (anti ds-DNA) were normal. Liver function tests were elevated; however, autoimmune and viral hepatitis serology was negative. Bone marrow aspiration was normal. No proliferation was observed in the throat, blood, and urine cultures. Abdominal ultrasonography (USG) revealed an increase in splenic size (145 mm) and a homogenous splenic parenchymal echo. Echocardiographic examination was normal. In light of the available examinations and tests, the patient was diagnosed to have ASD and was admitted to the internal medicine clinic. Non-steroidal anti-inflammatory drugs (NSAIDs) and steroid (prednisolone) were begun. She was then discharged on indomethacin 12 mg/kg/day and called for a follow-up appointment 1 month later.

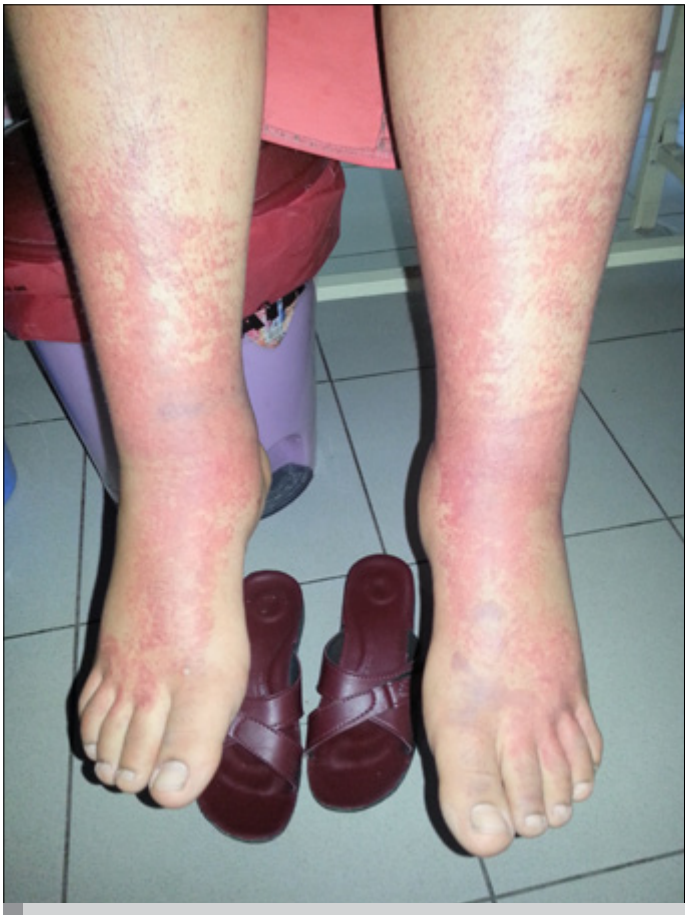

Figure 1. Diffuse maculo-papular erythema in legs

Discussion

It is a systemic inflammatory disease with unknown etiology and pathogenesis. ASD characterized by fever, rash, and articular manifestations. It has no pathognomonic findings. According to the Yamaguchi criteria (1992), its diagnosis first requires ruling out infectious, malignant, and rheumatological diseases, followed by the presence of at least five features, with at least two of these being major diagnostic criteria (6). Yamaguchi criteria are given in Table 1. Our patient was considered to have ASD, since her symptoms and signs met three major and four minor criteria. The major and minor criteria of the Yamaguchi criteria are given below:

Our patient had fever, skin rash, and neutrophilic leukocytosis from major criteria, and sore throat, splenomegaly, liver dysfunction, and RF and ANA negativity from the minor criteria. Lymphadenopathy and organomegaly may be observed in ASD as a result of reticuloendothelial involvement (7). Our patient had lymphadenopathy and splenomegaly but no hepatomegaly.

Serum ferritin and glycosylated ferritin levels are considered to be specific diagnostic criteria for ASD. A ferritin level 5-fold greater than the upper limit of normal has been reported to have a sensitivity of 80% and specificity of 46% for the diagnosis of ASD (8). ANA and RF negativity is important with respect to the differential diagnosis of ASD from other connective tissue disorders. Elevated ferritin levels may be observed as an acute phase reactant in rheumatological diseases, although levels in these diseases are not elevated as high

Table 1. Yamaguchi Criteria (1992)

Major Criteria	Minor Criteria
1- Fever of at least 39 °C	1- Sore throat
2- Arthralgia > 2 weeks	2- Lymphadenopathy or splenomegaly
3- Still rash	3- Liver dysfunction
4- Neutrophilic leukocytosis >10.000	4- RF and ANA negativity

as in ASD. Thus, it has been recommended to measure serum ferritin levels absolutely in cases with fever of unknown etiology, especially when rheumatological signs are also present. Excess elevation in ferritin level combined with elevated CRP and sedimentation rate supports the diagnosis of ASD.

Treatment protocols may include NSAIDs, aspirin, corticosteroids, and immune-modulating drugs, depending on disease severity and organ involvement. NSAIDs and acetylsalicylic acid should be given as first-line treatment in cases with musculoskeletal symptoms and fever (5). While 20% of cases respond to this therapy, adequate control of both arthritis and systemic signs requires modified antirheumatic drugs (DMARD) alone or combined with aggressive steroid treatment in the remaining 80% (9). Presence of high fever attacks, severe articular symptoms, or internal organ involvement may justify corticosteroid (usually prednisolone) use at a dose of 1 mg/kg (3). We began indomethacin 12 mg/kg/day combined with prednisolone 1 mg/kg/day, since our case had combined articular and internal organ (splenomegaly) involvement.

Hematological abnormalities in ASD vanish with remission or effective treatment of the disease (4). Control laboratory tests in our patient revealed normalized hematological (white blood cell count) and biochemical parameters (AST, ALT, ALP, GGT, ferritin) after combined NSAID and steroid therapy.

In patients with prolonged fever combined with musculoskeletal symptoms and macular rash, the differential diagnosis should include ASD. Timely diagnosis and treatment of the disease can prevent complications and lead to a favorable prognosis.

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