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Bilateral Low-Flow Type-D Dural Carotid-Cavernous Fistula: Diagnosis and Treatment with 3D Time-of-Flight Magnetic Resonance Angiography

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Patient: Female, 62-year-old
Final Diagnosis: Bilateral dural carotid cavernous fistula
Symptoms: Bilateral periorbital edema • conjunctival chemosis • diminished visual acuity • diplopia • ophthalmoplegia
Clinical Procedure: Endovascular coil embolisation
Specialty: Ophthalmology • Radiology

Objective: Rare disease

Background: Carotid-cavernous fistula (CCF) is a rare, atypical vascular shunt between the carotid arterial system and the venous channels of the cavernous sinus, classified according to the shunt's anatomy, by etiology (resulting from trauma or occurring spontaneously), or by hemodynamic characteristics (such as low- or high-flow fistulas).

Case Report: A 62-year-old female patient with poorly controlled arterial hypertension presented with bilateral periorbital edema, conjunctival chemosis, ophthalmoplegia, diplopia, and diminished visual acuity. On magnetic resonance angiography (MRA), abnormal arterial flow along the cavernous sinuses was noted, suggestive of bilateral CCF. The diagnosis of indirect dural low-flow CCF (Barrow Type D) was later confirmed by digital subtraction angiography, with feeding arteries from intracavernous internal carotid artery branches, and meningeal branches of the external carotid artery, draining bilaterally to ophthalmic veins, the intracavernous sinus, and the inferior petrosal sinus. The patient was successfully treated with endovascular embolization. At 7-month follow-up, no residual arteriovenous shunting was detected. This case highlights the importance of non-invasive radiological methods for CCF, and presents rarely published radiological findings of bilateral Type-D dural CCFs on 3-dimensional time-of-flight MRA with post-treatment MRA follow-up.

Conclusions: Regardless of the patient's history of possible trauma, a patient presenting with bilateral periorbital edema, conjunctival chemosis, ophthalmoplegia, diplopia, and diminished visual acuity should have a spontaneous bilateral CCF investigated to prevent delayed treatment. Experienced neuroradiologists are needed to accurately detect indirect CCF, since this condition often does not demonstrate classic symptoms.

Keywords: Carotid-Cavernous Sinus Fistula • Cavernous Sinus • Magnetic Resonance Angiography • Magnetic Resonance Imaging • Radiology, Interventional

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Introduction

Carotid-cavernous fistula (CCF) is characterized by aberrant arteriovenous shunting within the cavernous sinus. CCFs can be classified according to the shunt's anatomy, by etiology (resulting from trauma or occurring spontaneously), or by hemodynamic characteristics (such as low- or high-flow fistulas) [1]. Only 1% to 2% of people with CCFs have the bilateral type [2]. CCFs are divided into 2 groups: indirect (dural), which are more often low-flow fistulas with arterial supply arising from the internal maxillary, middle meningeal, accessory meningeal, and ascending pharyngeal branches of the external carotid artery (ECA), as well as cavernous segment branches of the internal carotid artery (ICA), and direct, usually high-flow fistulas with a direct connection between the ICA and the cavernous sinus [3]. Spontaneous direct CCFs are rare (20% of all Type-A CCFs) and typically result from ICA cavernous segment aneurysm rupture [2]. Angioarchitecture of the arterial side of the fistula determines the Barrow type, the most widely adopted system to classify CCFs [4]. Anatomically, CCFs are classified into 4 groups, from Type A to D, as follows:
Type-A fistulas are defined as a direct connection between the cavernous sinus and the intra-cavernous ICA; these are typically high-flow and high-pressure fistulas [2].
Type B fistulas consist of a dural shunt between intracavernous branches of the ICA and the cavernous sinus [2].
Type C fistulas are located between the cavernous sinus and the meningeal branches of the ECA, via a dural shunt [2].
Type-D fistulas consist of a connection between the cavernous sinus and ICA and ECA branches by dural shunts, in a combination of types B and C [2].

Debrun et al introduced a study of 132 patients presenting with CCFs (including traumatic and non-traumatic CCFs). Of these, 100 CCFs (75.8%) were classified as Type A, none were classified as Type B, 4 (3%) were classified as Type C, and 28 (21.6%) were classified as Type D [5].

