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CASE REPORT

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Paraneoplastic bullous pemphigoid in association with squamous cell carcinoma of the lung: A case report and literature review

Dominika Czarnecka, Ewa Pasierbska

Dermatology Department, Provincial Integrated Hospital in Elblag, Elbląg, Poland

ABSTRACT

Bullous pemphigoid (BP) is a common autoimmune subepidermal blistering disorder that predominantly affects the elderly and is characterized by autoantibodies against BP230 and BP180. While its aetiology remains uncertain, BP has been associated with medications, infections, and neoplasms, including paraneoplastic manifestations. This report highlights a rare case of paraneoplastic BP in a 72-year-old male with squamous cell carcinoma (SCC) of the lung, emphasizing the importance of recognizing BP as a potential cutaneous marker of internal malignancies. The patient presented with itchy, tense blisters on an erythematous base, erosions, and crusts, confirmed as BP through immunopathological testing. Imaging revealed a lung tumour, later diagnosed as SCC with mediastinal and right hilar lymphadenopathy. Despite topical steroid treatment for BP and subsequent oncologic consultations, the patient's condition progressed. The skin lesions exacerbated alongside the malignancy, and he was eventually referred to the hospital again. This case underscores the potential paraneoplastic nature of BP and its association with lung SCC, which remains poorly understood. Notably, recent reports indicate that BP may resolve following successful cancer treatment, further suggesting a pathogenic link. However, therapeutic challenges persist, particularly in cases of advanced malignancy or treatment resistance. Innovative therapies, such as omalizumab and Janus kinase inhibitors, have shown promise in managing refractory BP, including cases induced by immune checkpoint inhibitors. Clinicians should consider comprehensive cancer screening in patients with refractory BP, as early identification of associated malignancies may improve outcomes. Further studies are warranted to elucidate the underlying mechanisms connecting BP and neoplasms, refine diagnostic approaches, and expand treatment options. This case contributes to the growing evidence of BP as a paraneoplastic phenomenon, particularly in the context of SCC.

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Keywords: bullous pemphigoid, squamous cell carcinoma of the lung, SCC, lung cancer, paraneoplastic pemphigoid

INTRODUCTION

Bullous pemphigoid (BP) is a common autoimmune subepidermal blistering disorder and one of the most prevalent autoimmune bullous dermatoses. While typically diagnosed in elderly individuals, BP can also occur in children, with those over 80 being the most affected group. It occurs more often in men than in women. The condition arises from the production of autoantibodies against BP230 and BP180, transmembrane antigens associated with hemidesmosomes in basal keratinocytes and the lamina lucida. Despite extensive research, the exact cause of BP remains unclear. However, in about 15% of cases, BP has been linked to factors such as medications, neoplasms, active psoriasis, UV radiation, and bacterial or viral infections. Clinically, BP presents with itching, burning, and tense bullae filled with serous fluid, often on erythematous or edematous skin, as well as seemingly normal areas. Commonly affected sites include the upper extremities (especially the anterior surfaces), anterior thighs, and trunk. The main clinical subtypes described in the literature are classic, vegetans, localized, erythrodermic, dyshidrotic, and nodular pemphigoid [1–4]. Diagnosis is confirmed by immunopathological examination, revealing linear IgG and C3 deposits at the dermo-epidermal junction. Indirect immunofluorescence is also crucial in diagnosing blistering diseases. An additional test is a histopathological examination of the diseased skin [5, 6]. The most effective treatment for BP is topical 0.05% clobetasol propionate cream, applied to the entire body. Other treatment options include methotrexate, dapsone, prednisone, azathioprine, and the combination of tetracycline and nicotinamide [1]. BP is usually a chronic condition with periods of spontaneous exacerbation and remission.

Address for correspondence:

Ewa Pasierbska, Provincial Integrated Hospital in Elblag, Królewiecka 146, 82–300 Elbląg, Poland, e-mail: ewapasierbska@gmail.com

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Comorbidities are common, with cancer found in approximately 15–20% of BP patients [7].

Although there are reports in the literature linking bullous pemphigoid with internal malignancies, the exact cause-and-effect relationship is not well defined. Paraneoplastic bullous pemphigoid is rarely seen in lung cancers, especially of the squamous cell type. As a result, its occurrence should raise suspicion for a range of internal malignancies, including lung cancer.

This case highlights a rare association between paraneoplastic bullous pemphigoid and squamous cell carcinoma of the lung in a 72-year-old male, underscoring the importance of recognizing this unusual cutaneous manifestation of lung cancer among clinicians.

Objective

This article aims to present a case of a patient with paraneoplastic bullous pemphigoid in association with squamous cell carcinoma of the lung.

