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Research Article

Drug-Induced Bullous Pemphigoid: Emerging Evidence with Vildagliptin and Teneligliptin Use in a Tertiary Care Hospital – A Case Series

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ABSTRACT

Background: Bullous pemphigoid (BP) is an autoimmune subepidermal blistering disorder of the elderly. Dipeptidylpeptidase-4 (DPP-4) inhibitors ("gliptins") have been increasingly recognized as potential drug-induced triggers.
Objective: To describe eight cases of gliptin-associated drug-induced Bullous Pemphigoid and to highlight the emerging evidence implicating vildagliptin and teneligliptin use in Indian patients.
Methods: Eight patients with type 2 diabetes mellitus who developed BP during gliptin therapy were evaluated at a tertiary-care teaching hospital. Diagnosis was confirmed by clinical findings, histopathology, and direct immunofluorescence (DIF). All cases were reported to the Adverse Drug Reaction Monitoring Centre (AMC) under the Pharmacovigilance Programme of India (PvPI), R.G. Kar Medical College and Hospital, prior to causality assessment using the WHO–UMC and Naranjo scales.
Results: Six patients had received vildagliptin and two teneligliptin. Mean age was 63 years (range 52–74); female:male = 4:4. Latency period 2–8 weeks. All developed pruritic erythematous plaques and tense bullae over trunk and limbs, with mucosa spared. Histopathology revealed subepidermal blisters with eosinophilic infiltrates, and DIF showed linear IgG and C3 deposition along the basement membrane. Drug withdrawal led to remission within 1–3 weeks. No relapse occurred over three months. All cases were rated "probable" by causality assessment.
Conclusion: Vildagliptin and teneligliptin can precipitate drug-induced Bullous Pemphigoid in elderly diabetic patients. Early recognition, pharmacovigilance reporting, and drug withdrawal are crucial. Teneligliptin may represent an emerging pharmacovigilance signal.

Keywords*: Drug-induced Bullous Pemphigoid, Vildagliptin, Teneligliptin, DPP-4 inhibitors, Pharmacovigilance.*

INTRODUCTION

Bullous pemphigoid (BP) is the most common autoimmune subepidermal blistering disease of the elderly, mediated by autoantibodies against BP180 and BP230 hemidesmosomal proteins (1, 2). The resulting complement activation and inflammatory cascade lead to dermal–epidermal separation and tense bulla formation.

Several drugs have been linked to BP (diuretics, antibiotics, neuroleptics), but DPP-4 inhibitors used in Type 2 Diabetes Mellitus (T2DM) have emerged as important offenders (3–5). DPP-4 inhibition disturbs immune homeostasis and eosinophilic activity, precipitating autoantibody formation (4).

This case series describes eight patients from R.G. Kar Medical College and Hospital, Kolkata, who developed BP after gliptin use, adding to limited Indian pharmacovigilance data.

OBJECTIVES

- To report eight cases of drug-induced Bullous Pemphigoid associated with gliptin therapy.
- To highlight vildagliptin and teneligliptin use in T2DM patients as emerging offenders in Indian patients.

METHODS

Eight T2DM patients who developed BP during gliptin therapy were referred from the Department of Endocrinology to the Clinical Pharmacology and Therapeutics OPD and evaluated in the Department of Pharmacology, R.G. Kar Medical College and Hospital.

Diagnosis was confirmed by clinical features, histopathology, and direct immunofluorescence (DIF). All cases were reported to the Adverse Drug Reaction Monitoring Centre (AMC) under PvPI before causality assessment using the WHO–UMC and Naranjo scales (6, 7).

RESULTS

Eight patients (4 males, 4 females; mean age 63 years) presented with bullous lesions during gliptin-based dual oral antidiabetic therapy. Six were on vildagliptin, two on teneligliptin. Lesions involved the trunk and limbs, sparing mucosa. Mean HbA1c 7.7%. Histopathology showed subepidermal blisters with eosinophilic infiltrates; DIF demonstrated linear IgG and C3 deposits. Withdrawal of gliptin with systemic corticosteroids (Prednisolone 30-40 mg/day), topical steroids and antihistamines resulted in remission within 1-3 weeks. No relapses occurred over 3months follow-up. All cases were rated “probable.”

