Control Number: 45

Abstract Category: Clinical Case Challenge in Cardio-Oncology

Title: Delayed development of marked aortitis following treatment with pembrolizumab in a patient with metastatic melanoma

ABSTRACT BODY

Background and Purpose

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 aortitis developed two years after the treatment with pembrolizumab in a patient with metastatic melanoma.

Case Description and Outcomes

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 directly into the scalp nodules with excellent clinical and radiographic response upon PET-CT. The patient did very well without significant complications. Then, three years since the diagnosis, two years since the treatments with pembrolizumab, the patient's cancer surveillance PET-CT showed new, markedly increased FDG activity along near the entire thoracic aorta in a pattern most suggestive of aortitis. The patient was otherwise clinically stable and asymptomatic except for the interval development of hypertension. The patient is now being considered for high-dose steroid therapy.

Discussion

Large vessel vasculitis has been reported with ICIs. However, the frequency, severity, and timing of the ICI-associated vasculitis remains 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 and subsequent development of vasculitis. The patient described in this case developed marked thoracic aortitis nearly two years after the treatment with pembrolizumab. While the underlying mechanism remains yet to be uncovered, it is important to recognize vasculitis as a potential delayed complication following the ICI therapy.

References

Watanabe, R., Zhang, H., Berry, G., Goronzy, J.J., and Weyand, C.M. (2017). Immune checkpoint dysfunction in large and medium vessel vasculitis. Am. J. Physiol. Heart Circ. Physiol. 312, H1052–H1059. Zhang H, Watanabe R, Berry GJ, Vaglio A, Liao YJ, Warrington KJ, Goronzy JJ, Weyand CM. (2017). Immunoinhibitory checkpoint deficiency in medium and large vessel vasculitis. Proc Natl Acad Sci U S A. 114(6):E970-E979.

Image 1