Carotid cavernous fistula presenting as orbital cellulitis

Christopher J Peterson MD, MS, Benjamin Lee BS, and Mark D. Lacy MD

Abstract

Carotid cavernous fistula is a serious vascular disorder that is commonly misdiagnosed due to clinical signs that overlap with several other diagnoses and the need for sensitive imaging techniques, most notably digital subtraction angiography, to make the diagnosis. Here we present a case of carotid cavernous fistula mimicking orbital cellulitis, ultimately diagnosed with magnetic resonance venography.

Keywords: carotid cavernous fistula, cellulitis, embolization

Introduction

Carotid cavernous fistulas (CCFs) are arteriovenous shunts between the internal or external carotid arteries and the cavernous sinus.[1] They are classified as either direct (internal carotid artery) or indirect (external carotid artery or internal carotid artery branches).[1] They can be further classified using the Barrow classification system based on specific vascular communications: internal carotid (Type A), dural meningeal branches of internal carotid (Type B), dural meningeal branches of external carotid (Type C), and dural meningeal branches of both internal and external carotid (Type D).[2]

The cavernous sinus (CS) represents a unique site for fistulation as it completely envelopes the internal carotid artery as it travels anterodorsally to feed the ophthalmic artery and the cerebrum. This apposition of major venous and arterial structures creates an area of high risk if disrupted and can quickly lead to high flow fistulations, as a disruption in continuity of the carotid through this section would constitute immediate fistula. The cavernous sinus receives inflow from the sphenoparietal sinus and superior/inferior ophthalmic veins and outflows to the superior and inferior petrosal sinuses.[3] The external carotid artery is also at risk for fistulation with the cavernous sinus due to the proximity of the middle meningeal artery and its branches to the cavernous sinus, as seen in Barrow type C and D CCFs. Cranial nerves can be affected either due to their course through the cavernous sinus (III, IV, V1, V2) or their proximity to the internal carotid/venous sinusoids of CS contributing to potential targeted neuropathies.[3]

Corresponding author: **Christopher J Peterson**
Contact Information: Cjpeterson1@carilionclinic.org
DOI: 10.12746/swrccc.v11i46.1091

Case Report

A 68-year-old woman presented to the emergency department with a 5-day history of swelling and redness of the right eye with right periorbital erythema and vision obstruction. The patient had been admitted 4 days before to an outside hospital for nausea and vomiting, was given unspecified ophthalmic drops for suspected conjunctivitis, and discharged after 3 days. Her past medical history included hypertension, chronic obstructive pulmonary disease, chronic idiopathic thrombocytopenic purpura (ITP) s/p splenectomy, provoked deep venous thrombosis (DVT) (right thigh), and stage III renal cancer being treated with capecitabine and radiation therapy. Home medications included eltrombopag (50 mg daily), azathioprine (10 mg), and prednisone (10 mg BID). On the day of this presentation, the patient was seen by her primary care provider and had a computed tomography (CT) scan at an outside facility suggestive of periorbital cellulitis; she

was then transferred to our facility for a higher level of care. The patient denied blurry vision, pain with ocular movement, or ocular trauma. Physical examination revealed 4+ lid edema, 3+ hemorrhagic chemosis OD, with brunescent cataract, and she was subsequently diagnosed with periorbital cellulitis. Based on the ophthalmology consultant's recommendation, she was started on intravenous vancomycin (1.25 g BID) and cefepime (2 g BID) for periorbital cellulitis. On admission, labs were significant for a white blood cell count of 12.98 K/μL and a platelet count of 47 K/μL. Hematology was consulted due to her thrombocytopenia and history of ITP; these consultants initially recommended continuing azathioprine (25 mg daily) and prednisone (5 mg every other day), but discontinued the azathioprine on hospital day (HD) 3 due to lack of response (i.e., down-trending platelets). Intravenous immunoglobulin was started to treat thrombocytopenia (15 g on HD 3, 15 g on HD 5, and 30 g on HD 25). Infectious disease was consulted, cefepime was also discontinued on HD 3, and metronidazole (500 mg TID) and ceftriaxone (2 g BID) were added.

Magnetic resonance imaging (MRI) of the head with and without contrast on HD 3 showed findings consistent with cellulitis, inflammatory sinus changes, and a Chiari malformation with possible syrinx. A follow-up cervical MRI was planned, but the patient refused due to anxiety. Neurosurgery was consulted for the Chiari malformation and recommended surgery on HD 4, but the patient declined surgical intervention. On HD 5, maxillofacial CT showed periorbital edema and contrast enhancement of the right orbit with no post-septal edema and no intraconal or extraconal mass. Due to persistent periorbital swelling, high dose IV methylprednisolone (250 mg q6h) was started on HD 9. The ENT consultation service evaluated her on HD 11 to rule out sinus involvement, found none, and signed off. Magnetic resonance venography (MRV) and a repeat MRI were attempted on HD 13 but were delayed due to patient anxiety.

