TWO CASES OF DIPLOPIA CAUSED BY ARTERIOVENOUS FISTULAS AND A SHORT LITERATURE REVIEW

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Introduction: Dural arteriovenous fistulas (dAVFs) are vascular abnormalities involving abnormal connections between branches of the carotid or vertebral arteries and the dural leaflets of the venous sinuses. The most common location is the transverse–sigmoid sinus junction, although they may also occur in the cavernous sinus, in which case they are referred to as carotid–cavernous fistulas. Their clinical course depends mainly on the pattern of venous drainage. **Case presentation:** We present two cases from our department who presented to the Emergency Department with several months' history of diplopia. Clinical examination showed impaired abduction of the left eye, left eye proptosis and redness. The first patient had undergone imaging studies prior to admission and, in conjunction with the clinical findings, digital subtraction angiography (DSA) was deemed necessary, establishing the diagnosis of bilateral direct carotid–cavernous fistulas (Barrow type A). The second patient underwent brain and neck magnetic resonance imaging and angiography, which revealed multiple arteriovenous fistulas involving branches of the left external carotid artery and the ipsilateral internal jugular vein, with retrograde venous flow into the inferior petrosal sinus, the ipsilateral sigmoid sinus, the left superficial middle cerebral vein, the left inferior ophthalmic vein, as well as the left sigmoid and transverse sinuses (Cognard type IIa+b or Borden type II). **Conclusions:** Cranial nerve palsy even in the absence of overt signs of venous congestion does not exclude the presence of an arteriovenous malformation of the central nervous system. When clinical findings suggest a possible vascular aetiology, or when routine diagnostic work-up is inconclusive, appropriate imaging studies should be performed to ensure accurate diagnosis and optimal management.

Keywords: Arteriovenous fistula; carotid-cavernous sinus fistula; diplopia; magnetic resonance angiography; ophthalmoplegia

ΔΥΟ ΠΕΡΙΣΤΑΤΙΚΑ ΔΙΠΛΩΠΙΑΣ ΟΦΕΙΛΟΜΕΝΗΣ ΣΕ ΑΡΤΗΡΙΟΦΛΕΒΩΔΕΙΣ ΕΠΙΚΟΙΝΩΝΙΕΣ ΚΑΙ ΣΥΝΤΟΜΗ ΑΝΑΣΚΟΠΗΣΗ ΤΗΣ ΒΙΒΛΙΟΓΡΑΦΙΑΣ

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Εισαγωγή: Οι αρτηριοφλεβώδεις επικοινωνίες σκληράς μήνιγγας (dAVF) αποτελούν αγγειακές ανωμαλίες μεταξύ κλάδων των καρωτίδων ή των σπονδυλικών αρτηριών και των πετάλων της σκληράς μήνιγγας των φλεβωδών κόλπων. Η περιοχή συχνότερης εντόπισης είναι η συμβολή του εγκάρσιου με τον σιγμοειδή κόλπο, ενώ μπορεί να εμφανιστούν και στο σηραγγώδη κόλπο. Στην τελευταία περίπτωση ονομάζονται καρωτιδοσηραγγώδεις επικοινωνίες. Η κλινική τους πορεία εξαρτάται κυρίως από φλεβική παροχέτευση. **Παρουσίαση περιστατικών:** Παρουσιάζουμε 2 περιστατικά της κλινικής μας που προσήλθαν στο Τμήμα Επειγόντων Περιστατικών του νοσοκομείου μας λόγω διπλωπίας από μηνών. Η κλινική εξέταση ανέδειξε διαταραχή απαγωγής του αριστερού οφθαλμού με συνοδό εξόφθαλμο και ερυθρότητα. Η πρώτη ασθενής προσκόμισε απεικονιστικό έλεγχο που είχε διενεργηθεί προ της νοσηλείας και σε συνδυασμό με την κλινική της εικόνα κρίθηκε σκόπιμη η διενέργεια Ψηφιακής Αφαιρετικής Αγγειογραφίας (DSA) που έθεσε τη διάγνωση της καρωτιδοσηραγγώδους επικοινωνίας άμεσης επικοινωνίας αμφοτερόπλευρα (κατηγορία Α

