SHORT COMMUNICATION

Bullous Pemphigoid Following IgG/IgA Pemphigus: Possible Involvement of SGLT2 and DPP-4 Inhibitors

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IgG/IgA pemphigus is a relatively rare subtype of pemphigus. Only a limited number of cases of combined IgG/IgA pemphigus and bullous pemphigoid have been reported (1, 2). We report a case of bullous pemphigoid that developed during the course of IgG/IgA pemphigus, in which a possible drug involvement was considered.

CASE REPORT

A 60-year-old woman developed erythema and blisters on the back and upper arms 3 months before her initial visit and consulted a local dermatology clinic. Because serum anti-desmoglein 1 antibody was positive, she was referred to our department. She had been taking linagliptin (a DPP-4 inhibitor) for 6 years. Furthermore, she had been treated with tofogliflozin (an SGLT2 inhibitor) for 5 months, from 4 months before the onset of skin lesions until 2 months prior to her initial visit. Physical examination revealed erythema, flaccid blisters and erosions on the lower back and bilateral upper arms (**Fig. 1**a and b). A drug-induced lymphocyte stimulation test (DLST) was positive for tofogliflozin and negative for linagliptin. Histopathology showed intraepidermal blisters containing acantholytic cells, neutrophils and eosinophils. Small epidermal pustules were also seen scattered throughout. Vacuolar degeneration was observed at the epidermal–dermal junction, accompanied by neutrophilic infiltration with nuclear dust. In the dermis, infiltration of neutrophils and eosinophils was noted (Fig. 1c and d).

