

November 2017 Pulmonary Case of the Month

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History of Present Illness

A 67-year-old man developed a right neck mass and underwent a right radical neck dissection. It was initially thought to be a high-grade sarcomatoid cancer, but after review was determined to be metastatic melanoma.

Past Medical History, Social History and Family History

He had no significant past medical or family history. He was a nonsmoker.

Physical Examination

His initial physical examination showed a right neck mass but was otherwise unremarkable. No abnormal skin lesions were identified.

PET/CT Scan

A positron emission tomography/computed tomography (PET/CT) scan showed increase uptake in the neck (Figure 1A) but his chest showed no increased uptake (Figure 1B).

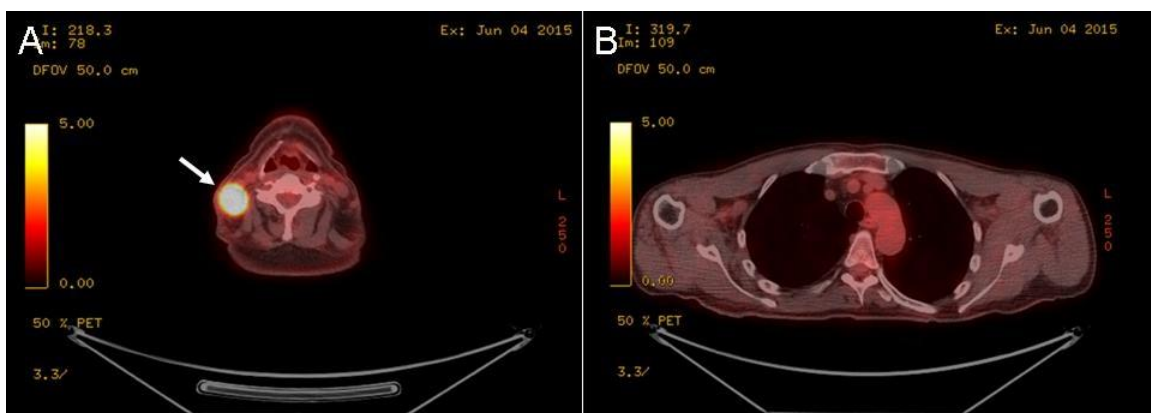


Figure 1. Panel A: PET/CT scan showing increased tracer uptake in the right neck (arrow). Panel B: No abnormal tracer uptake is seen within the chest.

Which of the following is/are **true**?

1. Bronchoscopy should be performed to search for bronchial melanoma
2. Radiation and oncology consultation should be obtained
3. The pathologic diagnosis is likely wrong since no primary melanoma can be identified
4. 1 and 3
5. All of the above

Correct!

2. Radiation and oncology consultation should be obtained

Metastatic melanoma without a primary site is seen in about 2-3% of patients with melanoma (1). There is no indication for bronchoscopy. Radiation therapy and oncology consultation were obtained and the patient received radiation therapy followed by gemcitabine and docetaxel. He was later switched to pembrolizumab (Keytruda®).

Nineteen months later a repeat PET/CT scan was suspicious for metastatic liver disease (Figure 2, Panel A) but his neck (Figure 2, Panel B) and chest (Figure 2, Panel C) showed no increased tracer uptake.

