Paraneoplastic Bullous Pemphigoid Resembling Erythema Gyratum Repens-like Figurate Erythema

Sarun Jantrakulroj MD, Sasima Thammarucha MD, Kowit Kampirapap MD, Pinnaree Kattipathanapong MD.
Institute of Dermatology, Bangkok, Thailand.

ABSTRACT:
Paraneoplastic bullous pemphigoid is a rare autoimmune blistering disease that is associated with an underlying malignancy. The clinical presentation can vary, but typically involves the appearance of multiple tense blisters and erosions. This case report describes an atypical manifestation of bullous pemphigoid characterized by the presence of bullous and erythematous figurate lesions closely resembling the clinical features of erythema gyratum repens-like figurate erythema, which poses diagnostic challenges. The histopathological examination, direct immunofluorescence and indirect immunofluorescence consistent with bullous pemphigoid. By integrating the patient's underlying condition of lung cancer with the clinical presentation and histologic finding, the diagnosis of paraneoplastic bullous pemphigoid resembling erythema gyratum repens-like figurate erythema was made. The treatment of paraneoplastic bullous pemphigoid involves addressing and treating underlying malignancy.
Key words: Paraneoplastic bullous pemphigoid, Bullous pemphigoid, Erythema gyratum repens, Non-small cell lung cancer

Case presentation

A 43-year-old man presented with tense bullous eruptions with urticarial plaques on his trunk, upper extremities, and lower extremities for three months prior to his hospital visit. He had been to primary care where he was diagnosed with a bullous disorder and given oral prednisolone 40 mg/day (0.6 mg/kg/day) and colchicine 1.2 mg/day for 2 months, but his condition had not improved. To receive a second opinion, the patient visited the Institute of Dermatology. Physical examination revealed multiple discrete well-defined wood-grain appearance figurate erythematous plaques on upper extremities and lower extremities with few tense bullous lesions on right forearm (Figure 1, 2). No mucosal lesion was present.

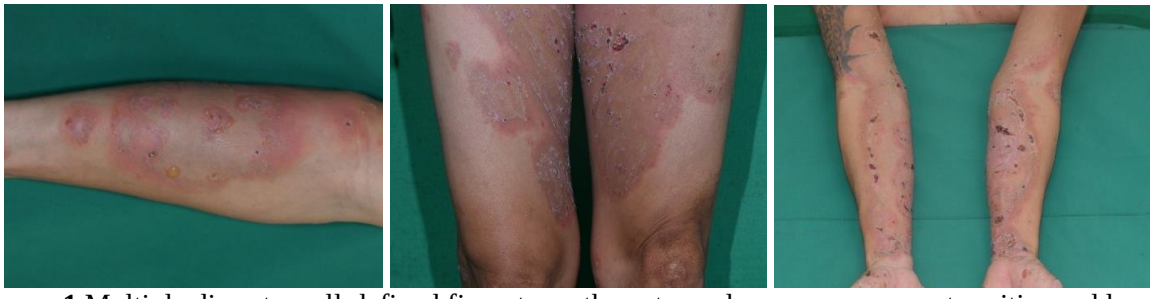

Figure 1 Multiple discrete well-defined figurate erythematous plaques on upper extremities and lower extremities with few tense bullous lesions on right forearm

Corresponding author: Pinnaree Kattipathanapong MD., email: pinnareek@yahoo.com

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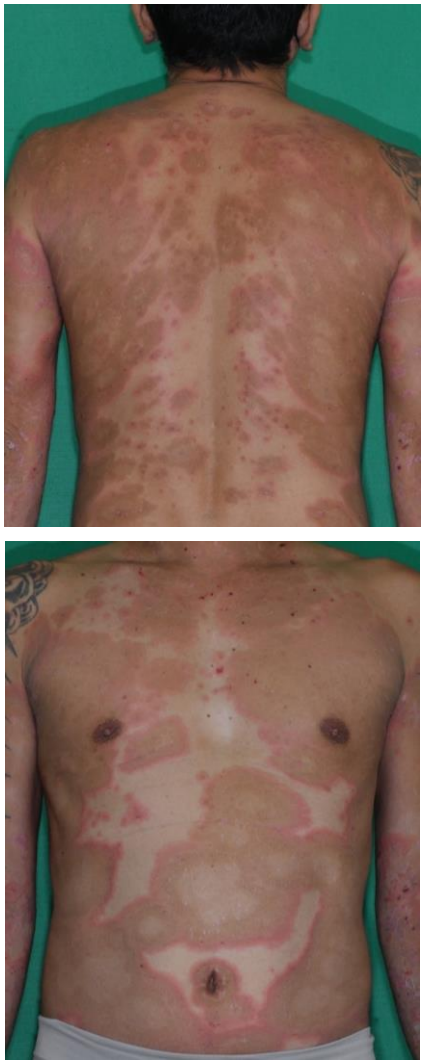

