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Case Report

Pembrolizumab-induced vasculitis demonstrated by FDG-PET/CT ☆,☆☆

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ABSTRACT

A 76-year-old man with a history of malignant pleural mesothelioma treated with pembrolizumab underwent FDG-PET/CT for restaging. The images demonstrated FDG uptake overlying the right hepatic and splenic artery, which were new from the previous FDG-PET/CT 2.5 years prior before the patient started pembrolizumab, suspicious for vasculitis. A follow-up MRI supported the diagnosis with evidence of celiac, splenic, common hepatic, and right hepatic artery involvement. Pembrolizumab was discontinued and the patient received a short course of oral glucocorticoids. Subsequent FDG-PET/CT performed 14 months after initiation of treatment for vasculitis demonstrated resolution of vasculitis. Immune checkpoint inhibitors can cause vasculitis, which can be recognized on FDG-PET/CT and lead to appropriate treatment.

Introduction

Pembrolizumab, a monoclonal programmed death-1 (PD-1) antibody, improves clinical outcomes in advanced pleural mesothelioma [1]. However, like other immune checkpoint inhibitors (ICI), immune-related adverse effects have been reported including vasculitis, which often affects medium to large vessels [2]. Pathogenesis likely involves uncontrolled stimulation of the immune system from the therapy [2]. Vasculitis has variable clinical, laboratory, and radiologic manifestations. This case highlights the importance of recognizing the FDG-PET findings of ICI-vasculitis, especially in asymptomatic patients, and its ability to guide therapy to avoid more serious complications such as thrombosis or end-organ damage.

Case report

A 76-year-old man with malignant pleural mesothelioma on pembrolizumab underwent restaging FDG-PET/CT. The patient had been treated with pembrolizumab for the past 10 months without new or changes in symptoms from baseline.

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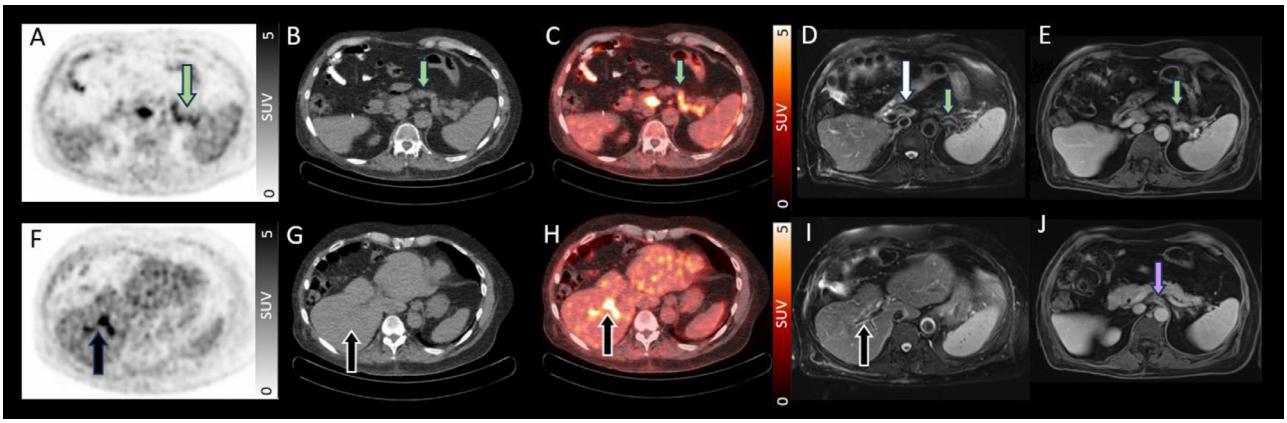

Fig. 1 – A 76-year-old man with malignant pleural mesothelioma on pembrolizumab underwent restaging FDG-PET/CT (A and F: PET only; B and G: CT only; C and H: fused PET/CT). FDG-PET/CT showed uptake along the splenic artery (panel A and C, green arrow, SUV_{max} of 5.7) and right hepatic artery (panel F and H, black arrow, SUV_{max} of 9.8) suspicious for vasculitis. Follow-up MRI (D and I: T2-weighted fat saturated MRI) for further characterization demonstrated mildly T2-hyperintense, thickened walls of the common hepatic (panel D, white arrow), splenic artery (panel D, green arrow) and right hepatic artery (panel I, black arrow). This MRI (E and J: T1-weighted post contrast-enhanced MRI [delayed phase]) also showed enhancement and wall thickening of the splenic artery (panel E, green arrow) and celiac artery (panel J, purple arrow), overall suggestive of medium-vessel vasculitis.

