

Case Report

Case report of bullous pemphigoid in a 65 year old woman

**Bolaji Otikeyodibi¹, Ekechi S. Amadi*¹, Dasetima D. Altraide¹, Belema O. Abbey¹,
Okezie Ugwa^{1,2}**

¹Department of Internal Medicine, ²Department of Anatomical and Morbid Pathology, University of Port Harcourt Teaching Hospital, Alakahia, Port Harcourt, River State, Nigeria

Received: 21 April 2020

Accepted: 28 May 2020

***Correspondence:**

Dr. Ekechi S. Amadi,

E-mail: ekechiamadi@yahoo.com

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ABSTRACT

The unique thing about this case is that it is the first reported case of bullous pemphigoid in the elderly that has been clinically diagnosed with histologic findings highly suggestive of this blistering disorder although an immunofluorescence could not be done due to unavailability in the centre. Patient was managed successfully and discharged home with improvement on subsequent hospital visits. This case report shows how diagnosis of an immunobullous disease was made and managed in a resource poor setting. A descriptive summary of 65-year old black Nigerian woman with bullous pemphigoid covering history, physical examination and management. The main diagnosis was bullous pemphigoid in a recently diagnosed type 2 diabetic. Patient was placed on corticosteroids as well as immunosuppressive agents and diabetes was managed with subcutaneous insulin and oral hypoglycemics with appropriate wound care. Patient showed remarkable improvement after management and was discharged home with subsequent follow up in the clinics. Bullous Pemphigoid (BP) can be diagnosed clinically with a high index of suspicion with the aid of skin biopsy and histology, and can be managed successfully even in a resource poor centre where immunofluorescence facilities are lacking.

Keywords: Autoimmune, Bullous pemphigoid, Drug-induced, Elderly

INTRODUCTION

The aim of this study is to report a case of an elderly woman who presented to the hospital with complains of blistering skin lesions and to elaborate on clinical history, physical examination findings, possible associated risk factors and the investigations carried out within the setting. This includes the diagnostic and management challenges faced at different times and also the patient and care giver's perception about the disease which has been shown to have an impact on the outcome of management.¹ This case of BP happens to be unique in that it was diagnosed clinically and histologically, this is the first time this is occurring at the tertiary centre since the inception of the dermatology unit over fourteen years ago. The patient was managed and discharged home and is being followed up on an outpatient basis. Being a rare

disease in itself can pose a diagnostic challenge, in that the diagnosis can be missed by the non-dermatologist's low index of suspicion thus ascribing the disease to other common blistering disorders in the community.²

CASE REPORT

Mrs. L.J, a 65-year old lady, farmer from Gokana in Rivers State in Nigeria. She is from the Ogoni ethnic group and is a Christian. She developed tense blisters following a 4 week's history of fever and a 3-week history of generalized skin rashes. Patient was in her usual state of health until 4 weeks prior to presentation when she developed fever, low grade, intermittent, and temporarily relieved by paracetamol. There was no associated history of neurological, chest, urinary symptoms or ear pain or discharge. Generalized skin

rashes were noticed a week later. It was sudden in onset, started as pruritic papules which 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 ranging between 1-4cm in diameter, which later broke down to become erosions and ulcers. There was no known relieving or aggravating factors. There was a previous history of ingestion of drugs such as paracetamol and antimalarial (artesunate based combination) prior to onset of blisters. There was no associated hematuria, dysuria, oliguria, pedal oedema nor facial puffiness or frothiness of urine, There were no acute symptoms such as polyuria, polydipsia or polyphagia or chronic symptoms such as blurring of vision or paraesthesia ; suggestive of diabetes mellitus . At onset of symptoms, patient and her family members who are also her care givers became agitated due to the development of the blisters. They were afraid it was infective and maybe contagious as a result of the fever and blisters.

She had no known chronic illness such as hypertension, epilepsy, dementia, or any other neuropsychiatric illness. She was not asthmatic or had any history of atopy. She had no malignancy or liver disease. There was no family history of diabetes, hypertension, asthma or atopy, malignancy, liver disease, renal or autoimmune disease. She has had no previous hospital admissions, surgery or history of blood transfusions.

She was married in a monogamous setting with 6 children, ages between 30 and 45years all alive and well. She was not known to take alcoholic beverages or use tobacco products in any form. Palm kernel oil and some herbal topical agents were applied on the skin following development of blisters before patient visited the primary care centre and was subsequently referred to the tertiary centre as disease persisted despite medical intervention.

