Isolated third nerve palsy with pupillary involvement resulting from carotid-cavernous sinus fistula
A case report
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Abstract
Rationale: Isolated third nerve palsy with pupillary involvement caused by a posterior drainage carotid-cavernous sinus fistula (CCF) is relatively rare. Diagnosis of a posterior drainage CCF can often be delayed due to its unapparent congestive signs.

Patient concerns: Here, we present the case of a young male patient with right-sided CCF, who presented with right-side headache and partial third nerve palsy with pupillary involvement. The diagnosis was confirmed using time-of-flight magnetic resonance angiography (TOF-MRA) and digital subtraction angiography (DSA).

Diagnoses: A right-sided CCF was detected, which was primarily supplied by the dural branch of the right middle meningeal artery and venous drainage into the right inferior petrosal sinus.

Interventions: The patient was treated with transarterial coil embolization.

Outcomes: At 2 months, right-side headache was significantly improved and ptosis and limited extraocular muscle movement were partially resolved.

Lessons: CCF might not always present with ocular congestion. Although uncommon, white-eye and painful third nerve palsy with pupillary involvement may be caused by a posterior drainage CCF.

Abbreviations: CCF = carotid-cavernous sinus fistula, CTA = computed tomography angiography, DSA = digital subtraction angiography, MRA = magnetic resonance angiography, TAE = transarterial embolization, TOF-MRA = time-of-flight magnetic resonance angiography.

Keywords: carotid-cavernous sinus fistula, diplopia, oculomotor nerve palsy

1. Introduction
Isolated third nerve palsy with pupillary involvement can result from numerous factors. The most common and life-threatening cause is intracranial aneurysm. Carotid-cavernous sinus fistula (CCF), which commonly presents with ocular congestion, proptosis, and audible bruits, is a rare cause of isolated third nerve palsy. CCF can be classified into “red-eye shunt” and “white-eye shunt” according to its clinical presentation and venous drainage direction.[1] The diagnosis of isolated third nerve palsy resulting from a posterior drainage CCF is easily delayed due to its unapparent congestive signs.[2,3] Here, we present the case of a young male patient with right-side CCF, who initially presented with right-side headache and partial third nerve palsy with pupillary involvement. The diagnosis was confirmed by time-of-flight magnetic resonance angiography (TOF-MRA) and digital subtraction angiography (DSA).

2. Case presentation
A 32-year-old man complained of progressive double vision that persisted for 4 months. He reported to have a medical history of diabetes mellitus for >10 years and a minor head trauma that occurred from a road accident 1 year ago. Two weeks before he visited our outpatient department, he started to experience right-side headache and periorbital pain. He had visited the neurology department at a local clinic, and painkillers were prescribed for the suspected cluster headache. However, the right-side headache did not improve with medication. One week later, he developed sudden onset of right-side partial ptosis. Ophthalmic examination revealed right-side mid-dilated pupil with poor reaction to light and limited right-side extraocular movement with impaired adduction and infraduction (Fig. 1). His best-corrected visual acuity and intraocular pressure of both eyes were normal. Other cranial nerve functions were normal. There was no chemosis, proptosis, conjunctival injection, swollen eyelids, or ocular bruits.
Assuming the presence of acute-onset third nerve palsy with pupillary involvement, emergent computed tomography angiography (CTA) was performed to exclude posterior communicating artery aneurysm. CTA revealed no obvious abnormal findings. MRA was then performed; however, it revealed no significant intracranial lesions. However, TOF-MRA showed a high-signal intensity at the right cavernous sinus (Fig. 2), raising the concern of dural CCF. A neuroradiologist was consulted, and cerebral angiography was performed, confirming a right-side CCF with Barrow type D. The fistula was primarily supplied from the dural branch of the right middle meningeal artery and venous drainage into the right inferior petrosal sinus (Fig. 3). He was treated with...
transarterial embolization (TAE). One month following TAE, his diplopia, ptosis, mid-dilated pupil, and limited extraocular muscle movement problems remained. However, the right-side headache significantly improved. Ptosis and extraocular muscle movement partially improved after 2 months. Informed patient consent was obtained from the patient for publication of this case report.