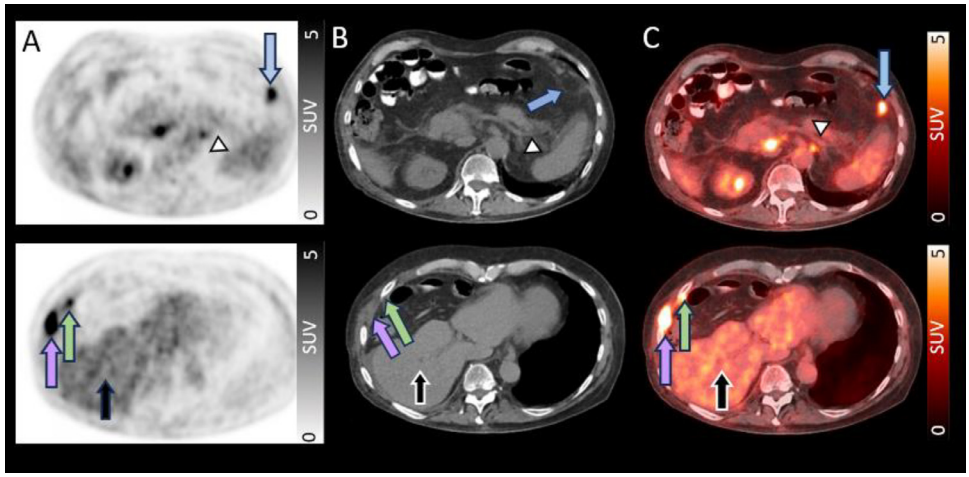

Fig. 2 – Follow-up FDG-PET/CT taken 14 months after discontinuation of pembrolizumab, initiation of steroid, and subsequent non-pembrolizumab systemic therapies showed a complete resolution of previous FDG avidity of the right hepatic artery (black arrow) and splenic artery (white arrowhead) in (A) PET only; (B) CT only; (C) fused PET/CT despite progression of malignant pleural mesothelioma, as seen with increased size of left upper abdominal implant with SUV_{max} of 11.2 (blue arrow), persistent right-sided chest wall mass with a SUV_{max} of 13.6 (purple arrow) and a new right pleural focus (green arrow) with SUV_{max} of 9.7, supporting the diagnosis of pembrolizumab-related vasculitis.

FDG-PET/CT showed uptake along the right hepatic artery (SUV_{max} of 9.8) and splenic artery (SUV_{max} of 5.7), suspicious for vasculitis (Fig. 1). Follow-up MRI for further characterization demonstrated mildly T2-hyperintense, thickened walls of the common hepatic, right hepatic and splenic arteries. This MRI also showed enhancement and wall thickening of the splenic artery and celiac artery, overall suggestive of medium-vessel vasculitis. Follow-up FDG-PET/CT taken 14 months after discontinuation of pembrolizumab, initiation of steroid, and subsequent non-pembrolizumab systemic therapies showed a complete resolution of previous FDG avidity in the right hepatic artery and splenic artery despite progression of malignant pleural mesothelioma, supporting the diagnosis of pembrolizumab-related vasculitis (Fig. 2).

Discussion

Since their first regulatory approval in 2011, ICIs have become a standard-of-care treatment option for an estimated 40% of all patients with cancer in the United States [3]. Despite

having fewer side effects than toxic chemotherapy, these medications can cause immune-related adverse events (irAE) such as vasculitis. Currently, ICI-induced vasculitis has only been described in case reports and case series as an emerging entity.

Previous reports on pembrolizumab-induced vasculitis have been associated with the retinal artery, aorta, and blood vessels that supply the brain parenchyma, spinal cord, or leptomeninges [4–7]. Our case demonstrates pembrolizumab-induced vasculitis involving multiple medium-size abdominal vessels shown on FDG-PET/CT and supported by MRI. Prior reports suggest the mean time of onset of vasculitis related symptoms from start of ICI can range from 3 to 7 months. Hence, vasculitis as a form of irAE can occur soon after therapy initiation [8,9]. A recent analysis of 20 case reports in the literature found the majority of reported symptomatic cases on ICI-induced vasculitis involved treatment with ipilimumab (n = 8), followed by pembrolizumab (n = 6) and nivolumab (n = 5) [9]. Two case reports demonstrated FDG-PET/CT signs of periaortitis associated with nivolumab [10,11].

FDG avidity from ICI-induced vasculitis can be seen before patients are symptomatic, allowing early identification and treatment of this potentially fatal immune-related adverse event. Treatment often includes glucocorticoids and discontinuation of immunotherapy with clinical improvement in most cases [8]. In our case, the patient demonstrated resolution of imaging findings suggesting ICI-vasculitis after treatment with glucocorticoids and change in therapy. This case emphasizes the importance of recognizing the FDG-PET findings of ICI-vasculitis, especially in asymptomatic patients, and its ability to guide therapy.

Conclusion

Immune checkpoint inhibitors can cause vasculitis, which can be detected on FDG-PET/CT and MRI. Recognition of the imaging findings can help direct patient care to avoid potential adverse events.

Patient consent

This statement is to document that written consent was obtained from the patient presented in this report for publication of their de-identified images and case information for educational purposes.

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