Clinical Reasoning: A 21-year-old woman with right eye swelling and bruising

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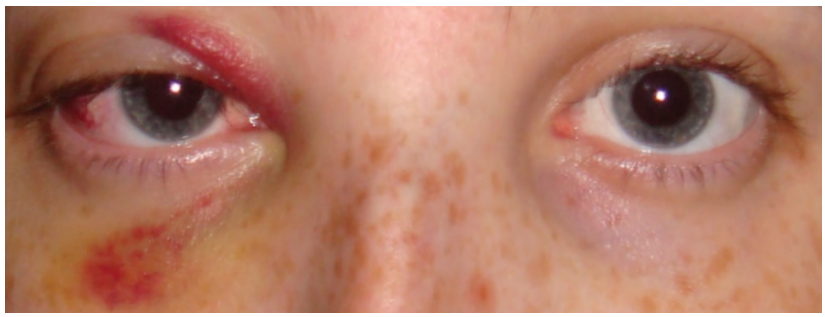
SECTION 1

A 21-year-old woman presented with right eye swelling and bruising. Several weeks prior to admission, she had bifrontal headaches associated with a "whooshing" pulsation in her right ear. She went to a local emergency department where CT scan of the brain was read as negative. One week later, she noticed that her right eye was turned toward her nose. She denied diplopia. On the day of admission, she awoke and noticed bruising under her right eye accompanied by swelling. She also had blurry vision. Her physical examination was remarkable for right eye ptosis, conjunctival injection, and mild proptosis with ecchymosis above and below the eye (figure 1). She was unable to abduct her right eye past midline, visual acuity was 20/30 bilaterally, and her visual fields were intact. There was an ocular bruit auscultated over the right eye.

Questions for consideration:

1. What other history is important to obtain?
2. What is the differential diagnosis?

Figure 1 Initial external eye findings



Right eye ptosis with proptosis, conjunctival injection, and ecchymosis surrounding the right eye.

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SECTION 2

The patient denied any history of trauma. Her past medical history was significant for Ehlers-Danlos type IV, complicated by bowel rupture 6 years prior, necessitating subtotal colectomy and colostomy. She also had chronic migraine and corrective surgery for amblyopia as a child. Family history was significant for her mother who died at age 35 of splenic rupture and maternal grandmother who died at age 43 of subarachnoid hemorrhage. The differential diagnosis included thyroid ophthalmopathy, tumor, infection, inflammation (e.g., Tolosa-Hunt), and carotid cavernous aneurysm or fistula.

Question for consideration:

1. What further testing should be considered?

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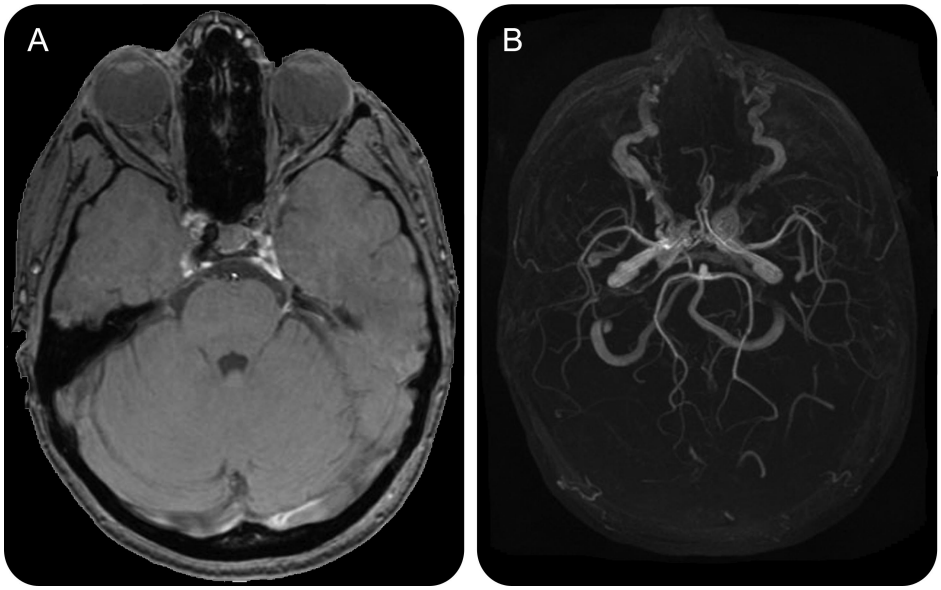
SECTION 3