However, the Barrow classification is not very practical from the clinical and therapeutic standpoints, as symptomology and current treatment approach are influenced largely by venous drainage [4].

Thomas et al proposed a Venous Drainage-Based Classification System for Carotid Cavernous Fistulae, which includes 5 subtypes:
Type 1: Posterior/inferior drainage only (posterior/inferior drainage: inferior petrosal sinuses, superior petrosal sinus, pterygoid, and parapharyngeal plexus) [4].
Type 2: Posterior/inferior and anterior drainage (anterior drainage: superior and inferior ophthalmic veins) [4].
Type 3: Anterior drainage only [4].
Type 4: Retrograde drainage into cortical veins ± other routes of venous drainage (cortical drainage: superficial middle cerebral veins, perimesencephalic, and cerebellar venous system) [4].
Type 5: High-flow direct shunt between the cavernous ICA and cavernous sinus (Barrow Type A) ± multiple routes of venous drainage [4].

Case Report

We present a rare case of bilateral (Barrow's Type D) spontaneous indirect low-flow CCF which was diagnosed by 3-dimensional time-of-flight MRA (3D TOF MRA) and treated with endovascular coil embolization, with post-treatment follow-up MRA imaging.

A 62-year-old woman presented with bilateral periorbital edema and subacute hyperemia of both eyes, ophthalmoplegia, diplopia, and diminished visual acuity. It was known that she had a history of poorly controlled systemic arterial hypertension. She had no history of prior head trauma. She was primarily seen by an emergency doctor and later by an ophthalmologist. On examination, her arterial blood pressure was 196/113 mmHg, with elevated intraocular pressure (IOP). On her blood workup, no evidence of infection was noted (normal white blood cell count, erythrocyte sedimentation rate, C reactive protein). Due to the clinical findings, an MRI with 3D time-of-flight (TOF) angiography of the brain was performed. The study revealed abnormal arterial flow between the cavernous sinuses (**Figure 1**), suggesting a fistula with ICA and ECA branches as feeding arteries, draining to the inferior petrous sinus and intercavernous sinus. Due to the MRI findings, a digital subtraction angiography (DSA) was performed, which confirmed the diagnosis of bilateral indirect dural low-flow CCFs with feeding arteries from intracavernous ICA branches, and meningeal ECA branches, draining bilaterally to ophthalmic veins, the intracavernous sinus, and the inferior petrous sinus (**Figure 2**). Eight days after the diagnosis, an endovascular embolization was performed by accessing the right femoral artery. The right jugular vein was catheterized, and, advancing through the right inferior petrous sinus, the left cavernous sinus was accessed via the right cavernous sinus through the intercavernous sinus, allowing advancement to the left ophthalmic vein. Embolization of the right and left cavernous sinuses and intercavernous sinus was performed with 24 detachable embolization coils, and resolution of the type-D carotid-cavernous arteriovenous flow was immediately noted (**Figure 3**). The embolization went successfully, and the patient fully recovered without any complications. The edema and hyperemia of both eyes resolved within a couple of days. The IOP was normalized on follow-up. The ophthalmoplegia, diplopia, and the patient's vision improved over the course of 3 months. A follow-up MRI was scheduled after 6 months; however, due to

