

## SHORT COMMUNICATIONS

### Oral Contraceptive Pills Inducing Bullous Pemphigoid in an Adolescent

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An 18-year-old African-American female with past medical history of autism spectrum disorder and polycystic ovarian syndrome presented with a four-month history of tense bullae and superficial erosions 1-2 weeks after starting oral contraceptive pills: norethindrone acetate 1mg-ethinyl estradiol 20mcg-ferrous fumarate 75mg (Figure 1). She discontinued the medication and the bullae resolved with a short course of methylprednisolone. A few weeks later she restarted the OCPs resulting in a worse flare that did not respond to discontinuation or methylprednisolone.

Histopathology revealed a subepidermal vesicular dermatitis with eosinophils and direct immunofluorescence showed linear IgG and C3 at the dermoepidermal junction, consistent with bullous pemphigoid. Her BP180 antigen was 163. Desmoglein 1, 3, and BP280 were all normal, a pregnancy test was negative, and a complete blood count and metabolic panel were unremarkable. She was started on 80mg prednisone daily with mild improvement that was unchanged with the addition of mycophenolate mofetil 1g twice daily. Subsequently, she was treated with rituximab 1000mg, two doses two weeks apart which cleared all bullae. One month after rituximab treatment she presented with one tense bullae and was started on doxycycline 100mg twice daily, niacinamide

500mg twice daily, and topical triamcinolone 0.1% ointment, with clearance of bullae. Of note, her BP180 four weeks following rituximab therapy was 63.6.

**Figure 1.** Bullous pemphigoid on the extremities and trunk after starting oral contraceptive pills.



Bullous pemphigoid (BP), recognized clinically by bullous skin lesions accompanied by pruritus, can be confirmed by biopsy findings revealing histopathological visualization of IgG and C3 against the components of the hemidesmosome. BP antigens are monitored with serum levels of BP180 and, lesser so, BP230.<sup>1</sup> BP180 constitutes part of the transmembrane hemidesmosome whose extracellular proteins can serve as a nidus for autoimmunity. BP180 levels help monitor the response to therapy in association with clinical improvement.<sup>4</sup>

This case represents a unique presentation of drug-induced bullous pemphigoid (DIPB) in that BP is rare in adolescents with most patients presenting after age 70. Cases in children are infrequent, with half occurring during the first year of life.<sup>1</sup> In contrast with adults, childhood BP has a more indolent course with resolution after initial treatment.

Though many drugs are associated with the development of BP in adults, OCPs have not been previously reported. Progesterone has been known to induce autoimmune dermatoses, though not in association with OCPs. Progesterone could be the causal factor of the development of BP in our patient. Though the mechanism is unknown, some suggest that synthetic progesterone induces molecular mimicry of the natural and synthetic hormones which may induce autoimmune disease.<sup>6</sup> Most cases of progesterone-associated autoimmune bullous dermatoses accompany pregnancy when progesterone levels are high. A case mentioning pemphigoid gestationis that resolved and later recurred with OCP use post-pregnancy has been reported.<sup>2</sup> Our patient represents a unique case in that she is an adolescent and not pregnant.

Two types of DIPB have been reported. DIPB-proper is self-limiting and resolves with cessation of the offending drug. The other resembles classical BP which takes a more severe, chronic course requiring treatment even after discontinuing the offending medicine.<sup>5</sup> Initial therapy is steroids. If the patient does not respond to oral prednisone, second line therapies are introduced such as azathioprine, mycophenolate mofetil, and tetracycline with niacinamide. Tetracycline and niacinamide are used as secondary agents even though the data supporting their role is not as robust as the others.<sup>3</sup> Rituximab can be utilized for refractory cases.<sup>4</sup>

Our patient required the use of rituximab as she did not improve with oral steroids or the addition of mycophenolate mofetil. Though rituximab has been approved for treatment of pemphigus vulgaris, it has been shown to provide improvement in patients with BP.<sup>4</sup>

**Conflict of Interest Disclosures:** None

**Funding:** None

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