Figure 2 Multiple discrete well-defined annular figurate erythematous plaques on trunk

Histopathology from a bullous lesion on right forearm performed on the same day reveals subepidermal separation, superficial perivascular infiltrate, and interstitial infiltrate with lymphocytes and eosinophils (Figure 3). Direct immunofluorescence along the dermo-epidermal junction was positive for C3 in a granular pattern, and indirect immunofluorescence of anti-basement membrane zone was positive with a titer of 1:10 for IgG but negative for IgA. Histopathology and immunohistochemistry demonstrated a correlation with bullous pemphigoid. After a diagnosis is made, prednisolone 30 mg/day (0.5 mg/kg/day), doxycycline 200 mg/day, and nicotinic acid 300 mg/day treatment is initiated.

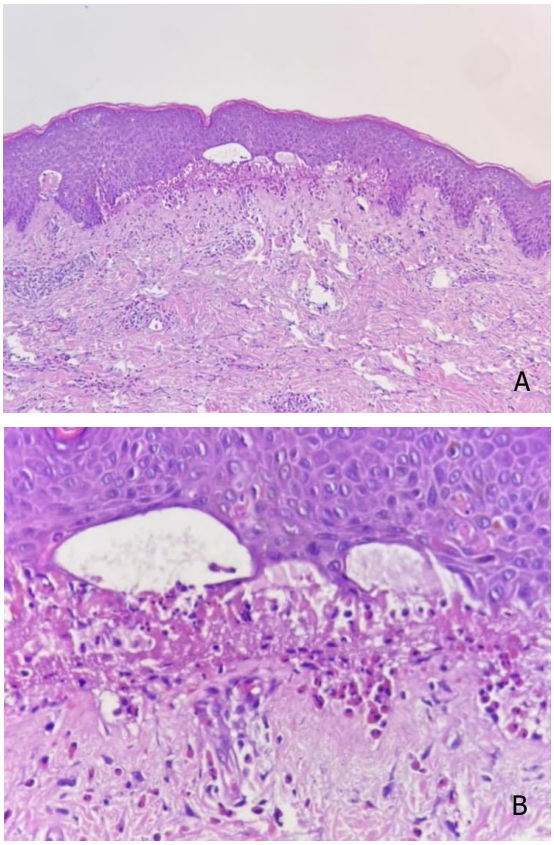

Figure 3 Skin biopsy specimen from right forearm demonstrated subepidermal separation with superficial perivascular and interstitial infiltrate with lymphocyte and eosinophils (A). Subepidermal separation with numerous eosinophils (B). (H&E; original magnification: A. X10, B. X40)

From the clinical presentation, erythema gyratum repens-like figurate erythema was considered a possibility. With a strong history of heavy smoking Despite the absence of chest symptoms, a chest radiograph performed as a

screening examination reveals the presence of a lung mass. The patient was referred to an oncologist, and chest computer tomography was performed. The imaging revealed multifocal irregular heterogeneous enhancing mass-like opacities mainly involving the right upper and middle lobes and superior segment of the right lower lobe with adjacent or surrounding infiltration, as well as a lobulated enhancing nodular opacity at the left lower lobe and mediastinal lymphadenopathy. A bronchoscopy with biopsy was performed, and non-small cell lung cancer was diagnosed.

Given the histopathological diagnosis of bullous pemphigoid and the clinical diagnosis of erythema gyratum repens-like figurate erythema with non-small cell lung carcinoma, paraneoplastic bullous was suspected. Erythema gyratum repens-like figurate erythema paraneoplastic bullous pemphigoid was our final diagnosis.

The patient was initiated on a combination chemotherapy regimen of paclitaxel and carboplatin at the oncology center. It was observed that the cutaneous manifestation of erythema gyratum repens-like figurate erythema paraneoplastic bullous pemphigoid gradually improved along with pulmonary symptoms of cough and chest pain after the patient received two cycles of chemotherapy. During chemotherapy, the dosage of prednisolone is progressively reduced to 20 mg/day, while the dosages of doxycycline and nicotinic acid remain unchanged at 200 mg/day and 300 mg/day, respectively. The patient experienced several complications during the course of chemotherapy, including deep venous thrombosis, severe infection, and pulmonary embolism. Following the third cycle of chemotherapy, the patient passed away due to respiratory failure.