CASE REPORT

A 72-year-old male with a history of hypertension, diffuse brain damage (clinically silent) and a history of smoking cigarettes a pack a day for 30 years, was admitted to the Dermatology Ward due to bullous skin lesions. According to the patient, the lesions appeared a week prior to admission, initially on the scalp and subsequently spreading to the trunk and limbs. The skin changes were accompanied by itching. Before admission, the patient used antiviral and antihistamine medications without improvement. The patient denied any family history of skin diseases.

On the day of admission, a physical examination revealed tense blisters on an erythematous base, erosions, and crusts. The lesions were most pronounced on the trunk and groin, with a few on the limbs and scalp (Fig. 1, 2). A biopsy was taken for direct immunofluorescence, which showed linear IgG and C3c deposits along the dermo-epidermal junction. Another skin biopsy for immunopathological examination confirmed the presence of BP180 and BP230 antibodies. A diagnosis of bullous pemphigoid was established.

During hospitalization, an abdominal ultrasound revealed no significant abnormalities. A chest X-ray described a rounded shadow measuring 40 × 38 × 40 mm near the upper pole of the right hilum, which required further evaluation via computed tomography (CT). Chest and abdominal CT scans identified a tumour in the right lung, mediastinal, and right hilar lymphadenopathy.

Topical steroid therapy was initiated during the hospital stay — clobetasol propionate 0.5 mg/g, 30 g daily, divided into two doses applied to the entire body except the face.

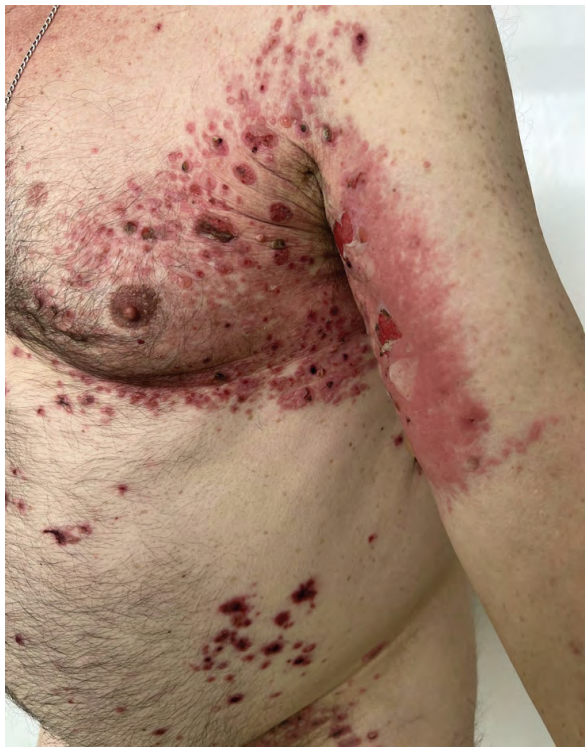

Figure 1. Blisters on an erythematous base, erosions, and crusts on the day of admission — patient's chest

The patient was referred to the Pulmonology Ward for further diagnostic and therapeutic management. A lung biopsy was non-diagnostic, but a lymph node biopsy revealed squamous cell carcinoma. A diagnosis of right lung squamous cell carcinoma T3N2Mx was made.

Following the completion of diagnostic procedures and worsening skin lesions due to bullous pemphigoid, the patient was readmitted to the Dermatology Ward for exacerbation of skin changes. On the day of readmission, the patient was bedridden and in moderate general condition. Physical examination revealed numerous tense blisters on an erythematous base, erosions, and crusts, most prominent on the limbs. Fungal changes in the oral cavity and honey-coloured crusts on the beard area were also noted.

During the hospitalization, the patient developed bacteremia. Empirical antibiotic therapy was initiated and subsequently adjusted based on antibiogram results, leading to clinical improvement and a reduction in inflammatory markers. The patient was also consulted oncologically. The oncologist concluded that the patient was in a palliative state and recommended symptomatic treatment in a hospice.

The patient was discharged to hospice care in stable condition with recommendations like topical use of clobetasol and topical antiseptic agents.

