Case 39

History of Present Illness

An 83-year-old man noted 3–4 months ago that he fell down, hit his head and afterward he could not open his right eye and could not move his right eye. An MRI at that time was read as normal. This has not gotten better or worse as far as he can tell. He has had headache behind his right eye for the past 2 months. The headache is deep, boring, and constant. He rates it at a 6–7/10. Acetaminophen takes the edge off. Nothing seems to make it worse or better. He denies ever having a headache in his life before this. He denies a family history of migraine. He has lost 17# in the past 6 months due to a poor appetite. He had a workup of a normal ESR and CRP and a normal CT angiogram.

Past medical and ocular history Mild dementia Atrial fibrillation Squamous cell and basal carcinomas Hypertension Hyperlipidemia Benign prostatic hypertrophy Gastric reflux Syncope Glaucoma	*Past surgical history* Cataract BE Retinal detachment LE 4 years ago Multiple skin cancers removed *Family history* Unremarkable
Medications Donepezil Finasteride HCTZ Ipratropium Latanoprost Lisinopril Metroprolol Omeprazole Simvastatin Warfarin	*Review of systems* Hearing loss bilaterally Runny nose Poor memory *Social history* Retired from the military 25 years ago Does not smoke 1–2 drinks a day

M.S. Lee, K.B. Digre, *A Case-Based Guide to Eye Pain*,
https://doi.org/10.1007/978-3-319-65121-7_39

Examination
Acuity with correction Right eye: 20/40 Left eye: 20/50
Pupils RE unreactive to light or near, larger than left APD LE
Intraocular pressure Right eye: 11 mmHg Left eye: 14 mmHg
Color vision All correct BE
External exam Complete ptosis RE Scar along right temple Hertel: 20 mm BE
Eye alignmentand motility Exotropic in primary gaze Unable to elevate, adduct, or depress his right eye at all No torsion with attempted downgaze 25% abduction deficit RE LE normal
Slit lamp examination Intraocular lenses BE
Visual field Altitudinal defect RE Significant constriction LE
Fundus examination Cupping LE ≫ RE
Neurologic examination Corneal reflex absent

Discussion

Ophthalmic Perspective—Dr. Lee

This patient has multiple cranial neuropathies. The complete ptosis and complete third nerve palsy are the biggest things here. However, he has a mild abduction deficit in the RE. When a patient has a third nerve palsy, you can determine fourth nerve function by having the patient look up and down. The eye should intort on downgaze if the fourth nerve is functioning properly. He has no torsion of the RE on downgaze. The patient also has facial numbness in the right V1 distribution. So, to summarize, he has right third, fourth, fifth, and sixth nerve dysfunction. These nerves all hang out together in the cavernous sinus.

The patient's ESR and CRP were negative arguing away from giant cell arteritis. I would like to look carefully at his previous MRI. If this does not show an abnormality, then I would likely repeat the scan with thin cuts through the right cavernous sinus. He may have Tolosa Hunt Syndrome (Case 40), but usually that does not

cause facial numbness. In this age group, I would be more concerned about a metastasis. Also consider that patients with skin cancers on the face can develop perineural spread if the margins were not clean with resection. The cancer spreads along the trigeminal nerve and causes numbness and/or pain. It can lead to an optic neuropathy and/or CN III, IV, and VI dysfunction if it makes it to the orbital apex and cavernous sinus. I would also look at V1 to see if it is enlarged or enhancing.

If there is an enhancing lesion in the cavernous sinus, one could consider steroid treatment vs. biopsy. The danger of steroids is that you do not know what you are treating and it may make it harder to identify lymphoma. A biopsy of the cavernous sinus can be fairly invasive at this age. If there is a lesion of V1, then a more anterior orbital biopsy can be considered.

Finally, as an aside, he has an APD in the LE. He has cupping of the optic nerves LE ≫ RE consistent with asymmetric glaucoma. The color vision is normal, which is what you would expect with glaucoma; whereas an optic neuropathy would typically show poor color vision. I do not think the APD is relevant to the other cranial nerve palsies.

Neurologic Perspective—Dr. Digre

Here is another older person with a new headache and an abnormal examination—this is worrisome. While we are told he has had a fall, his imaging is normal so we know he probably does not have a subdural hematoma and since he is awake and alert, he is not herniating—despite his pupil-involving third nerve palsy. He also has numbness in the V1 distribution. One important point is *pain plus numbness equals something bad*! For example the numb chin symptom is usually a sign of underlying malignancy until proven otherwise.

