Clinical Case Reports

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CASE REPORT

Skin nodule reveals lung cancer in a patient with granulomatosis with polyangiitis

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Key Clinical Message

A 69-year-old male with granulomatosis with polyangiitis presented with new skin nodules. Skin biopsy showed metastatic poorly differentiated lung adenocarcinoma. The skin nodule was the initial presentation of his lung cancer. There is need for increased vigilance for cancer risk in ANCA-associated vasculitis patients.

Keywords

Granulomatosis with polyangiitis, lung cancer, skin nodule.

Introduction

Granulomatosis with polyangiitis (GPA), formerly called Wegener's granulomatosis, is a small-vessel vasculitis that typically involves the upper and lower airways, and the kidneys although limited involvement can be seen in some patients. The standard of care for inducing remission in GPA used to be high-dose steroids and oral cyclophosphamide until the FDA approval of rituximab in combination with steroids for this indication in April 2011. Studies thus far have shown an increased predilection of bladder cancer, leukemia, and lymphoma in GPA patients [1]. The differential contribution of the disease and its treatment in cancer causation remains to be determined. We present a case of lung cancer in a patient with known history of GPA that initially presented with skin nodules.

Case Report

A 69-year-old Caucasian male smoker with a two-year history of granulomatosis with polyangiitis (GPA), manifested predominantly as difficult to control bilateral scleritis, asymptomatic cavitary lung lesions consistent with GPA, and positive c-ANCA and PR3. In the past, the patient had never experienced cough, shortness of breath, or hemoptysis and the cavitary lung lesions on imaging were stable/asymptomatic. Kidney function and urinalysis were monitored and remained normal. Initial treatment with oral cyclophosphamide was unsuccessful after 4 months; rituximab and methotrexate were also tried but were unsuccessful in controlling his scleritis. He was requiring high-dose corticosteroids to control the eye symptoms. He then presented to rheumatology clinic with a one-week history of multiple new skin nodules (Fig. 1A, arrow) that were nontender and nonpruritic. Besides the skin nodules, he had erythema in both sclerae that was chronic. His lung examination revealed expiratory wheezes, consistent with his smoking history. Remainder of the examination was unremarkable. At that time, he was taking prednisone 60 mg daily, methotrexate 15 mg weekly, and rituximab infusion every 6 months. The differentials for new skin nodules in an immunosuppressed patient included infectious etiology, manifestation of GPA, versus a malignant process. He was sent to dermatology that same day, and a skin biopsy was performed.

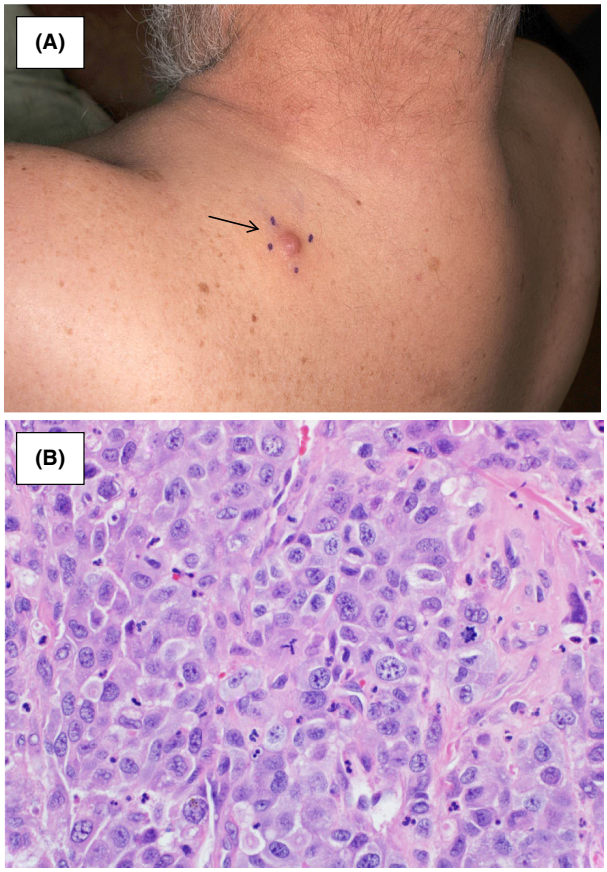

Figure 1. (A) New skin nodule in a patient with h/o GPA. (B) Higher magnification of skin biopsy showing atypical epithelioid cells with enlarged nuclei and numerous atypical mitotic figures.

Two days later, the patient reported mild shortness of breath with one episode of hemoptysis and presented to his local emergency department. CT chest revealed a new lung mass, and the patient was admitted locally. The skin biopsy returned in this time frame and showed metastatic poorly differentiated lung adenocarcinoma. Higher magnification showed atypical epithelioid cells with enlarged nuclei and numerous atypical mitotic figures (Fig. 1B; hematoxylin and eosin staining; 400x magnification). The epithelioid cells demonstrated strong diffuse pan-cytokeratin expression (not shown), consistent with a carcinoma. The tumor was TTF-1 positive. The patient chose hospice care and, unfortunately, passed away within 2 weeks of presentation of the skin nodules.

Discussion

ANCA-associated vasculitis (AAV) and its therapies are associated with an increased risk of malignancies. As reported by Mahr et al., prior studies have shown that the standardized incidence ratio of cancer in AAV is 1.6–2.0 compared to the general population and a possibly higher risk in GPA than in microscopic polyangiitis [2]. Cyclophosphamide has been implicated in the development of other malignancies, including bladder cancer and acute myeloid leukemia, especially if the cumulative dose exceeds 36 g [3]. To our best knowledge, this is the first case of skin nodules revealing metastatic lung cancer in a patient with GPA. This case highlights the need for increased vigilance for cancer risk in AAV patients, especially in patients who have other risk factors for cancer like smoking.

Authorship

TD: involved in preparation of the preliminary draft of manuscript and patient care. BS: involved in manuscript writing and drafted histopathology slides and legends. NS: involved in concept, patient care, writing of manuscript and was the corresponding author.

Conflict of Interest

All the authors have no conflicts of interest or funding sources to disclose.

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