Post-Vaccination Bullous Pemphigoid in Infants: A New Case
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Introduction: Bullous pemphigoid (BP) is an acquired autoimmune disease that primarily affects the elderly. It is considered rare in children, even less so in infants during the first six months of life. Bullous pemphigoid infantile post-vaccination is a rare presentation. We report a new case. Case report: A 2-month-old girl who presented two days after vaccination (hepatitis B, DPT, poliomyelitis, hemophilus, rotavirus, and pneumococcus) initially had a palmar-plantar vesiculobullous rash and thighs. The examination revealed multiple vesicles and tight bubbles resting on an erythematous and urticarial base, the presence of post-bullous erosions dry in places, the sign of Nikolsky was negative. Lesions affecting the whole body, the face, the scalp, the palms, the soles of the feet and then the oral and genital mucosa without any sign of infection. The diagnosis of bullous pemphigoid has been confirmed in histology. After steroid resistance, the patient was treated with immunoglobulin with a good response. Conclusion: It is difficult to prove that there is a genuine relationship between vaccination and the occurrence of bullous pemphigoid in infants. This is probably a pure coincidence justifying the continuation of the vaccination schedule. Nevertheless, it is important to know this clinical entity to be able to carry out an adequate treatment and to avoid any aggravation.

Keywords: Bullous pemphigoid - infant – vaccination.

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INTRODUCTION
Bullous pemphigoid (BP) is an acquired autoimmune disease that primarily affects the elderly. It is rare in children with only a hundred cases [1] described in the literature. Pediatric bullous pemphigoids distinguished from the adult variety by more frequent palmoplantar involvement, lack of association with neoplasm, and rapid resolution on steroids. Bullous pemphigoid infantile post-vaccination is a rare presentation. We report a new case of sterile-resistant post-vaccine infantile pemphigoidbullosa.

OBSERVATIONS
A 2-month-old female infant with no particular pathological history presented two days after vaccination (anti-polio, anti-rotavirus, anti-pneumococcal and pentavalent vaccine: anti-hepatitis B, DPT, hemophilus) a vesicular rash -bulleuse appeared initially on the thighs, the palms and soles of the feet evolving in a febrile context. Clinical examination revealed multiple vesicles and tense bubbles resting on erythematous and urticarial skin, mostly with clear contents and some acral hemorrhagic blebs, the presence of post-bullous dry erosions in places with a negative Nikolsky sign. The lesions spread to the entire body, face, scalp, and then the oral mucosa and genital area with no evidence of superinfection (Figure 1: A, B, C, D).

Cutaneous biopsy showed junctional detachment (Figure 2). Direct immunofluorescence revealed the presence of linear IgG and C3 deposits along the basement membrane, indirect immunofluorescence showed the presence of serum antibodies. Anti-basement membrane IgG type. The diagnosis of bullous pemphigoid was selected. The infant was put on prednisone orally at the dose of 2 mg / kg per day associated with a topical treatment with clobetasol propionate. A good initial response has been observed (Figure 3).

One month later and following an episode of viral bronchiolitis, the patient made a new outbreak identical to the initial episode; following which we opted for the addition of dapsone at a dose of 2 mg / kg / day. But before methemoglobinemia and the persistence of new lesions, dapsone was stopped and treatment with intravenous immunoglobulin was initiated at a dose of 2g / m2 with concomitant corticotherapy. The infant continued to present new bubbles with urticarial plaques and millium grains. A biopsy with NaCl cleavage found evidence of immune
deposits on the roof of the cleavage. Two other courses of intravenous immunoglobulin were administered to the patient with resolution of the lesions (Figure 4). The decline was a year and a half.

The parents do not choose to vaccinate their daughter even though they were informed of the absence of contraindications to continue the vaccination schedule.

**Fig-1:** Vesicles-blisters with clear or haemorrhagic contents + post-bullous erosions, A: lesions of the face, palmar and upper limb, B: trunk lesions, C: acral lesions and genital mucosa, D: damage to the scalp

**Fig-2:** Histological result in favor of bullous pemphigoid, A: Junctional detachment, B: Dense inflammatory infiltrate at the level of the dermis

**Fig-3:** Early healing of bullous lesions after corticosteroid therapy at the cost of hypopigmented macules
DISCUSSION

The first case of juvenile PB with confirmation by immunofluorescence was published in 1970 [2]. Infant PB is rare, to our knowledge. 110 whose reports are published in the literature [1] of which only 21 after the vaccination of all children affected by this disease [3].