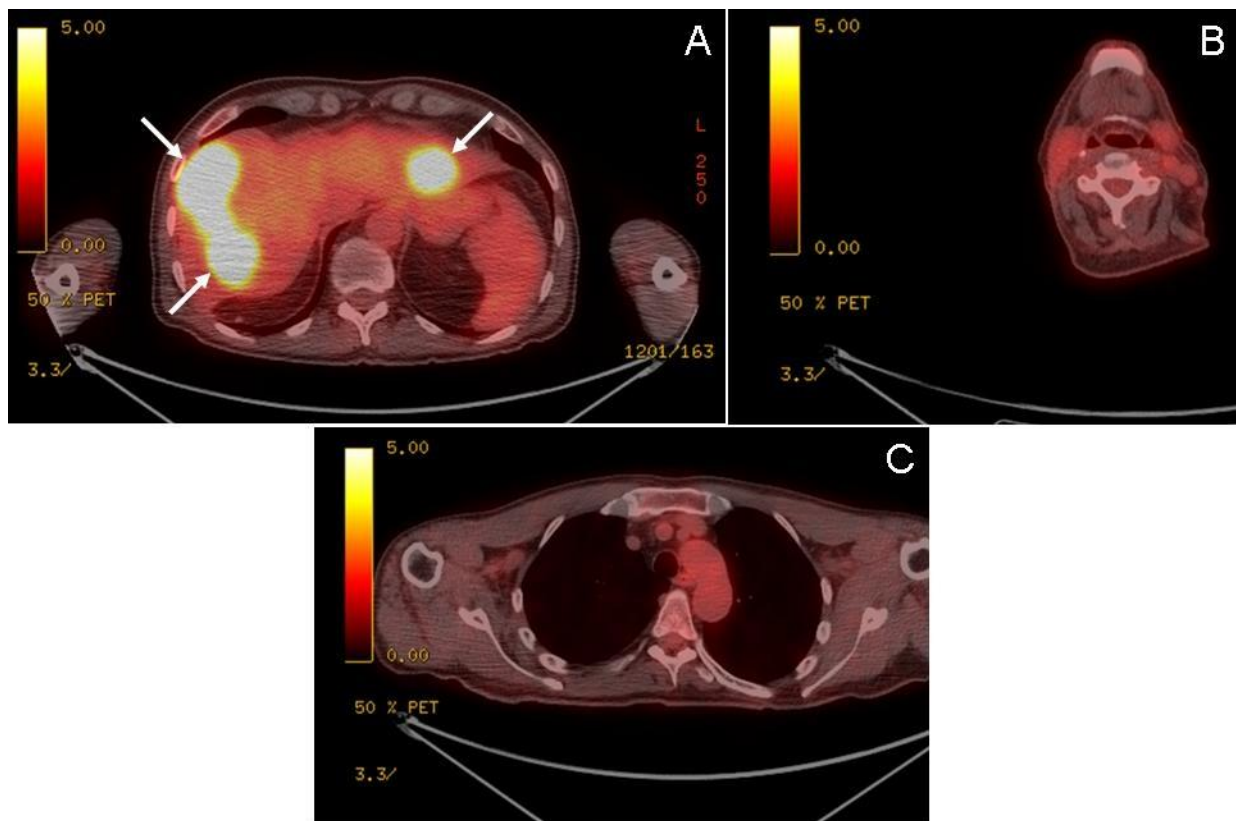


Figure 2. Panel A: Abdominal PET/CT scan showing increased uptake within the liver. Panel B: Neck PET/CT showing no increase in uptake. Panel C: Chest PET/CT showing no increased uptake.

His chemotherapy was subsequently switched to a combination of ipilimumab (Vervoy®) and nivolumab (Opdivo®).

A repeat PET/CT scan 3 months later showed the liver lesions were no longer present but increased uptake within the chest (Figure 3).

