A Rare And Unusual Association Between Central Retinal Vein Occlusion And Pemphigus Vulgaris

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Citation

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Abstract

Pemphigus vulgaris (PV) is an autoimmune bullous disease characterized by blistering and erosions within the skin and mucous membranes. Ocular involvement in patients with PV has rarely been reported. In this report, we describe a 40-year-old man affected by PV. Although the mucocutaneous lesions improved during treatment (oral prednisolone at a starting dose of 90 mg/day, and subsequently tapered to 17.5 mg/day), he developed central retinal vein occlusion (CRVO). To our knowledge, no previous report has described posterior segment ocular complications in a patient with PV. We discuss the possible mechanisms of this association.

INTRODUCTION

Pemphigus is defined as a group of autoimmune blistering diseases that cause lesions in the skin and mucous membranes. Pemphigus can be broadly classified into three major forms: (i) pemphigus vulgaris (PV); (ii) pemphigus foliaceus; and (iii) others. 1 PV is the most common form of pemphigus. The pemphigus antigen is desmoglein (Dsg), a cadherin-type cell-cell adhesion molecule found in desmosomes. The PV antigen is Dsg3, and the pemphigus foliaceus antigen is Dsg1. PV can be further classified as mucosal-dominant or mucocutaneous. Ordinarily, only anti-Dsg3 IgG antibodies are detected in mucosal-dominant PV, while both anti-Dsg3 and anti-Dsg1 IgG antibodies are detected in mucocutaneous PV. 1

Ocular involvement in patients with PV has rarely been reported. 2-7 To our knowledge, no previous report has described posterior segment ocular complications in a patient with PV.

Herein, we report the occurrence of central retinal vein occlusion (CRVO) in a patient with PV, and we discuss the possible mechanisms of this association.

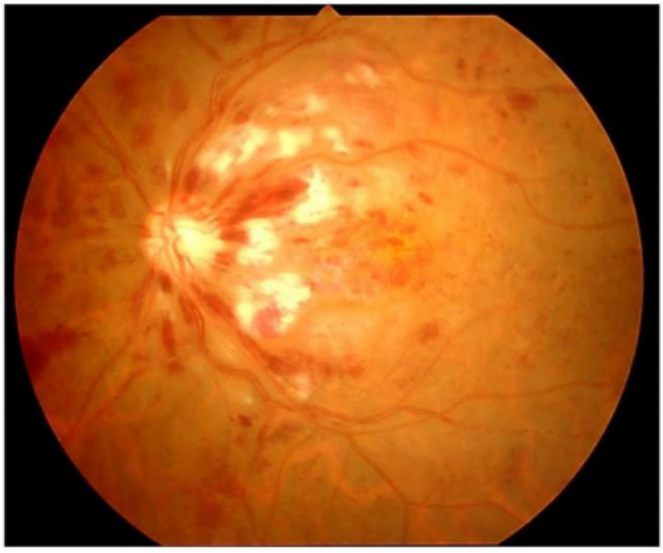
CASE REPORT

A 40-year-old man complaining of blurred vision in his left eye was referred to our hospital. The patient had a 7-month history of PV. The patient complained of blisters on his torso, face, and lip, and these were detected by physical exam; however, the oral mucosa and conjunctiva were not affected in this patient. Histopathological analysis confirmed acantholysis in the epidermis with intraepidermal blistering. Direct immunofluorescence showed intercellular deposition of IgG and C3 in the epidermis. The serum anti-Dsg 1 and 3 antibody titres were 88 U/ml and 610 U/ml, respectively. These results confirmed the diagnosis of PV. Treatment was initiated with prednisone at a dose of 90 mg/day (1 mg/kg) under the Japanese guidelines for the management of pemphigus. After 2 weeks of therapy, a significant reduction of skin lesions was not observed. Therefore, intravenous immunoglobulins were administrated as an adjuvant therapy, resulting in marked improvement of the skin lesions. A full clinical remission was achieved after 4 weeks of therapy. This was associated with a reduction of serum levels of pemphigus antibodies (anti-Dsg 1 and 3 antibody titres were 3 U/ml and 33 U/ml, respectively). The dose of prednisone was gradually reduced, and no relapse was observed.

The patient is currently being prescribed a tapering dose of prednisolone (17.5 mg/day). At the initial ophthalmological examination, the patient had a best-corrected visual acuity of 1.2 in the right eye and 0.1 in the left eye. The ocular pressures were normal. Slit lamp examination showed no abnormalities in both anterior segments. Fundus examination showed multiple retinal hemorrhages and soft exudates in the left eye (Figure 1).

Figure 1

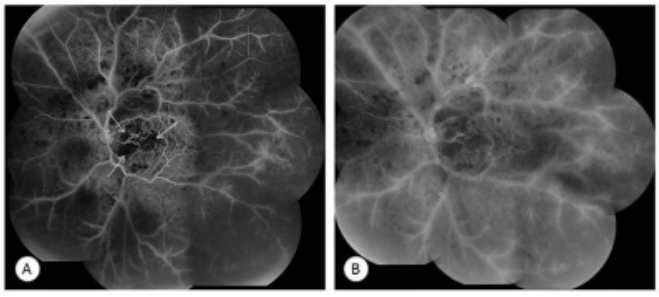
Fundus photograph showing multiple retinal hemorrhages and soft exudates in the left eye.



