Case Report

# Bullous pemphigoid as a paraneoplastic manifestation of metastatic adenocarcinoma of the lung

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## ABSTRACT

A 73-year-old male smoker presented with complaints of fever and multiple clear fluid-filled lesions for 3 months. He was initially being treated for primary bullous pemphigoid but lesions recurred. On a chest X-ray, he was found to have a right hilar mass, and contrast-enhanced computed tomography of the chest revealed a right lung mass lesion with cervical, hilar, and mediastinal lymphadenopathy. A bronchoscopy was done, and bronchoalveolar lavage cytology was suggestive of lung adenocarcinoma. An excision biopsy of the left supraclavicular lymph node showed features consistent with adenocarcinoma lung. Hence, he was diagnosed with metastatic adenocarcinoma of the lung with bullous pemphigoid as a paraneoplastic manifestation. He was subsequently treated with chemotherapy, and his skin lesions resolved.

**Key words:** Bullous pemphigoid, Lung cancer, Oncology, Paraneoplastic syndrome, Respiratory medicine

The term "paraneoplastic syndromes" describe the distant manifestations of cancer that is unrelated to the primary tumor or its metastasis. These might happen before the cancer is identified and could vary in severity depending on the original tumor's stage. Lung cancer (LC), which is recorded in around 10% of cases, is the condition most frequently linked with paraneoplastic syndromes [1]. Bullous pemphigoid is one of the most common chronic autoimmune subepidermal blistering skin diseases, majorly seen in the elderly population. Several case reports have described bullous pemphigoid as the paraneoplastic syndrome of several internal malignancies, but its association with LC is rare.

Here, we are reporting a case of bullous pemphigoid as a paraneoplastic manifestation of adenocarcinoma of the lung, which improved after starting carboplatin-based chemotherapy. This case serves to alert physicians about the rare presentation of lung adenocarcinoma as bullous pemphigoid.

## CASE REPORT

An elderly male patient who is a percussionist by occupation and a smoker with 30 pack years presented with complaints of fever and multiple clear fluid-filled lesions for 3 months. The lesions started over the right foot, medial aspect of the right thigh, then over the sole, palm, neck, axilla, and oral cavity, lesions were tense, remained intact, and burst upon trauma to form raw areas and showed a tendency to heal.

On a general examination, he was oriented to time, place, and person. The patient was moderately built and nourished, and his vitals were stable. On cutaneous examination, tense bullae, and vesicles contained serous fluid, a few with hemorrhagic fluid and crusted erosions were also present in the above-mentioned areas (Fig. 1). Subungual hyperkeratosis and onycholysis were also present. The Nikolsky sign (the top layers of the skin slip away from the bottom layers when rubbed) and the Bulla spread sign (the extension of bullae to the neighboring normal skin when pressure is applied on top of it) were negative.

An incisional biopsy done from the lesional skin with a bulla over the right axilla showed skin with epidermis and dermis. The epidermis showed mild spongiosis with a subepidermal bulla. There was interstitial and perivascular infiltrate of eosinophils, and a few neutrophils were also seen in the bullous cavity. Pigment incontinence was noted. The deep dermis shows eccrine glands. Direct immunofluorescence shows linear staining of the basement membrane zone with immunoglobulin G (IgG) and C3 which is suggestive of a bullous pemphigoid.

The patient was managed with an injection of dexamethasone followed by oral steroids, and other conservative measures and

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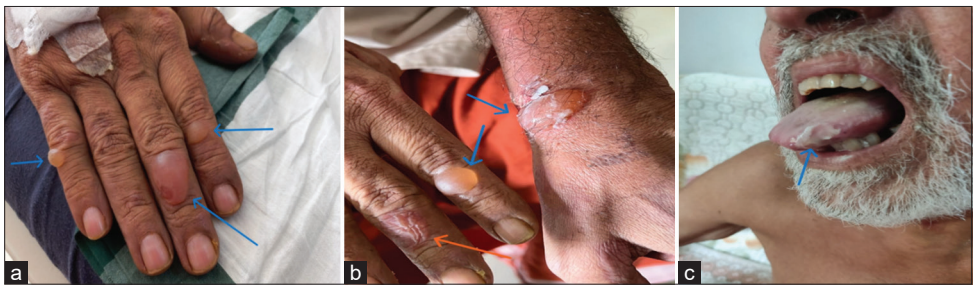

**Figure 1: (a) Multiple clear fluid-filled bullae are seen on the dorsal aspects of the fingers of the right hand (blue arrows); (b) multiple clear fluid-filled bullae (blue arrows) and old crusted lesions (orange arrow) are seen on the dorsal aspects of both hands; (c) ruptured bulla is seen on the left lateral aspect of the tongue (blue arrow)**

discharged with maintenance oral steroids. However, after 1½ months, the patient presented with complaints of coughing and breathlessness for 15 days. On evaluation, vitals were found to be normal, and a respiratory system examination found harsh vesicular breath sounds and occasional rhonchi. Other system examinations were found to be normal. Routine blood investigations were normal.

The chest X-ray showed a right hilar mass and infiltrates with mediastinal widening. Contrast-enhanced computed tomography of the thorax showed a right lung lower lobe-enhancing peripheral lesion with multiple bilateral parenchymal nodular lesions and multiple enlarged hila, mediastinal, left axillary, supraclavicular, and cervical lymph nodes' (Fig. 2).