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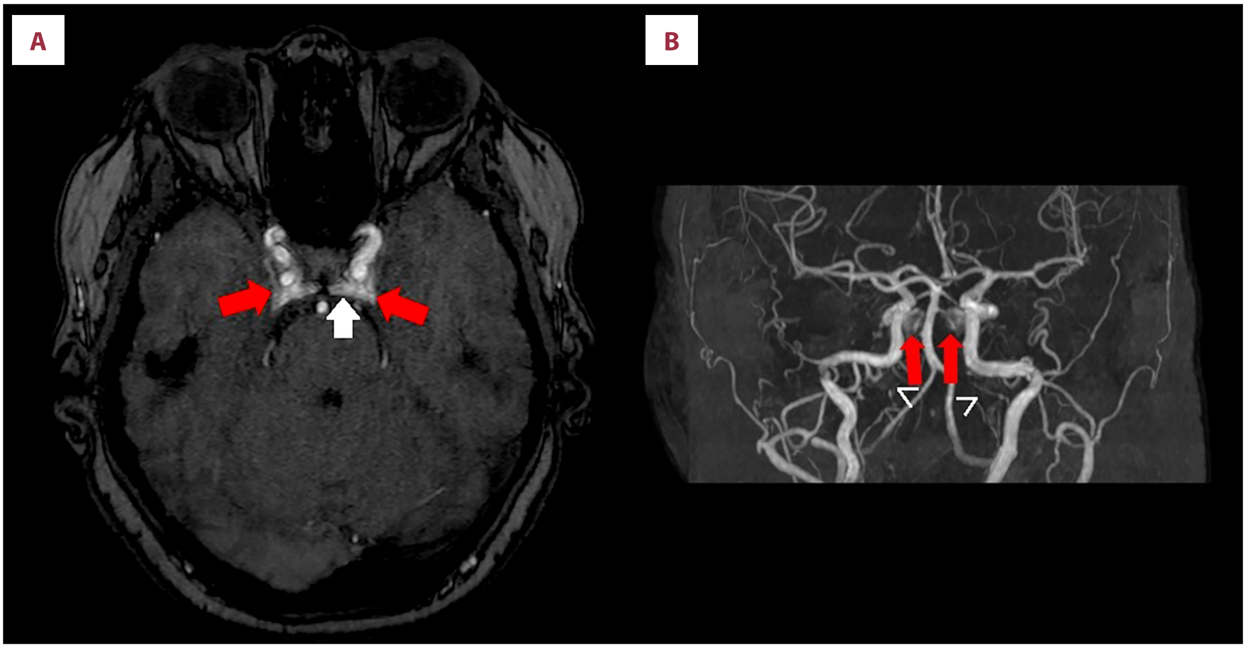

Figure 1. Initial axial (**A**) and 3D reconstruction (**B**) from 3D time-of-flight magnetic resonance angiography showing bilateral arterial flow in cavernous sinuses (red arrows), intracavernous sinus (white arrow), and inferior petrous sinus (arrowheads), suggesting bilateral dural carotid-cavernous fistulae.

personal reasons, it was performed after 7 months. It showed no abnormal fistulous arteriovenous shunting along the cavernous sinuses (**Figure 4**). As a part of the ongoing management plan, the patient was scheduled for continued clinical observation, and the next control follow-up MRA is planned for 2 years post-surgery.

Discussion

Although various classifications of CCFs have been cited in the literature, reports of bilateral, spontaneous, indirect Type-D CCFs diagnosed by MRI remain very limited, and only a few reports presenting low-flow CCFs diagnosed by MRA have been published.

We present a rare case of bilateral low-flow Type-D carotid-cavernous fistulas detected on 3D TOF MRA that were also visible on maximum intensity projection (MIP) imaging, along with post-treatment follow-up.

The angiographic criteria used to differentiate a high-flow from a low-flow fistula were described by Barrow et al in 1985 [2]. TOF is the most utilized MRA method, operating on the principle of diminishing signals from static background tissues while focusing on capturing images of inflowing spins, specifically blood, an effect known as "flow-related enhancement." In low-flow fistulas, the cavernous sinus opacification occurs in a slower fashion, thereby making 3D TOF MRA less sensitive. A study by Henderson et al comparing the sensitivities of computed tomography angiography (CTA), MRA, and DSA showed that the sensitivity of MRA was only 80%, which was significantly lower than either CTA or DSA [6]. However, the study included both direct and indirect CCF's, suggesting that the sensitivity purely for indirect low-flow CCF's may be even lower.

Upon searching the scientific literature by keywords, we found only 4 different cases of reported indirect CCF, and 1 case series including 2 patients with Type-D CCFs, diagnosed by 3D TOF MRA. The 3D TOF MRA in this case series showed only indirect signs suggesting the diagnosis, showing no abnormal flow voids in the carotid-cavernous sinuses [7-11]. In a report of 8 indirect CCFs, MIP images of 3D TOF MRA only revealed changes in half of the cases [12]; however, there were no cases of bilateral involvement.

