

Bullous pemphigoid: can it occur in pediatric age?

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RESUMEN

El penfigoide ampollar en niños es extremadamente infrecuente. La mayoría de los casos ocurre en adultos mayores, resultando fundamental considerar que en medicina todo es posible y esta enfermedad igualmente podría presentarse en niños, por lo que se debe prestar especial atención a sus manifestaciones clínicas, realizar los exámenes apropiados para descartar diagnósticos diferenciales y de esta forma, iniciar un tratamiento eficaz en el momento preciso. A continuación, presentamos un caso clínico de penfigoide ampollar que ocurrió en un paciente pediátrico atendido en nuestro hospital universitario.

Palabras claves: Penfigoide ampollar; Dermatología pediátrica; Enfermedades ampollares en niños; Dermatopathology.

SUMMARY

Bullous pemphigoid in children is extremely infrequent. Most of them predominate in elderly persons, resulting fundamental to consider that in medicine everything could be possible, and this disease could occur in children, so we must pay special attention to its clinical manifestations, to take the appropriate exams to rule out differential diagnoses and in this way perform an effective treatment at the precise moment. Following, we present a clinical case of bullous pemphigoid that occurred in a pediatric patient attended at our university hospital.

Key words: Bullous pemphigoid; Pediatric dermatology; Bullous diseases in children; Dermatopathology.

Bullous pemphigoid (BP) is an autoimmune blistering disorder characterized by tense blisters with itchy urticarial erythema and plaques that develop on the entire body.¹ Its incidence and prevalence during childhood is unknown, being extremely rare with only nine reports of cases occurred during early adolescence.²⁻⁴ Autoimmune bullous disorders are due to autoantibodies generated against target antigens; in this way one typical serologic characteristic of BP is the presence of circulating autoantibodies against BP180 (collagen XVII) and BP230.⁵ BP180 is a 180 kDa transmembrane glycoprotein with a 16th non-collagenous domain, and BP230 is an intracellular constituent of the hemidesmosomal

plaque which belongs to the spectraplaklin family.⁶

In the following report, we present a clinical case of bullous pemphigoid (BP) in a teenager, highlighting the unusualness of this disease at this age.

CLINICAL CASE

A 12 year-old female with no chronic diseases or other relevant medical history was referred to our hospital, for a disseminated dermatosis of a two-week evolution, which affected the face, trunk, limbs and genitals. It was characterized by large, tense and painful blisters, with serous or serohemorrhagic content (Fig-

ure 1). Nikolsky's sign was negative, and there was no compromise of mucous membranes (Figure 2). Also, the patient did not report taking medications, receiving vaccinations or having had infectious conditions during the last months. General laboratory tests showed no relevant alterations. The patient was hospitalized, and treatment with prednisone 1mg/kg/day was initiated. The following day, dermatologists took knowledge of the patient and under the suspicion of bullous pemphigoid, an incisional skin biopsy was performed on the edge of a blister for hematoxylin-eosin staining, showing a subepidermal blister with a viable roof, fibrin and eosinophils inside, and superficial perivascular inflammatory infiltrate with eosinophils in the dermis (Figure 3). Simultaneously, a second incisional skin biopsy was performed on perilesional skin for direct IF, which did not show the presence of antibody deposits. The diagnosis of BP was confirmed, and treatment with prednisone was continued at the same dose, adding azathioprine at a dose of 2 mg/kg/day. After three months, a progressive decrease of the administered dose of both medications was initiated, until it was completely suspended after six months. Three years later, the patient is without immunosuppressive treatment and has not presented new exacerbations of the disease.

DISCUSSION

Bullous diseases in children can be associated to different etiologies, being the most frequent dermatosis at this age, those of infectious type and those genetically inherited; however, autoimmune blistering diseases in childhood are extremely rare, with only nine reported cases during early adolescence, and highlighting that BP tends to occur in the elderly.² Considering the unusualness character of this dermatosis, we must pay special attention to its clinical manifestations, and its possible differential diagnoses.

BP is characterized by the presence of tense blisters, sometimes hemorrhagic, and arising from normal or inflamed skin. Urticarial plaques are commonly seen in annular or polycyclic patterns, and unlike adults; in children the mucosal involvement would be more common;³ however, our patient didn't present mucosal affection.

