Immune Checkpoint Inhibitor Associated Orbitopathy: A Rare Complication

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Background

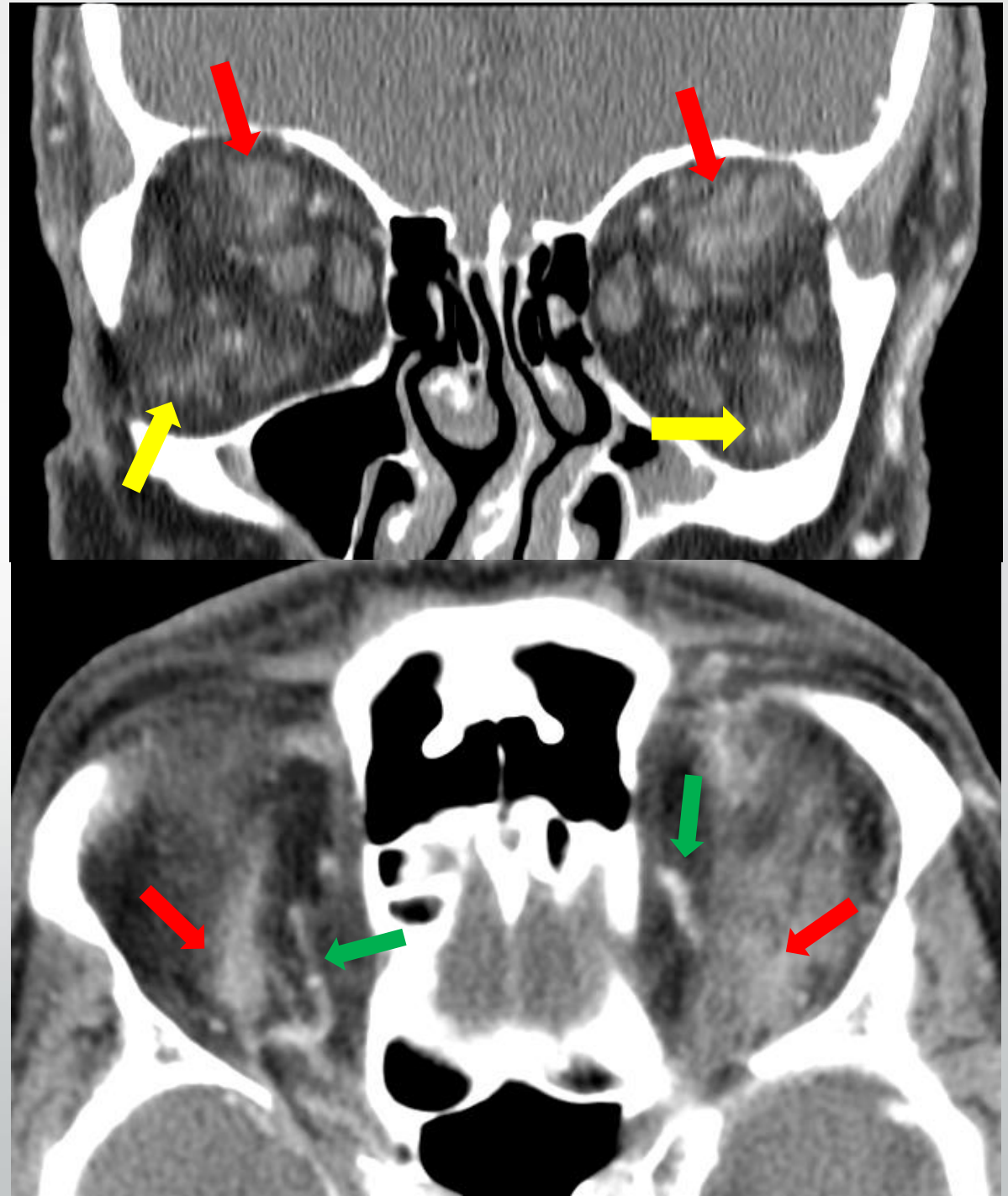
- Immune checkpoint inhibitors are a novel class of treatment for a variety of cancers.
- These agents act as antibodies directed against checkpoint proteins within the cell cycle.
- Due to their mechanism of action, these agents can lead to a multitude of immune-related adverse events across all organ systems, including the ophthalmic system.
- Orbital involvement can affect both the intraconal and extraconal spaces.