Discussion

The diagnosis of erythema gyratum repens-like figurate erythema paraneoplastic bullous pemphigoid is a dermatological condition that is infrequently reported in the literature. A thorough examination of previously reported cases and article is imperative in order to gain a more comprehensive understanding of its pathogenesis and clinical characteristics. The distinct components of each disease entity and their correlation with the clinical manifestation with a focus on its atypical characteristics.

Erythema gyratum repens is a paraneoplastic disease first identified in 1952. It manifested as a wood-grain pattern of erythematous dermatosis, with a fine-scale trailing edge predominating on the trunk and limbs[1]. 70–82% of erythema gyratum repens cases have been linked to an underlying malignancy[2] and treatment focuses on identifying and eliminating the underlying malignancy. Non-paraneoplastic erythema gyratum repens causes include idiopathic, pityriasis rubra pilaris, psoriasis, ichthyosis, hypereosinophilic syndrome, drug-induced, and others[2].

Bullous pemphigoid, the most common autoimmune bullous disease, occurs when autoantibodies bind to basement membrane zone, triggering multiple pathogenesis cascades that spread hemidesmosome-associated protein fragment and epidermal separation, resulting in blisters[3]. Bullous pemphigoid occurs 43 times per million in people over the age of 70 and can be caused by neurological disorders, medications, and other factors[3]. In most instances, tense bullae were the typical manifestation of bullous pemphigoid[3]. However, there have been several reports of different types of atypical bullous pemphigoid presentations[4,5].

Atypical presentations of bullous pemphigoid, such as figurate erythema or erythema gyratum repens-like figurate erythema bullous pemphigoid, have been linked to underlying malignancy and given the names paraneoplastic bullous pemphigoid and bullous pemphigoid associated with neoplasm

(BPAN)[1,4,6-9] There is anecdotal evidence to definitively establish whether this illness presentation is a bullous pemphigoid-like variation of erythema gyratum repens or vice versa. Yet, bullous pemphigoid patients without underlying malignancy can also develop erythema gyratum repens-like eruptions[2,8].

Apart from the aforementioned atypical bullous pemphigoid with figurate erythema, limited literature exists regarding certain potential factors that could establish a connection between bullous pemphigoid and malignancy, such as HLA-DR13, negative indirect immunofluorescence, mucosal involvement, erythema multiforme-like lesions, antibodies to BPAG2, ladder configuration on immunoblot between 180 and 230 kD bands, and heat shock protein-90[6]. There have been several reports linking bullous pemphigoid to various internal malignancies, including squamous cell carcinoma, mycosis fungoides, renal cell cancer, laryngeal cancer and lymphoid leukemia, gastric cancer, colon cancer, parotid cancer, gallbladder cancer, breast cancer, lung cancer, myelodysplastic syndrome, B-cell lymphoma, and chronic lymphocytic leukemia[6,7,10].

Several case studies have documented the presence of localized erythema gyratum repens in individuals with bullous pemphigoid, as well as the association of bullous erythema gyratum repens with underlying carcinoma[8,9]. The majority of published reports of either the typical or bullous type of erythema gyratum repens indicate an underlying malignancy, with lung (27-32%), esophageal (4-8%), stomach (4-5%), and breast (3-6%) carcinomas being the most prevalent, in descending order[1,2].

There are several possible pathogenesis for the association of erythema gyratum repens, bullous pemphigoid, and underlying malignancy. First, the bullous pemphigoid antibodies, anti-BP 180 and BP 230, as well as anti-laminin 332, may cross react as antibodies against tumor-specific antigens[1,7]. The second possible mechanism is the secretion of a hormone-like substance by tumor cells, which can cause damage to the epithelial basement membrane and the production of anti-basement membrane antibodies[1,7]. Third, an external etiology factor from a virus that can damage the epithelial basement membrane and cause the production of anti-basement membrane antibodies causes bullous pemphigoid[7,10]. Fourth, HLA-DR13 genetic predisposition is increasingly being found in patients with both bullous pemphigoid and underlying malignancy. Finally, heat shock protein 90 is linked to bullous pemphigoid and underlying malignancy[7,10].

Our patient has been diagnosed with erythema gyratum repens-like figurate erythema paraneoplastic bullous pemphigoid, a very unusual presentation of bullous pemphigoid for which there are only a small number of instances in the medical literature[1,9]. Although our data is limited due to the patient's untimely passing, we were able to confirm the diagnosis of a rare form of paraneoplastic bullous pemphigoid that resembled erythema gyratum repens-like figurate erythema and demonstrate its association with underlying malignancy, as evidenced by the disappearance of the skin lesion following therapeutic chemotherapy for the cancer.

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