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Case Report

Clinical Case Report: Bullous Pemphigoid

Juan Pablo Meza-Budani[1], Diana Ly-Liu[2], Ellen O'Riordan[3], Domingo Ly-Pen[4]

[1]*Thames Medical Centre. Thames. New Zealand.*
[2]*Department of Anesthesia, Basurto University Hospital, Bilbao, Bizkaia, Spain.*
[3,4]*Coothehill Medical Centre. Cootehill. Co. Cavan. Ireland.*

[4]*Corresponding Author : domingoly@gmai.com*

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Abstract *- A patient diagnosed with Bullous Pemphigoid is presented. This is not a very frequent disease in Primary Care. Nevertheless, general practitioners or family physicians should be aware of this entity so as not to misdiagnose and make a suspicious and differential diagnosis. General practitioners or family physicians should also be aware of the follow-up and side effects of the specialist´s treatments.*

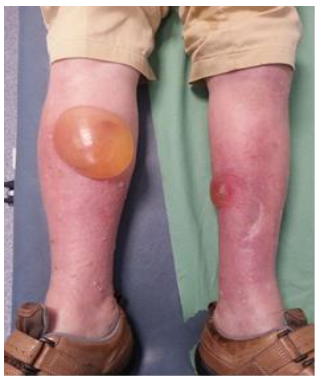
Keywords *- Bullous pemphigoid, Dermatology vesicular lesion, Primary Care*.

1. Introduction

Bullous Pemphigoid (BP) is the most common subepidermal blistering autoimmune disease. Nevertheless, it is seldom known in a primary care setting. There have been few cases of BP published for general practitioners. Of course, this should not be an excuse to ignore BP and to know the most frequent side effects of its treatments. BP is about 80% of all subepidermal immunobullous patients. It is more frequent in elderly patients (60 to 80 years old). The typical clinical presentation is tense bullae and generalized pruritus. In less frequent cases, bullae can be absent, therefore requiring high clinical suspicion. In these cases, a haematoxylin and eosin staining biopsy shows subepidermal split with eosinophils: direct immunofluorescence will show autoantibodies against the basement membrane zone. Although BP is associated with high morbidity and mortality, its burden worldwide remains unclear.

2. Clinical Case

A 66-year-old man comes to our consult with these lesions in his lower legs:



2. Epidemiology

In the USA, the incidence is 6 to 13 new cases per million people per year, while in Central Europe, it is 12 to 13 new cases per million. Despite its incidence is low, it seems to be increasing over time. BP is more frequent in elderly people, usually above 60. BP may present in childhood, but this is very uncommon. There is no preference related to gender, nor to any ethnic group. Different specific HLA class II alleles have been described in different ethnics [1-3].

3. Aetiology

Most BP cases have autoantibodies against proteins at the dermal-epidermal junction; nevertheless, some BP can be iatrogenic, caused by systemic medications (even two to three months after exposure to the specific medicine). Among the most frequently published these are diuretics (spironolactone, furosemide), antibiotics (amoxicillin), several NSAIDs, PD-1/PD-L1 inhibitors, TNF-alpha inhibitors, and gliptins [4, 5].

4. Pathophysiology

The main components regarding the pathophysiology of BP are immunologic and inflammatory. The immunologic consists of autoantibodies against BP antigen 230 and BP antigen 180, located in the basal keratinocyte hemidesmosomal proteins. The role of these antigens is based on the adhesion of epithelial-stromal complexes. Once the autoantibodies attach to their target antigen, complement and mast cells activate, providing the inflammatory component that causes eosinophils and neutrophils to release inflammatory cells, ending with the

release of proteolytic enzymes that destroy the dermal-epidermal junction [6, 7].

5. Histopathology

In the BP, the major histopathology feature shows a subepidermal blister with variable degrees of dermal inflammation.

Direct immunofluorescence consists of detecting tissue-bound autoantibodies and is the gold standard test in autoimmune blistering diseases; for this, it is mandatory to biopsy the site of the skin lesion. At least two punch biopsies should be obtained: one for haematoxylin and eosin staining, and the other will be from perilesional uninvolved skin for direct immunofluorescence [8, 9].