The clinical course was now worsening with the development of periorbital ecchymosis. On HD 14, CT and MRI of the head continued to show findings consistent with cellulitis and found no evidence of drainable abscess or mass in the right superior ophthalmic vein. However, MRV showed cavernous sinuses and superior ophthalmic veins patency, suspicious for a cavernous sinus fistula. Given this, a cerebral angiogram was performed on HD 17 and showed a direct right carotid-cavernous fistula with a rupture point on the dorsal aspect of the right internal carotid with rapid venous outflow through the superior orbital vein (Figure 1). The fistula was embolized on HD18 using an endovascular sheath deployed through the femoral

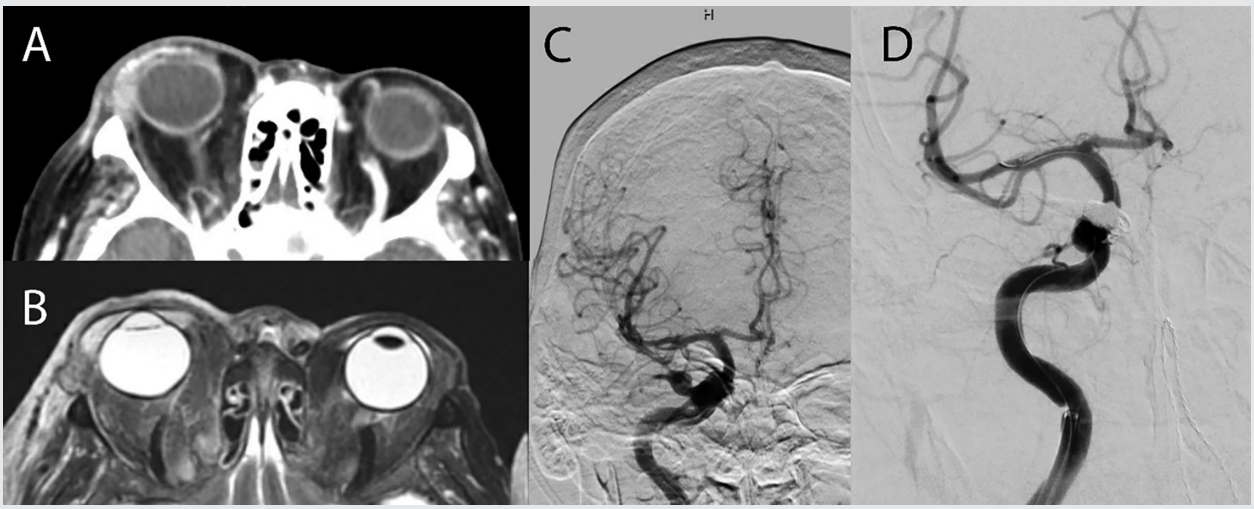

Figure 1. (**A**) CT Head w/ contrast on HD1, (**B**) MRI Head w/wo contrast HD14 prior to embolization, (**C**) HD16 pre-embolization, (**D**) HD17 post-embolization.

artery with confirmed hemostasis and no residual fistula. Patient had rapid improvement in symptoms and was discharged on HD 21 with appropriate follow-up.

Discussion

Direct CCFs are usually due to traumatic injury, represent 70–75% of CCFs encountered, are typically high flow connections, and are usually found in young males; CCF is rare in children (only 4% of all reported CCF cases).[4] Trauma and iatrogenic injuries are the most common etiologies,[5] with the presentation of these cases typically being abrupt.[6] Direct CCFs have been seen due to iatrogenic injury following mechanical thrombectomy[7] and transsphenoidal surgery.[8,9]

Indirect CCFs (Types B–D) are caused by rupture of the dural branches of the carotid artery, most commonly found in older female patients predisposed to vascular injury with risk factors, including atherosclerosis, diabetes, hypertension, and collagen diseases,[6] such as Ehlers-Danlos syndrome.[10,11] In fact, vascular diseases like fibromuscular dysplasia can make CCF possible even after minor stresses, such as cough[12] or the Valsalva maneuver.[13] Indirect fistulas typically occur with vascular disorders (e.g., aneurysm, Ehlers-Danlos) and are less likely to be high flow as these structures are not directly apposed with the cavernous sinus as is the cavernous segment of the internal carotid. Indirect fistulas must travel through other structures to form a fistula and are more likely to have an insidious onset.[1]

In this case, the pathogenesis is unclear, but it may have been due to increased intravascular pressure from vomiting due to chemotherapy agents, which the patient was taking prior to admission. There is no evidence of blunt or iatrogenic trauma in our patient. Whatever the initial breach of vessel integrity, a small vascular insult persisted and enlarged due to the immune thrombocytopenic purpura that the patient also had prior to the onset of this condition.