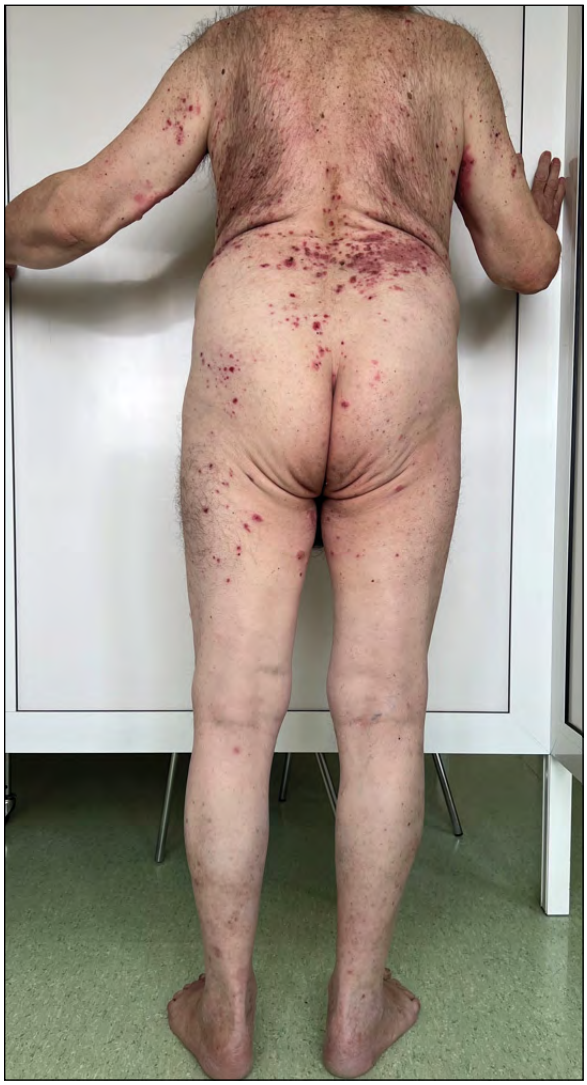

Figure 2. Blisters on an erythematous base, erosions, and crusts on the day of admission — full-body view

DISCUSSION

In 2004 Reich et al. [8] described a case of a 47-year-old male who was referred to their department due to disseminated tense vesicles and blisters, along with numerous erosions all over the body. Two years earlier, the patient had noticed a tumour in the left groin. The lesion was surgically removed, and histopathological examination revealed squamous cell carcinoma. Several months later, the lesion recurred. Immunohistochemical and histopathological examinations confirmed the clinical diagnosis of bullous pemphigoid. The patient was treated with intramuscular methylprednisolone acetate (80 mg/week) and oral cyclophosphamide (50 mg/day) without improvement. Only after the surgical removal of the tumour was a marked improvement in the skin lesions observed.

The other authors, Benhiba and Hassam [9], described a case report in 2015 of BP associated with squamous cell carcinoma of the lower lip has been described. They also noted that the link between BP and cutaneous malignancies has long been debated, with no definitive consensus established. Although numerous case reports and studies have been published, a clear association remains unproven.

In 2022 Shrestha et al. [10] described a case of squamous cell lung carcinoma, diagnosed after investigations for refractory bullous pemphigoid, which showed a marked response to carboplatin-based chemotherapy. Treatment with carboplatin and gemcitabine was initiated, and a significant response was observed within 3 days of starting chemotherapy. The skin lesions remained in remission even after the chemotherapy was discontinued.

In 2024 Youh et al. [11] described a similar case — a 72-year-old man who presented with pruritic skin lesions, including tense vesicles and bulles and was diagnosed with BP. The patient was treated with doxycycline, nicotinamide, and topical clobetasol; however, despite treatment, the lesions persisted. A chest X-ray, conducted as part of the diagnostic workup, incidentally, revealed a large mass in the right upper lung, which was later diagnosed as squamous cell carcinoma. After the surgical removal of the tumour, the patient's BP lesions completely resolved within seven weeks, without any changes to his dermatologic treatment. Unfortunately, the patient described in the present report was disqualified from surgical treatment.

In another article, Guan et al. [12] presented a case of a 69-year-old man with squamous cell carcinoma of the lung, in whom BP developed 3 weeks after starting therapy with the programmed cell death-1 (PD-1) inhibitor pembrolizumab and chemotherapy.

Another case of bullous pemphigoid induced by ICIs in patients with squamous cell lung cancer has also been described in the literature by Chen et al. [13]. Omalizumab (300 mg every 4 weeks) proved effective in treating BP, leading to the cessation of blister formation and significant symptom relief within a week. The total treatment duration was four weeks, and the improvement was stable. No recurrence was observed after four months.

Also, there should be mentioned a 74-year-old woman with recurrent metastatic squamous cell carcinoma of the head and neck, who developed drug-induced bullous pemphigoid in the context of immunotherapy with a new immunoglobulin-like transcript 4 inhibitor (MK-4830) in combination with pembrolizumab. Treatment with upadacitinib, a Janus kinase-1 inhibitor, was initiated for a significantly disabling disease that was unresponsive to standard therapies, and she ultimately transitioned to palliative care.

Follow-up at 4 weeks showed a good response. This is the first report describing the use of a Janus kinase inhibitor in the treatment of bullous pemphigoid [14].

This case highlights the importance of cancer screening in patients with persistent BP and suggests a potential connection between BP and hidden malignancies, especially when conventional treatments fail. Additional studies are needed to explore the mechanisms linking these conditions.

Article information and declarations

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Author contributions

Both authors have equal contributions.

Conflict of interest

The authors have no conflicts of interest to declare.

Ethics statement

All authors have been personally and actively involved in substantial work leading to the paper and will take public responsibility for its content. The paper reflects the authors' own case report. The contents of this manuscript have not been copyrighted or published previously.

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Supplementary material

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