Bronchoscopy was done which showed infiltrates and mucosal edema in the right upper lobe bronchus and lower lobe bronchus distal to the opening of the right middle lobe. Bronchoalveolar lavage cytology shows pleomorphic tumor cells which are suggestive of adenocarcinoma. Positron emission computed tomography showed a "hypermetabolic, heterogeneously enhancing soft tissue attenuating lesion with spiculated margins involving the lateral basal segment of the right lower lobe of the lung with multiple hypermetabolic intrapulmonary lesions involving both lung fields, hypermetabolic metastatic mediastinal, and cervical lymph nodes." Left supraclavicular lymph node excision biopsy showed metastatic carcinoma, for which immunohistochemistry showed tumor cells positive for thyroid transcription factor 1 (Fig. 3a). Napsin and PDL-1 expression are present in 2% of tumor cells and 6% of immune cells. Genetic studies showed positive for KRAS, p.G12C and TP53, p.E171 and were diagnosed as metastatic pulmonary adenocarcinoma (Fig. 3b), in which bullous pemphigoid was a paraneoplastic manifestation of the same.

The patient was managed with chemotherapy, including carboplatin 150 mg, pemetrexed 500 mg, and filgrastim 300 mcg, following which skin lesions drastically improved with subsequent cycles.

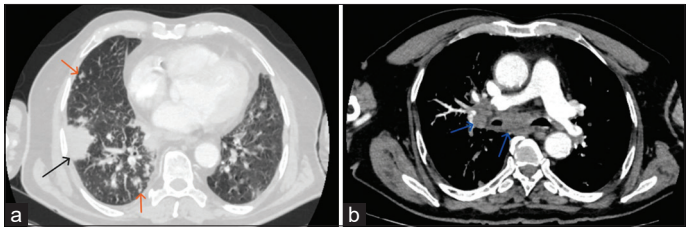

**Figure 2: (a) CECT thorax in the lung window showing the peripheral mass lesion in the right lung (black arrow) with multiple bilateral parenchymal lung nodules (orange arrows); (b) CECT thorax in the mediastinal window showing subcarinal and right hilar lymphadenopathy (blue arrows). CECT: Contrast-enhanced computed tomography**

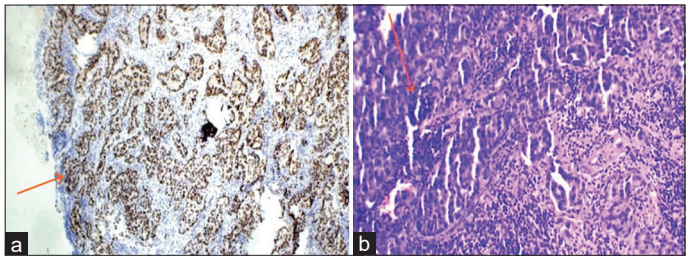

**Figure 3: (a) Histopathology microphotograph showing thyroid transcription factor-1 positivity in the tumor cells (orange arrow); (b) histopathology microphotograph showing tumor tissue arranged in the form of nests, glands, and papillae. The cells show moderate pleomorphism, vesicular chromatin, and prominent nucleoli (orange arrow)**

## DISCUSSION

LC is the cancer type that is most prevalent right now in the world [2]. LC-related paraneoplastic syndromes (PNS) are more common than in other types of cancer. They happen as a result of the cancer cells' immune response or as a result of the hormones and cytokines they produce [3]. In 50% of individuals with small cell LC and non-small cell LC, systemic symptoms and paraneoplastic syndrome (PNS) abnormalities appear [4].

Dermatologic manifestations as PNS in LC are very less, in that acanthosis nigricans, polymyositis/dermatomyositis, erythema gyratum repens, erythema annulare centrifugum, Bazex syndrome, tripe palms, and paraneoplastic pemphigoid are the most common ones [3].

Bullous pemphigoid is one of the most common chronic subepidermal blistering disorders which usually does not involve the mucus membranes like pemphigus vulgaris. It is most commonly seen in the elderly population [5]. About 10.4% of cases of bullous pemphigoid are linked to neoplasms [6].

Bullous pemphigoid is brought on by IgG autoantibodies that are directed against the hemidesmosome antigens BP230 (bullous pemphigoid antigen [BPAg]1) and BP180

(BPAg) [7]. It is also associated with several other conditions such as ulcerative colitis, multiple sclerosis, diabetes, myasthenia gravis, systemic lupus erythematosus, and rheumatoid arthritis [5] and is also stated to occur in several malignancies as paraneoplastic syndromes such as B-cell lymphoma, bladder cancer, colorectal cancer, breast cancer, renal cell carcinoma, esophageal carcinoma, parotid carcinoma, LC, endometrial cancer, and cholangiocarcinoma [7-10]. It is rarely reported in LC, especially in adenocarcinoma of the lung. Bullous pemphigoid that is paraneoplastic does not go away with standard treatment, which includes steroids and other immunosuppressants [5]. In some situations, LC therapy successfully heals the skin lesions.

In our case report, the patient's skin lesions appeared before the LC manifested, and after receiving appropriate steroid therapy, the bullous pemphigoid blister count persisted. After treatment, the blisters vanished, indicating that these skin lesions are paraneoplastic.

## CONCLUSION

Lung carcinoma can present as any one of its paraneoplastic manifestations. Bullous pemphigoid can present as a paraneoplastic manifestation of any internal malignancy. In that, lung carcinoma should be kept in mind as a possible diagnosis. Paraneoplastic bullous pemphigoid can be resistant to regular steroids and may improve after starting chemotherapy for lung carcinoma.

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