Pearls & Oy-sters: Isolated oculomotor nerve palsy due to pituitary apoplexy missed on CT scan

Sina Marzoughi, MD,* Aravind Ganesh, MD, DPhil,* Amro Qaddoura, MD, Pouya Motazedian, MD, and Simerpreet S. Bal, MD, FRCPC

Correspondence
Dr. Bal
simer.bal@ahs.ca

Neurology® 2020;94:e1774-1777. doi:10.1212/WNL.0000000000009298

Pearls

- Pituitary apoplexy is an important differential diagnosis for acute headache, particularly accompanied by cranial nerve palsies
- Apoplexy should be included in the clinician's differential for acute onset third nerve palsy in addition to the more common etiologies of compressive aneurysmal palsy and ischemic microvascular palsy
- MRI with dedicated views of the sella turcica is important to detect milder pituitary pathology

Oy-sters

- Limited presentations of pituitary apoplexy may only involve a single cranial nerve
- Patients with new headache of maximal intensity at onset should be admitted for extensive evaluation with a high index of suspicion for a serious intracranial pathology
- Headaches from secondary causes may subside by the time patients seek medical attention
- Midline lesions like pituitary apoplexy may be easily missed on standard emergency department neuroimaging, especially if findings are early or mild
- Reviewing the images themselves can help clinicians ensure that important secondary causes are not missed

A 70-year-old left-handed man presented to his family physician's office after waking up with a new 10/10 intensity headache and was prescribed acetaminophen and cephalexin for left ankle cellulitis. Over the next 3 days, his headache had improved to 1/10, but he then developed a new horizontal binocular diplopia and right-sided ptosis concurrent with a mild bifrontal headache, for which he presented to the emergency department. He had a medical history of type II diabetes, hypertension, stage IV chronic kidney disease with kidney transplantation for immunoglobulin A nephropathy and immunosuppression, left upper limb deep vein thrombosis, right-sided parotid mass, recurrent but locally limited squamous cell carcinoma (SCC), and dyslipidemia. His medications included amlodipine, bisoprolol, gabapentin, prednisone, tacrolimus, and warfarin. He had an unremarkable cardiovascular, respiratory, and abdominal physical examination. On neurologic examination, he had a mild anisocoria (right pupil: 3 mm, left pupil: 2 mm, worse in bright light vs dim light) but both pupils were briskly reactive to light and accommodation. His visual acuity was 20/20 bilaterally and he had full visual fields on bedside examination and unremarkable funduscopy. In addition to right ptosis (marginal reflex distance of 3 mm to lower lid margin), he had impaired right eye adduction, elevation, and depression (figure 1). No other deficits were identified.

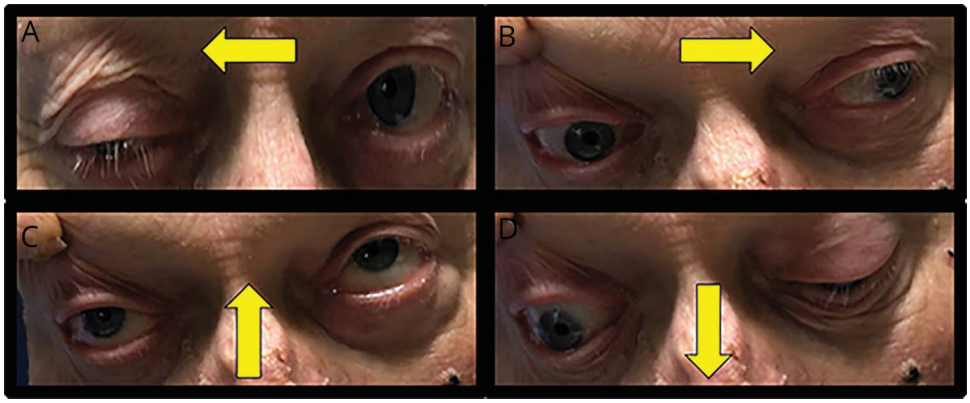
We localized these findings to the right oculomotor nerve. The differential diagnoses considered for these findings included a posterior communicating artery aneurysm resulting in a compressive third nerve palsy given the initial severe nature of the patient's headache

*These authors contributed equally to this work.