ΕΛΛΗΝΙΚΗ ΝΕΥΡΟΛΟΓΙΚΗ ΕΤΑΙΡΕΙΑ

κατά Barrow). Ο δεύτερος ασθενής υπεβλήθη σε μαγνητική τομογραφία και αγγειογραφία εγκεφάλου και τραχήλου που ανέδειξαν πολλαπλές αρτηριοφλεβώδεις επικοινωνίες μεταξύ κλάδων της αριστερής έξω καρωτίδας και της ομόπλευρης έσω σφαγίτιδας με ανάδρομη αρτηριακή ροή στον κάτω λιθοειδή σηραγγώδη κόλπο, στο σύστοιχο σιγμοειδή κόλπο, στην αριστερή επιπολή μέση εγκεφαλική φλέβα, στην αριστερή κάτω οφθαλμική φλέβα καθώς και στον αριστερό σιγμοειδή και εγκάρσιο κόλπο (κατηγορία κατά Cognard IIa+b ή κατά Borden II). **Συμπεράσματα:** Η πάρεση κρανιακού νεύρου ακόμα και χωρίς σημεία συμφόρησης δεν αποκλείει την ύπαρξη αρτηριοφλεβώδους δυσπλασίας κεντρικού νευρικού συστήματος. Όταν η κλινική σημειολογία υποδεικνύει πιθανή αγγειακή αιτιολογία ή ο λοιπός παρακλινικός έλεγχος είναι αρνητικός πρέπει να διενεργείται ο κατάλληλος απεικονιστικός έλεγχος για την ορθή διάγνωση και αντιμετώπιση της νόσου.

Two patients, a 78-year-old woman and a 65-year-old man, visited our Emergency Department due to blurred vision and diplopia that started 3 months and 2 months respectively before their admission. Both patients reported that the vision blurring preceded the diplopia. The neurological examination of the first patient showed diplopia with dysfunction of the left eye abduction, left eye proptosis, conjunctival injection, bilateral eyelid swelling and left eyelid ptosis with a positive ice pack test (defined as 2mm improvement), while the rest neurological examination revealed no other focal neurological deficit. Neurological examination of the second patient revealed dysfunction of the left eye abduction and diplopia at the leftward gaze, left eye proptosis, bilateral eye redness, while the rest of the neurological examination was unremarkable. Both patients had normal testing of thyroid function, while the first patient had also a negative testing for antibodies associated with Myasthenia Gravis.

The first patient underwent magnetic resonance imaging (MRI) examinations before coming to our Emergency Department, which showed dilation of right ophthalmic vein. Further work-up with Magnetic Resonance Angiography (MRA) verified this and demonstrated additional findings indicating a Carotid-Cavernous-Fistula (**Figure 1A-B**). Thus, a Digital Subtraction Angiography was performed confirming the diagnosis by displaying bilateral Carotid-Cavernous-Fistulas (**Figure 1 C-D**). Regarding the second patient, imaging studies were performed during hospitalisation. Brain MRI and Orbit MRI showed enlargement of the left superficial middle cerebral vein, as well as abnormal signal in the left transverse sinus and the ipsilateral sigmoid sinus. For further evaluation of the above findings, MRA of the intracranial and cervical arteries was performed, which revealed arteriovenous shunts between branches of the left external carotid artery (the most prominent of which being the ascending pharyngeal artery) and the ipsilateral internal jugular vein. Areas of retrograde venous flow were also depicted, affecting the inferior petrosal venous sinus, cavernous sinus, left superficial middle cerebral vein, left inferior ophthalmic vein and left sigmoid and transverse sinus (**Figure 1 E-F-G-H**).