Misdiagnosis of CCF is common, with one estimate as high as 45%, with the most common misdiagnosis being infectious conjunctivitis.[14] Carotid cavernous fistula has also been mistaken for other diseases, including Graves ophthalmopathy,[15–17] hemicrania continua,[18] and myasthenia gravis, for which nerve stimulation neuromonitoring can be helpful.[19,20] Cellulitis is also commonly misdiagnosed[21] and can mimic other conditions with estimates of misdiagnosis as high as 74%.[22] It has been recommended that dermatology consultations could reduce the number of inappropriate antibiotics prescribed and significantly reduce unnecessary costs to patients and hospitals.[23] Given the impressive nature of the periorbital swelling and discoloration, as well as the acute onset of this patient's presentation, cellulitis is an important diagnosis to rule out. However, given the lack of improvement with antibiotics, a digital subtraction angiography might have been considered sooner since it is the gold standard for diagnosis of CCF.[12]

Diagnosis of CCF can be suggested by a clinical presentation of targeted neuropathies, ocular bruits, although this is rare and more likely detected during Valsalva maneuvers, extraocular swelling, tortuous vessels in the eye, signs of venous congestion in the eye, restriction of extraocular muscles, and swelling of extraocular tissues and muscles on CT or MRI.[24] CCF should be considered in the differential diagnosis, especially with recent trauma, transsphenoidal surgery, or a history of vascular fragility. However, gold standard diagnosis is obtained through digital subtraction angiography, and this should be performed before any treatment is initiated.[24] Less common symptoms of CCF include hypopituitarism,[25] massive epistaxis,[26] migraine-like headache symptoms, though not common,[27] seizures, and cranial nerve deficits.[28] Other diagnostic tests to consider are ocular pressure comparison with standard tonometry, pneumotonometry, or ultrasound.

Treatment of CCF has both surgical and nonsurgical options; 20–60% of low-flow CCF will spontaneously thrombose.[29] First-line therapy is endovascular treatment with coils or liquid embolization. The transarterial route is recommended for high-flow CCF and transvenous route for low-flow CCF. Adverse outcomes are more likely among those with Ehlers-Danlos syndrome due to vascular fragility.[30] Surgical options, including, clipping or suturing the ICA, are more invasive but definitive treatment options. For low-flow CCF, patient-administered carotid compression and

radiotherapy can be considered, but radiotherapy may require months to years of treatment to be successful.

In summary, we present a case of carotid-cavernous fistula mimicking periorbital cellulitis treated with transarterial embolization. To our knowledge, this is the first reported case of carotid cavernous fistula mimicking periorbital cellulitis.

Article citation: Peterson CJ, Lee B. Lacy MD. Carotid cavernous fistula presenting as orbital cellulitis. The Southwest Respiratory and Critical Care Chronicles 2023;11(46):39–43
From: Department of Internal Medicine (CJP), Virginia Tech School of Medicine, Roanoke, VA; School of Medicine (BL), Texas Tech University Health Sciences Center, Lubbock, TX; College of Engineering (BL), Texas Tech University, Lubbock, TX; Department of Internal Medicine (MDL), School of Medicine, University of New Albuquerque, NM
Submitted: 9/25/2022
Accepted: 12/16/2023
Conflicts of interest: none