From the Departments of Clinical Neurosciences (S.M., A.G., S.S.B.) and Medicine (A.Q., P.M.), University of Calgary, Alberta, Canada.

Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

Figure 1 Physical examination findings of a right oculomotor nerve palsy in a 70-year-old man



Right oculomotor nerve palsy manifesting on examination as marked ptosis with normal abduction on right gaze (A), impaired adduction on left gaze (B), as well as limited elevation (C) and depression (D). In images B–D, the patient's eyelid has been lifted by the examiner.

(10/10), a microvascular third nerve palsy given his vascular risk factors, pituitary apoplexy (PA) given the combination of severe headache and third nerve palsy, infection or metastasis given the history of SCC and immunosuppression, as well as other cavernous sinus pathologies like cavernous sinus thrombosis and Tolosa-Hunt syndrome. Laboratory investigations were unremarkable. The patient's international normalized ratio was therapeutic. A CT scan of the head with angiography was performed (figure 2, A and B). On our independent review of the images, we were suspicious about a possible missed lesion in the sellar region. We admitted the patient for further workup.

The patient received an MRI scan with dedicated sella views, revealing a T1 hyperintense signal involving the pituitary gland with findings in keeping with a subacute hemorrhage in the sella. This was consistent with PA within an adenoma (figure 2, C and D), extending laterally into the superior aspect of the right cavernous sinus and abutting the superior and medial aspect of the right internal carotid artery. Whereas gadolinium-enhanced T1-weighted coronal sequences are typically obtained in this setting, our patient could not receive gadolinium owing to his severe kidney disease.

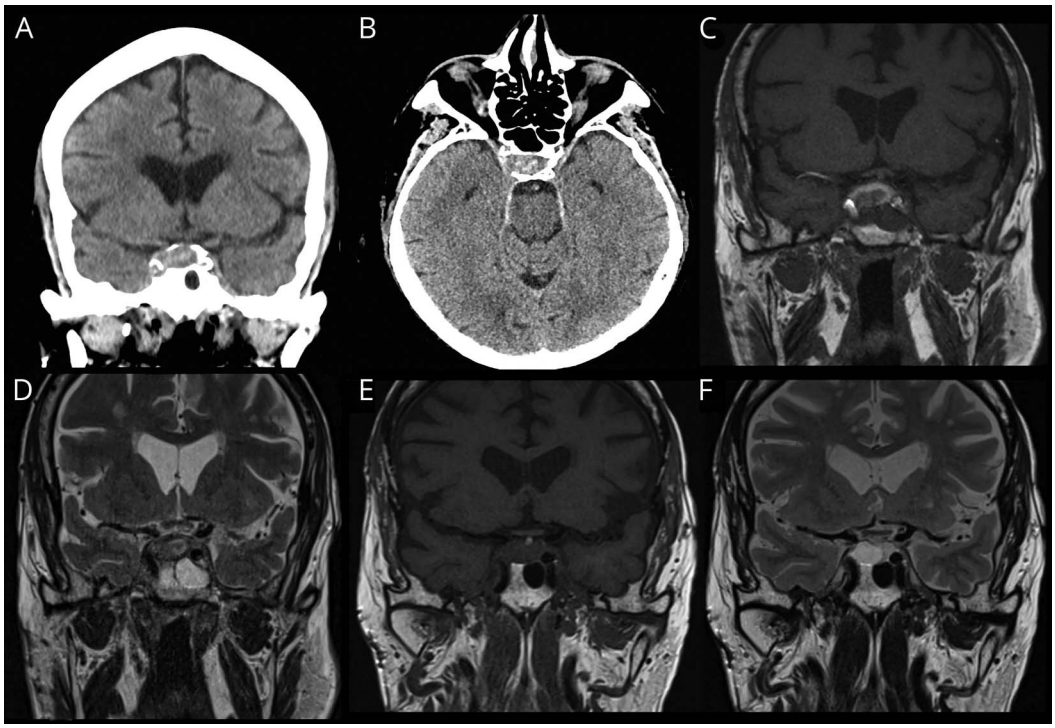
The neurosurgical team was consulted, who deemed surgery high-risk given the patient's comorbidities and recommended monitoring of clinical progression. He was also referred to endocrinology for evaluation of secondary hypopituitarism, which included serum AM cortisol, thyroid-stimulating hormone, free T4, prolactin, insulin-like growth factor 1, luteinizing hormone, follicle-stimulating hormone, and testosterone. There was no corticotropic deficiency, although the patient was already taking prednisone post kidney transplantation. He required levothyroxine replacement. His diplopia and third nerve palsy resolved within 2 months. A 4-month follow-up MRI showed slight decrease in the size of the sellar contents (figure 2, D and E).