During childhood the most common cause of blis-

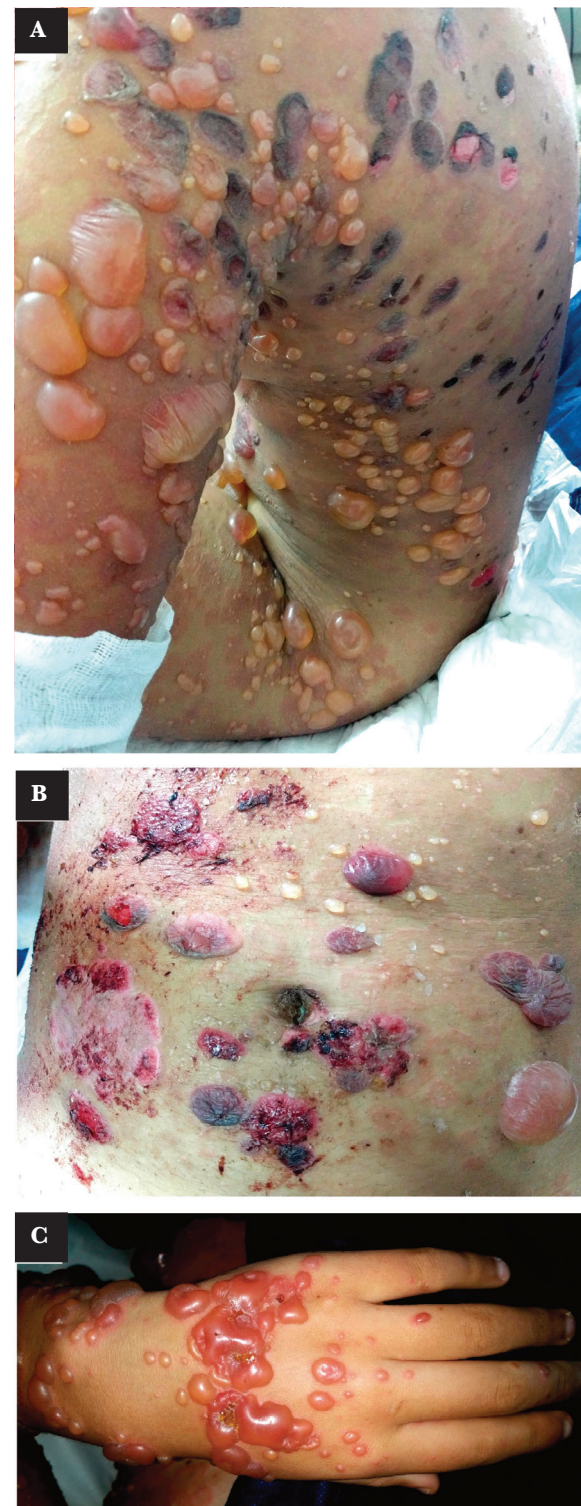


Figure 1
Bullous pemphigoid, clinical manifestation. Disseminated blistering dermatosis characterized by large, tense and painful blisters, with serous or serohemorrhagic content.
A. Left region of the trunk and left arm.
B. Anterior region of the trunk.
C. Dorsum of the left hand.



Figure 2

Bullous pemphigoid, clinical manifestation. Bullous dermatosis evidencing blisters around the mouth, and with no compromise of oral mucous membranes.

tering disorders are infections: viral (herpes simplex virus), bacterial or fungal.⁴ However, autoimmune bullous diseases could also be presented, and the most commonly seen is the linear IgA bullous dermatosis (LBD), which is characterized by tense bullae with an annular configuration in a “cluster of jewels” or “string of pearls”, evidencing predilection for perineum and perioral region. Mucous membranes can be involved in up to 80% of affected children.⁴ Another differential diagnosis that should be considered is dermatitis herpetiformis that is characterized

