Pembrolizumab-associated sarcoidosis

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INTRODUCTION

Pembrolizumab is a humanized antibody that targets the programmed cell death-1 (PD-1) receptor. It is currently approved by the US Food and Drug Administration for patients with advanced melanoma and metastatic non–small cell lung cancer. As an immune checkpoint inhibitor, pembrolizumab augments a patient's immune system against an underlying malignancy.

Systemic toxicities associated with use of PD-1 inhibitors such as fatigue, pyrexia, chills, and infusion reactions have been commonly reported.[1] We report a case of sarcoidosis flare associated with pembrolizumab, which is, to our knowledge, the first reported case of sarcoidosis linked to PD-1 inhibition.

CASE REPORT

A 72-year-old woman with refractory, stage IV Hodgkin lymphoma diagnosed in 2014 was placed on pembrolizumab, 200 mg intravenously every 3 weeks. Twelve years prior, the patient had gallstone pancreatitis, and a chest x-ray at that time found bilateral hilar adenopathy. Subsequent mediastinoscopy and lymph node biopsy were notable for sarcoidosis, although the patient was never symptomatic and was never treated.

Approximately 6 months after starting pembrolizumab, the patient presented to the dermatology clinic with slowly enlarging, asymptomatic subcutaneous nodules on her arms. Physical examination found 2 nontender, subcutaneous nodules on the right extensor forearm without overlying erythema, with the largest nodule measuring 10 cm in diameter (Fig 1, *A*). There was a similar, smaller nodule on the left forearm. Punch biopsy of the larger right forearm nodule found mild lymphohistiocytic perivascular dermatitis with a focal, dermal epithelioid granuloma (Fig 2, *A* and *B*). Infectious stains and tissue cultures were negative. Based on the clinical presentation and medical history, a diagnosis of cutaneous sarcoidosis was made.

Abbreviations used:

FDG: fludeoxyglucose
PD-1: programmed cell death-1

Pembrolizumab was held for the progressing skin lesions and a positron emission tomography/computed tomography scan was performed to reassess the status of the lymphoma. The imaging found new bilateral pulmonary parenchymal patchy ground glass opacities with septal thickening. There were also new hypermetabolic areas within multiple bones, including the left side of the scapula (Fig 3, *A*), sternum, and the right side of the iliac. Interval increases in fludeoxyglucose (FDG)-avid mediastinal and bilateral hilar lymph nodes (Fig 3, *B*), compared with 3 months prior were seen. It was unclear whether these changes were secondary to lymphoma or sarcoidosis.

Soon thereafter, the patient had left eye pain, and evaluation by an ophthalmologist found acute iritis attributable to sarcoidosis. In addition, she had dyspnea and was referred to cardiothoracic surgery for consideration of video-assisted thoracoscopic surgery to determine the etiology of the dyspnea and adenopathy. However, the patient declined to

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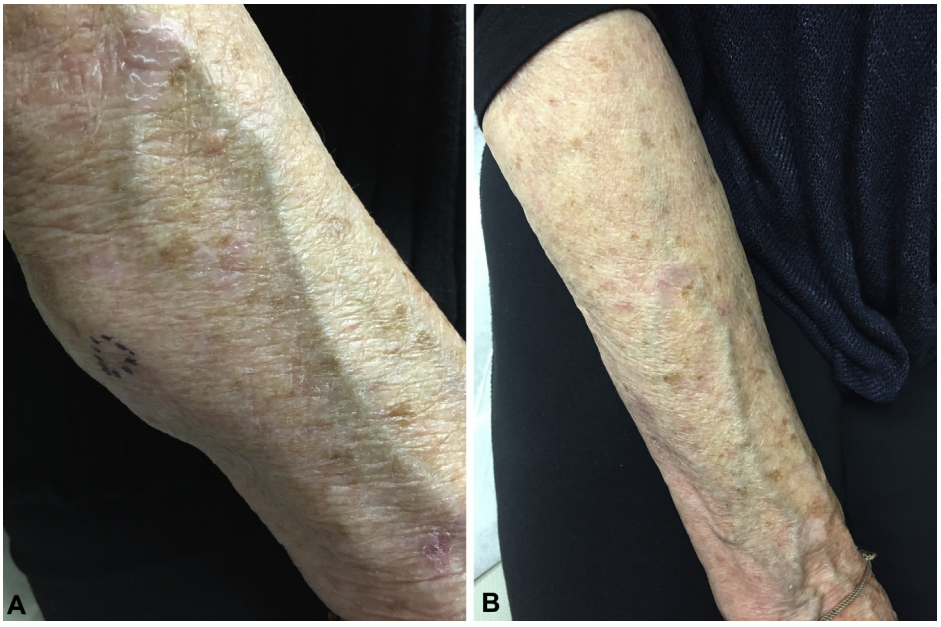