Discussion

PA is a rare but potentially fatal medical emergency that can present with a variety of clinical presentations. Most frequently, PA presents as a severe retro-orbital headache and can be accompanied by visual field deficits.[1–3] Other common presentations include changes in level of consciousness, panhypopituitarism, nausea and vomiting, and ophthalmoplegia. Due to the overlap between the presentation of PA and other conditions (including subarachnoid hemorrhage, cervical artery dissection, and cerebral dural sinus thrombosis), PA is not often suspected on initial presentation. In addition, the diagnosis of PA may be missed as its clinical presentation can be acute or subacute with symptom presentation being dependent on the extent of bleeding and edema extension.[4] There are numerous types of pituitary tumors that are known to be associated with PA but the most common types are chromophobe adenomas followed by eosinophilic adenomas; most tumor types associated with PA have been found to be endocrinologically significant.[5] Corticotropic deficiency is the most common endocrinologic deficit in PA, followed by thyrotropic and gonadotropic deficiency.[6]

Given the presentation of a third nerve palsy, it is important to understand the anatomy of the third nerve and the structures with which it is closely related. The third cranial nerve (oculomotor, CN III) nucleus extends in a rostrocaudal fashion near the midline of the midbrain at the level of the superior colliculus.[3] Nuclear oculomotor lesions are rare but can manifest with ipsilateral complete CN III palsy and contralateral ptosis and superior rectus paresis. Each third nerve passes between the superior cerebellar and posterior cerebral arteries in the subarachnoid space and ultimately enters the lateral wall of the cavernous sinus. Lesions of the oculomotor nerve in the cavernous sinus—which can result from compression or infiltration by adjacent sellar lesions—can present as complete CN III palsy and may involve other cranial nerves (IV, V1, V2, or VI).[7] Upon

Figure 2 Pituitary apoplexy within a macroadenoma in a 70-year-old man



(A) Coronal and (B) axial CT head show findings suspicious for a sellar lesion. (C) Coronal T1-weighted MRI brain sellar view shows peripheral T1 hyperintensity within a bulky pituitary gland, measuring 1.7 cm anteroposterior by 2.1 cm mediolateral by 1.3 cm vertical, extending laterally into the superior aspect of the right cavernous sinus and abutting the superior and medial aspect of the right internal carotid artery. (D) Corresponding view on coronal T2-weighted MRI. (E) Coronal T1 and (F) coronal T2 view of sellar contents at 4-month follow-up MRI show chronic blood products in addition to pituitary parenchyma or tumor, now measuring 1.3 × 2.0 × 1.1 cm.

reaching the superior orbital fissure, the oculomotor nerve splits into a superior division supplying the superior rectus and the levator palpebrae superioris and an inferior division that supplies the medial and inferior recti, inferior oblique, and the sphincter pupillae muscle and ciliary muscles. Lesions at the superior orbital fissure may manifest as a CN III palsy with or without additional involvement of CN IV, VI, and V1.

