Asian Journal of Case Reports in Medicine and Health

Volume 7, Issue 1, Page 45-50, 2024; Article no.AJCRMH.115141

Generalized Bullous Pemphigoid and Glycaemic Control in the Geriatric age Group: A Case Report

Amadi, Ekechi Stella [a,b*], Obioha, Solomon Uchenna [c], Gomba, Victoria Eno [d], Amaewhule, Mary Nnenda [a], Figilo, Ibeinmo Moses [e] and Altraide, Dasetima Dandeson [f]

[a] Department of Internal Medicine, Dermatology Unit, Rivers State University, Nkpolu-Oroworokwu, Rivers State University Teaching Hospital, Harley Street, Port Harcourt, Nigeria.
[b] Dermatology in Clinical Practice, Faculty of Life Sciences and Education, University of South Wales, Pontypridd, United Kingdom.
[c] Anatomical Pathology, Faculty of Basic Clinical Sciences, Rivers State University, Rivers State University Teaching Hospital, Harley Street, Port Harcourt, Nigeria.
[d] Department of Internal Medicine, Endocrinology, Diabetes and Metabolism Unit, Rivers State University, Nkpolu-Oroworokwu, Rivers State University Teaching Hospital, Harley Street, Port Harcourt, Nigeria.
[e] Department of Internal Medicine, Dermatology Unit, Rivers State University Teaching Hospital, Harley Street, Port Harcourt, Nigeria, Federal Medical Centre, Yenagoa, Nigeria.
[f] Department of Internal Medicine, University of Port Harcourt, Dermatology Unit, Rivers State University Teaching Hospital, Harley Street, Port Harcourt, Nigeria.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/115141

Case Report

Received: 26/01/2024
Accepted: 30/03/2024
Published: 06/04/2024

**Corresponding author: E-mail: ekechiamadi@yahoo.com;*

ABSTRACT

Bullous pemphigoid (BP) is a rare autoimmunobullous disease which is seen more in the elderly. There are many factors that have been associated with BP including medications, vaccines, and different diseases including diabetes mellitus. Diabetes mellitus is known to enhance the production of autoantibodies by glycosylation of dermal proteins and increase skin fragility. This case report looks at the management of BP with consideration for glycaemic control; the accurate interpretation of the values in the older adult and emphasis on the need for multidisciplinary approach while also taking note of medication side effects.

Keywords: Corticosteroids; diabetes mellitus; generalized bullous pemphigoid; geriatric age; glycaemic control; rivaroxaban

1. INTRODUCTION

Bullous pemphigoid (BP) is a rare autoimmunobullous disease that commonly occurs in older adults though any age group can be affected. It could be generalized or localized. Hyperglycemic states such as diabetes mellitus have been associated with an increased risk of developing bullous pemphigoid [1]. The mechanisms involved are increased skin fragility (due to hyperglycemia) and the production of autoantibodies by glycosalation of dermal proteins [2-5]. Ironically some anti-diabetic drugs have been implicated in also causing BP [6]. On the other hand, corticosteroids which are the first line therapy for BP have also been implicated in predisposing to hyperglycaemia and actually causing diabetes mellitus [3]. These make management of BP in patients with diabetes to be very challenging especially in the elderly who most often than not already have long term microvascular and macrovascular complications of diabetes [4,6]. Glycaemic control is essential in managing BP effectively because poor glycaemic control is associated with poor outcome of BP. Therefore, utmost care must be taking in the management of hyperglycaemia especially in geriatric patients with BP to ensure optimal glycaemic control for age without causing hypoglycaemia. The interpretation of glucose readings in geriatric patient with BP must therefore be carefully done to avoid hypoglycaemia or hyperglycaemia that can worsen the outcome of bullous pemphigoid. The aim of this case report is to effectively interpret hyperglycaemia in geriatric patients with BP with the purpose of adequate control of BP in spite of co- existing morbidities.

2. CASE REPORT

We present two cases of generalized bullous pemphigoid occurring in the geriatric age group seen within a 3month period in our centre that presented with documented evidence of poor glycaemic control.

