

Figurate Erythema: An Unusual Presentation of the Nonbullous Phase of Bullous Pemphigoid

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Background and Objective: Bullous pemphigoid, an autoimmune disorder, most commonly presents as a bullous eruption in patients over the age of 60. There may be a prodromal urticarial or papular eruption that evolves to bullae.

Conclusion: We report a 46-year-old woman with a figurate erythema presentation of bullous pemphigoid.

Renseignements de base et objectif: La pemphigoïde bulleuse, un trouble auto-immun, se présente très couramment comme une éruption disséminée chez les patients de plus de 60 ans. Une éruption urticarienne prodromique ou papulaire peut entraîner l'apparition de bulles.

Conclusion: Nous exposons le cas d'une femme de 46 ans qui présentait un érythème figuré de pemphigoïde bulleuse.

A 46-YEAR-OLD WOMAN was seen in July 2010 with a widespread skin eruption that began 2 weeks prior to presentation. The lesions first developed on her arms and then became generalized. The lesions were extremely pruritic, with minimal relief obtained from oral diphenhydramine. The patient denied any prodromal symptoms and had not begun any new medications.

Past history included an astrocytoma diagnosed and treated during childhood. Secondary to this, she had hearing loss, ongoing petit mal seizures, and a cerebrovascular accident approximately 10 years ago. Her medications included carbamazepine and acetylsalicylic acid, which she has taken since childhood.

On examination, there were multiple targetoid lesions with central erythema, a concentric zone of pallor, and a well-defined peripheral ring of erythema. The lesions were generalized, involving the extremities, trunk, and face. There was no mucosal involvement. The clinical appearance was suggestive of erythema multiforme. A skin biopsy was taken from one of the lesions. The histology showed a heavy dermal eosinophilic infiltrate.

When seen 2 weeks later, the morphology of the eruption had changed to large plaques with raised

erythematous borders and gray centers in a generalized distribution suggestive of a figurate erythema. There were also several isolated vesicles on normal skin on the thigh, ankle, and one arm. Biopsies were taken for routine histology and direct immunofluorescence. A lymphoeosinophilic infiltrate was noted. Linear deposition of IgG and C3 at the dermoepidermal junction was seen on direct immunofluorescence, in keeping with a diagnosis of bullous pemphigoid (BP) (Figure 1).



Figure 1. Figurate erythema: 2 weeks after initial presentation

A complete blood count showed an eosinophilia of $1.4 \times 10^9/L$ (normal range $< 0.45 \times 10^9/L$) with a normal leukocyte count of $9.1 \times 10^9/L$ (normal range $4\text{--}10 \times 10^9/L$). The patient was started on prednisone 60 mg/d, and

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clobetasol propionate cream was to be applied twice daily to affected areas. In an attempt to enable tapering of the prednisone, minocycline 50 mg twice daily was begun. This medication was not tolerated and was discontinued. New blisters continued to appear while the patient was on prednisone 45 mg daily. A second immunosuppressant agent, mycophenolate mofetil, was added. After 1 month on the combination of prednisone 45 mg and mycophenolate mofetil 1,000 mg daily, the eruption gradually improved, with no new blister formation.

Discussion

BP is the most common autoimmune blistering disease of the skin.¹ Typically a disease of the elderly, it presents with a generalized pruritic bullous eruption. Mucous membrane involvement is rare.² The initial presentation may consist of urticarial plaques, without any vesicles or bullae. The incidence has been reported from 7 to 30 cases per million people per year.² The cutaneous lesions of BP can be polymorphous in appearance and may be initially misdiagnosed, particularly in the early stages of the disease. A lesional skin biopsy is required to establish the diagnosis of BP. A biopsy of an urticarial plaque may show eosinophilic spongiosis, the presence of eosinophils within the epidermis, without any separation of epidermis and dermis. BP is a paradigm of an organ-specific autoimmune disease. The antigens targeted by patients' autoantibodies, BPAg1 and BPAg2, represent two normal components of the hemidesmosome, a structure that is necessary for the adherence of the epidermis to the dermis.³

Clinical Features: Nonbullous Phase

In the nonbullous phase of the disease, signs and symptoms are nonspecific, with mild to severe pruritus and papules and plaques that may be urticarial in appearance. It may be several weeks or months before bullae appear. In our patient, the lesions in this phase of the illness were clinically compatible with a figurate erythema. There are only two reported cases of figurate erythema with BP.^{4,5} Such nonbullous prodromal manifestations make the diagnosis of BP difficult to establish without a biopsy.

