

Childhood erythrodermic lichen planus pemphigoides after nonavalent human papillomavirus vaccination



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INTRODUCTION

Lichen planus pemphigoides is an uncommon autoimmune blistering disease characterized by clinical and microscopic findings of lichen planus, and a subepidermal blistering disease with antibodies to the basement membrane, similar to bullous pemphigoid. The disease is rare in adults and rarer in pediatric patients, with only 17 cases described so far.¹⁻⁷ It is usually idiopathic, although it has been related to some drugs in adults. As for children, lichen planus pemphigoides has been related to varicella infections^{2,3} and has been triggered by henna tattoos⁵ and the excessive application of an aromatic retinoid.⁷ To our knowledge, this is the first case of pediatric erythrodermic lichen planus pemphigoides described after nonavalent human papillomavirus (HPV) vaccination.

CASE REPORT

An 11-year-old boy presented with an extremely pruritic, diffuse rash for 7 weeks. The eruption started 2 weeks after he received the first dose of HPV vaccine (Gardasil 9), with isolated papules that coalesced into a widespread dermatitis. He had a history of atopic dermatitis, was up to date on all vaccines, and was receiving no medication. Physical examination found dry erythroderma involving more than 90% of his body surface according to the Wallace rule of 9, with the presence of purplish papules on the face, neck, trunk, and upper and lower extremities, including palms and soles, as well as tense hemorrhagic blisters on his legs and feet.

Abbreviation used:

HPV: human papillomavirus

Vesiculobullous lesions were present both on the papules and on normal skin, appearing 5 weeks after the development of papules (Figs 1 and 2). Mucous membranes and nails were spared. Nikolsky sign was negative. Histologic examination of a lichenoid lesion from the thigh showed hyperkeratosis with parakeratosis, focal hypergranulosis, and acanthosis with some apoptotic keratinocytes, interface dermatitis with a dense lichenoid infiltrate of lymphocytes, and rare eosinophils (Fig 3), whereas histopathology of a bullous lesion on the leg revealed a subepidermal blister containing eosinophils and neutrophils in the blister fluid and a mixed inflammatory infiltrate in the dermis (Fig 4). Direct immunofluorescence showed linear C3 deposits along the basement membrane. Enzyme-linked immunosorbent assay from serum was positive for PB180 antibody (120 U/mL; normal <9 U/mL) and slightly positive for PB230 antibody (10.50 U/mL; normal <9 U/mL). A diagnosis of lichen planus pemphigoides was made. The patient was treated with oral deflazacort 1.5 mg/kg/day, antihistamines, and topical steroids, with rapid improvement and clearing of the pruritic eruption. At 6-week follow-up, the patient had only residual postinflammatory hyperpigmentation. The patient's parents were advised to avoid further HPV vaccine injections to their son.

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Fig 1. Dry erythroderma with the presence of purplish isolate confluent buttocks and papules on the trunk and upper and lower extremities, including palms and soles.



Fig 2. Dry erythematous patches with vesicubullous elements.

DISCUSSION

Lichen planus pemphigoides is a rare, autoimmune, subepidermal bullous disease characterized by the coexistence of both lichen planus and bullous pemphigoid, although the relationship between these 2 disorders is more complex. Clinical findings include 2 primary skin lesions (ie, lichenoid papules and plaques and tense subepidermal blisters located both on the lichenoid plaques and on the uninvolved skin),⁸⁻¹⁰ different from bullous lichen planus, in which bullae are limited to long-standing lichen planus lesions. The onset of lichenoid lesions usually precedes the onset of bullae. Mucosal and nail involvement may occur but is uncommon. Palmoplantar involvement is observed more often in children. The erythrodermic form is rare, being reported in just 11 cases in adults but in only 1 case in pediatric patients. The pathogenesis of lichen planus pemphigoides can be explained by the

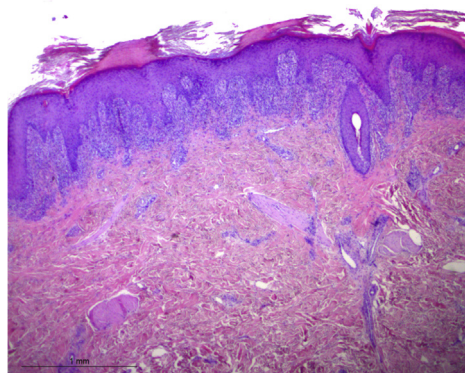


Fig 3. Histopathology of a papule showing hyperkeratosis with parakeratosis, focal hypergranulosis, acanthosis with some apoptotic keratinocytes, interface dermatitis with a dense lichenoid infiltrate of lymphocytes, and rare eosinophils. (Hematoxylin-eosin stain; original magnification: $\times 25$.)

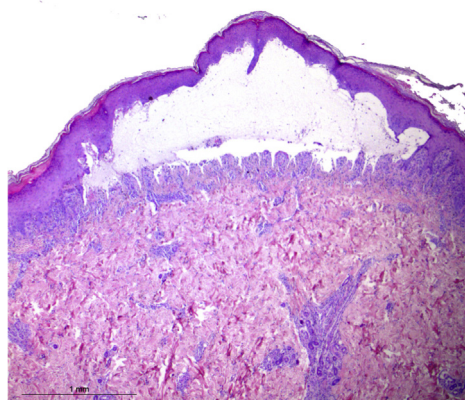


Fig 4. Histopathology of a bullous lesion from the leg, revealing a subepidermal blister containing eosinophils, neutrophils, and a mild mixed inflammatory infiltrate in the dermis. (Hematoxylin-eosin stain; original magnification: $\times 25$.)

phenomenon of “epitope spreading.” It has been hypothesized that a lichenoid inflammatory attack to the basal cell layers and basal membrane can expose antigens and promote the development of an autoimmune response, targeting proteins of the epidermal basement membrane, including type XVII collagen, also known as PB180 antigen.^{11,12}

Although usually idiopathic, lichen planus pemphigoides has been related to drugs such as cinnarizine, captopril, ramipril, simvastatin, antituberculous medications, gliptins, nivolumab, and enalapril; to phototherapy; and rarely to malignancies. Lichen planus pemphigoides has also been reported to be triggered by viral infections such as varicella,^{2,3} hepatitis B virus,^{13,14} and pharyngitis in the only pediatric case of erythrodermic lichen planus pemphigoides.⁶

Gardasil 9 is the nonavalent HPV vaccine licensed in 2014 that contains an additional 5 cancer-causing HPV types (HPV31, -33, -45, -52, and -58) in addition to the 4 more common HPV types (HPV16, -18, -6, and -11).¹⁵ It has twice the concentration (500 mg) of aluminum hydroxyphosphate as an adjuvant¹⁶ compared with 4-valent HPV vaccine.

Adverse events to HPV vaccination have been previously reported, including local reactions at the injection site such as granulomas, lipoatrophy, cellulitis, subcutaneous emphysema mainly related to the aluminum vaccine content, erythema multiforme, dermatographism, urticaria, erythema nodosum, and linear IgA bullous dermatosis.¹⁷⁻¹⁹ A lichenoid eruption after HPV vaccine has also been described.²⁰ To our knowledge, this is the first case of lichen planus pemphigoides in its erythrodermic variant after nonavalent HPV vaccination (Gardasil 9). In our patient, for ethical reasons, we could not perform a rechallenge, but the pattern of lichenoid reaction followed by the appearance of the bullae, the temporal relationship between the development of lichen planus pemphigoides and the vaccination, and the complete healing of the eruption suggest that the HPV vaccine was the probable triggering event.

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