2.1 Case 1

She was a 75 year old retired administrator, known to be living with diabetes and hypertension for more than 10 years with good adherence to therapy. She had complicating cerebrovascular disease with residual right hemi paralysis that caused her to be immobile most part of the day. She suddenly developed a vesicobullous rash which initially, started as pruritic papules which then progressed to form tense blisters. They were on normal looking skin, initially at the inner thighs and upper arm but rapidly progressed to involve the trunk and other parts of the body with very few lesions in the mouth. Blisters were itchy, tense, of varying sizes which later broke down to become ulcers. However, new lesions continued to appear to become blisters. There was no known relieving or aggravating factors. There was history of ingestion of rivaroxaban, two days prior to the development of the rash. She had been on insulin and metformin for her diabetes. She had also been on amlodipine, atorvastatin and clopidogrel with good blood pressure control. Her fasting blood glucose on the day of presentation was 14.3mmol/l. An initial diagnosis of Steven Johnson' syndrome in a known type 2 diabetes mellitus was made at the Accident & Emergency but the dermatologists on review felt it was an autoimmune bullous disease. The diagnosis of drug induced bullous pemphigoid was made from histology. She was co-managed by the endocrinologists and dermatologists. Insulin was maximised and adjusted daily. Topical 0.05% clobetasol propionate with oral prednisolone 30 mg daily was commenced, however the oral prednisolone had to be stopped due to worsening hyperglycaemia. Oral azathioprine

100mg daily was used in its place. Antipruritic agents such as chlorphenamine (piriton) certirizine and ketotifen were used, sometimes in combination due to the intense itching. Patient was discharged after she showed good clinical response to treatment and good glycaemic control was achieved. She is currently on follow up at the medical outpatient clinics.

2.2 Case 2

He is a 71 year old retired director not known to be living with diabetes who presented with a three month history of vesicobullous rash which was intensely pruritic, tense, discharging haemorrhagic fluid when ruptured. The rash was not photosensitive. The initial rash started as a blister on the leg and then spread rapidly over a period of days. There was no history of polyuria, polydipsia or polyphagia, but he had history of unintentional weight loss. He was initially managed as a case of staphylococcal scalded skin infection at a peripheral centre but was referred to the dermatologist after a couple of months of being on intravenous antibiotics without any improvement. Initial investigations showed, FBS was 5.2mmol/l and HbA1c was 6.9%. The endocrinologist requested a 2 hour post-prandial test after breakfast be done daily for 1 week which showed the range to 6.8-8.4 mmo/l which was within normal glucose range for his age. Skin punch biopsy initially done was suggestive of psoriasis but the samples left had to be reanalysed and bullae at dermal–epidermal junction was visualized. The clinical diagnosis of bullous pemphigoid was confirmed. Patient was treated with topical 0.05% clobetasol propionate and oral prednisolone 30 mg daily for 3months. The dose of oral prednisolone was later tapered down as patient made significant improvement and went into remission. He was later commenced on azathioprine as the bullae reoccurred and is currently being followed up on outpatient basis.