Magnetic resonance angiography revealed enlarged superior ophthalmic veins bilaterally, right greater than left, with an increased prominence in the right cavernous sinus (figure 2, A and B). The patient was diagnosed with carotid cavernous fistula. She was sent to the ophthalmology clinic where her intraocular pressures (IOP) were 22 mm Hg in the right eye and 12 mm Hg in the left eye. She was started on timolol for increased IOP. Transcranial Doppler revealed accelerated flow and reduced resistance in the right internal carotid siphon.

Questions for consideration:

1. What are the treatment options for a patient with a direct carotid cavernous fistula?
2. How does her diagnosis of Ehlers-Danlos affect her treatment?

Figure 2 MRI



MRI (A) and magnetic resonance angiography (B) showing mild proptosis of the right eye and enlarged ophthalmic veins (R > L), enlarged cavernous sinus (R > L), with multiple fistulous vessels connecting the right and left cavernous sinus.

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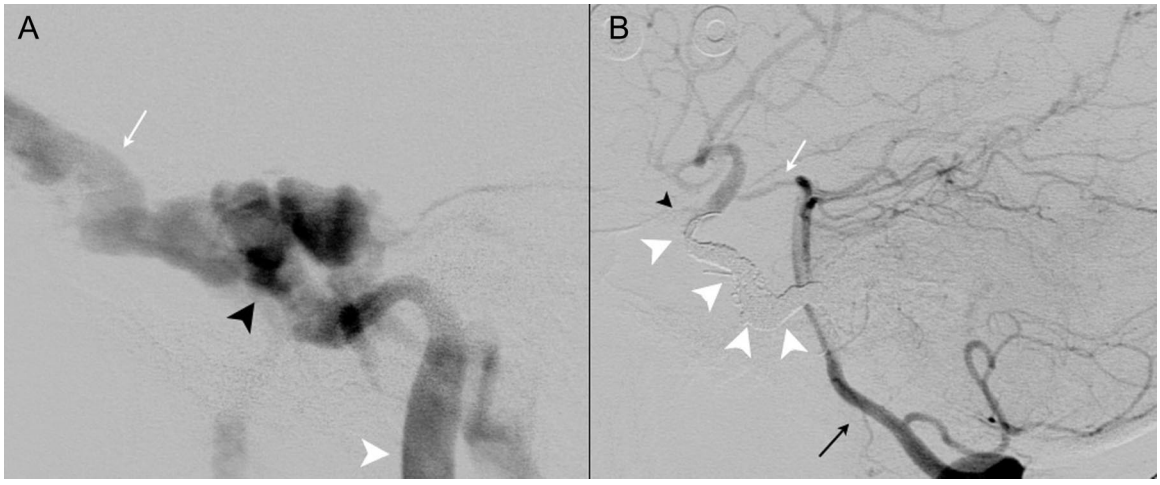
Because the patient had Ehlers-Danlos type IV, she had a high potential mortality rate from angiography alone. Therefore, management decisions had to be made very carefully, with extensive interdisciplinary discussions involving the family. Digital angiography showed complete steal of right internal carotid artery (ICA) flow into the cavernous sinus (figure 3). There was filling of the right middle cerebral artery and anterior cerebral artery via the anterior and posterior communicating arteries. Options for treating the direct carotid cavernous fistula included transarterial coiling via the ICA, transvenous coiling through the superior or inferior petrosal sinus, or ophthalmic approach via the ophthalmic vein. In addition, because of the high rate of treatment complications, the conservative option of observation alone was also considered. The last alternative was discarded because she would likely develop progressive visual loss without intervention. The carotid cavernous fistula was treated with transarterial endovascular coil occlusion extending from the clinoid to the petrous internal carotid artery segment, occluding the fistula between the ICA and the cavernous sinus. Immediately after the procedure, IOP in the right eye normalized to 10 mm Hg. The edema and erythema resolved within 1 day, and she was able to adduct her right eye 10 degrees past midline (figure 4).