The appearance of the lesions after vaccination varies from 1 to 4 weeks [1] after the administration of the anti DTP and polio [1, 2, 4, 5], the anti-hepatitis B [6] and the pneumococcal; just like our patient. BCG [7] and anti-meningococcal [8] were also incriminated.

The sex ratio of the literature is close to the literature (11M: 10F). The average age of overestimation is 3.5 months, of which a little less than half (12cas) before the first 6 months of life [3]. The cause of pediatric bullous pemphigoid is unknown and the possible triggers are nonspecific maternal antibodies and foreign antigens [1,9].

Although IgG antibody transfer is anti-pemphigoid, it can be explained by development in infants, no antibodies have yet been detected in the serum of affected mothers [3]. The possible relationship between vaccination and bullous pemphigoid is still unclear. It has been transformed into PB via a modulation of immunity [7].

Vaccination may help suppress subclinical bullous pemphigoid by enhancing an autoimmune response in immunologically predisposed individuals [10]. A study in adults failed to establish a link between BP and influenza vaccination [11]. Some aspects may suggest a possible relationship between vaccination and PB in infants: Most bullous pemphigoid cases have been found after the first vaccination dose [6, 12].

The incidence of pemphigoid is higher in infants in the first year of life; corresponding to age or vaccinations are performed more quickly. The time interval between the administration of the vaccination and the clinical manifestations. Recurrence after a new dose of vaccination [8, 13].

However, arguments refuting this hypothesis are the rarity of this entity in infants and hepatitis vaccinations in infants and children. Similarities between the structure and basement membrane proteins and a belief in the unlikely autoimmune hypothesis of PB after infant vaccination are lacking, with the mechanism of bubble formation induced by directed autoantibodies against the zone of the basement membrane. The absence of circulating anti-membrane antibodies in the mother's serum contradicts the theory of vertical transfer from the lip to the infant.

According to recent studies by Lo Schiavo et al. [14] it is worth mentioning the possible activation in inflammatory cascade mediated by the Th17 / IL17 pathway. It appears that the trauma caused by the injection of the vaccine led to the activation of Th17 cells with an increase in IL-17, capable of releasing cytokines and pro-inflammatory proteolytic enzymes, and recruiting and activating neutrophils, responsible for the clinical manifestations of bullous pemphigoid. Some infants, genetically predisposed, may be more sensitive to the stimulus of injecting the vaccine.

However, there is little conclusive evidence and it is difficult to prove that there is a genuine relationship between vaccination and the occurrence of bullous pemphigoid in infants. This is probably a pure coincidence.

Palmoplantar lesions are considered a diagnostic index of infantile pemphigoidbullosa. Schwieger-Briel et al. [12] proposed the following diagnostic criteria for retaining infantile pemphigoidbullosa: typical clinical presentation (acral distribution) and linear deposition of IgG and/or C3 at
the basement membrane in the IFD. The mucous membranes are constantly respected. To our knowledge, our patient is the second to have oral and genital mucosal involvement [15].

The infant PB usually has a favorable prognosis and disappears rather quickly with the treatment [16]. However, in post-vaccination PB cases previously reported, remission was achieved with topical or systemic steroids. Dapsone or intravenous immunoglobulins, as well as mycophenolate mofetil, methotrexate, azathioprine or rituximab are reserved for severe cases refractory to steroids [12, 17, 18]. Spontaneous remission is rare and is reported in one case [19]. Relapses of PB in children following a new dose of vaccine are extremely rare [12].

**CONCLUSION**

To our knowledge, there is currently no experimental data suggesting a link between vaccination and PB. As a result, this potential relationship is not meaningful from a practical point of view, which justifies the continuation of the immunization schedule in infants. In a few cases where there was recurrence after a new vaccine dose, the thrust was less intense and with a good response to treatment.

**REFERENCES**