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CASE REPORT/OLGU SUNUMU

A Case of Mediterranean Spotted Fever Misdiagnosed as Drug Allergy

Yanlış İlaç Allerjisi Tanısı Almış bir Akdeniz Benekli Ateşi Olgusu

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ABSTRACT

Skin rashes are observed in about 2-3% of patients taking medication for any reason. Since the cutaneous manifestations are also common in viral exanthemas, rickettsial-bacterial infections and rheumatologic diseases, it is important to exclude other conditions that may mimic drug-induced allergic reactions in patients having skin rashes. Here, we report a patient of Mediterranean Spotted Fever (MSF) who was initially misdiagnosed as a drug eruption. The clinician should take into account the skin manifestations that can also be seen in the course of infectious diseases and they should consider the possibility of various infections in the diagnosis of drug allergy such as a Mediterranean Spotted Fever.

Key words: Drug hypersensitivity, exanthema, Mediterranean spotted fever, rickettsia

ÖZ

Deri döküntüleri herhangi bir nedenle ilaç kullanan hastaların yaklaşık %2-3'ünde gözlenmektedir. Cilt bulguları aynı zamanda viral döküntüler, riketsiyal-bakteriyel enfeksiyonlar ve romatizmal hastalıklarda da sık görülen bir bulgu olduğundan, deri döküntüsü olan hastalarda ilacın neden olduğu allerjik reaksiyonları taklit eden diğer durumları dışlamak önemlidir. Burada, başlangıçta yanlış ilaç allerjisi tanısı almış bir Akdeniz Benekli Ateşi olgusu sunulmuştur. Klinisyenler enfeksiyon hastalıklarının seyrinde de görülebilen cilt bulguları konusunda dikkatli olmalı ve ilaç allerjisi ayırıcı tanısında Akdeniz Benekli Ateşi gibi çeşitli enfeksiyonların olasılığını düşünmelidir.

Anahtar kelimeler: Akdeniz benekli ateşi, ekzantem, ilaç allerjisi, riketsiya

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INTRODUCTION

The skin is frequently affected organ of drug hypersensitivity reactions and skin rashes are observed in about 2-3% of patients taking any particular medication (1). Maculopapular rash is the most common presentation of the drug allergy which appears within days to 3 weeks after drug exposure (1). Antibiotics such as sulfonamides, penicillins, anticonvulsants and allopurinol are the most common culprit drugs with the rate of 5% of drug allergy reactions (2,3). Since the cutaneous manifestations are also common in viral exanthemas, rickettsial-bacterial infections and rheumatologic diseases, the drug allergy diagnosis is often challenging (1). It is important to exclude other conditions that may mimic drug-induced allergic reactions. Referral to an allergist in identification and diagnosis of drug allergy is recommended if a drug-induced allergic reaction is suspected (3). The aim of this

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case report is to point out the cooperation between allergists and other disciplines at the diagnostic work up of a patient with suspected drug-induced maculopapular allergic reaction. Here, we reported a patient of Mediterranean Spotted Fever (MSF) who was initially misdiagnosed as a drug allergy.