As a result, according to angiography findings, our first patient suffered from bilateral direct ICA-cavernous sinus fistulas (CCF categorised as type A according to the Barrow classification).[1] Interestingly, she had eyelid ptosis with a positive ice pack test which is indicative of a neuromuscular junction deficit leading to diagnostic pitfall. This underlies the importance of imaging studies when additional clinical findings and/or seronegativity are present.

On the other hand, our second patient had a jugular bulb/transverse-sigmoid sinus dural AVF with retrograde flow in dural sinuses and cortical venous reflux (Cognard type IIa+b or Borden type II dural AV fistula), which is a non-cavernous DAVF mimicking a CCF.[2] Both patients were referred to the Interventional Radiology Department for assessment and further treatment.

Arteriovenous fistulas (AVFs) are abnormal communications between an artery and a vein that result in shunting of blood from the former to the latter. These vascular lesions are uncommon. They can range from asymptomatic to fatal depending on the location. Their cause can vary from congenital to surgically created for hemodialysis treatments or pathologic processes, such as neoplasms, trauma, or erosion of an arterial aneurysm.[3]

Dural arteriovenous fistulas (dAVF) are vascular abnormalities in which arteries arising from branches of the carotid or vertebral arteries drain directly into the dural leaflets of the venous sinuses. The transverse-sigmoid junction is the most common location, with a slight left-sided predominance. They can also be found at tentorial, petrosal, ethmoidal, Sylvian, cavernous sinus, spinal dura, and superior sagittal sinus locations. Histopathologic examination has showed that the main abnormality in dAVFs is a connection between the dural arteries and veins within the venous sinus wall via small vessels, 30 micrometres on average. In some cases, neovascularisation is induced by a thrombosis in a dural venous sinus. The clinical course of dAVFs, including the risk of intracranial hypertension and haemorrhage depends mostly on the venous drainage patterns.[4] The two most well-known classification systems used for predicting the aggressiveness of dAVFs are the Borden (based on the direction of flow and presence of cortical venous drainage) and the Cognard (based on the

location, the direction of flow, presence of cortical venous drainage, and presence of venous ectasia). Our second case corresponds to Cognard type IIa+b (drainage into a venous sinus, retrograde flow, reflux into cortical veins with a 66% risk of haemorrhage with or without intracranial hypertension) or Borden type II (anterograde flow into a dural venous sinus with retrograde cortical venous reflux and a 39% aggressive behaviour) classifications.[1,2,4]

Carotid cavernous fistulae (CCF), a type of intracranial AVF, represent abnormal arteriovenous communications, in which arterial blood from the carotid system enters the cavernous sinus, resulting in elevated sinus pressure. CCFs are characterized as direct when they arise from the internal carotid artery (ICA) proper, most commonly via a ruptured cavernous segment aneurysm, or from traumatic ICA injury or indirect, in which the arterial supply is via dural branches of the ICA and/or external carotid artery (ECA) to the cavernous sinus. The Barrow classification is the most commonly used system to stratify CCFs. Type A fistulae, such as the one depicted in patient one, are characterized as a direct, high-flow shunt between the ICA (intracavernous) and cavernous sinus, whereas types B to D constitute variants of dural arteriovenous fistulae (dAVF) between the cavernous sinus and arterial feeders from the internal carotid artery only in type B, meningeal branches of the external carotid artery in type C, and type D by contributions from both carotid systems.[1]

In 2015, Thomas et al. proposed a new classification system for CCFs based on venous drainage:[6]

Type 1—posterior/inferior venous drainage only (inferior petrosal sinuses, superior petrosal sinus, pterygoid, and parapharyngeal plexus)

Type 2—posterior/inferior and anterior venous drainage

Type 3—anterior venous drainage only (superior and inferior ophthalmic veins)

Type 4—retrograde cortical venous drainage (superficial middle cerebral veins, perimesencephalic, and cerebellar venous system)

Type 5—direct ICA-cavernous sinus fistulae (type A Barrow classification).

