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Dipeptidyl peptidase-4 inhibitor–associated mucous membrane pemphigoid leading to severe vision loss treated with rituximab

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A 61-year-old man was admitted to the Department of Dermatology because of tense blisters arising on erythematous and apparently normal-looking skin of the trunk, neck and extremities (Figure 1A and 1B). The patient had a history of arterial hypertension, bronchial asthma and cataract. A dipeptidyl peptidase-4 inhibitor (DPP-4), sitagliptin, had been introduced several months earlier for the treatment of type 2 diabetes mellitus. The patient's drug history included metformin, acarbose, valsartan, hydrochlorothiazide, and inhaled salmeterol/fluticasone propionate. Initial blood results showed mildly elevated C-reactive protein levels, renal impairment with an estimated glomerular filtration rate of 20 ml/min/1.73 m^2, and markedly increased serum glucose and glycated hemoglobin levels, consistent with poorly controlled diabetes mellitus. Physical examination also revealed erosions of the oral mucosa and conjunctival hyperemia (Figure 1C and 1D). The patient underwent an ophthalmological consultation, during which conjunctivitis was diagnosed. Visual acuity was 0.32 in the right eye and 0.32 in the left eye. Direct immunofluorescence of perilesional skin demonstrated linear deposits of immunoglobulin G, immunoglobulin A, and complement component C3 along the

basement membrane zone (Figure 1E and 1F). Circulating antibodies associated with autoimmune blistering diseases were not detected by indirect immunofluorescence or enzyme-linked immunosorbent assay. Based on the clinical presentation and immunopathologic findings, mucous membrane pemphigoid with ocular involvement was diagnosed. During hospitalization, the patient received intravenous methylprednisolone pulses followed by systemic corticosteroids and methotrexate. Complete improvement of cutaneous and oral mucosal lesions was achieved. A possible association with DPP-4 inhibitor therapy was considered, and the treatment was discontinued on admission. However, the patient continued to report worsening vision. Immunosuppressive treatment was intensified with further methylprednisolone pulses, oral prednisone, azathioprine, and dapsone. Ocular treatment included autologous serum eye drops, topical cyclosporine, and perilimbal injections of anti–vascular endothelial growth factor agents. The patient also underwent cataract surgery. Despite intensive dermatological and ophthalmological treatment, progression of ocular involvement continued to be observed. Ophthalmologic examinations revealed progressive deterioration of vision. Visual acuity was hand motion in the right eye and 0.15 in the left eye. A corneal defect with neovascularization, endophthalmitis, and posterior synechiae were observed. Because of severe, progressive, and treatment-refractory ocular mucous membrane pemphigoid, the patient was qualified for rituximab therapy. Corneal transplantation was considered as a further therapeutic option.

This case highlights the potential role of DPP-4 inhibitors as one of the most frequently reported drug-associated triggers of bullous pemphigoid and mucous membrane pemphigoid [1,2]. Although withdrawal of DPP-4 inhibitors may lead to remission in some patients, the clinical course after drug discontinuation is variable, and disease progression may occur despite cessation of the suspected trigger [3]. In patients with ocular involvement, the disease course may be sight-threatening, even leading to blindness [4]. Therefore, close interdisciplinary

collaboration between dermatologists, ophthalmologists and diabetologists is crucial to ensure early recognition, prompt initiation of therapy, and intensive management aimed at preventing irreversible visual impairment. Rituximab may be considered in severe or refractory mucous membrane pemphigoid when conventional immunosuppressive therapy fails [5].

Article information

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Conflict of interest None declared.

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Figure 1 Clinical and immunopathological presentation of autoimmune subepidermal blistering disease; **A**, **B** – cutaneous involvement characterized by multiple tense blisters and erosions arising on an erythematous and normal-looking skin; **C** – involvement of the oral mucosa, with visible erosions affecting the hard palate; **D** – ocular involvement presenting with conjunctival erythema and hyperemia, indicating inflammatory changes of the ocular surface; **E**, **F** – direct immunofluorescence findings from a perilesional skin biopsy demonstrating linear deposition of C3 and immunoglobin A along the basement membrane zone.

Short title: DPP-4 inhibitor–associated mucous membrane pemphigoid