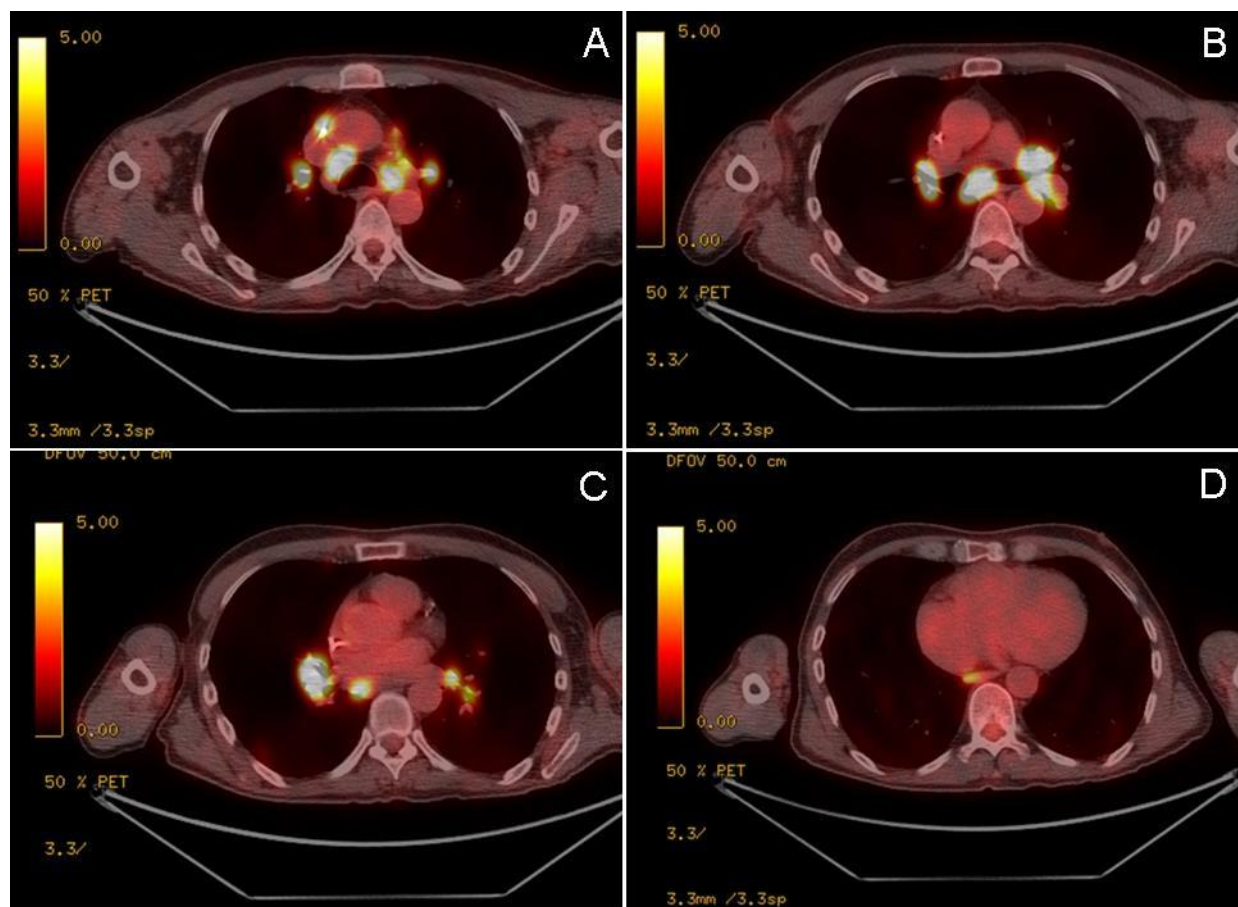


Figure 3. PET/CT scan of the chest showing multiple areas of increased uptake.

Which of the following are ***indicated at this time?***

1. Bronchoscopy with endobronchial ultrasound (EBUS) biopsy
2. Liver biopsy
3. Mediastinoscopy
4. S100 calcium-binding protein B (S100B)
5. Video-assisted thorascopic biopsy

Correct!

1. Bronchoscopy with endobronchial ultrasound (EBUS) biopsy

Although the most likely diagnosis seems to be metastatic melanoma to the mediastinal lymph nodes, it seems unusual that while the presumed metastases in the liver have regressed, new lesions have occurred in the chest. A tissue biopsy is probably indicated. The easiest procedure to obtain tissue from the mediastinal lymph nodes is bronchoscopy with EBUS. For lung cancer, the most common situation for performing mediastinal lymph node biopsy, bronchoscopy with EBUS has largely supplanted mediastinoscopy (2). There does not appear to be any parenchymal lung lesions which would be more readily sampled by VATS and there is now no increased uptake in the liver making it an unlikely source to obtain a tissue diagnosis. S100 calcium-binding protein B (S100B) has been touted as a biomarker for melanoma, but in this case, it seems tissue is needed (3).

Bronchoscopy with EBUS was performed. All lymph node stations were negative for malignancy. Station 7 (right upper hilum) showed a biopsy with noncaseating granulomas.

Which of the following should be **done next**?

1. Corticosteroids for presumed sarcoidosis
2. Perform mediastinoscopy
3. Stop the of ipilimumab and nivolumab
4. 1 and 3
5. All of the above

Correct!
4. 1 and 3

A slight increase in sarcoidosis has been reported in melanoma (0.58%) compared to 0.005% in the general population (4). Both nivolumab and ipilimumab have been reported to induce a sarcoid-like granulomatosis reaction (5-7). Based on these reports his chemotherapy was stopped and he was treated with oral corticosteroids, prednisone initially 60 mg/day followed by tapering doses over 3 months. Three months later a repeat PET/CT of his chest did not show any areas of increased tracer uptake (Figure 4).