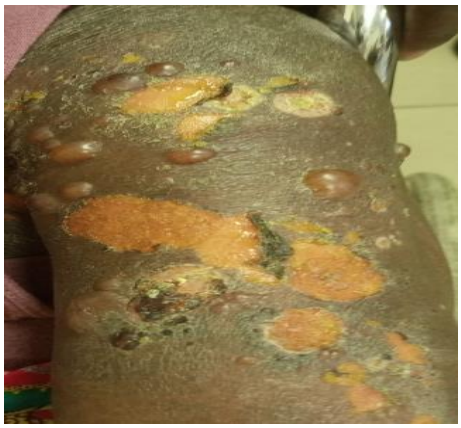

Fig. 1. Bullae and ulcers on the upper arm

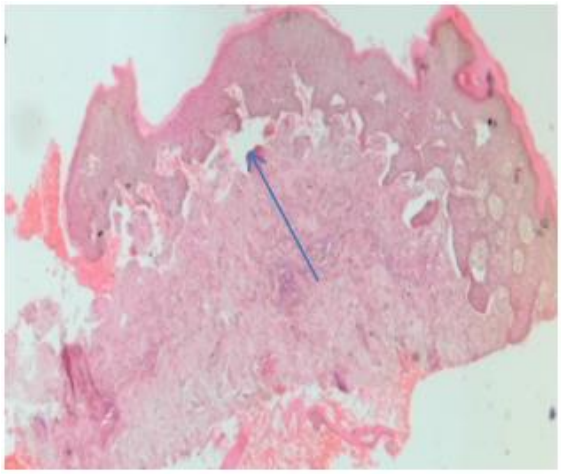

Fig. 2. Micrograph showing sub-epidermal split

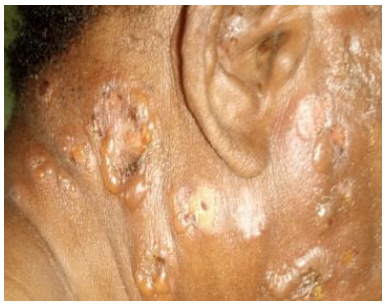

Fig. 3. Bullae, eschar and ulcers on the head and neck

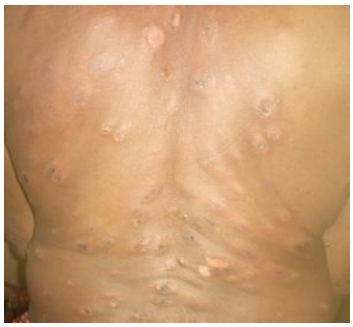

Fig. 4. Bullae, eschar and ulcers on the trunk

3. DISCUSSION

The cases above typify the classical cases of generalized bullous pemphigoid which is known to be commoner in the elderly if they occur. T2DM and BP share a common epidemiological factor which is older age but this alone cannot fully explain the rarity of BP even in older adults when compared to T2DM. The aging process has been associated with alteration in the immune status of patients [7]. Co-morbidities such as cerebrovascular diseases (as in the first case) dementia, multiple sclerosis and epilepsy have been implicated but the mechanisms involved are not known [8, 9]. In BP there is self-induced destruction of the membrane of the epidermis by the antibodies and white blood cells. It is known to be an autoimmune sub-epidermal blistering disorder, as a result of damage by the basement collagen protein known as type 17(XVII) collagen which is also called BP 180 and a plakin (BP 230). The antibodies responsible are the immunoglobulin G and E, while the T-lymphocytes are the white blood cells implicated [10]. These autoantibodies are enhanced by the glycosalation of dermal proteins leading to increased skin fragility [11]. It has been established that DM is a predisposing factor to BP even as reported in an older patient in similar settings who after few months of developing asymptomatic DM came down with BP [12]. Poorly controlled T2DM has also been shown to have a negative impact on the management of BP. It has been shown in patients with DM and BP that it is more difficult to achieve remission particularly if there is poor glycaemic control as was seen in the first case [1,13,14]. Multidisciplinary approach is needed particularly good collaboration between endocrinologists and dermatologists as a study has shown that up to one third of BP patients are diabetic [13]. Establishing a correct diagnosis of diabetes in the elderly is very important The second case showed that using glycated haemoglobin alone may give a false diagnosis of DM. The combination of HbA1c and fasting plasma glucose increased diagnostic sensitivities and specificities [15]. The glycated haemoglobin is not always reliable. It is influenced by several factors one of which is anaemia which the elderly are predisposed to [16].

Several drugs have been implicated as causal factor in BP including drugs being used for treatment of T2DM particularly the gliptins [2, 6,17 ,18]. Recalcitrant BP has been shown with the gliptins, metformin and sulphonylureas. This hyperglycemic state is likely to predispose to formation of more autoantibodies resulting in a re-occurrence of BP [2, 6]. There are about ninety or more medications and vaccines that have been identified to cause drug induced BP.

These drugs have been classified into likely, probable and uncertain association and include (in addition to the anti-diabetic agents) anti-hypertensives, antibiotics, anti-platelets, and diuretics which the older adult are likely to receive for co-morbidities as it was in the first case [18]. Rivaroxaban has good safety profile in persons living with diabetes; however the report of rivaroxaban associated bullous pemphigoid is increasing across the globe [19]. The mechanism is not fully understood but the treatment modality is to stop the offending agent and start corticosteroids as it was done in this case report. Corticosteroids have their own adverse effects on glucose control. Corticosteroids are known to cause hyperglycaemia by stimulating hepatic gluconeogenesis, muscular non-esterified fatty acid production, adipose lipolysis, and inhibition of pancreatic beta cells insulin response [20]. In the two patients discussed corticosteroids had to be discontinued and azathioprine started. In the first case the patient was a known diabetic whose glucose control was poor while in the second case the patient was not diagnosed with T2DM; however had the potential to fully become diabetic with the risk factors of using corticosteroids for more than 3 months and being in the geriatric age group.

4. CONCLUSION

Bullous pemphigoid is an autoimmune blistering disease that has been known to be induced by several external factors including hyperglycaemic states such as diabetes mellitus and a variety of drugs. Corticosteroid which is the first line of treatment in most cases of BP has the potential to cause hyperglycaemia if used for a prolonged period hence worsening outcomes for BP care. Dermatologists and endocrinologists need to collaborate with other specialists in developing guidelines in managing patients with these co-morbidities.