The cavernous sinus is located in the parasellar region at the confluence of the anterior and central skull base. In addition to venous blood, the cavernous sinus contains the cavernous segment of the ICA and multiple cranial nerves, including the oculomotor (III), trochlear (IV), abducens (VI), and the ophthalmic (V1) and maxillary (V2) components of the trigeminal. It also receives input from the superior and inferior ophthalmic veins, Sylvian veins, and veins associated with the anterior and middle fossae and communicates with surrounding dural venous sinuses, such as the basilar or clival sinus, the inferior and superior petrosal sinuses, and the sphenoparietal sinus, as well as the pterygoid plexus. Each cavernous sinus is interconnected via the inferior and superior intercavernous sinuses.[5]

Clinical manifestations of CCFs vary widely and are largely determined by the pattern of arterial supply and, more importantly, venous drainage. Direct CCFs usually produce more pronounced symptoms because of their high-flow shunting. In contrast, indirect dural fistulas often develop spontaneously and may present with subtle ocular findings, such as chronic conjunctival injection related to low-grade episcleral venous congestion, or isolated cranial nerve VI palsy depending on drainage patterns.[5] CCFs with anterior venous drainage typically demonstrate proptosis or pulsatile exophthalmos (in the case of direct CCFs) due to arterialisation of the superior and inferior ophthalmic veins. Ischemic optic neuropathy can also develop in setting of elevated venous pressure and vascular compromise.[5] In the setting of posterior venous drainage, patients may develop "white-eyed shunt syndrome" where orbital congestion is absent and bruit is less commonly reported. Posteriorly draining CCFs may be asymptomatic or present with isolated cranial neuropathy often with associated orbital pain.[7] Diplopia may result from direct compression of the CNs in the engorged cavernous sinus, and ptosis and/ or pupillary changes may be seen with CN III involvement. Horner syndrome may accompany VI palsy due to compression within the cavernous sinus. Compression of V1 and V2 may cause ipsilateral decreased facial sensation.[5] Facial weakness and hemiparesis may occur in the setting of brainstem oedema.[8]

Digital subtraction angiography (DSA) remains the diagnostic gold standard given its superior spatial and temporal resolution. Non-invasive alternatives include CT of the brain with CT-Angiography (CTA) and brain MRI with MRA.[5]

In rare circumstances, the arteriovenous shunts are localised outside the cavernous sinus, but mimic symptoms and radiographic characteristics of a cavernous shunt. Kobkitsuksakul C et al. examined a series of 350 patients with provisional diagnoses of carotid cavernous sinus fistulae or cavernous sinus dural AVF. 10 patients in this series had a final diagnosis of noncavernous sinus AVF. The writer concluded that the clinical presentation depends mainly on the outflow, which is the result of the venous anatomy of the central nervous system and skull base.[9]

The presentation of isolated nerve palsy without prominent congestion features does not exclude the arteriovenous malformation of the cavernous sinus. Reviewing the literature there have been cases of isolated cranial nerve palsies that were ultimately the result of a carotid-cavernous sinus fistula. Lin and Hu presented the case of a young male patient with right-side CCF, who initially presented with right-side

