November 2016 Pulmonary Case of the Month

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History of Present Illness

Our patient is a 76-year-old gentleman who was referred based on an abnormal CT scan. He has a history of metastatic melanoma and had begun immunotherapy with pembrolizumab 10 months prior to admission. He had low grade fevers and chills and some dyspnea on exertion and dry cough. He also had a 6-8 pound weight loss over 4 weeks.

PMH, SH and FH

He has a history of hairy cell leukemia since 2009; squamous and basal cell cancers; and diabetes on insulin. He is a retired commercial banker and has a 15 pack-year smoking history.

Physical Examination

Physical examination showed and SpO2 of 90% on room air. His lungs were clear. He had numerous depigmented lesions on his skin.

Radiography

A thoracic CT scan was performed (Figure 1) and compared to a scan done 3 months prior which was considered unremarkable.

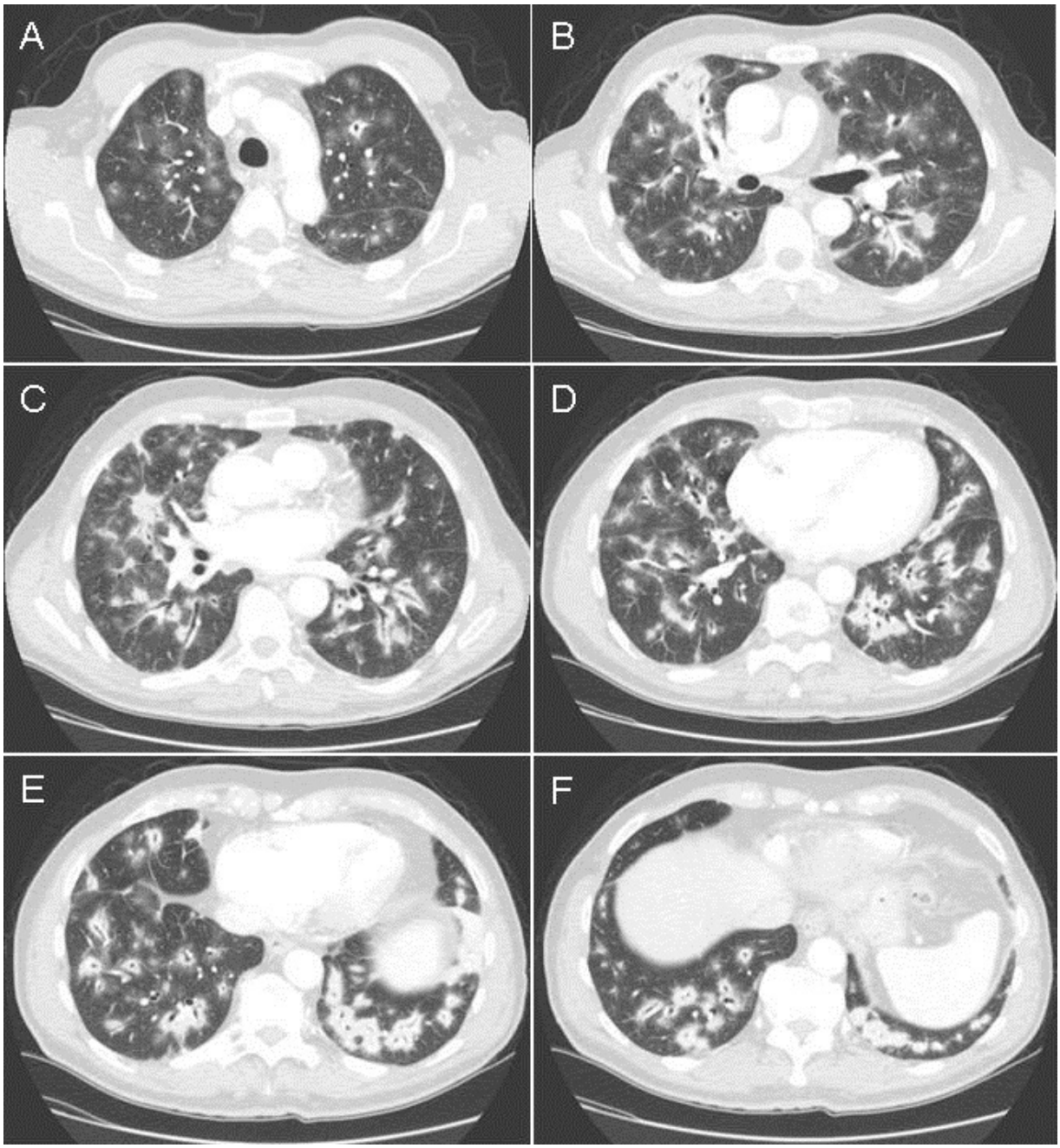

Figure 1. Representative images from contrast-enhanced thoracic CT scan in lung windows.

Which of the following ***best describe*** the CT scan?

1. Normal
2. Mosaic pattern of lung attenuation
3. Numerous bronchial-associated ground glass opacities
4. Numerous pulmonary nodules
5. Numerous pulmonary nodules with a halo sign

Correct!
3. Numerous bronchial-associated ground glass opacities

The thoracic CT scan is clearly abnormal with numerous rounded densities most of which have a bronchus in the center. The bronchi are well preserved and this would favor an acute pneumonitis over metastatic carcinoma although this is not diagnostic. A mosaic pattern is