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Simvastatin-induced Toxic Epidermal Necrolysis

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ABSTRACT

Toxic epidermal necrolysis comprises a severe immune-complex mediated hypersensitivity reaction that typically involves the skin and mucous membranes. Herein, we describe a 68-year-old man who presented with the condition after simvastatin administration.

1. Introduction

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are severe immune complex mediated hypersensitivity reactions that typically involve the skin and mucous membranes. The incidence of SJS is approximately 6 cases per million persons per year, and incidence of TEN is approximately 2 cases per million persons per year[1].

2. Case report

A 68-year-old man was admitted to our hospital for a scheduled coronary artery bypass grafting operation due to three-vessel coronary artery disease. The treatment scheme before the operation included aspirin, atenolol, ramipril and atorvastatin. In the post-operative therapeutic scheme, 10 mg of atorvastatin daily was replaced with 20 mg of simvastatin daily. On the second post-operative day, the patient complained malaise and arthralgia. A macular rash was covered the thorax and lower extremities also started to appear, and within hours necrotic lesions covering the entire body surface were formed (Figure 1). Histopathologic examination of the skin revealed dermal inflammatory infiltration and full-thickness necrosis of the epidermis. The former, combined with keratinocytes apoptosis and specific CD+ T lymphocytes dermal stratification patterns were diagnostic for TEN. Simvastatin was removed and the patient fully recovered within four weeks.

3. Discussion

SJS was first described in the 1920's, as an acute mucocutaneous syndrome. French LE described four patients with an eruption resembling scalding of the skin which he called TEN[2]. Genetic predisposition and a strong association between human leukocyte antigen, drug hypersensitivity and ethnic background

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are believed to be associated with the syndrome's appearance[3].

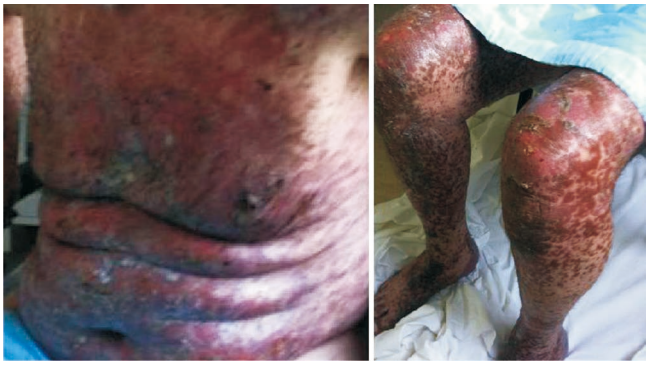

Figure 1. Necrotic lesions covering the thorax and lower extremities.

Typical prodromal symptoms of SJS/TEN include headache, malaise, arthralgia and productive cough with thick, purulent sputum. Patients may complain of a burning rash that begins symmetrically on the face and the upper part of the torso. Signs of mucosal involvement may include erythema, edema, sloughing, blistering, ulceration or necrosis, as in our patient. Finally, ocular involvement can be present including the cornea, the eyelids and conjunctiva[4].

Dermal inflammatory cell infiltrate and full-thickness necrosis of the epidermis are typical histopathologic findings in patients with SJS/TEN. Histopathologic examination of the skin can also reveal the following: changes in the epidermal-dermal junction ranging from vacuolar alteration to subepidermal blisters, perivascular dermal infiltrate, keratinocytes apoptosis and specific CD+ T lymphocytes dermal stratification patterns. Additionally, conjunctival biopsies from patients with active ocular disease reveal subepithelial plasma cells and lymphocyte infiltration[5]. The differential diagnosis of SJS/TEN includes autoimmune blistering diseases, including linear immunoglobulin A dermatosis and paraneoplastic pemphigus, but also pemphigus vulgaris and bullous pemphigoid, acute generalized exanthematous pustulosis, disseminated fixed bullous drug eruption and staphylococcal scalded skin syndrome[6].

Management of SJS/TEN requires early diagnosis, immediate discontinuation of the causative drug(s), and supportive care. Some authors have advocated the use of corticosteroids, cyclophosphamide, plasmapheresis, hemodialysis, TNF antagonists and immunoglobulin; however these treatments remain controversial[7].

The statin medications for lowering of blood cholesterol have been reported to associate with "chameleon-like" cutaneous eruptions but also a variety of other adverse cutaneous eruptions, including SJS/TEN, porphyria cutanea tarda, linear immunoglobulin A bullous dermatosis, and lupus and dermatomyositis-like pustular reaction patterns[8].

According to adverse drug reaction probability scale proposed by Naranjo *et al.*, the described condition is designated as a probable reaction to simvastatin[9]. However, we claim that in the absence of an alternative cause that could have elicited the reaction. A high level of suspicion for an unexplained necrotic cutaneous eruption in an individual on statins is important to identification of the disorder and discontinuation of the offending medication.

Conflict of interest statement

The authors report no conflict of interest.

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