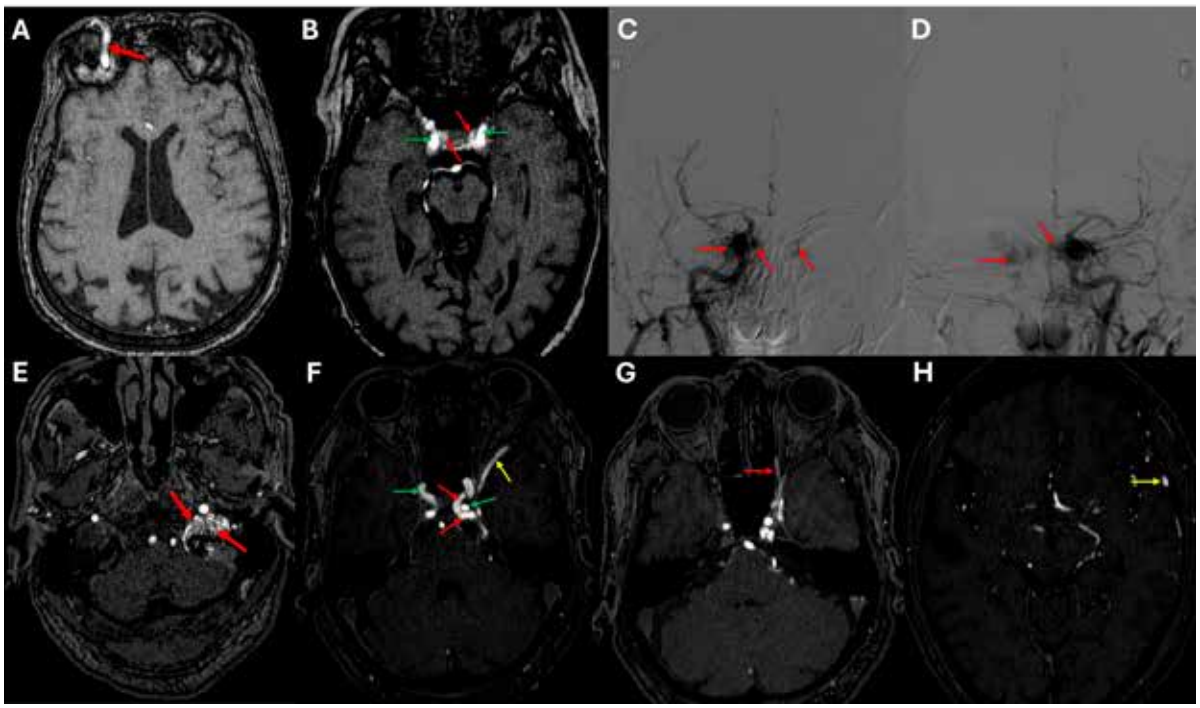

Figure 1. (**A-D**, Patient 1). Magnetic resonance angiography using a 3D time-of-flight (TOF) technique demonstrates dilatation and flow-related signal hyperintensity of the right superior ophthalmic vein (red arrow). (**B**) A more caudal 3D TOF image shows the expected flow-related signal hyperintensity within the cavernous segments of both internal carotid arteries (green arrows), along with similar hyperintensity within the cavernous sinuses (red arrows). Because TOF angiography depicts increased intravascular flow, the presence of high signal intensity within the cavernous sinuses and superior ophthalmic vein indicates increased flow within these venous structures, which is referred to as arterialisation, because of its similarity to arterial signal characteristics. (**C, D**) Digital subtraction angiography during right (**C**) and left (**D**) carotid angiography demonstrates immediate contrast opacification of the cavernous sinuses (red arrows). These findings are consistent with bilateral carotid–cavernous fistulas.
(**E-H, Patient** 2). Magnetic resonance angiography using a 3D time-of-flight (TOF) technique demonstrates multiple arteriovenous shunts between branches of the left external carotid artery and the ipsilateral internal jugular vein (red arrows, **E**). Areas of retrograde, "arterialized" venous flow are also identified within the ipsilateral inferior petrosal sinus and cavernous sinus (red arrows, **F**), the left superficial middle cerebral vein (yellow arrows, **F** and **H**), the left inferior ophthalmic vein (red arrow, **G**), and the left sigmoid and transverse sinuses. The green arrows in panel **F** correspond to the expected flow-related signal hyperintensity within the cavernous segments of both internal carotid arteries.

