

# Is it metastatic melanoma or is it sarcoidosis? Non-caseating granulomas due to pembrolizumab

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## DESCRIPTION

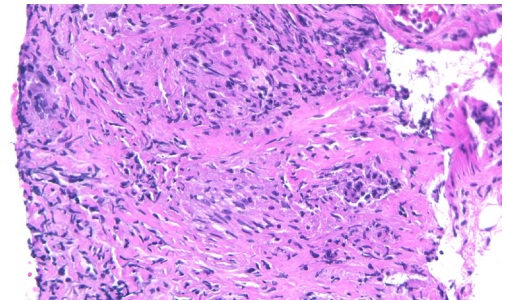
A 61-year-old man with a history of multiple basal cell carcinoma presented with a nodular, pigmented lesion on the left side of his scalp. A shave biopsy revealed malignant melanoma. The patient then underwent wide local excision of the melanoma, with left occipital sentinel lymph node negative for tumour involvement. However, 2 months later, he noticed a swelling on the left side of his neck. A subsequent left neck excisional biopsy revealed one of six lymph nodes positive for melanoma. A follow-up positron emission tomography (PET) scan did not reveal distant metastasis. Final staging was IIB, pT3a, pN1b and cM0.

This patient received adjuvant intensity-modulated radiotherapy, followed by intravenous pembrolizumab 200 mg every 21 days with a planned total duration of 1 year. He tolerated six cycles of pembrolizumab with only mild fatigue and cough. Follow-up PET/CT scan after these cycles revealed possible progression of his disease. There was fluorodeoxyglucose-avid adenopathy throughout the mediastinum, bilateral infraclavicular and supraclavicular nodes, and likely periaortic and porta hepatis nodes ([figure 1](#)).

Given the extent of his, possible, recurrent disease, he did not receive further radiotherapy. He was



**Figure 1** Follow-up positron emission tomography/CT scan after six cycles showing possible marked disease progression with diffuse fluorodeoxyglucose-avid adenopathy of the mediastinum, bilateral hilar and periaortic regions. Not pictured are the clavicular lymph nodes.



**Figure 2** Photomicrograph illustrating non-necrotising granulomatous inflammation with numerous epithelioid histiocytes and a few lymphocytes in the background (H&E, 10 $\times$ ).

switched to intravenous ipilimumab 3 mg/kg every 21 days. He tolerated the first treatment well with minor stomach upset. Prior to his second cycle of ipilimumab, he underwent endobronchial ultrasound-guided biopsy of subcarinal, right paratracheal level IV and right hilar lymph nodes level X. Bronchial washings for cytology was also performed. A biopsy to confirm recurrence was planned prior to starting ipilimumab; however, there was a delay as the interventional radiology team requested a pulmonology evaluation first. Once performed, the subcarinal and paratracheal lymph node biopsies showed non-necrotising granulomatous inflammation ([figure 2](#)).

No melanoma was found in these samples. After cycle two of ipilimumab, he was admitted to the hospital with colitis that improved with high-dose corticosteroids. He was recommended to complete a prednisone taper over a few weeks and then was restarted on pembrolizumab. A follow-up CT chest showed near resolution of the lymph nodes.

Pembrolizumab is a programmed death receptor-1 indicated in melanoma with lymph node involvement following resection, and for unresectable or metastatic disease. This drug (Keytruda), along with other immune checkpoint inhibitors, has been known to cause unique adverse effects, such as thyroiditis, enterocolitis and organising pneumonia.<sup>1</sup> As in this patient, granulomatous, or sarcoid-like, lesions involving the lungs, and hilar and mediastinal lymph nodes have been reported.<sup>2</sup> A possible mechanism for this adverse effect is the expansion of CD4+ TH17 cells, which are associated with sarcoidosis.<sup>3</sup>

The management of sarcoidosis-like reactions in these patients generally consists of withholding the drug with or without starting steroids, or continuing therapy with the addition of steroids. In either case, the reactions improve or even resolve in most



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patients.<sup>2</sup> This case highlights the continued need for awareness of this adverse effect of pembrolizumab. One should consider biopsy of lymph nodes favouring possible metastatic disease in cases like this as it can have a great effect on management.

### Learning points

- ▶ Non-caseating granulomatous inflammation is an important adverse effect of checkpoint inhibitors such as pembrolizumab.
- ▶ A biopsy of an area of possible metastatic disease or recurrence should be considered in patients with lymphadenopathy while on checkpoint inhibitors.
- ▶ Sarcoid-like reactions from checkpoint inhibitors have a favourable prognosis regardless of whether the offending drug is stopped with steroids added, or steroids are started and therapy is continued.

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