An Unforeseen Complication of Diabetes Therapy: Skin Revelations

Sir,

We describe a 46-year-old nonsmoker gentleman with type 2 diabetes mellitus who presented with bullous pemphigoid (BP) while on combination therapy with metformin 500 mg and sitagliptin 50 mg once daily. He was diagnosed with diabetes mellitus 5 years back and was well controlled on glimepiride till a year ago when his medication was changed to a combination of metformin and sitagliptin. He was apparently well for 6–7 months when he noticed pruritic, erythematous lesions over his abdomen, buttocks, and thighs. He did not have oral erosions, ocular symptoms, fever, or weight loss. He had history of allergic rhinitis. He was also on long-term treatment with atorvastatin and febuxostat for dyslipidemia and hyperuricemia, respectively. He consulted a dermatologist and was started on topical clobetasol and oral doxycycline for these lesions. The lesions regressed following the treatment but reappeared on his cheeks, chest, abdomen, and thighs after a few weeks. At presentation, he had two tense bullae, measuring

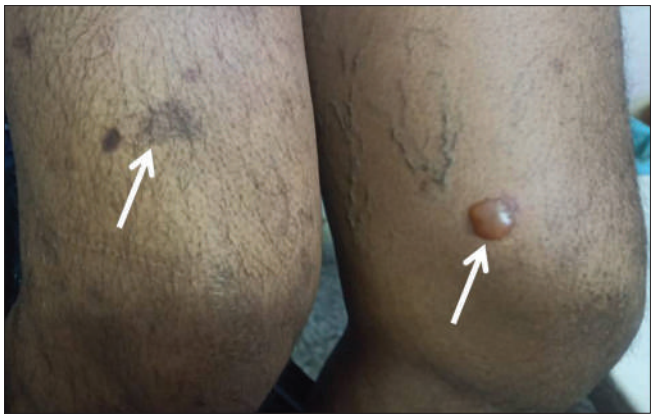

Figure 1: Tense bullous lesion (left thigh) and healed lesion (right thigh)

2 × 2 cm over the right side of abdomen and over the left thigh with healing erosions with surrounding erythema on the right thigh. On evaluation, he was found to have an elevated Immunoglobulin E of 181.1 U/mL (normal range: 5–100 U/mL) and anti BP230 of 113.4 RU/mL (normal value <20 RU/mL). Skin biopsy was performed and direct immunofluorescence showed subepidermal linear basement membrane positivity for IgG and C3 consistent with bullous pemphigoid. Sitagliptin was stopped and he was started on glimepiride along with metformin. After 3 months of discontinuing sitagliptin, he reported remarkable improvement and all the lesions except the one on the right thigh had resolved. The lesion on the right thigh though present had decreased considerably in size [Figure 1]. New lesions did not occur thereafter. He was asked to review after a month.

Bullous pemphigoid (BP) is the most common autoimmune bullous skin disorder, frequently encountered in the elderly as an idiopathic phenomenon. Neurological diseases with decreased cognitive functions and some drugs have been associated with BP. Since the introduction of gliptins in 2006, they have been associated with many skin lesions including bullous pemphigoid.[1,2] Typically BP begins as nonspecific pruritic erythematous lesions that later evolve into fluid-filled tense bullae, which may be localized or generalized. It has a long and variable latency period, ranging from 1 month to 3 years although most cases occur within a year of treatment initiation with gliptins.[3] BP autoantibodies target two major hemidesmosomal components BP180 and BP230 leading to increased fragility at dermal epidermal level.[4] Dipeptidyl peptidase-4 (DPP4) is ubiquitously expressed and its inhibition by dipeptidyl peptidase-4 inhibitors (gliptins) may alter the immune response, but the exact pathomechanism causing a break of immunotolerance is still not fully understood. Gliptin-induced BP is extremely rare, with a reported incidence of <0.1%.[4] It responds to topical clobetasol but tends to recur if the drug (gliptin) is not discontinued. Hence, a high degree of suspicion and a detailed drug history is required to differentiate gliptin-induced BP from idiopathic BP.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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