DISCUSSION Carotid cavernous fistulas are classified as direct or indirect.[1] Direct fistulas are characterized by carotid arterial blood shunting directly into the venous cavernous sinus, whereas indirect fistulas take place when another vessel connects the internal or external carotid to the cavernous sinus. Indirect fistulas may occur between the meningeal branches of the ICA and cavernous sinus, between the meningeal branches of the external carotid artery and cavernous sinus, or both. Fistulas most commonly occur secondary to trauma, but may happen spontaneously in patients with diseases that weaken the vessel wall, including Ehlers-Danlos.[2-4]

Ehlers-Danlos type IV is an autosomal dominant disorder, associated with easy bruising, thin skin, and spontaneous rupture of bowel, the uterus, or arteries. The disease is caused by mutation of *COL3A1*, which encodes type III collagen.[3] Cultured skin fibroblasts from patients are shown to secrete reduced type III procollagen, which confirms the diagnosis of Ehlers-Danlos. Since arterial vessel walls have impaired collagen formation, this predisposes patients to cerebrovascular complications including arterial dissection, rupture, and aneurysms.[2,4] Although neurologic sequelae arise in a minority of patients, it is a major cause of morbidity and mortality in this disease.[2]

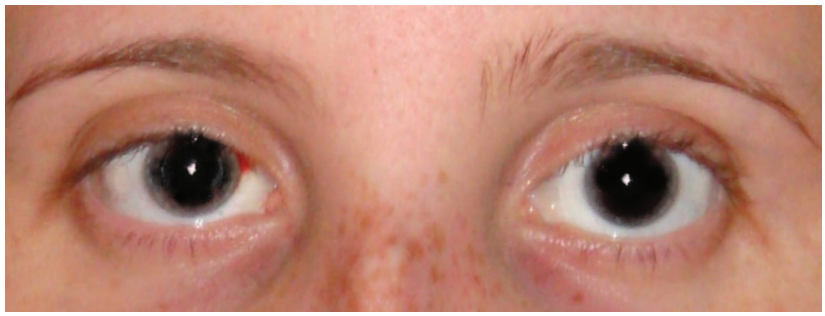
Symptoms of carotid cavernous fistulas are more prominent with patients who have a direct fistula. Patients develop conjunctivitis and chemosis because of high-pressure arterial blood flow in the cavernous sinus transmitted to the ophthalmic veins and conjunctival vessels. Additional symptoms include pulsating exophthalmos from venous congestion in the orbit and decreased visual acuity from optic nerve ischemia. Because the fistula involves the cavernous sinus, cranial nerves III, IV, V1, V2, VI, sympa-

Figure 3 Digital angiography



(A) Magnified lateral view of the fistula at the posterior petrous portion of the right internal carotid artery (ICA) (dark arrowhead) with massively dilated superior ophthalmic vein (white arrow). Total steal of the ICA (white arrowhead) into the fistula is seen. (B) Lateral view of the right vertebral artery injection (dark arrow) shows flow through the posterior communicating artery (white arrow) with back filling to the level of the ophthalmic artery (small dark arrowhead). A coil cast is demonstrated just below the ophthalmic artery extending into cavernous and petrous portion of the ICA (white arrowheads).

