

Pemphigus vulgaris and amyotrophic lateral sclerosis

Fatemeh Mokhtari, Marzieh Matin, Fatemeh Rajati¹

Department of Dermatology, Skin Diseases and Leishmaniasis Research Center, School of Medicine, Isfahan University of Medical Sciences, Isfahan, ¹Department of Public Health, Faculty of Health, Kermanshah University of Medical Sciences, Kermanshah, Iran

Pemphigus vulgaris (PV) is an autoimmune bullous and erosive mucocutaneous disease. Rarely, it occurs in patients with other autoimmune disease. The relation between PV and neurological disorders is unclear and needs to be more studied. Here, we report a case of amyotrophic lateral sclerosis (ALS), followed by dermatologic involvement. Histopathological evidence and direct immunofluorescence are consistent with PV. Systemic corticosteroid and azathioprine were effective in the treatment of mucocutaneous lesions. PV seems to be accidentally associated with ALS. Expression of major histocompatibility complex Class II in autoimmune disease and production of autoantibodies have been proposed to describe the association of PV with ALS.

Key words: Amyotrophic lateral sclerosis, major histocompatibility complex Class II, pemphigus vulgaris

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INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disorder that affects the upper and lower nervous system. 1.5–2 cases per 100,000 persons develop ALS each year.^[1] In Iranian patients, the annual incidence is 0.42/100,000.^[2] It most commonly afflicts people who are 60 years old. Clinical features are progressive weakness, muscle atrophy, fasciculation, muscle spasms, dysarthria, dysphagia, and dyspnea.^[1,3]

Pemphigus is an autoimmune blistering disease that affects skin and mucous membrane and usually occurs in adults with a mean age of 40–60 years. The incidence of pemphigus ranges from 0.1 to 0.5/100,000 per year.^[4] In Iran, the incidence rate is estimated approximately 5/100,000.^[5] The common manifestations of the disease are painful erosions in oral mucosa and flaccid blisters on the normal skin or erythematous base.^[4]

We report a case of an ALS in a male patient, followed by pemphigus vulgaris (PV). To the best of our knowledge, we describe the first case.

CASE REPORT

A 60-year-old male patient was admitted to our clinic with painful mucocutaneous lesions since 1 week before admission. He had a history of ALS for 1/5 years ago. Due to ALS, the patient suffered from dysphagia and odynophagia about 6 months ago. Nutritional support through a nasogastric tube was performed and percutaneous endoscopic gastrostomy (PEG) was inserted after several days. The patient's functional status and quality of life (QoL) decreased gradually over time.

In general, physical examination of the patient appeared ill but not toxic. His vital signs were stable. The dermatologic examination showed erosions on the buccal mucosa that superimposed with candidiasis. We observed flaccid blisters in different sizes and multiple erosions on his trunk, lower extremity, and flexural area [Figure 1]. We proposed PV, Hailey-Hailey, and bullous pemphigoid as differential diagnosis.

A complete blood count and serum biochemical studies showed normal results. Skin biopsy was

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Address for correspondence: Dr. Marzieh Matin, Department of Dermatology, Skin Diseases and Leishmaniasis Research Center, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran. E-mail: matin_med302@yahoo.com

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performed to examine histology which revealed suprabasal acantholysis [Figure 2]. An immunofluorescence study demonstrated intercellular deposition of IgG and C3, confirming the diagnosis of PV.

The patient was treated with systemic prednisone (60 mg/day in divided doses, 1 mg/kg) and azathioprine 50 mg 3 times a day (2/5 mg/kg/day). Topical application of corticosteroid with antiseptic care was also prescribed concomitantly.

Clinical improvement of the skin lesions was observed since the 2nd week of treatment. The maximum response was obtained after 4 months follow-up. The prednisone dosage was tapered gradually up to 10 mg/day. After 9-month follow-up, oral feeding was improved and the improvement in QoL was achieved. Therefore, the PEG tube was removed. He was close in follow-up and was doing well [Figure 3]. The written consent form was obtained from the patient.