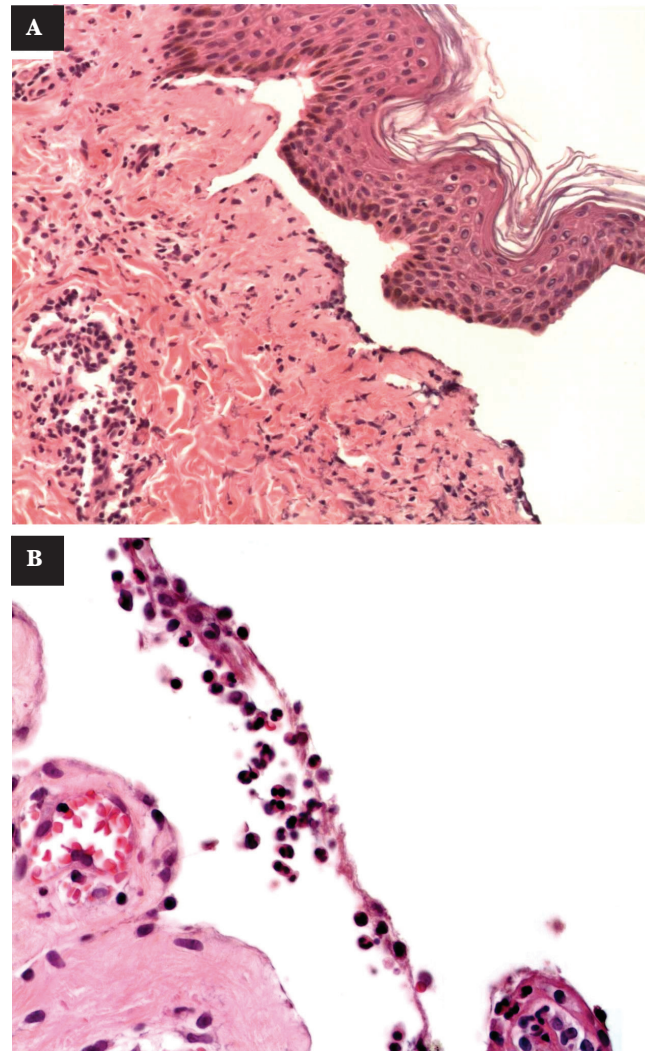


Figure 3

Bullous pemphigoid, histopathology with hematoxylin & eosin stain.

A. Subepidermal blister (20x, original magnification).

B. Fibrin and eosinophils are evidenced inside of the blister (40x, original magnification).

by intensely pruritic vesicles, and eroded papules on extensor surfaces and scalp, in patients with family or personal history of celiac disease.

Histopathology and direct IF are essential to corroborate the presumptive diagnosis, and to rule out differential diagnoses. In this way, light microscopy of lesioned skin from patients with BP evidences a subepidermal blister, with an eosinophilic or neutrophilic infiltrate within the papillary dermis; additionally, direct IF microscopy of perilesional skin typically shows linear deposits of IgG and C3 at the dermal-epider-

mal junction.⁷ According to rule out LBD, we have to consider that its anatomopathological examination could be similar, revealing subepidermal bullae with neutrophilic infiltrate, and occasionally evidencing eosinophils and lymphocytes. Considering the aforementioned, it is essential to perform direct IF, which shows linear and homogeneous deposition of IgA at the basement membrane zone.⁸ On the other hand, dermatitis herpetiformis is also a subepidermal blister dermatosis that usually shows neutrophilic microabscesses within dermal papillae, and fibrin deposition; however, direct IF shows granular deposits of IgA within dermal papillae.

Considering what was mentioned in the previous paragraphs, we emphasize the importance of performing the biopsy at the right moment and before starting corticosteroid treatment, avoiding the occurrence of false negative results of direct IF, as we believe that happened with our patient, where the clinical presentation was fundamental to clarify the diagnosis.

About the treatment of BP, systemic corticosteroids are effective for its management; nevertheless, we emphasize that corticosteroids should be administered for the shortest possible time and using the lowest effective dose;⁴ so we must add other medications such as azathioprine, which in our case was satisfactorily used. Other drugs used as steroid-sparing in pediatric patients are mycophenolate mofetil, methotrexate, and less commonly mycophenolic acid.⁹ In addition, other treatments described include antibiotics (erythromycin, dapsone, and sulfapyridine).⁴ While less well described in BP than in pemphigus, rituximab has demonstrated some efficacy in the treatment of BP; however, its high incidence rate of infections has been a limitation, and some authors recommend its combination with intravenous immunoglobulin to decrease this risk.⁹ In light of the improved understanding of the role of eosinophils in the development of BP,¹⁰ current clinical trials are underway of the IL-5 inhibitor mepolizumab, and the eotaxin-1 inhibitor bertilimumab.

Finally, it is important to specify that BP has an excellent prognosis during pediatric age, evolving towards complete remission after a few months, and presenting rare recurrences.⁴

CONCLUSION

BP in children is an extremely rare illness, and we should not be intimidated by its presence, proceeding quickly and with precision, when deciding the exams to be taken according to the proposed differential diagnoses. We must have an open mind, which allows us to remember that typical pathologies of elderly people can also occur during pediatric age.

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