Clinical Presentation

- 78 year-old male with past medical history significant for newly diagnosed metastatic renal cell carcinoma presents to the ED for headache, eye redness, eye pain, eyelid swelling and blurry vision.
- The patient was recently started on ipilimumab and nivolumab prior to presentation in the ED, with the first dose just two days prior.
- On physical examination, there was decreased vision acuity and color vision. On the ophthalmologic exam specifically, there was bilateral ptosis, decreased extraocular motion, and injection in the bilateral sclera and conjunctiva with chemosis.
- Lab work was significant for elevated ESR at 72 and CRP at 42.6. A CT head and CT orbits with IV contrast were ordered.

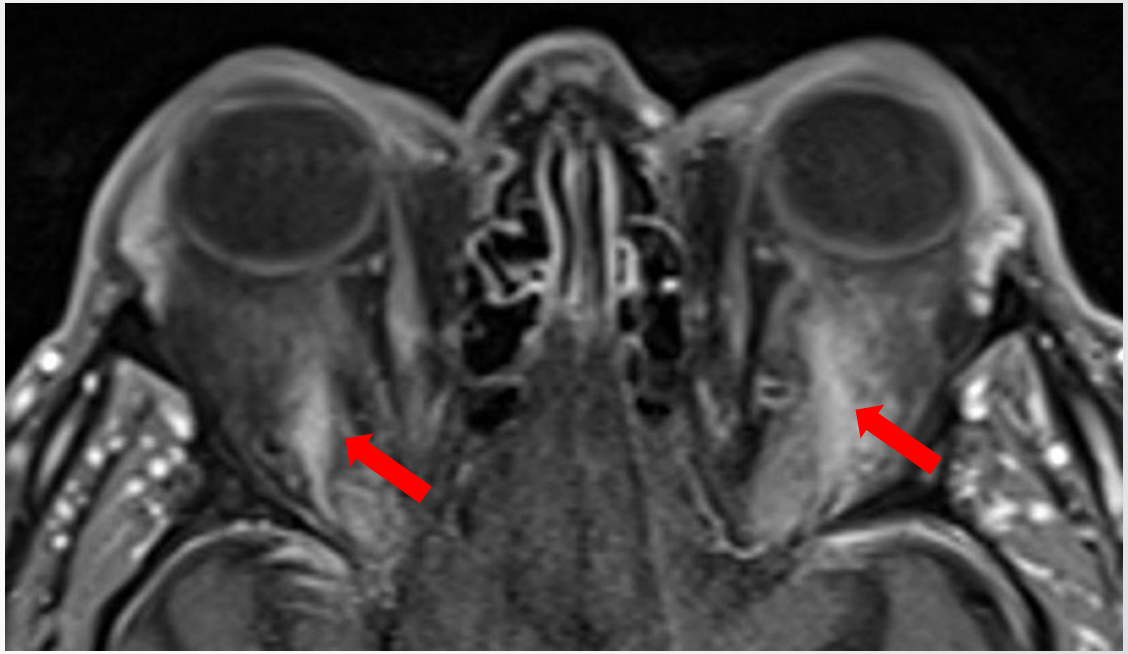
Imaging Findings

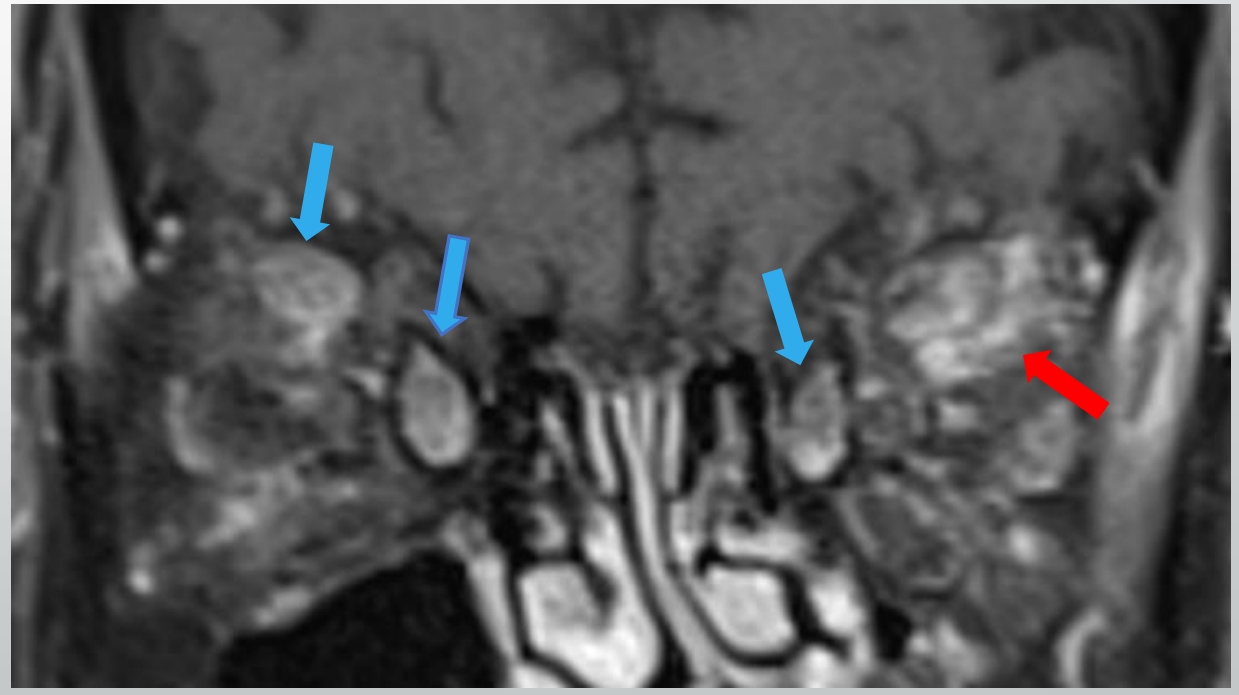
- Coronal and axial CT demonstrates heterogenous, amorphous enhancement within the bilateral globes, mostly within the intraconal compartments.
- More specifically, heterogenous enhancement is most notably seen surrounding the superior ophthalmic veins (green arrows) and inseparable from the superior rectus muscles, left worse than right (red arrows).
- Irregular area of heterogenous enhancement is also seen within the left lower quadrant of the orbit and abutting the inferior rectus muscles bilaterally (yellow arrows)



Imaging Findings

- MRI redemonstrates abnormal signal and enhancement within the bilateral intraconal and extraconal spaces similar to previous CT orbits.
- Axial MR T1 Post contrast (top image) shows heterogenous enhancement surrounding the superior ophthalmic veins and inseparable from the superior rectus muscles (red arrows). The bilateral superior ophthalmic veins appear patent and are not dilated.
- On Coronal T1 Post contrast sequence (bottom image), there is also mild expansion with fatty infiltration and enhancement within the bilateral extraocular muscles, better appreciated on MRI (yellow arrows)





Pertinent Negatives

- Optic nerves were grossly unremarkable. No abnormal signal or enhancement.
- The bilateral orbital rims and orbital floors are intact.
- The optic chiasm appears within normal limits.
- The cavernous sinuses enhance with contrast homogeneously bilaterally.

