

Furosemide induced bullous pemphigoid: a case report**Venu D., Vijendra R.***

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ABSTRACT

Bullous pemphigoid is an acquired autoimmune disease characterized by subepidermal vesicles and bullae. The etiology is mostly idiopathic with the highest occurrence in elderly patients. However, it is now well-accepted that bp has been triggered by or associated with drug therapy. Over 50 agents have been implicated as a cause of Drug-induced bullous pemphigoid, including diuretics, ace inhibitors, and antibiotics. We present a case of Bullous pemphigoid in a 75 year old male probably induced by furosemide. A 75 year old male was admitted to the dermatology department of KIMS hospital, Bengaluru. Presented with multiple tense bullae and vesicles over both upper limbs, forearm and few collapsed bullae and vesicles over the extensor aspect of forearm. Patient had a past history of myocardial infarction and undergone coronary artery bypass grafting for the same and treated with multiple medications. Among the treatment given injection furosemide was the one of the drug, after which he developed lesions and also presented with fluid filled bullae. A diagnosis of bullous pemphigoid was made based on clinical history and was treated with prednisolone, halobetasol and antibiotics. The lesions improved significantly with the above management and patient recovered enough to be discharged from the hospital after 5 days. Severe and serious reactions such as bullous pemphigoid can be caused by used drugs like furosemide.

Keywords: Adverse drug reaction, Bullous pemphigoid, Diuretics, Drug induced cutaneous reaction, Furosemide, Naranjo ADR Probability Scale

INTRODUCTION

Bullous pemphigoid (BP) is an acquired autoimmune disease characterized by subepidermal vesicles and bullae. The etiology for BP is mostly idiopathic with the highest occurrence in elderly patients; however, it is now well-accepted that BP has been triggered by or associated with drug therapy.¹ Over 50 agents have been implicated as a cause of Drug-induced bullous pemphigoid (DIBP), including diuretics, ACE inhibitors, and antibiotics.² Commonly reported drugs inducing bullous pemphigoid includes NSAIDs, furosemide, penicillamine, terbinafine, captopril, spironolactone, celecoxib, serratiopeptidase, mefenamic acid, beta-blockers, psoralens, sulphonamides, Chloroquine, ciprofloxacin.³

Furosemide is a widely used medication for treatment of congestive heart failure, hypertension, and various other conditions for its diuretic action. Available in parenteral and oral forms depending on need of therapy. Furosemide is one of the important drug attributed for causation of drug induced bullous pemphigoid.⁴

CASE REPORT

A 75 year old male was admitted to the dermatology department of KIMS hospital, Bengaluru, presented with multiple tense bullae and vesicles over both upper limbs (Figure 1), forearm and few collapsed bullae and vesicles over the extensor aspect of lower limbs (Figure 2) and chest (Figure 3). Patient had a past history of myocardial

infarction, undergone coronary artery bypass grafting (CABG) for the same and treated with multiple medications in a private hospital. Among the pharmacological treatment provided injection furosemide was one of the drug.



Figure 1: Bullae and vesicles over the forearm and hand.



Figure 2: Collapsed bullae seen over the lower limb.

After 2 days of administration of the drug, he developed fluid filled bullae and itching. First over the chest and upper limbs extensor aspect. After that bullae were drained and anti-histamine drug was administered, then patient was discharged from hospital after 2 days with continuing the treatment for Hypertension and Ischemic heart disease. Post discharge treatment included Furosemide, aspirin, bisoprolol, silodosin, ranitidine, levocetirizine and motelukast. After 5 days of discharge lesions increased in both the lower limbs and upper limbs, for which he admitted to dermatology department of our hospital. A diagnosis of bullous pemphigoid was made based on clinical findings. Causation by drug was suspected and furosemide was removed from therapy and treated with prednisolone, halobetasol and antibiotics. The lesions improved significantly with the above management and patient recovered enough to be discharged from the hospital after 5 days. ADR causality assessment done with Naranjo's scale shown this ADR as probable (Table 1) and WHO scale shown it as probable/likely (Table 2).



Figure 3: Collapsed bullae over the chest.

