

Case Report

Etanercept induced Bullous pemphigoid skin lesion in rheumatoid arthritis: A case report

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Abstract

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Tumor necrosis factor-alpha (TNF- α) is a proinflammatory cytokine produced predominantly by activated macrophages, and involved in the up-regulation of inflammatory reactions, and plays a pivotal role in the pathogenesis of rheumatoid arthritis and some other autoimmune disorders. Since their introduction anti-TNF- α agents have been revolutionized the treatment of these disorders. However, some adverse events such as skin reaction, hypersensitivity, infection, reactivation of tuberculosis, and various autoimmune diseases can occur in patients using these agents. In this report, we present a female case who was diagnosed as bullous pemphigoid while receiving etanercept for treatment of rheumatoid arthritis.

Keywords: Anti-tumor necrosis factoralpha, Bullous pemphigoid, Rheumatoid arthritis

INTRODUCTION

Bullous pemphigoid (BP) is defined as an autoimmune skin disease, characterized by the presence of antibodies against mucous membranes and skin. Patients present with erythematous skin lesion, urticarial papules and plaques that evolve to form large bullous lesions. It occurs in the elderly (Patton and Korman, 2008). Bullous pemphigoid may occur as an adverse effect of different drugs or as a consequence of autoimmune diseases. Different medications can induce Bullous pemphigoid such as angiotensin converting enzyme inhibitors, B-adrenergic blockers, non-steroidal anti-inflammatory drugs, calcium channel blockers, antibiotics, antipsychotics, omeprazole, and even with radiation (Patton and Korman, 2008; Wozniak et al., 2006), and anti-tumor necrosis factor (TNF- α). In this article, we report a patient with rheumatoid arthritis who developed bullous pemphigoid during treatment with anti-TNF- α (etanercept).

CASE REPORT

A 56-year-old female patient visited our biologic therapy

center with erythema on the upper anterior aspect of the right leg, knee and lower abdomen. The patient was diagnosed with rheumatoid arthritis 14 years before and had used different types of drugs. The patient was treated with methotrexate (15 mg/week), folic acid (5mg/day), and omeprazol (40 mg/day) for the last several years, when she was deteriorated and developed high disease activity. Etanercept was added to the treatment regimen. The patient described morning stiffness of more than one hour, joint pain and swelling. On physical examination, metacarpophalangeal (MCP) joints of both hands revealed swelling and tenderness and increased heat, both knees painful, swelled with limited range of movement. Laboratory findings were determined as: erythrocyte sedimentation rate: 80 mm/h, C-reactive protein: 19 mg/L, leukocytes: 8900/ μ L, hemoglobin: 8.7 g/dl, and platelets: 154.000/ μ L. Skin lesions suddenly appeared at the day of administration of the second dose of subcutaneous etanercept and increased within a few days. The erythematous bullous lesions were present on her upper anterior aspect of left leg and knee (Figures 1 and 2). Her blood pressure was 120/70 mmHg and pulse was 76/min. Other system



Figure 1. Erythematous bullous lesions anterior upper aspect of right leg and knee



Figure 2. Hands not involved by the lesion

examinations were normal. The patient's lesions were diagnosed as bullous pemphigoid confirmed by dermatologist and histopathological examination of a biopsy taken from the lesion (Joly et al., 2004). The patient had already stopped her treatment at the same day, and treatment was restarted with the same previous regimen except etanercept, prednisolone increased to 60 mg/day, and topical steroid was added. Lesions improvement was observed after 10 days of treatment.

DISCUSSION

Bullous diseases are a group of autoimmune skin

disorders characterised by bullous lesions with erosions and associated with antibodies developed against skin, mucous membranes and against structural proteins occupying space between cells and matrix. Bullous pemphigoid (BP) is the commonest autoimmune bullous disease in older age populations (Patton and Korman, 2008; Wozniak et al., 2006). In our patient, the lesions begin as urticarial papules on the upper anterior aspect of the right leg, knee and lower abdomen. The left leg, left knee, oral mucous membrane, and genital area was not involved. Bullous pemphigoid may occur in association with different autoimmune diseases like, pernicious anemia, rheumatoid arthritis, diabetes mellitus, and chronic inflammatory diseases such as psoriasis vulgaris.

It may be associated with some malignancies and different drugs. The development of this autoimmune disorder after administration of certain drugs is reported in the literatures. It may occur with angiotensin converting enzyme inhibitors, B-adrenergic blockers, non-steroidal anti-inflammatory drugs, calcium channel blockers, antibiotics, antipsychotics, omeprazole, and even with radiation (Patton and Korman, 2008; Suárez-Fernández et al., 2008). Anti-TNF- α induced BP has been reported in patients who have required such medications for psoriasis or rheumatoid arthritis (Stavropoulos et al., 2014; Altindag et al., 2010; Bordignon et al., 2009; Stausbol-Gron et al., 2009). Kijima et al. (2008) reported a female patient who had developed bullous pemphigoid with minocycline use. BP cases have also been reported with the use of penicillin, furosemide and simvastatin (Wozniak et al., 2006; Lee and Downham, 2006; Stoebner et al., 2003). TNF- α has been implicated in the pathogenesis of bullous skin disease in (Asashima et al., 2006). Because of this relationship between TNF- α and pemphigoid, anti-TNF- α agents is used in the treatment of this disorder. Anti-TNF- α drugs are used effectively for the treatment of rheumatoid arthritis as well and various adverse events including, injection reaction, allergic reaction, infection, reactivation of tuberculosis, malignancy, demyelinating syndromes, and autoimmune diseases have been reported. Production of autoantibodies increased in patients receiving anti-TNF- α , but the correlation remains unclear. Antinuclear antibody and anti-dsDNA antibodies induced by anti-TNF- α agents can range from 23% to 57% and 9% to 33%, respectively (Mongey and Hess, 2008). Skin lesions in patients with rheumatoid arthritis are rheumatoid nodules, skin vasculitis, palmar erythema, vasculitis, purpuric or necrotic skin lesions, livedo reticularis, drug adverse events and pyoderma gangrenosum (Rashtak and Pittelkow, 2008).

CONCLUSION

Our patient was advised switching to rituximab, prednisolone was tapered to 5mg/day after the disappearance of the skin lesions and clinical remission was achieved.

Informed consent

It was taken from the patient.

Conflict of Interest

Authors have no conflict of interest

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