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Introduction

Immunotherapy with immune checkpoint inhibitors (ICIs) has revolutionized the care of advanced melanoma. However, ICIs have been associated with various immune-related adverse events including vasculitis, a rare cardiovascular complication. Herein, we describe a case of marked thoracic and abdominal aortitis as well as medium-vessel arteritis developed two years after the treatment with pembrolizumab in a patient with metastatic melanoma.

Case Presentation

A 58 year-old man was diagnosed with stage IIIa melanoma of the right scalp. The patient underwent wide local excision with positive sentinel lymph node biopsy and negative completion lymph node dissection. He was randomized to pembrolizumab in a clinical trial and treated with 7 cycles. However, subsequent PET-CT showed local recurrence in the area of the right parietal skull concerning for cancer progression. He also suffered from multi-joint arthritis, involving both small and large joints throughout the whole body as a complication of pembrolizumab. Given the lack of therapeutic response along with immune complications, the patient was ultimately taken off the trial.

He was subsequently treated with talimogene laherparepvec injected directly into the scalp nodules with excellent clinical and radiographic response upon PET-CT. The patient did well without significant complications although he continued to suffer from arthritis and myositis as complications of pembrolizumab therapy. Then, three years since his cancer diagnosis, two years since the treatments with pembrolizumab, and approximately one year since the discontinuation of pembrolizumab therapy, the patient's cancer surveillance PET-CT showed new, markedly increased FDG activity along the entire thoracic aorta in a pattern most suggestive of aortitis. PET-CT also noted probable involvement of subclavian, iliac, and femoral arteries. Thoracoabdominalpelvis MRI and CT showed thickened vessel wall with evidence of active inflammation in the vascular territory consistent with PET-CT. No aneurysm or functionally significant vascular stenosis was identified. The patient is otherwise clinically stable and asymptomatic except for the interval development of hypertension. The patient is currently being observed clinically with supportive care. Pending a followup PET-CT, a steroid therapy will be considered to prevent long-term complications of vasculitis

Imaging Studies and Clinical Course

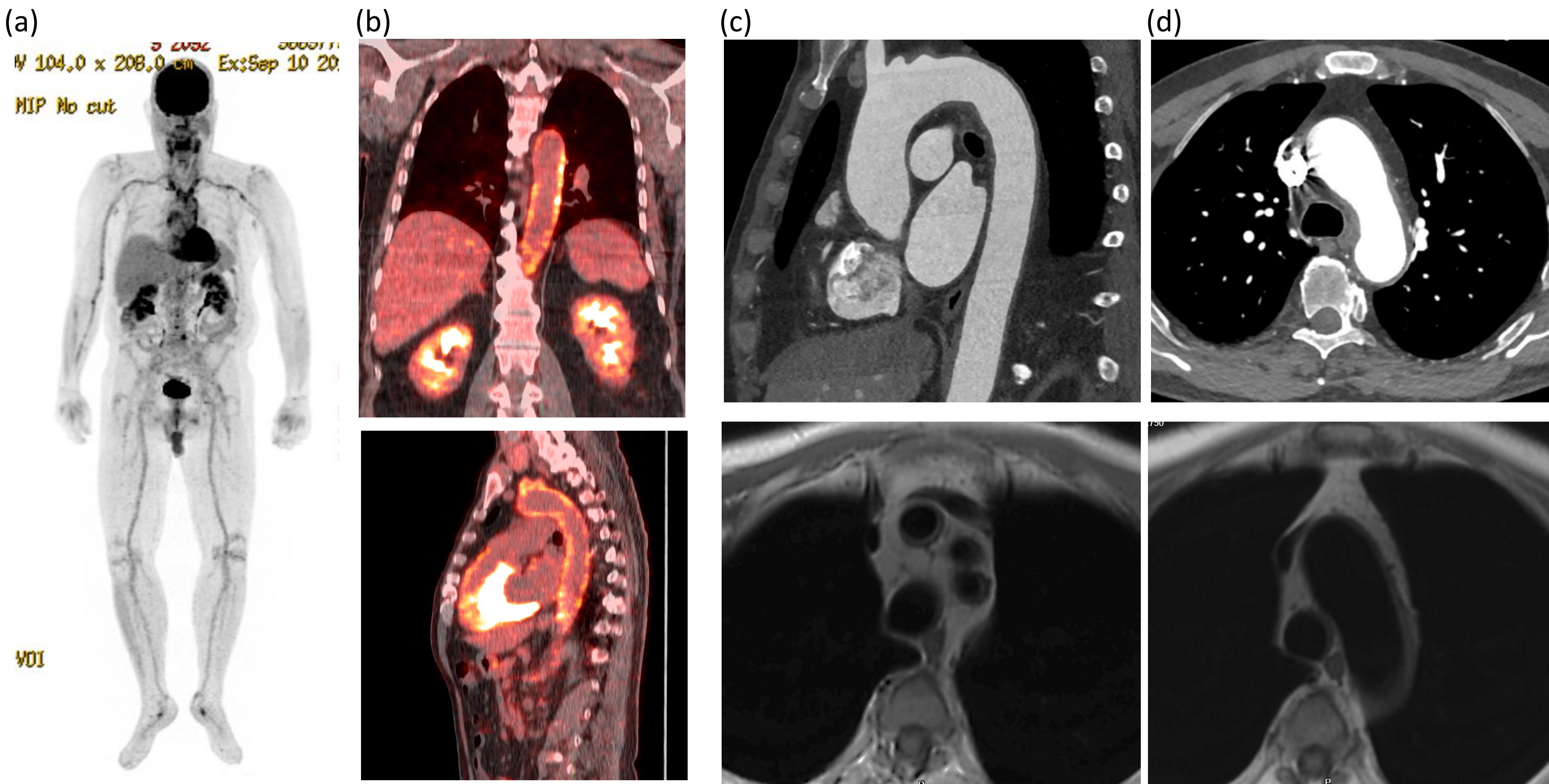


Figure. Multimodality vascular imaging studies show diffuse large vessel vasculitis. A-B. PET-CT showing markedly increased FDG activity along near the entire thoracic aorta in a pattern most suggestive of inflammation. While not as well defined, increased FDG uptake is also noted in subclavian, iliac, and femoral arteries bilaterally. **C.** MR Chest Abdomen Pelvis Angiography showing circumferential wall thickening of the thoracoabdominal aorta extending from the sinotubular junction to the bifurcation with involvement of the proximal arch branches. There is mild arterial wall contrast enhancement, consistent with vasculitis. **D.** CT Chest Abdomen Pelvis Angiography showing wall thickening of the thoracic and abdominal aorta, with thickening of the proximal arch branches, consistent with vasculitis.

Conclusions

Large vessel vasculitis has been reported with ICIs. However, the frequency, severity, and timing of the ICI-associated vasculitis remain poorly understood. Studies have suggested that the reduced levels of inhibitory programmed cell death ligand-1 (PD-L1) in human arteries may lead to uninhibited T-cell proliferations in response to injury when treated with ICIs and predispose them to develop subsequent vasculitis. The patient described in this case developed marked vasculitis involving thoracic, abdominal, and iliac arteries and their major branches nearly two years following the treatment with pembrolizumab. While the underlying mechanism of his aortitis remains yet to be understood, it is important to recognize vasculitis as a potential delayed complication following the ICI therapy.

Reference

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