6. Clinical Presentation

About 20% of patients will not have bullae or erosions in the initial cases.

The bullous phase typically presents with bullae and vesicles on normal or erythematous skin. Blisters are tense, measuring up to 1 to 4 centimetres in diameter, and sometimes they can be haemorrhagic. Typically, they contain clear fluid that will leave erosions and crusts after several days.

General symptoms are not frequent, but they may occur in severe, widespread disease [10, 11].

7. Diagnosis

BP diagnosis is based on clinical findings and laboratory tests. Histology immunofluorescence studies (direct and indirect) are crucial in the diagnosis [12].

Direct immunofluorescence is considered the gold standard in BP (also in other autoimmune blistering diseases), directly revealing deposits of IgG (mainly IgG4 and IgG1) in the dermal-epidermal junction. Two or more punch biopsies of the area of the skin lesion will be needed for direct immunofluorescence: one for haematoxylin and eosin staining and another for direct immunofluorescence using perilesional, uninvolved skin [13].

8. Differential Diagnosis

Bullae are nonspecific features that can appear in different pathologies, depending on the timing in the clinical presentation: contact dermatitis (and allergies that cause this), drug interactions, arthropod reactions, urticarial dermatoses, scabies, and other autoimmune bullous disorders such as cicatricial pemphigoid, pemphigus vulgaris, herpes gestationis, Stevens-Johnson syndrome, dermatitis herpetiformis, pseudo-porphyria, porphyria cutanea tarda, dyshidrotic eczema. If bullae are seen in childhood, epidermolysis bullosa, bullous variants of mastocytosis, and bullous impetigo must be considered [14, 15].

9. Treatment

The main treatment for BP is systemic corticosteroids, but the extent of the disease and other comorbidities will determine the definitive treatment. For focal disease, or in an elderly patient with less than 20% of the total body surface affected, potent topical steroids such as clobetasol are indicated. Also, nicotinamide, combined with topical steroids plus tetracycline, is effective in many cases [16].

For cases where the disease is more extensive, systemic prednisone from 0.5 to 1.0 mg/kg per day should be used. In about two weeks, this dose should control the disease, and the prednisone dose can be reduced over six to nine months. This treatment is, of course, tailored according to the patient's comorbidities, age and possible side effects. Generalized BP can be controlled with potent topical corticosteroids. Other drugs act as steroid-sparing drugs, acting as immunosuppressives. They will only be considered when there are contraindications for treatment with systemic corticosteroids or when corticosteroids cannot control the disease. Examples of these are methotrexate, azathioprine, cyclophosphamide, chlorambucil and mycophenolate mofetil.

If all these options for treatment fail, then omalizumab and anti-CD20 (rituximab) could be useful. Recently, dupilumab showed very promising results [17-19].

Table 1. Treatment of bullous pemphigoid

LOCAL DISEASE (-20% body surface): - Potent topical steroid (e.g. clobetasol) - Nicotinamide + topical steroids + tetracycline
EXTENSIVE DISEASE (+ 20% body surface): - Limited by comorbidities, age and side effects - Prednisone IV 0.5-1 mg/kg/day; dose reduced over 6 months.
IMMUNOSUPPRESSIVE THERAPY: - It is only to be considered when treatment with IV steroids is contraindicated or has no efficacy. - First line: methotrexate, azathioprine, cyclophosphamide, chlorambucil, mycophenolate mofetil - Second line (after the previous treatment failed): omalizumab, ituximab, dupilumab

10. Prognosis and Complications

Usually, BP spontaneously resolves in a few months, but in some cases, it can last for up to five years. Complications of BP can include skin infections, sepsis, and adverse effects of treatment [20].

11. Contributions

J-P M-B selected articles for inclusion and helped in writing the paper. DL-L helped write the paper and select articles for inclusion. EOR helped in writing the paper and reviewed the paper. DL-P conceived and supervised the work, helped in writing the paper, and did all the paperwork. All the authors have revised and participated actively in the elaboration and approved the final draft.

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