On physical examination she was in painful distress, anxious, acutely ill-looking, afebrile, pale, anicteric, acyanosed, dehydrated, no peripheral lymphadenopathy and nil pedal oedema. Her weight was 55kg and height was 1.55m with a body mass index (BMI) of 22.9kg/m²

Her integumentary system revealed widespread blistering and scalded lesions with erosions all over her body measuring from 1cm to about 4cm. Bullae were tense. There were few oral lesions over the lips and oral mucosa. Erosions were clean with absence of slough. Nikolsky sign was negative. Her neurological, chest and abdominal findings were normal. Her pulse rate was 88beats per minute and blood pressure was 120/70mmHg, both within normal limits

She was referred to the medical unit on call and admitted into the ward. On the second day of admission patient was transferred to the dermatology unit.

Initial investigations done were a random blood glucose that showed >33.3mmo/l (using glucometer). Bed side urinalysis showed 3+ of glucose. Retroviral screen was negative. Hepatitis B surface antigen and Hepatitis C antibody were also negative. Serum electrolytes, urea and creatinine and liver function tests were all within normal limits; however, the complete blood count showed eosinophilia of 24%. Urine microscopy culture and sensitivity (MCS) showed heavy growth of candida. Glycated haemoglobin was 9.4%.

A blood sample for culture and skin punch biopsy was requested for, culture result revealed staphylococcus aureus which was sensitive to quinolones. Thiopurine methyl transferase (TPMT) activity was 61U/ml which was within normal limits. Malaria parasite was negative.

On light microscopy the sections of tiny skin biopsy showed scanty basal layer cells. There were focal sub epidermal bullae which displayed mixed inflammatory cell infiltrate including eosinophils. The dermis was composed of irregular fibres of collagenous tissue and normal looking adnexial structures as well as pockets of mixed inflammatory cells infiltrates. There was no obvious neoplastic lesion. These findings were consistent with bullous pemphigoid.

She was not previously diabetic however was diagnosed as such on admission, at accident and emergency with a random blood glucose of > 33.3 mmol /L using a bed side glucometer.

The initial care of the patient was with intravenous normal saline, to correct dehydration. Intravenous and intramuscular soluble insulin was given initially and later converted to the subcutaneous route to correct hyperglycemia. Strict input and output chart for urine was kept with continuous monitoring of patient. Barrier nursing was instituted and normal saline was used to clean the wounds, which were dressed with petroleum jelly (Vaseline). Broad spectrum antibiotics like ceftriaxone at 1g 12 hourly and tinidazole 800mg daily for five days was instituted prior to result of blood culture. Blood glucose was monitored daily. Tabs albendazole 400mg, stat was given to take care of possible helminthic infections since the patient was put on tabs prednisolone 50mg daily (a.m.). She was also put on subcutaneous clexane(low molecular weight heparin-LMWH) 40mg daily and tabs vitamin C 200mg thrice daily.

Tabs metformin 1g b.d was added to control the hyperglycemia, tabs loratidine 10mg (a.m.) and tabs cetirizine 10 mg nocte was given to control the persistent pruritus. Glucose monitoring was done daily and the endocrinology unit was invited to co- manage the patient.

On the 7th Day of admission (DOA), several new lesions were noticed, topical betamethasone cream b.d was added and tabs Azathioprine 50mg daily (a.m.) was added.



Figure 1: Generalized blisters noticed on the 7th DOA.

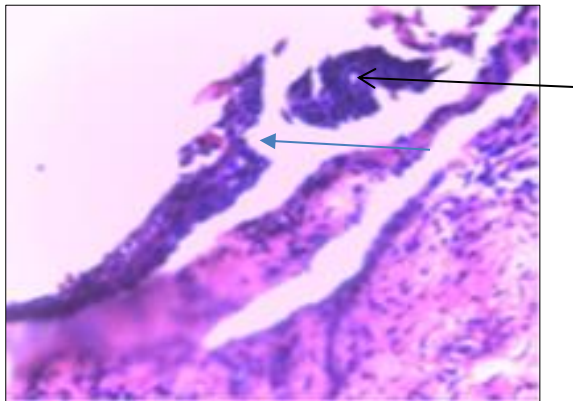


Figure 2: Denudation of the epidermis in most places with just the basal layer remaining (Black arrow). There is sub-epidermal non-acantholytic bullae (Blue arrow).