The nonbullous phase of BP was first described in the 1970s, and over the decades, there have been numerous reports of BP without the typical large, tense bullae. Lesions of BP have presented as pruritus without skin manifestations, urticaria, erythema, eczema, dyshydrotic patches, prurigo nodularis-type lesions, vegetating lesions, and erythroderma.⁶ Given the wide range of possible

presentations, confirming the diagnosis of BP can be difficult and requires a high index of suspicion.

Clinical Features: Bullous Phase

The bullous stage of BP is characterized by the development of vesicles and bullae on normal or erythematous skin together with urticarial papules and plaques. Tense blisters form, up to 1 to 4 cm in diameter, contain clear fluid, and may persist for several days, leaving eroded and crusted areas as they resolve. The blister fluid may become blood tinged. The lesions may have a symmetrical distribution and may predominate on the flexural aspects of the limbs and the lower trunk. Residual postinflammatory changes include hyper- and hypopigmentation. Involvement of the oral cavity is observed in 10 to 30% of patients.⁷

Differential Diagnosis

The following conditions should be considered part of a thorough differential diagnosis of BP⁸:

- Erythema multiforme
- Dermatitis herpetiformis
- Linear IgA dermatosis
- Drug-induced bullous disorders
- Epidermolysis bullosa acquisita
- Lupus erythematosus, bullous form
- Figurate erythema cicatricial pemphigoid

Diagnosis

Skin biopsies are required for the diagnosis of BP. Two biopsies should be performed. The biopsy for routine hematoxylin-eosin staining may be most informative if an entire intact vesicle is removed. The second biopsy should be taken from perilesional uninvolved skin for direct immunofluorescence.

Histopathologic examination shows subepidermal separation of the epidermis and dermis with a dermal inflammatory infiltrate, with eosinophils. Direct immunofluorescence shows linear deposits of C3 along the basement membrane. Linear deposits of IgG, as well as other immunoglobulins, may also be seen.⁹

Management

The mainstay of therapy for BP is systemic corticosteroids. A regimen of oral prednisone (dosed at 0.5–1 mg/kg/d) usually controls the disease. Once blister formation has

stopped and there is significant healing of the skin lesions, the dose of prednisone may then be gradually tapered over 6 to 9 months. A large controlled study highlighted the use of potent topical corticosteroids in controlling mild to generalized BP.^{10,11} A second immunosuppressant, such as azathioprine or mycophenolate mofetil, may be required to allow the prednisone to be tapered. The prognosis for patients with BP is generally excellent. Poor prognostic factors are comorbidities, such as heart disease, diabetes, dementia, stroke, and poor general health. No factors directly related to the disease, including the severity at the time of presentation, influence the prognosis.^{12,13}

Although there are reports of an association between BP and underlying malignancy, both diseases tend to occur in the elderly, and case-control age-matched studies do not support an increased incidence of malignancy in those with BP.¹⁴ In general, other than a physical examination, an extensive workup for malignancy in patients with BP is not indicated.

Conclusion

Although it is well known that BP may not be bullous at the time of presentation, a more unusual morphology with targetoid lesions and annular lesions that are consistent with a figurate erythema can be seen. A high index of clinical suspicion is important in making the diagnosis and initiating treatment in a timely manner. BP can be polymorphous in presentation, and bullous lesions may be completely absent. Oral corticosteroids (prednisone) and other immunosuppressant agents are generally required to treat widespread BP.

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