Fluorescein angiography revealed a marked filling delay of the macular area in the early stage (Figure 2A, arrows) and staining of the venous wall was detected in the late stage (Figure 2B).

Figure 2

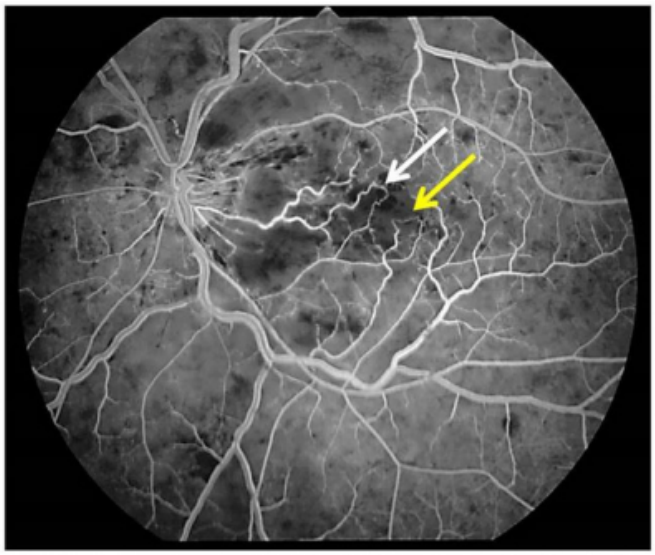
Fluorescein angiography revealed a marked filling delay of the macular area in the early stage (A: arrows); staining of the venous wall was detected in the late stage (B).



Additionally, a cilioretinal artery communicated directly with an inferotemporal branch retinal artery (Figure 3, white arrow) and retinal arterioarterial communication was also detected (Figure 3, yellow arrow). From these findings, the patient was diagnosed with CRVO associated with retinal arterial circulatory disturbance.

Figure 3

Fluorescein angiography: a cilioretinal artery communicated directly with an inferotemporal branch retinal artery (white arrow) and retinal arterioarterial communication was detected (yellow arrow).



Initially, we suspected antiphospholipid antibody syndrome (APS) in this patient on the basis of the combination of CRVO and retinal arterial circulatory disturbance. 8 However, the anticardiolipin antibody and lupus anticoagulant tests were negative, and 2-glycoprotein I was normal. In addition, based on staining of the venous wall on late phase fluorescein angiography, we also suspected anti-neutrophil cytoplasmic antibody (ANCA)-vasculitis. However, proteinase 3-ANCA and myeloperoxidase -ANCA were negative in this case.

Systemic administration of an anti-platelet agent was initiated after the initial examination. In addition, sub-Tenon triamcinolone acetonide injection was performed for macular edema.

After therapy, his visual acuity and the retinal edema gradually improved. These findings remained stable during the 3-month follow-up period.

DISCUSSION

In a 15-year cohort study, the population incidences of branch retinal vein occlusion (BRVO) and CRVO were 1.8% and 0.5%, respectively. 9 RVO is mainly related to cardiovascular diseases. There were associations of presence of diabetes, glaucoma history, larger cup disc ratio, higher intraocular pressure, and history of current use of antihypertensive medications and barbiturate sedatives at baseline with an increased 15-year cumulative incidence of

CRVO. 9

Ocular involvement in patients with PV has been rarely reported. 2-7 Most commonly, ophthalmologic examination reveals bilateral conjunctivitis, conjunctiva congestion, and inflammation of the eyelid margin, which is occasionally accompanied by blisters and erosions of the bulbar/palpebral conjunctiva or eyelid margin. 2-7 To our knowledge, no previous reports have been described posterior segment ocular complications in a patient with PV. Although the mucocutaneous lesions and anti-Dsg 1 and 3 antibody titres improved on corticosteroids, CRVO and cilioretinal artery occlusion developed in this case. Therefore, the association of CRVO and PV in this patient most probably is coincidental rather than causative.

However, we speculate that a relationship might be exist between CRVO and PV. We propose two possible explanations for this relationship. First, the pemphigus antigen (Dsg) is a cadherin-type cell-cell adhesion molecule found in desmosomes. 1,10 Ocular involvement in PV may be explained by the presence of Dsg 3 in the ocular epithelium. Dsg 3 was found to be strongly expressed in the basal cells of the conjunctival epithelium, with fading in the suprabasal layer. 11 In contrast, the presence of Dsg at the posterior segment has not been studied. However, desmosome-like junctions exist in the retinal periendothelial junctions. 12 Therefore, we speculate that an autoimmune reaction due to PV contributed to the retinal vascular endothelial changes observed in this case. Second, the p38 mitogen-activated protein kinase (MAPK) pathway regulates both cellular and humoral autoimmune responses. Recently, autoantibody-induced p38 phosphorylation was shown to occur in pemphigus 10 and ANCA-vasculitis. 13 Additionally, data from previous in vivo studies show that p38 MAPK activation occurs in platelets, monocytes, and endothelial cells after incubation with anti-phospholipid antibodies. 14 Therefore, the other possible explanation for CRVO in this patient is the occurrence of an inflammatory reaction through p38 MAPK. Additional cases will need to be examined in order to characterize these rare and unusual associations between CRVO and PV definitively.

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