

Serum Sickness-like Reaction induced by Antituberculous Drugs

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Abstract

Observation: Tuberculosis verrucosa cutis is a rare form of tuberculosis and it is typically seen as a chronic verrucose plate. At the first stage treatment of disease, rifampicin, isoniazid, pyrazinamide and ethambutol are quite effective. However, side effects developing due to antituberculosis drugs can cause a significant level of morbidity and mortality. Cutaneous medicine reactions are among major side effects being widely observed. Serum sickness-like reaction is a rare immunologic disease that can develop as relating with medicines such as penicillins, cephalosporins and trimethoprim-sulfamethoxazole. It is defined as type III hypersensitive reaction that classically develops against heterologous proteins. Its real mechanism could still not be fully understood. In this case presentation, we are introducing a female patient aged 28 who developed a serum sickness-like reaction following antituberculosis treatment.

Introduction

Tuberculosis verrucosa cutis occurs by direct inoculation of *Mycobacterium tuberculosis*. It is a rare form of cutaneous tuberculosis and it is seen at regions that are frequently subject to trauma. At the first stage treatment of disease, rifampicin, isoniazid, ethambutol and pyrazinamide are quite effective [1].

Side effects of medicines being used in the treatment of tuberculosis for long years have become an important health problem. Problems caused by medicines reveal a spectrum varying from simple skin lesion to death. It is important for a patient having tuberculosis to be monitored during the treatment period, for

side effects relating with medicines to be determined and for necessary measures to be taken [2].

In literature, serum sickness-like reactions (SSLR) depending on rifampicin have been notified. It has been presented due to its being the single case that was notified following skin tuberculosis treatment in our country.

Case Report

A 28-year-old female patient who was receiving quartet antituberculosis treatment (isoniazid, ethambutol, rifampicin and pyrazinamide) following

diagnosis of tuberculosis verrucosa cutis has applied to our polyclinic 20 days after starting of treatment with complaints of face, body, neck, redness and swelling of the hands and feet, fever, joint, muscle aches, abdominal pain and weakness. During the dermatologic examination of the patient, it was observed that there was diffuse edema of face, neck, hand and foot, urticarial plaques on the trunk, macular erythema on the hands and feet (Figures 1, 2, 3 and 4). The patient had a subfebrile fever (37.8 °C). In the laboratory findings of the patient, there was leukocytosis (13.000/mm³), erythrocyte sedimentation speed increase (25 mm/hour) and high level of c-reactive proteins (57.8 mg/L). Eosinophilia was not present. Complementary levels (C3c: 1.39 g/L, C4: 0.19 g/L) were within normal limits. Liver and kidney functions and full urinary examination of the patient were normal. As being based on the story, physical and dermatologic examination and laboratory findings SHBR diagnosis was given for the patient. Antituberculosis drugs which she mentioned that she was using during her application were stopped to be given. Parenteral 60 mg/day methylprednisolone and antihistamine treatments were initiated for the patient. On the third day of treatment, symptoms of the patient were significantly reduced. Systemic corticosteroid dose was

cut by being reduced. Following that it was continued only with oral antihistamines. General status of the patient was corrected with treatment and her dermatologic lesions were reduced.

Discussion

MSerum sickness was first defined in the year 1905 by von Pirquet and Schick as clinical picture revealed with fever, skin lesions, arthralgia, lymphadenopathy which developed days later in children who were applied antiserum treatment (rabies, diphtheria, tetanus). It is a complement-dependent systemic immune complex disease against an antigen which is in protein structure. SSLR is a lighter clinical picture developing against medicines not having a protein structure that is observed more frequently than serum sickness. Pathophysiology of SSLR could not be fully understood. But by many researchers, SSLR have been evaluated within type III hypersensitivity reactions. It has been defined as a medical reaction that showed itself with skin rash, fever and joint involvement without any vasculitis finding being present [3,4].



Figure 1. Common edema of the eyelid, lips and face



Figure 2. Right hand edema and erythema



Figure 3. Left edema and erythema



Figure 4. Erythematous macules in the body

This disease can be observed in all age groups and frequently in children. Clinical picture occurs 2 to 21 days following medicine intake. Skin lesion that is most frequently observed in patients is urticaria. Morbilliform, erythema multiforme-like lesions, edema and purpuric lesions are other cutaneous eruptions. Fever, diffuse muscle and joint pain, arthritis, and polyneuropathy are other clinical findings being observed. renal, cardiac and pulmonary involvement may also be rarely observed [5]. In our case, there were common facial, neck and hand-standing edema accompanied by a sub-febrile fever, urticarial lesions on the trunk and extremities and a common weakness and joint pain which were present. In our patient, no lymphadenopathy or systemic involvement was observed.

Most common reason of SSLR is medicines. Especially antibiotics, anticonvulsants, anti-neoplastics, antiarrhythmics, antihypertensives, nonsteroidal anti-inflammatory drugs and rarely infections were held to be responsible [3].

During the treatment of tuberculosis, serious side effect problems are confronted with. Serious side effects relating with antituberculosis drugs can cause a significant level of morbidity and mortality. Cutaneous medicine reactions relating with tuberculosis drugs are among frequently observed side effects. In a study conducted by Tan et al in 2007 in 47 (%5.7) out of 820 patients with active tuberculosis reported cutaneous drug reactions. Among these cutaneous medicine reactions the most frequently

observed one was morbilliform rashes (%72.3). Besides erythema multiforme, urticaria, exfoliative dermatitis, facial edema, diffuse purpura and lichenoid eruptions were also notified. The agent that was most frequently held responsible was shown as pirazinanad [2].

SSLR developing as depending on antituberculosis medicines was very rarely notified. Until now, only two cases relating with rifampicin were published [6,7]. As the first case, it was notified in 1994 by Parra et al [6]. that SSLR has developed in a patient with HIV who was getting antituberculosis treatment. In the patient as being different from our case, circulating immune complexes and reduction in serum complement levels were detected. Intra-dermal test that was done with rifampicin was found as positive. As the second case in 2014 Kim et al [7]. have published that combination of SSLR and anaphylaxis was observed in a patient getting quartet antituberculosis treatment with the diagnosis of tuberculosis meningitis. In this case with dermal and oral provocation tests being done with antituberculosis medicines, it was shown to have developed as depending on rifampicin. In our case as it was in acute period and as treatment of patient continued, allergy tests could not be done.

As a conclusion, it should be kept in mind that SSLR can develop in patients using antituberculosis medicines and these patients should be monitored closely for other cutaneous medicine reactions that can develop.

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