Recalcitrant bullous pemphigoid responsive to dupilumab in an adolescent patient

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Bullous pemphigoid (BP) is an autoimmune blistering disorder characterized by pruritic cutaneous blisters and erosive mucosal lesions. It predominantly affects elderly individuals and rarely manifests in pediatric populations. Here, we describe a pediatric patient with recalcitrant BP successfully treated with dupilumab.

CASE REPORT

A 17-year-old girl with no significant medical or family history reported a pruritic blister on the left breast 2 months prior to presentation. She later began noticing vesicles on the inner legs. Her primary care physician initially prescribed doxycycline for possible impetigo; however, the lesions continued to rapidly spread so she was immediately referred to dermatology. On examination, there were multiple tense bullae symmetrically distributed on the face, trunk, and extremities with hemorrhagic features (Fig 1, A). There was a single erosion of the hard palate and excoriated vesicles of the labia majora.

Quantitative human chorionic gonadotropin was negative. A punch biopsy showed a subepidermal split with a predominance of neutrophils and eosinophils (Fig 2, A and B). Direct immunofluorescence revealed continuous, linear, homogenous C3 and IgG deposition along the dermoepidermal junction (Fig 2, C). Indirect immunofluorescence demonstrated positive IgG basement membrane zone reactivity with epidermal localization on salt split (Fig 2, D). BP-180 antibodies were elevated (574 units, reference: <9). An extensive workup for underlying malignancy and rheumatologic diseases with imaging and laboratory test results proved unremarkable. She was diagnosed with bullous pemphigoid and admitted for extensive disease.

Intravenous 25 mg methylprednisolone every 8 hours improved pruritus and pain, though attempts to transition to high-dose oral prednisone and other conventional therapies either did not control her symptoms or were poorly tolerated. For unknown reasons, her condition worsened after starting rituximab, which led to concomitant plasmapheresis sessions in the interval. She experienced significant symptomatic relief but had continual vesicle development. A combination of intravenous immunoglobulin (IVIG) in addition to steroids, rituximab, and plasmapheresis eventually caused BP-180 titers to downtrend and plateau, although she had persistent flares and never reached full clinical remission.

Abbreviation used:
BP: bullous pemphigoid
hCG: human chorionic gonadotropin
IVIG: intravenous immunoglobulin
IL: interleukin
FDA: Food and Drug Administration

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We then trialed a loading dose of dupilumab with 300 mg maintenance doses every other week. In 2 weeks, she began reporting improved pruritus and absence of new lesions. All other interventions were gradually discontinued within 2 months of dupilumab initiation. Ultimately, we had administered rituximab every 2 weeks for 2 months and then every 4 weeks for 3 months, IVIG (2 g/kg) every 4 weeks for 3 months, and a total of 13 plasmapheresis sessions. At a 4-month follow-up, she had complete blister resolution and undetectable BP-180 levels (Fig 1, B). She had no relapses on maintenance dosing in any subsequent visits.

DISCUSSION

Pediatric (ie, childhood, juvenile) BP is a rare condition with similar clinical features to the adult form, though acral distribution and mucosal involvement tend to be more common. Levels of circulating BP-180 (type XVII collagen) autoantibodies correlate positively with clinical activity in both subtypes. Treatment often entails topical/systemic corticosteroids, dapsone, antibiotics, azathioprine, methotrexate, and mycophenolate mofetil. These regimens carry significant adverse effects, and careful consideration is warranted in pediatric patients. IVIG, omalizumab, rituximab, and dupilumab are reserved for refractory disease. Evidence surrounding adjuvant plasmapheresis has been conflicting but in our case, provided rapid symptomatic improvement.

Several etiologies have been implicated in the pathogenesis of BP which include genetics, infections, medications, neurologic disorders, and malignancy. While use of dupilumab in BP has only been studied in geriatric populations thus far, its effectiveness in both recalcitrant adult and pediatric BP suggests similar inflammatory mediators, despite the former being associated with neurologic disease. Dupilumab, an anti-IL4 and anti-IL13 antagonist, likely modulates type II cytokines involved in blister formation, pruritus, eosinophil activity, and IgE secretion. It has been shown in a multicenter case series to achieve high patient satisfaction and disease clearance in 12 of 13 (92%) patients with BP and can prevent new blister formation as soon as 8 days.

Dupilumab is currently Food and Drug Administration approved for allergic diseases and...
has a favorable safety profile. Our case highlights its potential as a long-term and first-line therapy for all BP subtypes, particularly in those who are young or have aggressive/refractory disease. Future trials investigating the efficacy of dupilumab in BP should include children and compare its effectiveness to other biologics.

Conflicts of interest

None disclosed.

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