References

1. D'Angelo L, Paglia F, Caporlingua A, et al. Atypical manifestation of direct low-flow carotid-cavernous fistula: case report and review of the literature. *World Neurosurg.* 2019;125: 456–460.
2. Gorner AT, Luong M. Carotid cavernous fistula presenting as common red eye. *Cjem.* 2021;23(1):123–125.
3. Munawar K, Nayak G, Fatterpekar GM, et al. Cavernous sinus lesions. *Clinical Imaging.* 2020;68:71–89.
4. Morais BA, Yamaki VN, Caldas J, et al. Post-traumatic carotid-cavernous fistula in a pediatric patient: a case-based literature review. *Childs Nerv Syst.* 2018;34(3):577–580.
5. Kohli GSP, Bhupendra C. Carotid Cavernous fistua. StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK535409/. Published 2021. Accessed.
6. Bailey CR, Ray-Mazumder N, Sedighi Manesh R. Carotid Cavernous Fistula. *J Gen Intern Med.* 2017;32(4):483–484.
7. Grüter BE, Kahles T, Anon J, et al. Carotid-cavernous sinus fistula following mechanical thrombectomy in acute ischaemic stroke: a rare complication. *Neuroradiology.* 2021;63(7): 1149–1152.
8. Cossu G, Al-Taha K, Hajdu SD, et al. Carotid-cavernous fistula after transsphenoidal surgery: a rare but challenging complication. *World Neurosurg.* 2020;134:221–227.
9. Lister RJ, Yonas H, Sypert GW. Traumatic false aneurysm and carotid-cavernous fistula: a complication of sphenoidotomy. *Neurosurgery.* 1979;5(4):473–475.
10. Girardin M, Puzenat E, Humbert P, et al. [Bilateral spontaneous carotid-cavernous fistula revealing Ehler-Danlos disease]. *Ann Dermatol Venereol.* 2013;140(4):296–299.
11. Mitsuhashi T, Miyajima M, Saitoh R, et al. Spontaneous carotid-cavernous fistula in a patient with Ehlers-Danlos syndrome type IV–case report. *Neurol Med Chir (Tokyo).* 2004; 44(10):548–553.
12. Simić S, Radmilo L, Villar JR, et al. Hemicranial Cough-Induced Headache as a First Symptom of a Carotid-Cavernous Fistula-Case Report. *Medicina.* 2020;56(4):194.
13. Qi Y, Liu H, Jia J, et al. Endovascular treatment for spontaneous carotid cavernous sinus fistula caused by fibromuscular dysplasia: A rare case report and literature review. *Clin Neurol Neurosurg.* 2020;195:105882.
14. Jacobs SM, Arias EJ, Derdeyn CP, et al. Carotid cavernous sinus fistulas without superior ophthalmic vein enlargement. *Ophthalmic Plast Reconstr Surg.* 2015;31(3):191–196.
15. Celik O, Buyuktas D, Islak C, et al. The association of carotid cavernous fistula with Graves' ophthalmopathy. *Indian J Ophthalmol.* 2013;61(7):349–351.
16. Loré F, Polito E, Cerase A, et al. Carotid cavernous fistula in a patient with Graves' ophthalmopathy. *J Clin Endocrinol Metab.* 2003;88(8):3487–3490.
17. Grados A, Matonti F, Maalouly G, et al. [Carotid-cavernous sinus fistula: an unusual cause of exophthalmia. Report of three cases]. *Rev Med Interne.* 2012;33(7):396–400.
18. Arnold Fiebelkorn C, Lanzino G, Chen JJ, et al. Carotid cavernous fistula mimicking hemicrania continua: a case report. *Headache: The Journal of Head and Face Pain.* 2019;59(8): 1365–1369.
19. Eswar A, Pomeranz HD, Vishnubhakat SM, et al. Carotid-cavernous fistula as a mimicker of myasthenia gravis. *Surg Neurol Int.* 2014;5:140.
20. Leishangthem L, Satti SR. Indirect carotid cavernous fistula mimicking ocular myasthenia. *BMJ Case Reports.* 2017;2017: bcr-2017-222048.
21. Raff AB, Kroshinsky D. Cellulitis: A review. *Jama.* 2016; 316(3):325–337.
22. Strazzula L, Cotliar J, Fox LP, et al. Inpatient dermatology consultation aids diagnosis of cellulitis among hospitalized patients: A multi-institutional analysis. *J American Academy of Dermatology.* 2015;73(1):70–75.

23. Li DG, Xia FD, Khosravi H, et al. Outcomes of Early Dermatology Consultation for Inpatients Diagnosed With Cellulitis. *JAMA Dermatol.* 2018;154(5):537–543.
24. Henderson AD, Miller NR. Carotid-cavernous fistula: current concepts in aetiology, investigation, and management. *Eye.* 2018;32(2):164–172.
25. Yarandi SS, Khoshnoodi MA, Chandra P. Hypopituitarism caused by carotid cavernous fistula. *Intern Med.* 2011; 50(10):1105–1108.
26. Mankahla N, LeFeuvre D, Taylor A. Delayed massive epistaxis from traumatic cavernous carotid false aneurysms: A report of two unusual cases. *Interv Neuroradiol.* 2017; 23(4):387–391.
27. Yamada SM, Masahira N, Shimizu K. A migraine-like headache induced by carotid-cavernous fistula. *Headache.* 2007;47(2):289–293.
28. Klevtsova E, Nguyen-Min C, Lalani T, et al. Posttraumatic carotid cavernous fistula that presented as seizure and focal neurological deficits with symptom resolution after therapeutic coil embolization. *J Emerg Med.* 2015;48(2):186–190.
29. Tiwari S, Garg PK, Khera PS, et al. Delayed Spontaneous Thrombosis of Neglected Direct Carotid-Cavernous Fistula: A Case Report. *Neurointervention.* 2020;15(2):96–100.
30. Schievink WI, Piepgras DG, Earnest FT, et al. Spontaneous carotid-cavernous fistulae in Ehlers-Danlos syndrome Type IV. Case report. *J Neurosurg.* 1991;74(6):991–998.