CASE REPORT

Paraneoplastic bullous pemphigoid presenting with erythema gyratum repens-like figurate erythema

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INTRODUCTION

Bullous pemphigoid (BP) is an idiopathic, immunobullous disease rarely associated with internal malignancy. In contrast, erythema gyratum repens (EGR) is a rare, paraneoplastic eruption most commonly linked to primary lung and breast carcinomas.

Classically, BP presents with vesicles and bullae overlying normal-to-erythematous skin. Histopathology shows a subepidermal split with a prominent eosinophilic inflammatory infiltrate. Direct immunofluorescence reveals linear basement membrane deposition of IgG and complement component 3 antibodies. The most common circulating antibodies are against BP antigen 180 (BPAG2, Collagen XVII) and BP antigen 230 (BPAG1). EGR presents with rapidly migrating concentric erythematous plaques often described as wood-grain in appearance with a trailing scale.

CASE REPORT

We describe the case of a 76-year-old man concomitantly diagnosed with squamous cell carcinoma of the lung and paraneoplastic BP with gyrate erythema. The patient was admitted with a 3-week history of cough and a diffuse, pruritic, bullous, and figurate eruption with no mucosal involvement (Fig 1, A and B). Chest computed tomography showed a cavitating left lower-lobe mass and multiple other masses concerning for metastasis. Bronchoscopy and bronchial lymph-node biopsy confirmed squamous cell carcinoma of the lung. Cutaneous biopsies revealed a subepidermal split with numerous eosinophils (Fig 2). Direct immunofluorescence showed linear complement component 3 deposits with negative immunoglobulin staining. Indirect immunofluorescence demonstrated positive IgG basement membrane antibodies on split skin substrate with an epidermal (roof-staining) pattern and a titer of 1:1280. Enzyme-linked immunosorbent assay was positive for IgG antibodies to BP180 at 124 units (positive range, ≥ 9 units). Additional, indirect immunofluorescence panels for pemphigus and paraneoplastic pemphigus showed weakly positive IgG cell surface staining on monkey esophagus (1:160) and on rat bladder basement membrane zone (1:20). Enzyme-linked immunosorbent assay test for desmoglein 1 and desmoglein 3 were negative. Combination treatment with oral prednisone (60 mg/day; ~1 mg/kg/day), doxycycline, nicotinamide, and topical clobetasol was initiated with marked improvement in pruritus and cutaneous findings at the 1-month follow-up. The morphology of the cutaneous disease also changed, now exhibiting scattered, well-defined, nummular, erythematous, edematous plaques more consistent with urticarial phase BP (Fig 3). The same treatment regimen was maintained to avoid further immunosuppression in the setting of malignancy.

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Unfortunately, prior to initiation of chemoradiation, roughly 2 months after presentation, the patient died from squamous cell carcinoma of the lung.

DISCUSSION

Based on the diagnostic studies and clinical findings, the patient was diagnosed with paraneoplastic BP with EGR-like erythema. Although rare, there are a few similar case reports in the literature. Saikia et al\(^1\) reported a case of metastatic colonic adenocarcinoma associated with BP and figurate erythema. A case of EGR-like figurate eruption with BP reported by Breathnach et al\(^2\) was investigated for associated malignancy. Despite thorough evaluation, and follow-up for 14 months, no neoplasm was identified though atypical transitional cells were found on urine cytology.\(^2\) Graham-Brown published a case of BP with figurate erythema associated with carcinoma of the bronchus.\(^3\) The patient underwent radiation therapy, and the eruption resolved within 2 months after discontinuation of all treatment. Lastly, Gilmour and colleagues reported a case of paraneoplastic BP and figurate

**Fig 1.** A, Axillary vault and chest with well-defined erythematous concentric plaques. Note the erosions consistent with unroofed bullae in the axillary fold. B, Left thigh, buttocks, and trunk with large violaceous-to-erythematous figurate plaques with scattered erosions.

**Fig 2.** Routine histology showing subepidermal split with numerous eosinophils. (Hematoxylin-eosin stain; original magnification: X20.)

**Fig 3.** Left palm and forearm at the 1-month follow-up showing well-defined nummular edematous plaques consistent with urticarial phase BP. BP, Bullous pemphigoid.
erythema diagnosed 4 months preceding cecal carcinoma. Barium enema showed significant mucosal ulceration, and direct immunofluorescence on tumor tissue showed complement component 3 positivity along the basement membrane. Furthermore, BP completely resolved in the week following tumor resection and had not recurred at the 4-year follow-up.

BP and EGR differ greatly in their associations with internal malignancy. EGR is associated with malignancy in over 80% of the cases. In a review of EGR, lung cancer was the most commonly associated malignancy (32%), followed distantly by esophageal (8%), and breast (6%) cancer. Drugs have rarely been reported to cause EGR (including pegylated interferon alpha and azathioprine). Other diseases reported in association with EGR include: pityriasis rubra pilaris, psoriasis, ichthyosis, systemic scleroderma, rheumatoid arthritis, hypereosinophilic syndrome, and Mycobacterium infection.

Meanwhile, malignancy and BP have a less certain association. A case-control study of 84 cases with BP and 168 controls revealed a malignancy rate of 17.9% and 5.3%, respectively. However, after removing malignancy diagnoses of dubious association, the malignancy rate decreased to a similar 6% among BP patients. Hadi et al followed 50 BP patients longitudinally for up to 7 years, recording any diagnosed malignancy. The 9 patients diagnosed with a neoplasm reflected a malignancy rate expected for the patient age group. Notably, 33% (3/9) patients with an associated malignancy presented with BP and figurate erythema. All 3 of these patients died of their malignancy.

While the cause of BP is known to be related to antibodies to the basement membrane antigens BP 180 and BP 230, the etiology of EGR is unknown. In most cases, EGR is paraneoplastic. Paraneoplastic syndromes may be caused by an immune-system reaction to the tumor with either humoral antibodies or T cells, including the following: 1) Antibodies to tumor antigens cross-reacting to cutaneous antigens; 2) tumor alteration of surrounding tissue rendering it immunogenic; or 3) tumor antigen plus host antibody immune complexes with deposition and inflammation. Paraneoplastic syndromes may also be caused by tumor-secreted factors, such as hormones and growth factors as with lung cancer and syndrome of inappropriate antidiuretic hormone secretion or parathyroid hormone related peptide. It is unclear if simultaneous BP and EGR-like eruptions reflect 2 separate etiologies or 2 cutaneous reaction patterns to the same BP antibodies. Due to the short clinical course, we were unable to test the patient’s serum or lung carcinoma for antibodies or secreted factors that might cause the EGR pattern. Our case emphasizes that when features of BP and EGR-like eruptions occur simultaneously, investigation into an underlying malignancy should be actively pursued, and the prognosis may be grave.

Conflicts of interest
None disclosed.

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