Differential Diagnosis

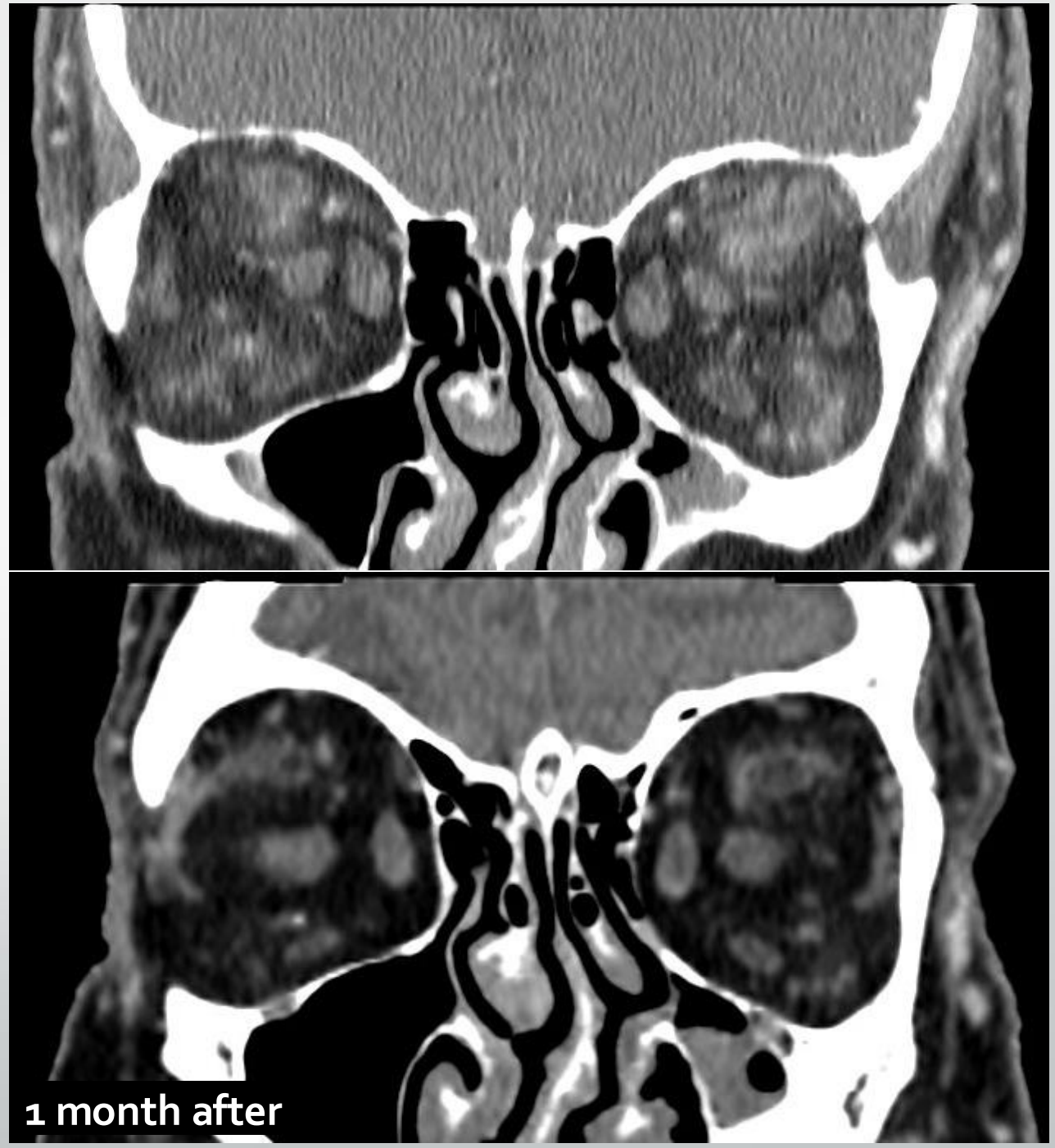
- Idiopathic Orbital Inflammatory Disease (Orbital Pseudotumor)
- IgG4 Orbital Disease
- Orbital Lymphoma
- Sarcoidosis
- Metastatic disease

Management

- The patient was treated with IV steroids for a few days with significant improvement in symptoms.
- Patient's treatment regimen was stopped during this time.
- They were discharged from the hospital and transitioned to a course of oral steroids.

Outcomes

- A follow-up CT orbits with IV contrast was performed 1 months afterwards which showed decreased inflammation within the orbits.
- As shown on the images on the right, there is interval near-complete resolution of the previous noted areas of enhancement.
- The patient was discontinued on ipilimumab and nivolumab and switched to cabozantinib, a tyrosine kinase inhibitor.



Take Home Points

- Immune checkpoint orbitopathy is a rare side effect for patients on immune checkpoint inhibitors such as ipilimumab and nivolumab.
- Imaging findings demonstrate signs of inflammation including abnormal signal intensities on MRI and enhancement on both CT and MRI. Bilateral involvement is typically appreciated.
- However, these findings may be nonspecific and clinical history must be applied. Awareness of this potential adverse side-effect of immune checkpoint inhibitors can help guide radiologic findings and lead to a timely diagnosis.

References

Furtado V., Melamud K., Hassan K., Rohatgi S., & Buch K. 2020. Imaging manifestations of immune-related adverse effects in checkpoint inhibitor therapies: A primer for the radiologist. Clinical Imaging 63; 35-49.

Thank You!

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