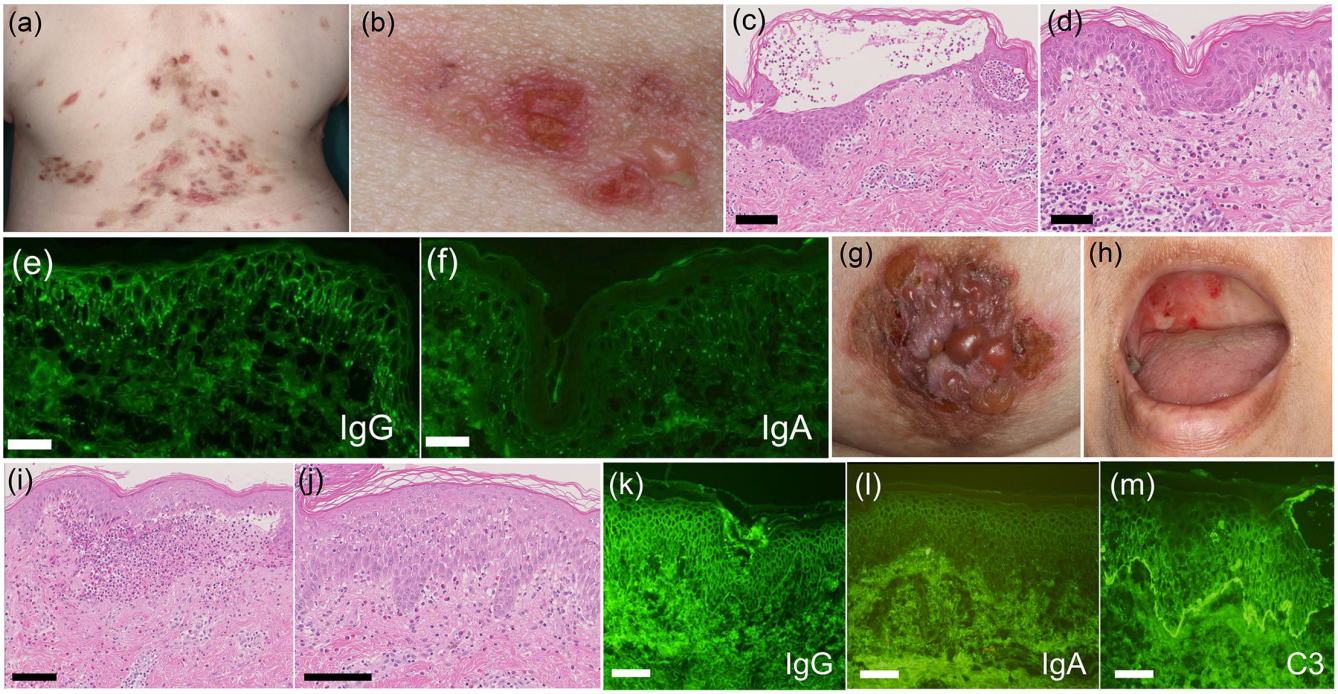

Fig. 1. Clinical and skin biopsy findings. (A, B) Initial presentation showing erythema, flaccid blisters and erosions on the lower back. (C) Hematoxylin-eosin (H&E) staining of a skin biopsy showing intraepidermal blisters with acantholytic cells, neutrophils, eosinophils and small neutrophilic pustules. Scale bar: 100 μm. (D) H&E staining of a skin biopsy showing vacuolar degeneration at the epidermal–dermal junction and perivascular infiltration of neutrophils and eosinophils in the dermis. Scale bar: 100 μm. (E,F) Direct immunofluorescence showing intercellular deposition of IgG and IgA in the epidermis. Scale bar: 100 μm. (G) Clinical presentation at recurrence showing erythema with both tense and flaccid blisters on the left breast. (H) Clinical presentation at recurrence showing oral erosions. (I) H&E staining of a skin biopsy showing subepidermal blisters with inflammatory infiltrates containing eosinophils and neutrophils. Scale bar: 100 μm. (J) H&E staining of a skin biopsy showing vacuolar degeneration at the epidermal–dermal junction with focal eosinophilic spongiosis and perivascular infiltration of eosinophils and neutrophils in the dermis. Scale bar: 100 μm. (K,L,M) Direct immunofluorescence showing intercellular deposition of IgG, IgA and C3 in the epidermis, along with linear IgG and C3 deposition along the basement membrane zone. Scale bar: 100 μm

Direct immunofluorescence (DIF) revealed intercellular deposition of IgG and IgA in the epidermis (Fig. 1e and f). A chemiluminescent enzyme immunoassay (CLEIA) showed an anti-desmoglein (Dsg) 1 antibody level of 75.5 U/mL (normal level<20.0 U/mL), while anti-Dsg 3 and anti-BP 180 antibody levels were negative. An enzyme-linked immunosorbent assay (ELISA) showed the presence of IgA antibodies to Dsg1 (OD of 1.19; cut-off value of<0.15) and IgG antibodies to desmocollin 3 (Dsc3) (OD of 0.338; cut-off value of<0.12). Based on these findings, a diagnosis of IgG/IgA pemphigus was made. Treatment with topical corticosteroids was initiated, and by six months after the initial visit, only two erythematous lesions remained on the back. Thereafter, the patient subsequently discontinued follow-up on her own.

Eighteen months after the initial visit, the skin lesions relapsed and the patient returned. Physical examination revealed a mixture of erythema, tense blisters and flaccid blisters on the trunk and extremities, along with oral erosions (Fig. 1g and h). Histopathological examination demonstrated subepidermal blisters containing eosinophils and neutrophils (Fig. 1i). Spongiosis was observed in the epidermis, with infiltration of eosinophils and neutrophils. Vacuolar degeneration was present at the epidermal–dermal junction, accompanied predominantly by eosinophilic infiltration with admixed neutrophils (Fig. 1j). DIF revealed epidermal intercellular deposition of IgG, IgA and C3, as well as basement membrane zone deposition of IgG and C3 (Fig. 1k, l and m). CLEIA revealed anti-Dsg1 and anti-BP180 antibody levels of 93.8 and 660.2 U/mL, respectively. Anti-Dsg3 antibody was negative. ELISA revealed the presence of IgA antibodies to Dsg1 (0.29 OD). Collectively, these findings supported a diagnosis of concomitant IgG/IgA pemphigus and bullous pemphigoid. Linagliptin was discontinued, and oral prednisolone was initiated at a dose of 0.5 mg/kg/day, resulting in clinical improvement of the skin lesions and a reduction in antibody titres. At the latest follow-up (3 years and 3 months after treatment initiation), linagliptin had not been resumed, and the patient remained free of skin relapse while receiving oral prednisolone at a dose of 4 mg/day.