High-flow CCFs, such as traumatic CCFs, can be easily detected by MRI and MRA, but in low-flow CCFs, the cavernous sinus opacification occurs belatedly, because of the slow flow in the constituent veins [11]. Even though 3D TOF MRA is known to be very sensitive in detecting CCFs [13], it is not specific, and confirmation with DSA is needed.

Prompt diagnosis, treatment, and improved outcomes will result from a complete understanding of the pathophysiology of carotid-cavernous fistulas and associated disorders. Computed tomography performs better, especially for bony structures, and this is crucial for traumatic CCFs. However, MRI offers the

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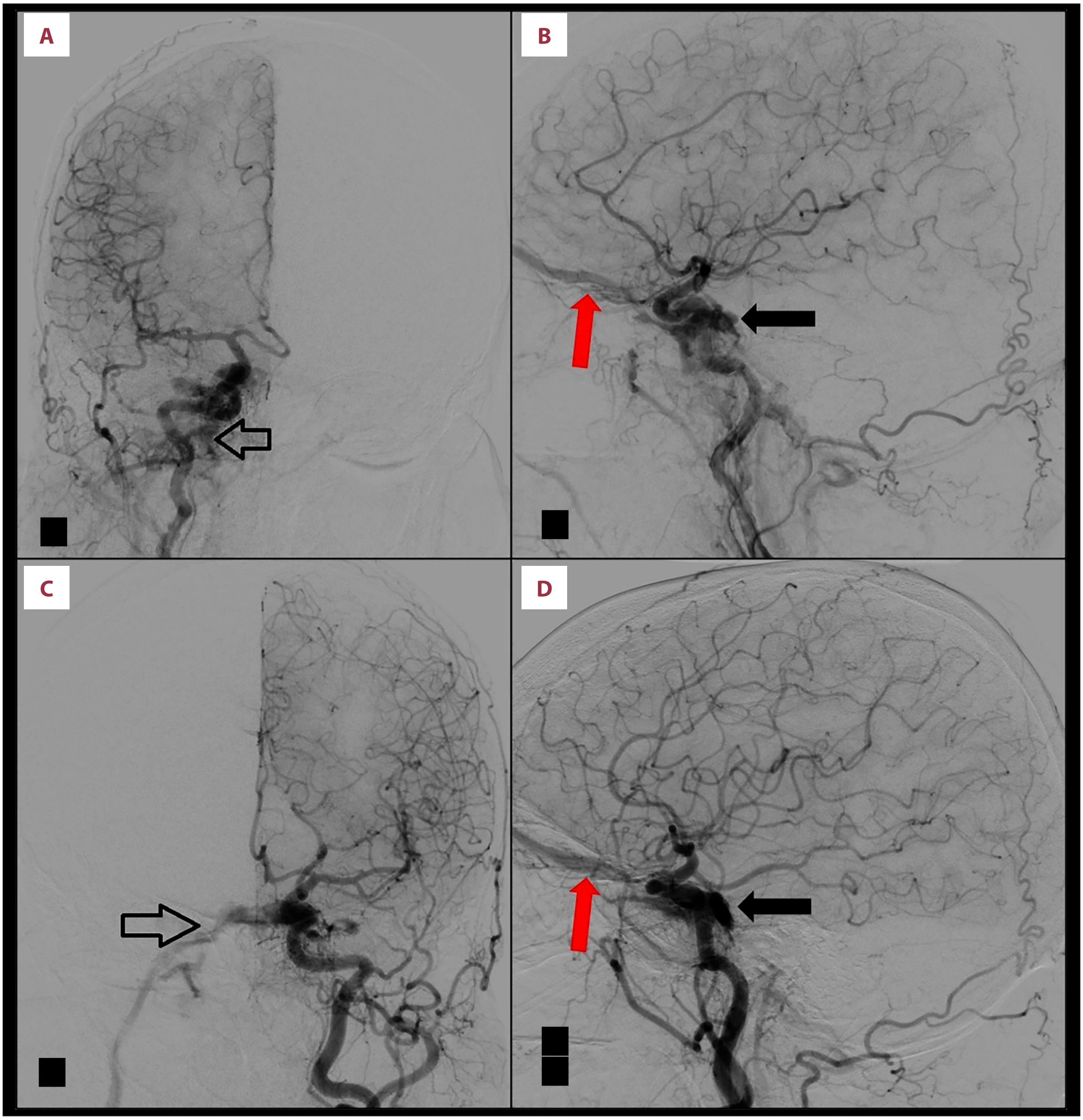