Table 1. Clinical Profile of Gliptin-Associated Drug-Induced Bullous Pemphigoid (n = 8)

Case	Age	Sex	DM Duration (Months)	Gliptin + OHA	Dose	Latency (weeks)	Lesion Sites	Mucosa	HbA1c	Causality (WHO-UMC)
1	52 Yrs	M	7	Vilda + Glimepiride	50 mg BD	4	Trunk, arms	No	7.0	Probable/Likely
2	56 Yrs	F	10	Vilda + Gliclazide	50 mg BD	5	Trunk, legs	No	7.5	Probable/Likely
3	60 Yrs	M	6	Tene + Glimepiride	20 mg OD	3	Trunk, arms	No	7.4	Probable/Likely
4	63 Yrs	F	12	Vilda + Gliclazide	50 mg BD	2	Trunk, thighs	No	8.0	Probable/Likely
5	65 Yrs	M	9	Tene + Glimepiride	20 mg OD	6	Trunk, back	No	7.8	Probable/Likely
6	68 Yrs	F	5	Vilda + Gliclazide	50 mg BD	8	Trunk, limbs	No	8.1	Probable/Likely
7	71 Yrs	M	15	Vilda + Glimepiride	50 mg BD	7	Generalized	No	8.3	Probable/Likely
8	74 Yrs	F	11	Vilda + Gliclazide	50 mg BD	4	Trunk, legs	No	7.9	Probable/Likely

DISCUSSION

DPP-4 inhibitors have been increasingly implicated in drug-induced Bullous Pemphigoid (1–5). The consistent latency, typical histopathology, and recovery after gliptin withdrawal support causality. All the cases were treated with Systemic & topical Corticosteroids and anti-histamines.

Pharmacovigilance context: Global databases, including WHO–UMC and EudraVigilance, contain >1,000 ICSRs linking vildagliptin and ~400 ICSRs implicating teneligliptin (3, 5). Our eight cases reported through AMC–PvPI align with these signals and strengthen regional evidence.

Pathophysiology: DPP-4 (CD26) modulates immune regulation and cytokine balance; its inhibition disrupts T-cell function and promotes eosinophil-mediated inflammation and autoantibody generation (4). Vildagliptin's lipophilicity may enhance this effect (5).

Clinical relevance: Given the extensive use of gliptins in India, clinicians should maintain a high index of suspicion for Bullous Pemphigoid in diabetic patients presenting with new bullous eruptions. Prompt discontinuation of the suspected gliptin generally leads to remission.

Limitations and Future Directions

Small sample size and absence of BP180/BP230 antibody testing were limitations. Larger, multicentric studies with genetic profiling are needed to define risk factors for gliptin-induced BP in Indian patients.

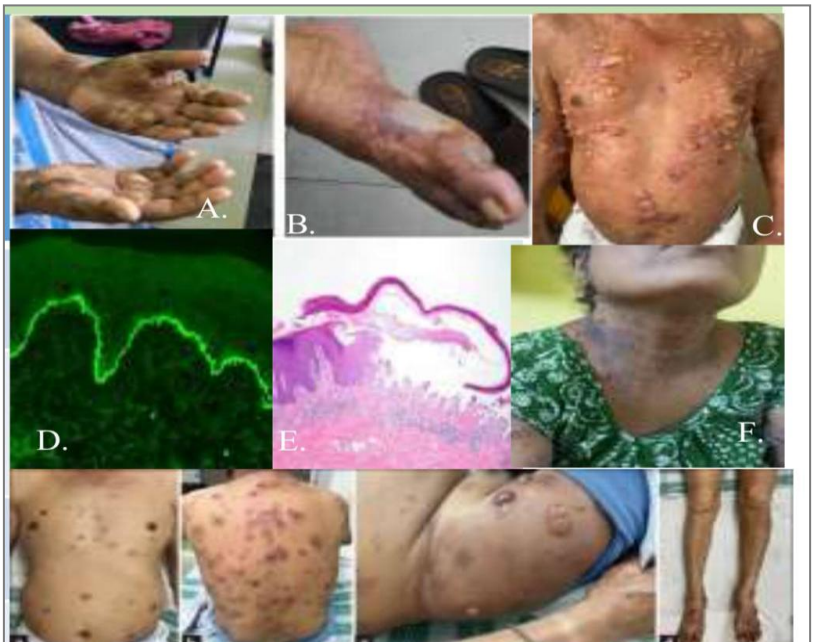

Figure. A,B,C & F: showing tense, pruritic subepidermal bullae distributed over both palms, soles, chest and along the neck & flexor aspect of the arms.
Figure D: HPE showing sub-epidermal blister with a detached overlying epidermis
Figure E: DIE showing linear deposition of IgG in the basement membrane
Figure G1-4: Teneligliptin induced Bullous pemphigoid

CONCLUSION

Vildagliptin and Teneligliptin, though effective for T2DM management, can act as offenders causing drug-induced Bullous Pemphigoid. Early recognition, drug withdrawal, and systemic and topical corticosteroid therapy ensure recovery. Pharmacovigilance reporting via AMC–PvPI is vital for signal detection and safe drug use.

Declarations

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Conflict of Interest: None declared
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Patient Consent: Written informed consent obtained

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