CONSENT

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Nuttapatch J, Padcha P, Sinee W. Bullous pemphigoid and diabetes mellitus: a systematic review and meta-analysis, International journal of dermatology; 2024. Available:https://doi.org/10.1111/ijd.16970, Accessed (02-03-2024)
2. Geller S, Kremer N, Zeeli T, Spreacher F. Bullous pemphiigoid and diabetes mellitus, Are we missing a bigger picture?' JAAD case reports. 2018;79(2):e27,
3. Persson MS, Harman KE, Thomas KS, Chalmers JR, Vinogradova Y, Langan SM, Hippisley-Cox J, Gran S. Long-term oral prednisolone exposure in primary care for bullous pemphigoid: population-based study. Br J Gen Pract. 2021;71(713):e904-e911.
4. Milanesi A, Weinreb JE. Diabetes in the Elderly. [Updated 2020 Sep 25]. In: Feingold KR, Anawalt B, Blackman MR, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc; 2000 Available:https://www.ncbi.nlm.nih.gov/books/NBK279147/, Accessed (02-03-2024)
5. Kilvert A, Fox C, Diagnosis and management of diabetes in older people . Pract. Diabetes. 2017; 34(6):195–199.
6. Huang L, Liu Y, Li H, Huang W, Geng R, Tang Z, Jiang Y. Bullous Pemphigoid and Diabetes medications: A disproportionality analysis based on the FDA Adverse Event Reporting System. Int J Med Sci. 2021;18(9):1946-1952.
7. Bastuji- Garin, B. et al, French study Group for Bullous diseases Risk Factors for Bullous pemphigoid in the elderly: a prospective case control study, J Invest Dermatol. 2011;131(3): 637-643.
8. Khosravoni S. Handjani F. Alimohammadi R, Saki, N. Frequency of Neurological Disorders in Bullous Pemphigoid patients: A cross sectional study Available:https://www.hindawi.com/journals/isrn/2017/6053267/,Accessed (21-02-2024)
9. Lai Y, Yew Y, Lambert, W. Bullous pemphigoid and its association with neurological diseases: a systematic review and meta- analysis, J Eur Acad Dermatol Venereol.n 2016;30(12):2007-2015.

10. Oakley A, Bullous Pemphigoid; dermanetNZ; Available:https://www.dermnetnz.org/topics/bullous-pemphigoid/, Accessed (02-03-2024)
11. Raghav A, Ahmad J, Alam K. Nonenzymatic glycosylation of human serum albumin and its effect on antibodies profile in patients with diabetes mellitus. PLoS One. 2017;12(eCollection 2017):e0176970.
12. Otike-Odibi B, Amadi ES, Altraide DD, Abbey BO, Ugwa O. Case report of bullous pemphigoid in a 65 year old woman. International Journal of Research in Medical Sciences. 2020;8(7): 2669–2673.
13. Downham TF, Chapel TA. Bullous pemphigoid: therapy in patients with and without diabetes mellitus. Arch Dermatol. 1978;114:1639-1642.
14. Alexandre MI, Garrido PM, Filipe P. Treatment of Diabetes in Bullous Pemphigoid Patients: Where Do We Stand? Dermatol Pract Concept. 2023 ;13(1):e2023063
15. Yan ST, Xiao HY, Tian H, Li CL, Fang FS, Li XY, et al. The cutoffs and performance of glycated hemoglobin for diagnosing diabetes and prediabetes in a young and middle-aged population and in an elderly population. Diabetes Res Clin Pract. 2015;109(2):238-45.
16. Guo W, Zhou Q, Jia Y, Xu J. Increased Levels of Glycated Hemoglobin A1c and Iron Deficiency Anemia: A Review. Med Sci Monit. 2019; 25:8371-8378.
17. Chouchane K, Di Zenzo G, Pitocco D, Calabrese L, De Simone C. Bullous pemphigoid in diabetic patients treated by gliptins: the other side of the coin. J Transl Med. 2021;19(1):520
18. Verheyden MJ, Bilgic A, Murrell DF. A Systematic Review of Drug-Induced Pemphigoid. Acta Derm Venereol. 2020;100(15)
19. Liang JC, Raman K, Chan SH, Tashakkor AY. Rivaroxaban-Associated Bullous Pemphigoid in a Patient With Atrial Fibrillation. CJC Open. 2021;3(10):1316-1319
20. Sari DA, Samodra G, Kusuma IY. Molecular mechanism of glucocorticoid-induced hyperglycemia. Pharmacy Reports. 1(1):1.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/115141