Figure 2. Digital subtraction angiogram confirming bilateral indirect Type-D carotid-cavernous fistulae (black arrows) with feeding arteries from intracavernous internal carotid artery branches and meningeal external carotid artery branches, draining bilaterally to ophthalmic veins (red arrows), and the inferior petrous sinus (empty arrows), on the right (**A, B**) and left (**C, D**) side.

advantage of detecting flow voids as well as orbital edema, which makes it more helpful in diagnosing non-traumatic CCFs [14]. These methods can be helpful for primary judgment and provide more information for clinical diagnosis to distinguish from other craniocerebral diseases such as arteriovenous malformations and cavernous hemangiomas. Small arteriovenous malformations within the cavernous sinus or adjacent structures might have a similar appearance in imaging studies, and cavernous hemangiomas can involve the cavernous sinus and might show similar imaging features as well [15].

Congestion from poor orbital venous drainage to the cavernous sinus leads to subsequent threats to the patient's vision [16] and increases the risk of cerebral venous infarction [17]. Finding the right diagnosis frequently requires a team effort, with the team including emergency physicians, radiologists,

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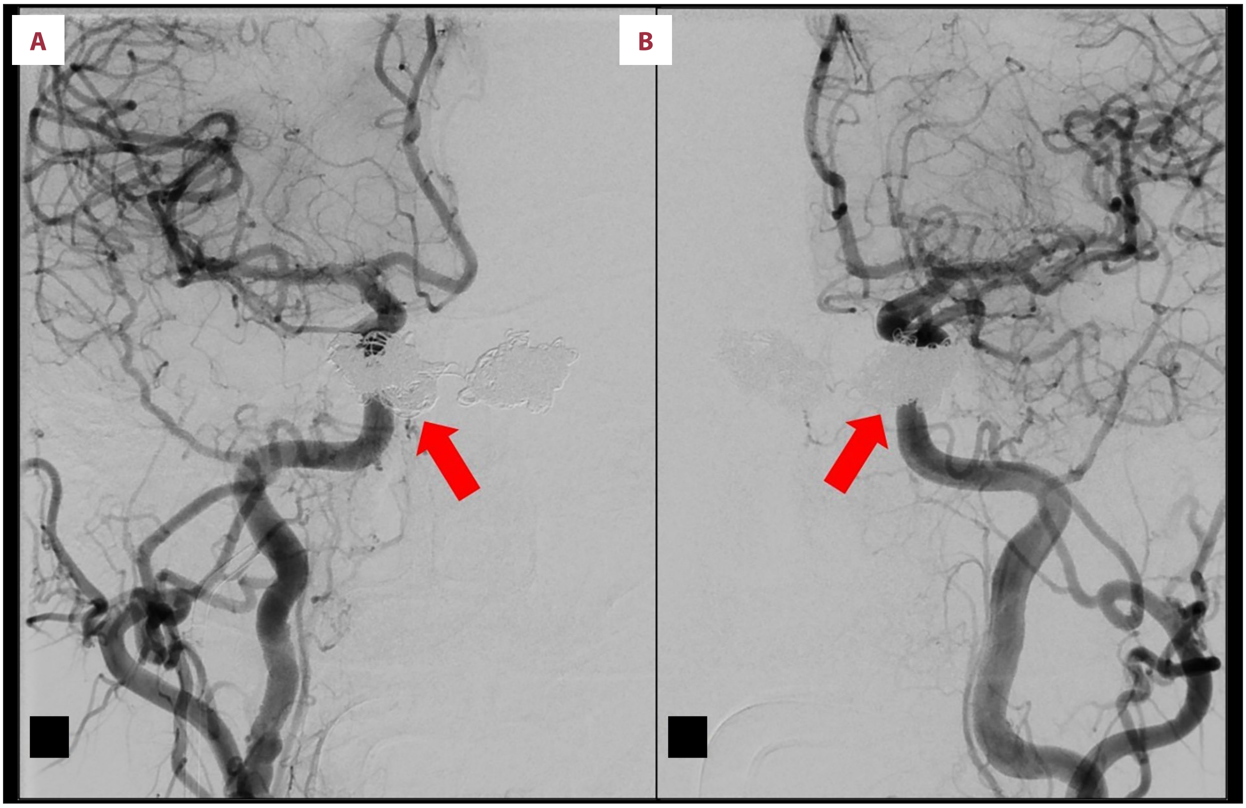

Figure 3. (**A, B**) Immediate post-coiling digital subtraction angiogram demonstrating no residual fistula following coil embolization of right and left cavernous sinuses (red arrows).