produced with interlobular and intralobular septal thickening (see July 2015 Pulmonary Case of the Month: A Crazy Case for an example). The halo sign occurs when a solid nodule is surrounded by a ground-glass opacity (see September 2015 Imaging Case of the Month for an example).

What is the ***best next step*** in evaluating the patient?

1. Bronchoscopy with bronchoalveolar lavage and transbronchial biopsy
2. Empiric antibiotics with careful observation
3. Repeat the thoracic CT scan
4. Thoracic CT angiogram
5. Video-assisted thorascopic biopsy (VATS)

Correct!

1. Bronchoscopy with bronchoalveolar lavage and transbronchial biopsy

The patient is an immuncompromised host. Most pursue a diagnosis aggressively in these patients since the patients are prone to unusual infections and can decompensate quickly. In our practice bronchoscopy with bronchoalveolar lavage is the usual procedure of choice. Transbronchial biopsy is also done by some. Depending on the hospital and the local expertise VATS could also be considered correct but is more invasive. Repeating the thoracic CT would probably have little utility and a thoracic CT angiogram, usually done for pulmonary emboli, would not seem indicated since that pulmonary embolus is unlikely based on the clinical situation.

The transbronchial biopsy (Figure 2) was interpreted as being negative for malignancy with nonspecific inflammatory changes including organizing pneumonia. Silver, S100 and HMB45 immunohistochmeical stains were negative. Coccidioidomycosis and aspergillus serologies were negative. Gram stain for bacteria and acid-fast stains tuberculosis were also negative.