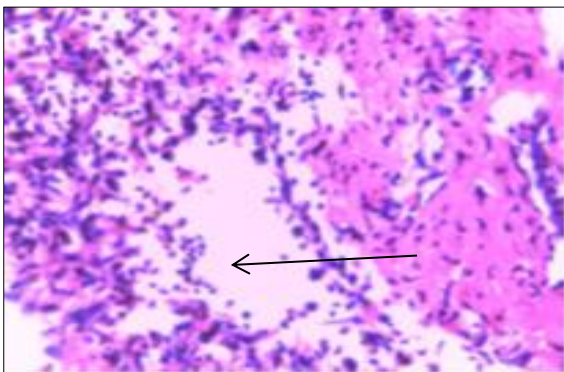


Figure 3: The dermis and the bullae contain a heavy infiltration by eosinophilic rich inflammatory cells that tend to collect as abscess.

On the 14th DOA, the blisters had greatly reduced. The fasting blood glucose (FBG) and RBG were normal. However, prednisolone was gradually increased to 100mg daily and Azathioprine to 150mg daily. Betamethasone cream was changed to the more potent clobetasone cream.

On the 16th DOA, patient developed an episode of irrational behaviour for which the neuropsychiatry team was invited and patient was certified to be stable and her

prednisolone was finally stepped down to 90mg daily and no new drugs were added

On the 43rd DOA, Subcutaneous clexane (LMWH) was discontinued. Patient was noted to be anaemic and declined blood transfusion on religious grounds. Iron deficit was calculated and correction commenced with iron sucrose on alternate days after a test dose as well as subcutaneous erythropoietin 4000units was given after the last dose of iron. She was converted from IV levofloxacin to tabs levofloxacin 500mg daily. As a result of the anaemia her drug was changed from azathioprine to mycophenolate mofetil 500mg twice a day. Prednisolone was tapered down gradually by 10mg every 5days.

On 47th DOA, patient showed remarkable improvement, she became ambulant and could sit out of bed with minimal pain, blood glucose has been well controlled for the past 1wk, few lesions were still coming out, but they were small in size.

She was discharged home in a stable condition with most of the skin lesions healed on the 54th day. The antibiotics and insulin were stopped but she continued on a tapered dose of prednisolone, metformin and mycophenolate mofetil. She had two follow up visits which showed most of the lesions has healed. Patient's caregivers (daughters) complained of the distance that she had to make to come to the hospital for follow-up and requested for referral to a centre nearer them. She was then referred to a tertiary hospital nearer to her home.

DISCUSSION

This is a case of BP in a black elderly female adult who resides in an oil producing area in the south-south region of Nigeria. The risk factors for BP in this patient are female sex and older age group.³ The patient was diagnosed with type 2 diabetes mellitus on admission from elevated blood glucose and was confirmed with elevated glycated haemoglobin (HbA1c) despite not having symptoms. Diabetes mellitus in itself has been associated with BP without prior administration of corticosteroid which can predispose to DM as seen in a case control study, although there has not been association with a specific type.⁴ The mechanisms involved are increased skin fragility due to hyperglycemia and the production of autoantibodies by glycosylation of dermal proteins.⁵ It can be argued that Type 1 diabetes is more closely linked with autoantibodies and autoimmune disease; however, Type 2 DM is more likely to be in this patient since it presented in her old age.

The use of dipeptidyl peptidase IV inhibitor drugs such as vidagliptin and sitagliptin have been linked with increased occurrence of BP.^{6,7} The patient took paracetamol and antimalarial tablets (artemisinin based combination therapy-ACT) Paracetamol has been

implicated in cases of bullous eruptions such as fixed drug eruptions and also bullous pemphigoid.^{8,9} Antimalarial drugs such as ACT are not known to be associated with BP.

On physical examination the generalized tense, tender blisters with minimal mucosal involvement made bullous pemphigoid highly suggestive on clinical examination. It is also noted that the blisters of BP heal with no or minimal scarring. Other blistering disorders such as pemphigus vulgaris (PV), pemphigus foliaceus (PF), bullous systemic lupus erythematosus (BSLE) and epidermolysis bullousa acquisita (EBA) are possible too, but were ruled out on thorough medical examination and history. BP is the commonest autoimmune bullous disorder even in our environment.¹⁰ The blister of pemphigus vulgaris and pemphigus foliaceus are usually flaccid and could also be painful with clear fluid on an erythematous skin or healthy skin.¹¹ EBA blisters can also be tense and tender with minimal mucosal involvement with a peak in the older age group like that of BP, however it leaves a dense scarring on trauma prone areas. It has no racial or sexual predilection.¹² BP, EBA and BSLE are all subepidermal blisters while PV and PF are intraepidermal. The autoantibodies for BP are against the basement collagen protein known as type 17(XVII) collagen which is also called (BPAG1) 180Kdalton and a plakin (BPAG2) 230Kdalton while both EBA and bullous SLE have autoantibodies against type VII collagen. The response to treatment with dapsone is more favourable in those with BSLE.¹³ Cicatricial pemphigoid (CP) also closely resembles BP and can be difficult to distinguish but it differs that it almost always displays its clinical activity on the mucosal membrane.¹⁴

