LETTERS

First case of acquired hemophilia A in the context of vildagliptin-induced bullous pemphigoid

Dear Editor,

A 68-year-old man with type two diabetes mellitus (T2DM), hypertension, and chronic kidney disease stage IIIb, presented to the Emergency Department due to multiple leg ecchymoses, recurrent macroscopic hematuria and epistaxis during the preceding week, along with fatigue, dyspnea in exertion and anorexia. Six months before his presentation, he was diagnosed with bullous pemphigoid (BP) in the context of vildagliptin treatment. He was on oral methylprednisolone 4 mg once daily without any sign of recurrence during the previous two months.

Physical examination only revealed large ecchymoses (Figure 1). Initial laboratory evaluation documented severe, normocytic, and normochromic anemia (hemoglobin level on admission: 6.7 g/dL) and significantly prolonged partial thromboplastin time (>100 seconds). The rest coagulation panel, d-dimmer, and fibrinogen levels were within normal range. The blood smear test was insignificant. An abdominal computed tomography scan was performed, excluding intra-abdominal or retro-peritoneal hemorrhage. An intrinsic coagulation pathway defect was highly speculated. Measurement of factors VIII and IX was ordered, demonstrating normal levels of factor IX; however, levels of active factor VIII were less than 1 % of normal, which, along with increased levels of factor VIII inhibitor, was suggestive of hemophilia A. FVIII inhibitor titers were measured 34 Bethesda units/mL. Based on his former medical history and the absence of relevant family history, the patient was ultimately diagnosed with BP-related acquired hemophilia A (AHA) after excluding neoplastic and other autoimmune diseases.

He initially received two units of red blood cell count and fresh frozen plasma; thereafter, he received recombinant activated factor VII (rFVIIa), 90 mcg/kg intravenously bolus every two hours, with a prompt achievement of hemostasis. He was then initiated on combined treatment with intravenous prednisone (one mg/kg/day) and cyclophosphamide (15 mg/kg/week). He was discharged in good general condition two weeks later on oral prednisone after restoring his previously abnormal laboratory markers. At the same time, he was placed on a regimen of monthly intravenous cyclophosphamide for six months. Three months later, he remains asymptomatic, without any symptoms.

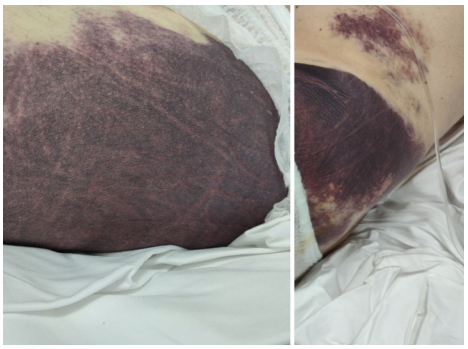

Figure 1: Clinical image demonstrating multiple ecchymoses in patient's left leg and abdomen on presentation.

AHA is a rare disorder, mainly affecting the elderly, caused by circulating autoantibodies against coagulation factor VIII[1]. There is increasing evidence of the association between AHA and BP[2]. AHA in the context of dipeptidyl peptidase-4 inhibitor-induced BP is extremely rare, previously observed with alogliptin and sitagliptin[3,4]. A high clinical suspicion index is required to identify this infrequent clinical association early.

Conflict of interest
None.

Keywords: Acquired hemophilia A, ecchymoses, vildagliptin, dipeptidyl peptidase-4 inhibitor, bullous pemphigoid

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