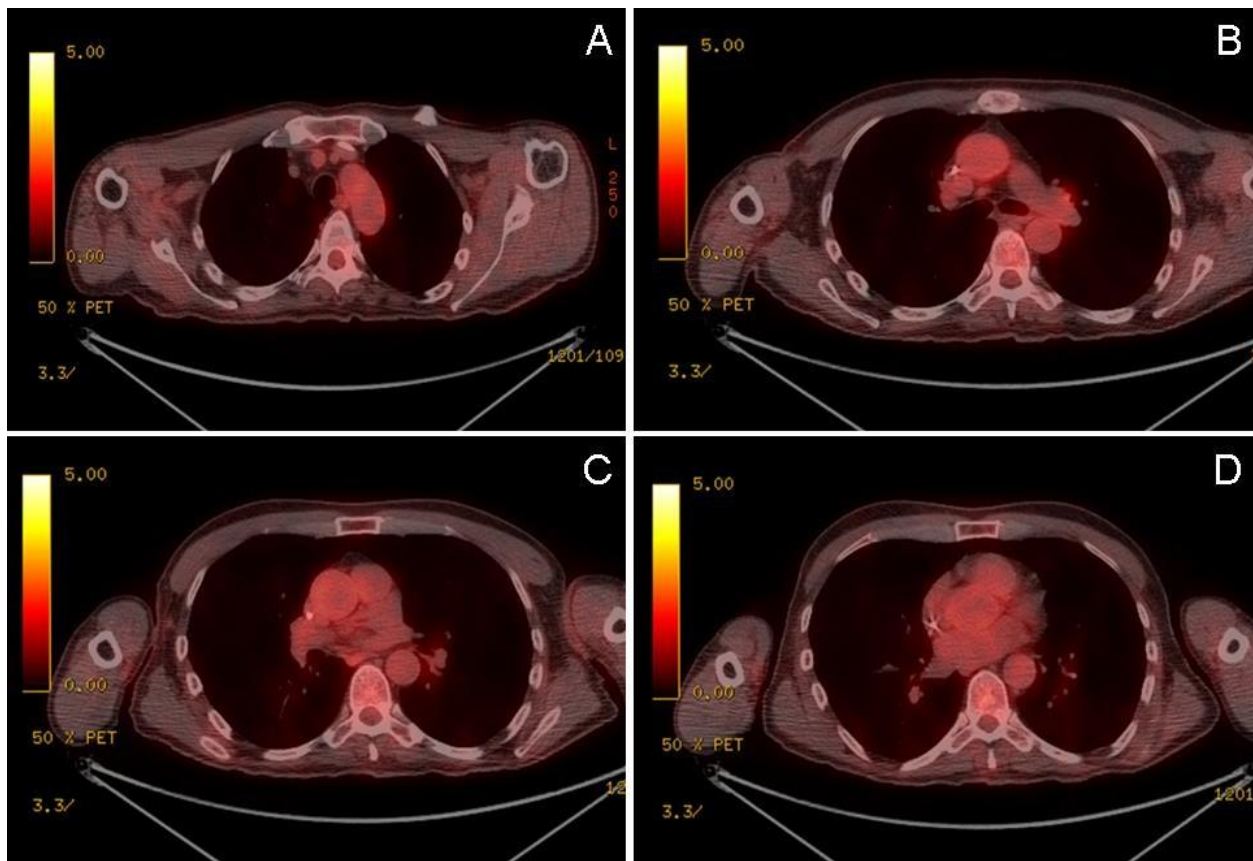


Figure 4. Representative images from PET/CT of chest 3 months after nivolumab and ipilimumab were stopped and corticosteroids were begun.

No other areas of increased tracer uptake were observed. Clinically he is doing well off chemotherapy and off corticosteroids.

Nivolumab is a human immunoglobulin G4 (IgG4) monoclonal antibody that binds to the PD-1 receptor and blocks its interaction with PD-L1 and PD-L2, releasing PD-1 pathway-mediated inhibition of the immune response, including the anti-tumor immune response. Ipilimumab is a monoclonal antibody that works to activate the immune system by targeting CTLA-4, a protein receptor that downregulates the immune system.

As these and other immune checkpoint inhibitors are increasingly used in malignancies such as non-small cell cancer of the lung, it seems likely that the sarcoid-like reaction observed in this patient may become more common.

References

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