Table 1 : ADR Causality assessment (Naranjo scale).⁵

Question	Yes	No	Do Not Know	Score
1. Are there previous conclusive reports on this reaction?	+1	0	0	1
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	2
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	1
4. Did the adverse event reappear when the drug was re-administered?	+2	-1	0	0
5. Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	+2	0	0
6. Did the reaction reappear when a placebo was given?	-1	+1	0	0
7. Was the drug detected in blood (or other fluids) in concentrations known to be toxic?	+1	0	0	0
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	0
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	0
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	1
Total				5

Score: ≥ 9 = definite ADR; 5-8=probable ADR; 1-4=possible ADR; 0=doubtful AD

Table 2: WHO-UMC Causality assessment.⁵

Causality term	Assessment criteria*
Certain	Event or laboratory test abnormality, with plausible time relationship to drug intake
	Cannot be explained by disease or other drugs
	Response to withdrawal plausible (pharmacologically, pathologically;
	Event definitive pharmacologically or phenomenologically (i.e. an objective and specific medical disorder or a recognized pharmacological phenomenon)
	Rechallenge satisfactory, if necessary
Probable / Likely	Event or laboratory test abnormality, with reasonable time relationship to drug intake
	Unlikely to be attributed to disease or other drugs
	Response to withdrawal clinically reasonable
	Rechallenge not required
Possible	Event or laboratory test abnormality, with reasonable time relationship to drug intake
	Could also be explained by disease or other drugs
	Information on drug withdrawal may be lacking or unclear
Unlikely	Event or laboratory test abnormality, with a time to drug intake that makes a relationship improbable (but not impossible)
	Disease or other drugs provide plausible explanations
Conditional / Unclassified	Event or laboratory test abnormality
	More data for proper assessment needed, or
	Additional data under examination
Unassessable / Unclassifiable	Report suggesting an adverse reaction
	Cannot be judged because information is insufficient or contradictory
	Data cannot be supplemented or verified

* All points should be reasonable complied with

Table 3: Hartwig’s severity assessment scale.⁶

Assessment criteria	
Level 1	An ADR occurred but required no change in treatment with the suspected drug
Level 2	The ADR required that treatment with the suspected drug be held, discontinued, or otherwise changed. No antidote or other treatment requirement was required. No increase in length of stay (LOS).
Level 3	The ADR required that treatment with the suspected drug be held, discontinued, or otherwise changed. AND/OR an Antidote or other treatment was required. No increase in length of stay (LOS).
Level 4	Any level 3 ADR which increases length of stay by at least 1 day (OR) The ADR was the reason for admission.
Level 5	Any level 4 ADR which requires intensive medical care.
Level 6	The adverse reaction caused permanent harm to the patient.
Level 7	The adverse reaction either directly or indirectly led to the death of the patient.

Mild=level 1 and 2; Moderate=level 3 and 4; Severe=5, 6 and 7.

Table 4: ADR preventability assessment (Schumock and Thornton Preventability Scale).

Assessment criteria	
Definitely preventable	
1	Was there a history of allergy or previous reactions to the drug?- YES
2	Was the drug involved inappropriate for the patient's clinical condition?
3	Was the dose, route or frequency of administration inappropriate for the patient’s age, weight or disease state?
4	Was a toxic serum drug concentration (or laboratory monitoring test) documented?
5	Was there a known treatment for the adverse drug reaction?
Probably preventable	
6	Was required therapeutic drug monitoring or other necessary laboratory tests not performed?
7	Was a drug interaction involved in the ADR?
8	Was poor compliance involved in the ADR?
9	Were preventative measures not prescribed or administered to the patient?
Not preventable	
10	If all above criteria not fulfilled

Severity was moderate according to Hartwig's severity assessment scale (Table 3). ADR preventability assessment with Schumock and Thornton Preventability Scale shows it was probably preventable (Table 4). All the above assessments are summarized as analysis of ADR and depicted in (Table 5).

Table 5: Analysis of the ADR.

Type	Results obtained
Causality- Naranjo	Probable
Causality- WHO-UMC	Probable/likely
Severity- Hartwig	Moderate
Preventability- Schumock and Thornton	Probably preventable

DISCUSSION

Bullous pemphigoid is one of the serious adverse drug reaction that leads to mortality and morbidity in elder patients, if timely care not taken. In our case the drug Furosemide injected as a routine medication for his cardiac manifestations along with other drugs such as beta-blockers (bisoprolol), NSAIDs (aspirin), which also known to cause DIBP. But the later two drugs were previously given in patient as elicited by history for his hypertension and ischemic heart disease and the duration of onset of reaction from the time of administration of furosemide was relatable. A UK case control study shown that diuretics and neuroleptics are more commonly associated drugs with DIBP.⁷ Another UK case control study stated that loop diuretics are the most frequent cause of DIBP.⁸ Several case reports before has shown the role of furosemide in DIBP in the past, but the events keep on repeating most probably due to decreased awareness of possibility of ADR in different population.^{4,9} One of the study done in tertiary care hospital in Karachi by Ahmed B et al shown that polypharmacy is the one of the main cause of drug induced adverse drug reactions.¹⁰ The concern on individual treatment and monitoring of drug reaction when a patient is on poly-pharmacy in specific population to be addressed to prevent this kind of reactions in future.

CONCLUSION

Serious reactions such as bullous pemphigoid can be caused by commonly used drug like furosemide. Proper history taking and tailoring treatment for individual, early detection and treatment of ADR is needed in such cases.

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