In the cavernous sinus, compressive lesions often involve the other ocular motor nerves and the ophthalmic branch of the trigeminal nerve although isolated third nerve palsies are possible, as seen in our case. Medial lesions in the cavernous sinus including carotid artery aneurysms can selectively affect the ocular motor nerves and spare the laterally located ophthalmic branch of the trigeminal nerve.[3] In contrast, lesions that start laterally can present with retroorbital pain initially and ophthalmoplegias subsequently. In this case, the subacute hemorrhage in the sella extended into the superior aspect of the right cavernous sinus, compressing the right third cranial nerve at this location. Acute onset of a third nerve palsy in PA also has been associated with compression of the vasa nervorum originating in the internal carotid artery, whereas chronic palsy has been associated with compression of the petroclinoid segment against the interclinoid ligament.[7] Given its location within the cavernous sinus, the third cranial nerve tends to be more susceptible to laterally placed compression by an expanding pituitary mass.

In this report, we present a 70-year-old man who developed a right oculomotor nerve palsy secondary to apoplexy within a pituitary adenoma, missed on initial CT, further emphasizing the limitations of CT in diagnosing sellar lesions and specifically PA. MRI brain is therefore the favored mode of imaging for cases with a high degree of suspicion for PA.[4] A key take-home point is maintaining a high degree of suspicion given a new-onset headache accompanied by neurologic findings. Despite a CT scan that was initially reported as unremarkable, our high index of suspicion led us to review the CT images in more detail to assist us in eliciting the diagnosis. This facilitated our approach towards reaching the correct diagnosis. Finally, pursuing more definitive MRI to visualize the sellar region was key in confirming our suspicion of PA.

Study funding

No targeted funding reported.

Disclosure

S. Marzoughi reports no relevant disclosures. A. Ganesh serves on the *Neurology*® editorial board. A. Qaddoura, P. Motazedian, and S.S. Bal report no relevant disclosures. Go to Neurology.org/N for full disclosures.

Appendix Authors

Name	Location	Contribution
Sina Marzoughi, MD	University of Calgary, Canada	Concept, acquisition of data, and writing and revising of the manuscript
Aravind Ganesh, MD, DPhil	University of Calgary, Canada	Concept, acquisition of data, and writing and revising the manuscript
Amro Qaddoura, MD	University of Calgary, Canada	Acquisition of data and critical revision of manuscript for intellectual content
Pouya Motazedian, MD	University of Calgary, Canada	Acquisition of data and critical revision of manuscript for intellectual content
Simerpreet S. Bal, MD, FRCPC	University of Calgary, Canada	Concept and critical revision of manuscript for intellectual content

References

1. Wakai S, Fukushima T, Teramoto A, Sano K. Pituitary apoplexy: its incidence and clinical significance. J Neurosurg 1981;55:187–193.
2. Bonicki W, Kasperlik-Zaluska A, Koszewski W, Zgliczynski W, Wislawski J. Pituitary apoplexy: endocrine, surgical and oncological emergency: incidence, clinical course and treatment with reference to 799 cases of pituitary adenomas. Acta Neurochir 1993;120:118–122.
3. Park HK, Rha HK, Lee KJ, Chough CK, Joo W. Microsurgical anatomy of the oculomotor nerve. Clin Anat 2017;30:21–31.
4. Goyal P, Utz M, Gupta N, et al. Clinical and imaging features of pituitary apoplexy and role of imaging in differentiation of clinical mimics. Quant Imaging Med Surg 2018;8:219–231.
5. Reid RL, Quigley ME, Yen SS. Pituitary apoplexy: a review. Arch Neurol 1985;42:712–719.
6. Briet C, Salenave S, Bonneville JF, Laws ER, Chanson P. Pituitary apoplexy. Endocr Rev 2015;36:622–645.
7. Saul RF, Hilliker JK. Third nerve palsy: the presenting sign of a pituitary adenoma in five patients and the only neurological sign in four patients. J Clin Neuroophthalmol 1985;5:185–193.

Pearls & Oy-sters: Isolated oculomotor nerve palsy due to pituitary apoplexy missed on CT scan

Sina Marzoughi, Aravind Ganesh, Amro Qaddoura, et al.

Neurology 2020;94;e1774-e1777 Published Online before print March 27, 2020
DOI 10.1212/WNL.0000000000009298