Figure 4 External eye findings after coiling



thetic, and parasympathetics may be affected. Ophthalmoplegia may be secondary to cranial nerve palsies from increased pressure in the cavernous sinus or because of engorged extraocular muscles. Sensory changes in the V1 and V2 distribution may also be seen. Ptosis and miosis occur because of parasympathetic involvement. The presence of an ocular bruit is characteristic of carotid cavernous fistulas. Transcranial Doppler of the distal ICA via the ophthalmic or temporal window shows high-velocity and low-resistance flow characteristic of a direct shunt from artery to vein. Venous distension and rupture may lead to intracranial hemorrhage.[5]

Imaging can aid in the diagnosis of carotid cavernous fistula. CT and MRI may both show proptosis of the affected eye, and CT may detect a bony fracture if trauma is the cause. CT and magnetic resonance angiography can diagnose a carotid cavernous fistula by showing ophthalmic vein and cavernous sinus expansion, but it is difficult to distinguish between direct and indirect fistulas by these modalities because the resolution generally does not allow visualization of small vessels connecting the carotid artery and the cavernous sinus. The gold standard is digital angiography, which can demonstrate both the anatomy of the fistula as well as the extent of collateral flow from the contralateral hemisphere, which is important if the treatment requires occlusion of the involved ICA.[6]

Repair of a carotid cavernous fistula is indicated if visual acuity is compromised, IOP is >40 mm Hg, there is retrograde cortical venous drainage from the cavernous sinus causing the patient to be at high risk for intracranial hemorrhage, or neurologic symptoms are unbearable for the patient. Indirect fistulas are more likely to close without intervention by spontaneous thrombosis because of the lower pressure flow. Some studies show that repeated, intermittent carotid compression performed by patients may be used to successfully close these fistulas.[7]

For direct fistulas, repair is usually achieved through closure of the fistula by endovascular techniques. The transarterial approach involves directing a catheter from the femoral artery to the internal carotid, and then placing detachable coils in the arterial tear to close off the fistula. Complete occlusion of the ICA at the site of the fistula may be necessary, but this can only be accomplished safely if the contralateral ICA or PCA provides adequate collateral flow to supply the ipsilateral hemisphere.[4,6] A balloon test occlusion can be performed prior to ICA takedown to determine adequacy of collateral flow. The transvenous approach is reserved for patients with dissections or stenosis of the carotid artery that would make transarterial approach difficult. In the transvenous approach, a catheter is placed into the femoral vein and threaded through the inferior petrosal vein to the cavernous sinus. This approach can be challenging, as the opening of the inferior petrosal into the cavernous sinus is small. Another transvenous approach involves directly inserting a catheter through the superior ophthalmic vein into the cavernous sinus.[8] In some cases, direct surgical closure may be warranted.[9]

In the general population, angiography carries a risk of 2.5% morbidity, but in patients with Ehlers-Danlos type IV, angiography has been associated with morbidity rates of 36%–67% because of the increased risk of carotid dissection, arterial perforation, and hematoma.[4,10] Both the transarterial and transvenous approaches carry these high risks because of the fragility of the vessels. Arteries in these patients are also often more tortuous, making it difficult to navigate a catheter through the vasculature.[4]

DISCLOSURE

Dr. Ruff, Dr. Strozyk, Dr. Rahman, and Dr. Szeder report no disclosures. Dr. Pile-Spellman has filed patents re: Adjustable tubular medical device including a catheter; Systems and methods for determining a temperature differential using temperature sensitive magnetic resonance imaging; Systems and methods for imaging a blood vessel using temperature sensitive magnetic resonance imaging; Systems and methods for determining metabolic rate using temperature sensitive magnetic resonance imaging; Systems and methods for determining a cardiovascular parameter using temperature sensitive magnetic resonance imaging; Systems and methods for intravascular cooling; System for autonomous robotic navigation; En-

dovascular brush; Devices and methods for protecting against distal embolisms; and Steerable devices; and is a founder of Hybernia Medical, LLC. Dr. Marshall has filed a patent re: Novel use of a drug for post-stroke dystonia; receives royalties from the publication of *OnCall Neurology* (Elsevier, 2003-present); has received speaker honoraria from Ferrer International SA; and receives research support from the NIH/NINDS (R01 NS048212-01A1 [PI], 5P50NS049060 [PI], 3P50NS049060-05S109 [PI], and NS42167 [Coinvestigator]).

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