DISCUSSION

Here, we report two rare diseases that both diagnosed in a patient. Iranian patients have a higher incidence rate of pemphigus in comparison with previous studies.^[4,5] Studies show that the incidence and prevalence rate of ALS in Iranian populations, in comparison to other countries, are lower.^[2] PV is an autoimmune blistering disease caused by antibodies against keratinocyte surface antigen. The disease is associated with human leukocyte antigen (HLA) Class II, in particular HLA-DR and HLA-DQ.^[6] In keeping with previous studies, HLA-DR, HLA-DP, and HLA-DQ staining are marked in ALS and immune response can lead to neuronal degeneration.^[7,8]

In addition to these straightforward descriptions, autoimmunity may justify the association between PV and ALS. Limited studies have been reported the coexistence of bullous disorders with other autoimmune diseases. Some of them are referred here.

Chosidow *et al.*^[9] reported that three cases out of 168 patients suffering from ALS in 2000 and showed clinical and histological features of bullous pemphigoid. As a recent epidemiologic study, the association between bullous pemphigoid and ALS is more than coincidental. They discussed that the interrelation between bullous pemphigoid antigen 1 (Bp Ag1) and neurofilaments may lead to cutaneous consequence. Hence, it seems that neurological disorders may be associated with bullous dermatitis.

In another study, Foureur *et al.*^[10] reported an 84-year-old woman with right hemiparesis secondary to ischemic cerebral stroke in 2001. The patient developed bullous



Figure 1: Flaccid blisters, erosions, and crusted plaques were observed on the patient's trunk and inguinal areas

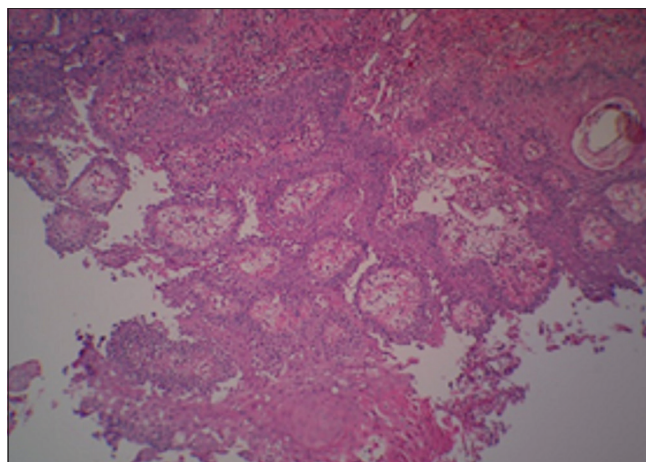


Figure 2: Biopsy section from the trunk showing suprabasal acantholysis (H and E, ×10)



Figure 3: Healed skin lesions with remained hyperpigmentation after 9 months of treatment

pemphigoid on her hemiparetic side. In this study, two hypotheses were proposed for the coexistence of these two diseases:

- The neuroautoimmunity association with the aging process
- The autoantibody reactivity against dystonin, which shares homology with Bp Ag1 in C-terminal location.

Cenk Kohen and Beril Kucumen^[11] described that a 53-year-old male ALS patient in 2011 whose disease had started 10 years ago. Four years after initial presentation, he developed PV. The patient had undergone cataract surgery due to high dose corticosteroid therapy. It is the only study that reported a case of PV accompanied with ALS.

In 2013, Thongprasom *et al.* published a case report of a 36-year-old Thai woman with oral pemphigus. The patient suffered from discoid lupus erythematosus, dermatomyositis, asymmetric polyarthritis, and multiple enthesopathy during a long-term follow-up. In this rare case, several autoimmune diseases were suggested.^[12]

PV is an uncommon condition in ALS patient. According to mentioned studies and the existence of autoantibodies in pathogenesis of both diseases, it seems that the association between PV and ALS is more than being coincidental. However, further studies are needed to be investigated.

This case demonstrates that PV can occur in ALS. If patients present with bullous skin lesions in the course of advanced neurologic disorder, physicians should consider an autoimmune bullous disease such as PV and BP. In summary, the early successful detection in control of both neurologic disease and skin lesion is important.

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Conflicts of interest

There are no conflicts of interest.

AUTHORS' CONTRIBUTION

FM contributed to the conception of the work, conducting the study, drafting and revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work. MM contributed to the conception of the work, conducting the study, drafting and revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work. FR contributed to the conception of the work, conducting the study, drafting and revising the

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