Fig 1. Clinical presentation. **A**, Nontender subcutaneous nodule of right forearm without overlying erythema while taking pembrolizumab for refractory Hodgkin lymphoma. **B**, Resolution of right forearm subcutaneous nodule while not taking pembrolizumab during course of prednisone.

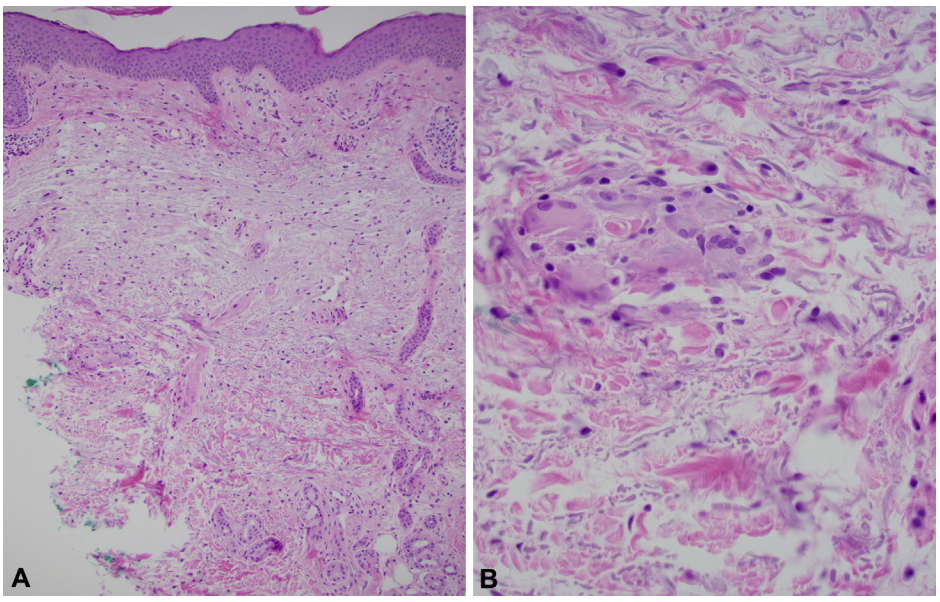

Fig 2. Microscopic examination. **A**, Normal epidermis with mild perivascular lymphohistiocytic inflammation. **B**, Focal dermal epithelioid granuloma. (**A** and **B**, Hematoxylin-eosin stain; original magnifications: **A**, ×10; **B**, ×20.)

pursue lung/lymph node biopsy. A decision was made to initiate an empiric trial of prednisone at a dose of 60 mg orally daily, to see if there would be a favorable clinical/radiographic response, based on the presumption that sarcoidosis induced by pembrolizumab, and not lymphoma, was the etiologic culprit for the clinical and imaging features.

Shortly after the initiation of prednisone, the left eye pain and dyspnea resolved, and within 1 month, the skin nodules resolved (Fig 1, *B*). Reimaging performed approximately 3 months after the prior scans (1 month after starting prednisone) found complete resolution of the FDG-avid skeletal regions previously noted (Fig 3, *C*) as well as resolution of