headache and partial third nerve palsy with pupillary involvement, who had a history of diabetes mellitus and minor head trauma.[10] The diagnostic approach with MRA, following a normal CTA, showed a high-signal intensity at the right cavernous sinus and the diagnosis was confirmed with a DSA. Wu et al. presented 11 cases of isolated ocular motor nerve palsy without any prominent congestive ocular features. The patients underwent a diagnostic workup consisting of CTA and/or MRI/MRA with DSA confirming the hypothesis. They also showed that MRA was less sensitive than DSA in the diagnosis, missing 3/9 patients that it was conducted on.[11] Caiza-Zambrano et al. showed a case of a woman presenting with abduction limitation in the right eye, with no proptosis or chemosis. The rest ophthalmological examination showed visual acuity at 20/30 bilaterally, visual fields, pupillary reflexes, intraocular pressure, and funduscopic exam were normal. The remaining neurological exam was unremarkable. Digital subtraction angiography (DSA) confirmed an intracavernous aneurysm communicating to the Cavernous Sinus as a high-flow direct CCF which was suspected from the MRA.[12]

In conclusion, our cases highlight that when the clinical symptoms and signs suggest a possible vascular lesion, then proper imaging studies should be conducted first and foremost in order to continue with the correct treatment as also shown in a case presented by Melanis et al. of a patient with multiple cranial nerve palsies, ocular proptosis and conjunctival hyperaemia that underwent a transvenous endovascular coiling of the CCF via inferior petrosal sinus and showed a remission of the symptoms.[13]

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Barrow DL, Spector RH, Braun IF, et al. Classification and treatment of spontaneous carotid-cavernous sinus fistulas. J Neurosurg. 1985 Feb;62(2):248-56.

[2] Cognard C, Gobin YP, Pierot L, et al. Cerebral dural arteriovenous fistulas: clinical and angiographic correlation with a revised classification of venous drainage. Radiology. 1995 Mar;194(3):671-80. PMID: 7862961.

[3] González SB, Busquets JC, Figueiras RG, et al. Imaging Arteriovenous Fistulas. AJR Am J Roentgenol. 2009 Nov;193(5):1425-33.

[4] Zyck S, De Jesus O, Gould GC. Dural Arteriovenous Fistula. [Updated 2023 Aug 23]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-.

[5] Howard BM, Barrow DL. Carotid Cavernous Fistula. Neurosurg Clin N Am. 2024 Jul;35(3):319-29.

[6] Thomas AJ, Chua M, Fusco M, et al. Proposal of Venous Drainage-Based Classification System for Carotid Cavernous Fistulae With Validity Assessment in a Multicenter Cohort. Neurosurgery. 2015 Sep;77(3):380-5

[7] Acierno MD, Trobe JD, Cornblath WT, et al. Painful oculomotor palsy caused by posterior-draining dural carotid cavernous fistulas. Arch Ophthalmol. 1995 Aug;113(8):1045-9. PMID: 7639656.

[8] Elhammady MS, Ambekar S, Heros RC. Epidemiology, clinical presentation, diagnostic evaluation, and prognosis of cerebral dural arteriovenous fistulas. Handb Clin Neurol. 2017;143:99-105. PMID: 28552162.

[9] Kobkitsuksakul C, Jiarakongmun P, Chanthanaphak E, et al. Noncavernous arteriovenous shunts mimicking carotid cavernous fistulae. Diagn Interv Radiol. 2016 Nov-Dec;22(6):555-559.

[10] Lin HL, Hu TT. Isolated third nerve palsy with pupillary involvement resulting from carotid-cavernous sinus fistula: A case report. Medicine (Baltimore). 2019 Feb;98(6)

[11] Wu HC, Ro LS, Chen CJ, et al. Isolated ocular motor nerve palsy in dural carotid-cavernous sinus fistula. Eur J Neurol. 2006 Nov;13(11):1221-5

[12] Caiza-Zambrano F, Gómez Lastra M, Garbugino S, et al. High-flow carotid cavernous fistula and 'white eye': A rare and easily misdiagnosed presentation - A case report and literature review. J R Coll Physicians Edinb. 2024 Jun;54(2):144-8.

[13] Melanis K, Magoufis G, Spiliopoulos S, et al. Carotid-cavernous fistula: A potential treatable cause of bilateral abducens palsy and conjunctival hyperemia. J Stroke Cerebrovasc Dis. 2024 May;33(5):107623. PMID: 38311093.