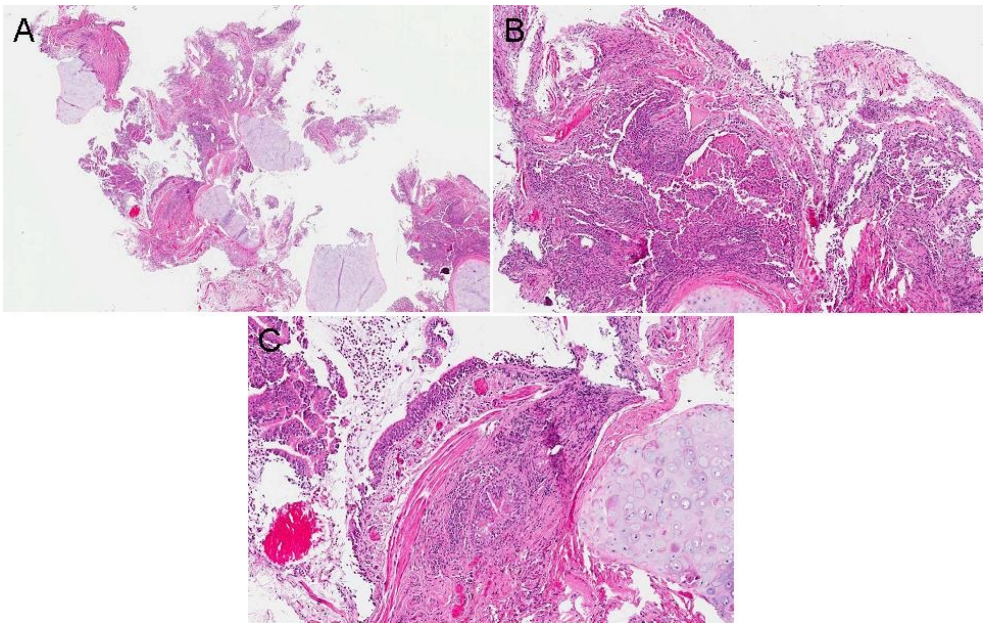

Figure 2. Transbronchial biopsy. Panel A: low power (H&E stain). Panel B: higher power (H&E stain). Panel C. High power (H&E stain).

Which of the following is the ***best next step***?

1. Begin empiric antibiotics while awaiting culture results
2. Perform open lung biopsy
3. Begin empiric corticosteroids for presumed organizing pneumonia secondary to pembrolizumab
4. 1 and 3
5. All of the above

Correct!
4. 1 and 3

The use of antibodies against programmed cell death 1 (PD-1), which block inhibitory T-cell checkpoints, is a promising new therapy for advanced cancers. One example of drugs in this class is pembrolizumab which is a humanized IgG4 monoclonal antibody (mouse antibody grafted to human immunoglublin). The Dana-Farber Cancer Institute reported three patients with pneumonitis secondary to pembrolizumab (1). in these patients pneumonitis onset was 7 to 24 months after starting treatment (1). The CT findings included diffuse ground-glass opacities, reticular opacities, consolidation, traction bronchiectasis, and effusions and CT scans were interpreted as showing acute interstitial pneumonia, adult respiratory distress syndrome (ARDS) or nonspecific interstitial pneumonitis (NSIP). Others have reported similar cases with pembrolizumab and the closely related immunotherapy nivolumab (2,3).

Naidoo *et al.* (4) proposed an algorithm for possible interstitial pneumonitis secondary with immune checkpoint blockade. For patients with severe , life-threatening symptoms and/or worsening hypoxia they propose hospitalization and discontinuing the immunotherapy. They also recommend corticosteroids and prophylactic antibiotics while awaiting cultures. Lung biopsy is not necessarily wrong but give the excellent transbronchial biopsies it seems unlikely this would add much in this case.

Our patient had his pembrolizumab discontinued and was started on prednisone with rapid resolution of his symptoms and radiographic abnormalities.

References

1. Nishino M, Sholl LM, Hodi FS, Hatabu H, Ramaiya NH. Anti-PD-1-related pneumonitis during cancer immunotherapy. N Engl J Med. 2015 Jul 16;373(3):288-90. [CrossRef] [PubMed]
2. Fragkou P, Souli M, Theochari M, Kontopoulou C, Loukides S, Koumarianou A. A case of organizing pneumonia (op) associated with pembrolizumab. Drug Target Insights. 2016 May 22;10:9-12. [CrossRef] [PubMed]
3. Sano T, Uhara H, Mikoshiba Y, Kobayashi A, Uchiyama R, Tateishi K, Yamamoto H, Okuyama R. Nivolumab-induced organizing pneumonia in a melanoma patient. Jpn J Clin Oncol. 2016 Mar;46(3):270-2. [CrossRef] [PubMed]
4. Naidoo J, Page DB, Li BT, Connell LC, Schindler K, Lacouture ME, Postow MA, Wolchok JD. Toxicities of the anti-PD-1 and anti-PD-L1 immune checkpoint antibodies. Ann Oncol. 2015 Dec;26(12):2375-91. [CrossRef] [PubMed]