We are told that he has had multiple skin cancers (both basal and squamous) removed. This is an important historical point. Reviewing the previous MR would be my first step—many times focusing the attention of the neuro-radiologist to the area of interest is helpful. In this case, cranial nerves 3, 4, 5, and maybe 6 localizes to the superior orbital fissure and cavernous sinus region. You may need to "run" the nerves with the neuro-radiologist!

In general, perineural spread in skin cancer is through the fifth and seventh cranial nerve since the skin has direct access to these nerves in the face and head. These cancers can track along these nerves centrally via the orbit and superior orbital fissure, foramen rotundum (V2) and foramen ovale (V3) where they gain access to other cranial nerves such as in this case. Squamous cell is slightly more common in perineural invasion than basal cell. Involvement of V or VII carries a worse prognosis.

While skin cancers can have perineural spread so can other tumors like adenocystic carcinoma, lymphoma, and nasopharyngeal carcinomas. The differential diagnosis in most cases other than cancer (for example metastasis) would be sarcoid and infections (like mucormycosis). MR imaging with gadolinium is most important. Treatment depends on the extent of infiltration and radiotherapy is usually what is recommended.

Non-ophthalmic/Non-neurologic Perspective

This patient was presumed to have a right, microvascular third nerve palsy. When it did not improve in 3–4 months, he was sent for further evaluation. If someone had checked facial sensation, then that would indicate that this is not an isolated third. Additionally, his original MRI was described as normal, but maybe it is not. Not everyone is comfortable looking at MRIs by themself, but a phone call to a radiologist asking him/her to take a closer look at the cranial nerves may have yielded a diagnosis.

Follow-up

The MRI (Fig. 39.1) showed enlargement and enhancement of a right V1 branch of the trigeminal nerve and also the right cavernous sinus. Biopsy of the branch showed poorly differentiated adenocarcinoma from a primary lung or gastrointestinal cancer. Full body PET scan showed a hot spot in the colon. Colonoscopy with biopsy was consistent with a colon adenocarcinoma but the immunohistochemical properties did not match! He was diagnosed with an orbital adenocarcinoma of unknown etiology. He underwent cranial radiation and chemotherapy. There was no improvement in his eye movements, but he continues to do well 4 years after diagnosis. *Final diagnosis: Metastatic adenocarcinoma to the cavernous sinus*.

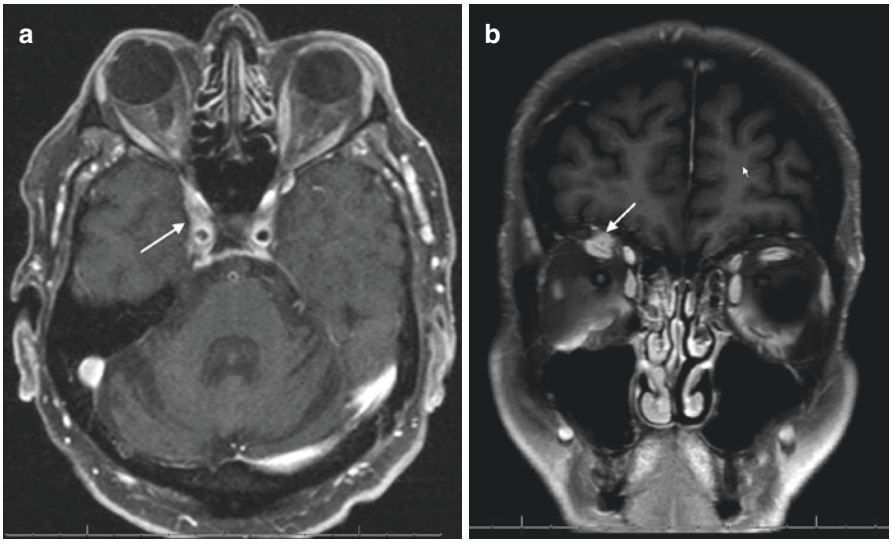

Fig. 39.1 (**a**) Axial MRI shows widening of the right cavernous sinus compared to the left (*arrow*). (**b**) Post-contrast Coronal T1 MRI shows enlargement and enhancement of the supraorbital nerve (*arrow*). Note the displacement of the superior rectus inferiorly

For Further Study

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