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Case Letter

Diagnostic dilemma? Rethinking how to diagnose bullous pemphigoid in older adults

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Dear Editors,

This letter discusses the difficulties in diagnosing bullous pemphigoid. We present the case of a man in his 80 s with pruritic, nonspecific, eczematous papules and plaques of the upper body for 3 weeks. The patient had a history of phospholipase A2 receptor membranous nephropathy treated with rituximab (1000 mg 6 and 7 months prior) and an angiotensin-converting-enzyme inhibitor, statin, and loop diuretic beginning 9 months prior. Initial pruritus treatment with triamcinolone and hydroxyzine yielded no improvement. One month later, there were numerous erythematous excoriations and papules (Fig. 1), several with pseudovesiculation, and no oral lesions. Biopsy indicated subacute spongiosis with eosinophils and negative direct immunofluorescence (DIF). A presumed diagnosis of adult-onset atopic dermatitis prompted treatment with narrow band ultraviolet B light.

Three months later, with persistent pruritus, there were new firm bullae on the foot. Biopsy showed subepidermal vesicular dermatitis with an eosinophilic-rich infiltrate. DIF was once again negative, but bullous pemphigoid (BP) 180 and 230 serologies were positive. Upon establishing the diagnosis of BP, doxycycline 100 mg and clobetasol 0.5% ointment twice daily were initiated. New blisters while the patient was on this regimen prompted prednisone 20 mg every other day with a plan to administer rituximab infusion for previous renal disease and BP.

Clinical problem

Bullous pemphigoid is a well-known diagnosis in dermatology; however, this case illuminates nuanced diagnostic difficulties, particularly in older adults, which are otherwise undescribed in the literature. Negative assays and polypharmacy contributed to an overdue diagnosis for this patient, highlighting the limitations of current diagnostic practices.

Approximately 20% of patients with BP present with nonbullous pemphigoid, of whom a reported 9.8% develop blisters at a later date (Lamberts et al., 2018; Meijer et al., 2019). Thus, BP is an important diagnosis to consider in elderly patients with pruritus. Conventionally, DIF is reported as the most sensitive test for BP (Meijer et al., 2019; Sárdy et al., 2013); however, this recommendation does not consider the comorbidities and medications that may affect results. Studies establishing the sensitivities and specificities of BP diagnostic assays (DIF, indirect immunofluorescence, and enzyme-linked immunosorbent assay) were based on patients before the introduction of immunosuppressive therapy, which has the potential to alter this disease and our diagnostic abilities.

Patients commonly receive at least topical steroids before directed diagnostic testing for BP. The real-world presentation of patients with multiple confounders can leave providers in the dark for the true diagnostic yield of assays. Furthermore, immune dysregulation associated with aging may uniquely affect results. With this in mind, some studies report delays in diagnosis for an average of 6 to 22.6 months from symptom onset, contributing to disease morbidity and affecting quality of life (della Torre et al., 2012; Lamberts et al., 2018). For this patient's 4-month diagnostic delay, rituximab (a monoclonal CD-20 antibody) and topical triamcinolone could have contributed to the negative DIF results because they are conceivable BP treatments (Polansky et al., 2019).

Therapeutic solution

We propose that the conventional workup for BP should be reconsidered in pruritic older adults whose skin disease has been recently treated. Rather than a skin biopsy and DIF alone, enzyme-linked immunosorbent assay or indirect immunofluorescence may be necessary because prior or concurrent treatments could affect the diagnostic yield of DIF. This case highlights the interplay of clinical intervention and diagnosis, aiming to improve care for our most vulnerable populations.

Conflicts of Interest

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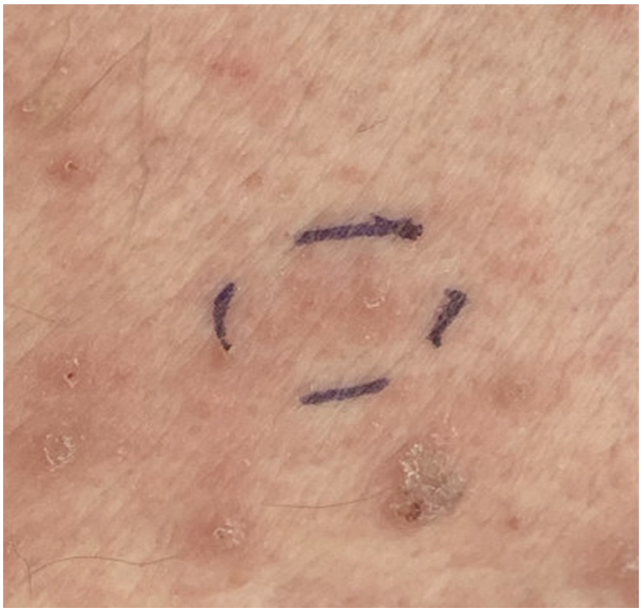

Fig. 1. Nonspecific pruritic papules at initial presentation.

Study Approval

The author(s) confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies.

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