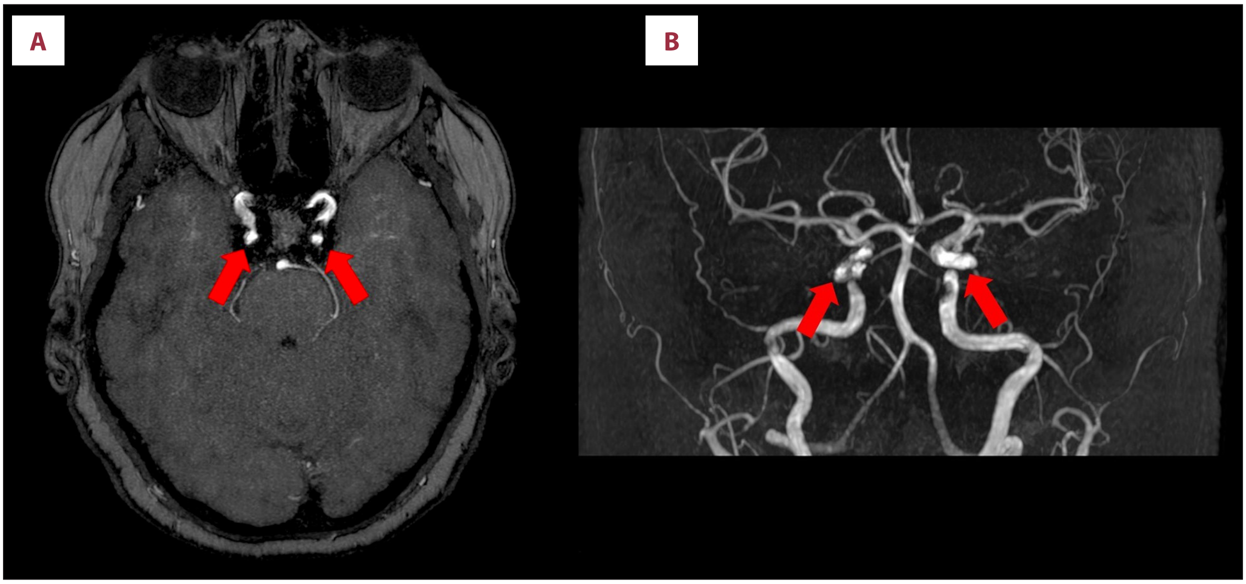

Figure 4. Seven-month follow-up axial (**A**) and 3-dimensional reconstruction (**B**) 3-dimensional time-of-flight magnetic resonance angiography demonstrating stable occlusion of the bilateral indirect carotid-cavernous fistulae.

neurosurgeons, ophthalmologists, and otolaryngologists [18]. The spontaneous resolution of untreated indirect CCF has been reported to occur in 10-60% of cases, usually due to re-thrombosis of affected segments of the cavernous sinus [2,3]. The decrease in the pressure gradient between the ICA and the fistula may result in thrombosis of the feeding arteries and subsequent fistula closure because of stagnation and reduced blood flow [19]. Intravascular intervention such as coil embolization should be considered if patients show indications of increased IOP, exophthalmos or proptosis, decreased vision, ophthalmoplegia, or persistent headaches [20].