3. Discussion

CCF is an abnormal communication between the carotid vascular system and cavernous sinus. The clinical presentation of ocular features is primarily associated with the venous drainage pattern and shunt flow rate, rather than the arterial supply.[4] The anterior drainage pattern, which drains into the superior ophthalmic vein or inferior ophthalmic vein, might cause chemosis, exophthalmos, or ocular bruit. This is the so-called red-eye shunt and is usually easier to diagnose compared with white-eye shunt caused by the posterior drainage pattern. The posterior drainage pattern, which drains into the superior petrosal sinus or inferior petrosal sinus, might cause ocular motor nerve palsy without congestive ocular signs. The “white-eye shunt” commonly remains undiagnosed and untreated because of unapparent congestive signs.[1–3]

In the presented case, the patient possessed risk factors for third nerve palsy, namely, diabetes mellitus and minor head trauma. The differential diagnosis of third nerve palsy includes ischemic microvascular disease (diabetes and hypertension), intracranial aneurysm, intracranial tumor, trauma-related, inflammation, and infection. Ischemic microvascular lesions usually have intact pupillary function and spontaneously resolve within 3 months. On the contrary, intracranial aneurysms and other compressive lesions can cause compressive stress on superficial parasymptotic fibers, resulting in incomplete or complete pupillary motor dysfunction. When the patient first visited our department, we suspected intracranial aneurysm. After early imaging excluded aneurysms, we focused on other compressive causes. The posterior drainage CCF is usually not the primary concern among such patients.

However, in numerous cases, delayed diagnosis and treatment might change the flow direction from a posterior drainage pattern to an anterior drainage pattern.[7] In such a condition, the patient might start to develop prominent ocular congestion, which is easily noticeable.

The third cranial nerve, fourth cranial nerve (trochlear nerve), ophthalmic and maxillary divisions of the fifth cranial nerve (trigeminal nerve), and sixth cranial nerve (abducens nerve) pass through the cavernous sinus. The sixth nerve is the only ocular motor nerve not protected within the dural wall. Therefore, theoretically, if only one ocular motor nerve is involved in the cavernous sinus, it is usually the sixth nerve. However, when the shunt drains posteriorly, an isolated third nerve palsy is reported to be the most common compromised nerve, followed by the sixth cranial nerve and then the fourth cranial nerve.[3,5,6] Third cranial nerve involvement can be presented as complete palsy with pupil involvement, incomplete palsy with pupil involvement, or incomplete palsy with pupil sparing.[7] The mechanism by which the third cranial nerve is the most commonly influenced in posterior drainage CCF remains unclear. In the presented case, imaging reveals that the fistula was located at the superior-lateral wall of the cavernous sinus. Anatomically, the third cranial nerve penetrates through the upper lateral part of the cavernous sinus, which increases its susceptibility to compression by dilated sinus.

Diagnostic tools include CT/CTA, MRI/MRA, and DSA. CT/CTA and MRI/MRA are relatively noninvasive and can provide information regarding the size and location of the CCF. Nevertheless, CT/CTA or MRI/MRA image alone sometimes is not sufficient for detecting a fistula.[5,6] Wu et al.[3] have reviewed 11 patients with isolated third nerve palsy caused by CCF and demonstrated that MRI/MRA showed a higher detection rate of isolated third nerve palsy resulting from CCF than did CT/CTA. The detection rate of MRI/MRA was 66.6% (6/9 cases), which still mismatched with that of DSA, suggesting that image evaluation alone is insufficient to provide detailed
information. DSA remains the golden standard method to confirm the diagnosis and complete characterization of CCF.\cite{5,7,12} CT/CTA and MRI/MRA can be used as early screening tools of CCF, which also differentiate other life-threatening causes, including intracranial aneurysms or hemorrhage.

Isolated third nerve palsy arising from a CCF is not exceptional. Similar cases have been reported.\cite{3,5,6,8–11} Yon Kwon Ihn et al.\cite{9} reported a case of isolated third nerve palsy caused by a posterior drainage CCF. The patient underwent coil embolization; improvement of ptosis and diplopia was noted in 2 months. The time to recovery varied from 1 month to 12 months regardless of the treatment method.\cite{5} Generally, the outcome of third nerve palsy caused by CCF is favorable.\cite{6,9} In our case, the patient underwent coil embolization 4 months after symptom onset. Given the long period of compression, his recovery might take months.

4. Conclusion

In patients presenting with isolated third nerve palsy without significant ocular congestion, CCF should be considered as one of the differential diagnosis. Diagnosis and consequent management of posterior drainage CCF are easily delayed. Early MRI/MRA should be performed as an initial study to exclude the possibility of aneurysms and other possible causes. The detection rate of CT/CTA or MRI/MRA is not comparable with that of DSA. DSA should be considered if CCF is not detected in previous radiography.

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