There was marked eosinophilia in blood count in this patient. This is a finding that can be seen in those with BP although it is non-specific and this patient being a rural farmer has a predisposition to helminthic infection such as *Ancylostoma duodenale*, a hookworm that penetrates the skin via contaminated soil.¹⁵ BP is known to be a type 2 hypersensitivity reaction and is known to have perivesicular eosinophilic infiltrate.¹⁵ There was also eosinophilic predominance of the dermal infiltrates in the subepidermal blister on histology of patient's skin. This is highly suggestive of BP.¹⁶ The marked eosinophilia in this patient might be multifactorial due to the possibility of helminthic infection, but mostly from the bullous pemphigoid.¹⁷ In BSLE it is usually a neutrophilic predominance.¹³ Although there was no use of immunofluorescence to make the diagnosis the clinical history, examination findings and histological diagnosis on light microscopy was highly suggestive of BP.

The management of this patient was multidisciplinary including the endocrinologist and dermatologist specialist care. Topical and oral steroids were both used. A medium potent steroid was initially used- bethametasone, It had to be changed to a highly potent steroid -clobetasone.

Steroid (oral prednisolone) was given and increased accordingly. Patient showed improvement upon commencement. It was tapered down when the patient developed irrational behaviour. It has been known that corticosteroids can have a lot of complications including neuropsychiatric problems such as mood swings, behavioural problems, confusion or delirium and these complications are worse in the elderly patient.^{18,14} It can also worsen the diabetic state of the patient however in this setting, these drugs are the most readily available to aid in reducing the blister formation, relieve pain and inflammation. A study done in France showed that there is an increased risk of neuropsychiatric problems in BP patients.¹⁹ Azathioprine is an immunosuppressive agent that can be used in the management of BP and it has steroid sparing effects, although its use is not without its own side effects.^{14,20} Azathioprine is the pro-drug for 6-mercaptopurine and is a substance that is metabolized in the alternate pathway by enzymes which include the thiopurine methyl transferase enzyme. It is known that up to 6 in 1000 patients can have mutation in the gene that produce this enzyme thus resulting in its deficiency. The implication is that there would be severe bone marrow toxicity when treating with azathioprine or mercaptopurine, hence the need to screen for the TPMT deficiency mutation.^{21,22} There are varying ways in which azathioprine can be used when treating BP. It is believed that it can be given together with prednisone particularly in the acute stage as was done in the treatment of this patient. This is because it acts slowly.¹⁹ Azathioprine can also be used alone in the initial stage of the disease particularly if the disease was limited.¹⁴ This patient had extensive BP and the combination of the two drugs was beneficial. Azathioprine was changed to mycophenolate mofetil when the haemoglobin and other blood parameters became reduced.

Other care patient received such as barrier nursing, wound care, rehydration, treatment of infections and correction of anaemia were also vital to the recovery of the patient. She declined blood transfusion due to her religious beliefs. Patient had to be given intravenous iron sucrose which she tolerated during initial test dose and later received two doses of 200mg of IV iron sucrose in appropriate dilutions of normal saline. The main complications in cause of treatment were severe anaemia and irrational behaviour.

Perception and consent

Initial perception about the disease was that she had an infection and it may have been complicated by drugs taken. This perception was also shared by her care givers who were family members (two daughters and a son). Patient and care givers who were her family members received counselling from the onset about the cause of illness. Their perception of the disease was assessed and they were informed of possible complications of treatment and disease. Consent was obtained from the patient and caregivers. She gave consent for her

photographs to be taken for this case report and was willing to be part of it, particularly when she was informed that what she suffered from was rare in our environment

CONCLUSION

BP though not a common disease, can occur in resource poor settings lacking the specific diagnostic tool such as immunofluorescence, however diagnosis can still be made based on clinical history, physical examination and skin biopsy and histology with light microscopy. Adverse reactions can occur in the course of treatment. Treatment is multidisciplinary. Patient perception of the disease can influence response to care. Caregivers are important and provide both financial and psychosocial support for the patient.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Otikeyodibi B, Amadi ES, Altraide DD, Abbey BO, Ugwa O. Case report of bullous pemphigoid in a 65 year old woman. *Int J Res Med Sci* 2020;8:2669-73.