DISCUSSION

The coexistence or transition between pemphigus and bullous pemphigoid (BP) has been sporadically reported in the literature (3). In recent years, the concept of epitope spreading, in which the autoimmune response expands or shifts to additional target antigens during disease progression, is thought to be a key mechanism underlying such overlapping autoimmune blistering diseases (4). IgG/IgA pemphigus is defined by the presence of both IgG and IgA autoantibodies against keratinocyte cell surfaces, as demonstrated by immunofluorescence or ELISA (5). Few cases have suggested a possible association between IgG/IgA pemphigus and bullous pemphigoid. Hashimoto et al. (1) analysed 30 patients who showed simultaneous intercellular IgG and IgA deposition by immunofluorescence. Among these patients, 2 cases exhibited subepidermal blister formation, 4 cases showed immune reactivity at the basement membrane zone detected by immunofluorescence or ELISA and 1 case was positive for anti-BP180 antibodies (1). In contrast, Kanwar et al. (2) reported a case with intercellular IgG and IgA deposition as well as IgG, IgA, IgM and C3 deposition along the basement membrane zone; however, neither subepidermal blister formation nor positivity for anti-BP180 antibodies was observed (2). To the best of our knowledge, only a limited number of cases have been reported in which IgG/IgA pemphigus coexists with BP, and the present case may be associated with drug exposure. In the present case, during the clinical course of IgG/IgA pemphigus, we identified the following newly developed findings: (*i*) histopathological evidence of subepidermal blister formation, (*ii*) immunoglobulin deposition along the basement membrane zone detected by immunofluorescence and (*iii*) serological positivity for anti-BP180 antibodies. These findings are consistent with the diagnostic criteria for the rare coexistence of IgG/IgA pemphigus and BP.

Another noteworthy aspect of this case is the possible involvement of medications. IgG/IgA pemphigus developed 1 month after the initiation of tofogliflozin. A drug-induced lymphocyte stimulation test showed a positive result for tofogliflozin. In addition, histopathological examination revealed vacuolar degeneration at the epidermal–dermal junction and eosinophilic infiltration in the dermis. These findings are atypical for IgG/IgA pemphigus and may be characteristic of drug-related interface reaction. Taken together, these findings indicate a concomitant drug eruption, with tofogliflozin potentially serving as a trigger for the development of IgG/IgA pemphigus. Furthermore, the patient had been treated with DPP-4 inhibitor for approximately 7.5 years before the onset of BP. Among previously reported cases describing coexistence or transition between pemphigus and BP, no cases associated with DPP-4 inhibitor therapy have been reported in the literature. Nevertheless, DPP-4 inhibitors are known to significantly increase the risk of BP (6), and the latency period between the initiation of DPP-4 inhibitors and the onset of BP has been reported to range from several months to several years, indicating that BP may develop even after long-term treatment (7). Therefore, the potential contribution of DPP-4 inhibitors to the development of BP in the present case cannot be excluded.

In conclusion, this case adds to the limited literature on concomitant IgG/IgA pemphigus and BP and suggests a possible involvement of both SGLT2 and DPP-4 inhibitors in disease development. This case may provide further insight into the complex pathogenesis of overlapping autoimmune blistering diseases.

ACKNOWLEDGEMENTS

Data Availability: The data that support the findings of this study are available from the corresponding author upon reasonable request.

The authors have no conflicts of interest to declare.

REFERENCES

1. Hashimoto T, Tsuruta D, Koga H, Fukuda S, Ohyama B, Komai A, et al. Summary of results of serological tests and diagnoses for 4774 cases of various autoimmune bullous diseases consulted to Kurume University. Br J Dermatol 2016; 175: 953–965. https://doi.org/10.1111/bjd.14692
2. Kanwar AJ, Vinay K, Saikia UN, Koga H, Teye K, Tsuruta D, et al. IgG/IgA pemphigus reactive with desmoglein 1 with additional undetermined reactivity with epidermal basement membrane zone. Indian J Dermatol Venereol Leprol 2014; 80: 46–50. https://doi.org/10.4103/0378-6323.125499
3. Recke A, Rose C, Schmidt E, Bröcker EB, Zillikens D, Sitaru C. Transition from pemphigus foliaceus to bullous pemphigoid: intermolecular B-cell epitope spreading without IgG subclass shifting. J Am Acad Dermatol 2009; 61: 333–336. https://doi.org/10.1016/j.jaad.2008.10.061
4. Didona D, Di Zenzo G. Humoral epitope spreading in autoimmune bullous diseases. Front Immunol 2018; 9: 779. https://doi.org/10.3389/fimmu.2018.00779
5. Cho YT, Fu KT, Chen KL, Chang YL, Chu CY. Clinical, histopathologic, and immunohistochemical features of patients with IgG/IgA pemphigus. Biomedicines 2022; 10: 1197. https://doi.org/10.3390/biomedicines10051197
6. Kridin K, Bergman R. Association of bullous pemphigoid with dipeptidyl-peptidase 4 inhibitors in patients with diabetes: estimating the risk of the new agents and characterizing the patients. JAMA Dermatol 2018; 154: 1152–1158. https://doi.org/10.1001/jamadermatol.2018.2352
7. Kridin K, Cohen AD. Dipeptidyl-peptidase IV inhibitors confer an increased risk for bullous pemphigoid: a population-based study with emphasis on latency and duration of exposure. Arch Dermatol Res 2023; 315: 727–734.