CASE PRESENTATION

A 52-year-old female patient who lives in Gaziantep (located in the south-east region of Turkey) was referred to emergency unit of state hospital with the symptoms of sore throat, chills, malaise and generalized muscle and joint pain. She was diagnosed as a urinary tract infection. Trimethoprim/sulfamethoxazole (TMP/SXT) treatment was initiated. After two days of the antibiotherapy, generalized rash on her trunk, high fever, increased muscle-joint pain and severe headache was added to her symptoms. TMP/SXT treatment was stopped; she was diagnosed as drug allergy. Local dexamethasone and paracetemol was recommended. During the follow-up, high fever persisted, her rash improved. She was hospitalized to the Infectious Disease inpatient clinic. On physical examination she was conscious, cooperative and fully oriented. She had hyperemic oropharynx. There were maculopapular rashes on her extremities and trunk. All major joints were tender but no erythema or swelling was observed. There was not any other pathologic sign at physical examination. She was non-smoker. She had no history of any allergic and/or systemic disease. Initial laboratory findings were as follows: white blood cells: 13300 cells/mm^3, hemoglobin:10.2 g/dl, hematocrit: 30.5%, platelets: 304 000 cells/mm^3, albumin; 2.4 g/dl, ALT: 130 U/L, AST: 86 U/L, GGT: 143 U/L, ALP: 368 U/L, CK: 603 U/L, LDH: 631 U/L. ESR, CRP, and total Ig-E was 105 mm/hour, 19.4 mg/dl and 77 IU/L, respectively. Hepatitis A, B, C, CMV, Rubella, Toxoplasma ELISA tests, Brucella and Salmonella serologies and VDRL tests were all negative. Plasmodium was not observed in thick drop smear. There was not any infiltration on chest X-ray. No growth was observed in samples of blood, urine, throat and feces cultures. Thorax, cranial and abdominal tomography was normal. The patient was pre-diagnosed as adult-onset Still's disease and/or drug allergy. Prednisolone 10 mg/day was initiated. On the 4th day of steroid treatment, the patient was evaluated at our Allergy and Immunology outpatient clinic for her symptoms of high fever, severe headache, hallucinations and rash. Personal history of patient revealed that she had close contact with dogs, and sheep. Patient had a suspicious history of a tick bite. She was not using any antibiotherapy and the rash was increasing with the steroid treatment. There were purpuric rashes on her both lower extremities while the character of the rashes on her trunk was still maculopapular. Skin biopsy and *Rickettsia conori* IFAT serological assay was performed because of the suspected rickettsial infection. Skin biopsy demonstrated a lymphocytic vasculitis. *Rickettsia conori* IFAT (Rickettsia conori-Spot IF, BioMerieux, Marcy L'Etoile, France) IgG test was positive at >1/1240 titers. Doxycycline treatment at a dose of 200 mg/day was initiated, steroid treatment was stopped. The rash disappeared gradually after antibiotic treatment. Body temperature decreased and regression in leucocytosis, the ESR and CRP level was also observed. At the 14th day of the treatment, the symptoms were fully regressed.

DISCUSSION

Characterization of cutaneous lesions in drug allergy is important to determine the cause, further diagnostic tests, and management of disease (3). Numerous cutaneous reaction patterns have been reported in drug allergy such as exanthemas, urticaria, purpura and fixed drug eruption. However, exanthemas are most common cutaneous lesions (3). These lesions are pruritic, often begins as macules that can evolve into papules and may coalesce into plaques. They generally originate from the trunk, and eventually show bilateral symmetric pattern (3).

MSF is a tick-borne rickettsial infection caused by a gram-negative, intracellular bacterium (4). In Mediterranean region including Italy, Spain, Greece and Turkey MSF is primarily caused by *Rickettsia conorii* which is transmitted with tick bite (4). Human infections are seen during May-September due to an increase in recreational activities like picnics and trekking and close contacts with pets or wild animals in working and/or residing areas where ticks are abundant (5). MSF is relatively less common in Turkey (5,6). It presents with high fever and maculopapular rash is seen after high fever. The rash first appears on the hands and feet, then spreads to the trunk (4,5). A black scar may be seen where tick is located (4). The possible mechanism involved in the pathogenesis of MSF is endothelial tissue damage, perivascular edema, dermal and epidermal necrosis (4,5).

Detailed history of our patient revealed that generalized maculopapular rash was first observed on extremities and then has spread to the trunk (Centripetal spread). The characteristic of the rash changed from exanthema to

vasculitis form during the follow up. Withdrawal of TMP/SXT did not make any change in her symptoms. The rash was unresponsive to steroid. She had high fever and high levels of ESR and CRP. She was admitted to our outpatient clinic during the spring season when the tick bites are most frequently seen in Turkey. She had close contact with animals and she had a suspicious history of a tick bite. She was diagnosed as MSF on the basis of clinical history and laboratory findings. However, the first differential diagnosis was drug allergy for this patient. Probably, if this patient had a good anamnesis, a rickettsial infection would have been suspected before. On the other hand, the appearance of a skin rash after the introduction of a new drug forces clinicians to include an allergic etiology in the differential diagnosis of rash. Clinicians should observe rush after withdrawal of the drug. If the rush does not improve after withdrawal of the suspected drug, it is more likely not drug allergy.

In conclusion, the clinician should take into account that the symptoms that appear in the course of infectious diseases do not all occur at the same time. The successive appearance of the symptoms can guide us for the right diagnosis. Clinicians should be alert for the possibility of differential infectious diseases that mimic drug allergy such as a Mediterranean spotted fever. Referral to an allergist may be helpful for correct diagnosis in patients having suspected drug-induced maculopapular allergic reactions.

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