TOF MRA plays a significant role in CCF diagnosis; among the non-invasive magnetic resonance procedures, it is the most frequently used method for the assessment of cerebrovascular diseases [21]. It is based on flow-related enhancement by applying the pre-saturation band, which eliminates the venous flow in the craniocaudal direction and shows the intracranial arteries. When an abnormal venous signal is seen on TOF MRA, the presence of an arteriovenous fistula could be suspected. It is important to clarify that while TOF MRA is a frequently used non-invasive technique for assessing cerebrovascular diseases, its specificity can be limited. The study by Ouanounou et al suggests that TOF MRA may show venous flow signals in the cavernous or inferior petrosal sinus even in the absence of CCF [22]. This finding indicates a potential for false-positive results, emphasizing the need for cautious interpretation of TOF MRA results in diagnosing CCF. The gold standard for definitive diagnosis remains DSA, due to its higher specificity and ability to accurately depict vascular anatomy and pathology.

Clinicians should be aware of the symptoms of CCF and always consider it in their differential diagnosis for patients presenting with these symptoms, even if it is quite uncommon. Despite previous clinical studies of non-invasive techniques showing that CTA outperformed MRA in diagnosing CCFs [6], our own clinical experience serves to question this conclusion. Technical advancements of MRI techniques have served to enhance the depiction of smaller vessels. These adaptations include the employment of magnetization transfer saturation pulses, the overlaying of multiple slabs, fat suppression, and variable (ramped) flip angles [23,24].

Also, the introduction of 7T MRI scanners have been shown to be advantageous for 3D TOF MRA compared with lower field MRI due to their utilization of a longer T1 relaxation time, resulting in improved vessel-to-background contrast [25].

The technical improvements of the latest generation of MRI technology raise the need to conduct further studies comparing the sensitivity and specificity of these methods, focusing on long-term outcomes, residual shunting, and the accuracy of detecting high-risk features like cortical venous reflux. Such studies would provide further insights into the optimal imaging approach for dural CCF diagnosis and follow-up.

One limitation of this case was the delayed follow-up MRI examination. While the post-treatment evaluation time should be 6 months, due to personal reasons, the earliest the patient was able to be examined was after 7 months. At this follow-up visit, the 3D TOF MRA demonstrated stable occlusion of the bilateral indirect carotid-cavernous fistulae. In the presence of metallic coils, there are artifacts on MRA imaging, which could interfere with evaluation, but despite that, there were no direct signs of abnormal flow, and the patient is, at the time of publication of this case report, still being observed clinically. Post-treatment assessment for residual or recurrent disease, which can often be subtle, is another area where the limitations of TOF MRA become evident. This is especially pertinent in scenarios where detection of subtle residual or recurrent disease is critical [26]. It is important to emphasize that post-coiling, the patient experienced resolution of symptoms, and the recovery period was free from complications.

In cases of dural CCFs, a follow-up that focuses solely on ophthalmological examination may not be sufficient to ensure the absence of risks such as ischemic stroke or cerebral hemorrhage. There may be limitations in detecting complications outside the orbit, like cortical venous hypertension and stroke risk, which are not evident through ocular assessments alone. Hence, going beyond just ophthalmological examinations, such as follow-up MRA, is essential for accurately assessing these risks in patients with dural CCFs.

The next follow-up MRA is scheduled for 2 years post-surgery, and if the patient is clinically stable, the evaluation for residual arteriovenous shunting will be deemed adequate. Artifacts due to metallic coils might interfere with image interpretation in post-treatment scenarios where metallic embolization materials are used. The presence of such artifacts can obscure or mimic pathology, leading to potential diagnostic inaccuracies. This is a crucial consideration in post-treatment assessments where accurate interpretation of the imaging is vital for determining the success of the treatment, and for planning further management. Adjusting imaging parameters like shortening the echo time or increasing flip angle can help reduce artifact presence while enhancing the visibility of the vascular structures of interest [27].

While 3D TOF MRA is a valuable, non-invasive tool for diagnosing and evaluating dural CCFs, it has certain limitations in sensitivity, particularly in identifying venous drainage. This therefore also limits the risk stratification ability with regard to dural CCF. It is useful in demonstrating arteriovenous shunt of a dural arteriovenous fistula but is relatively insensitive to cortical vein dilation or sinus occlusion [28]. This is largely due to

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the technique's dependence on flow velocity, which can sometimes render it ineffective in distinguishing abnormal shunt flow from normal flow. This limitation is particularly concerning since correctly identifying these patterns is vital for determining severity and potential risk [29].

Techniques like time-resolved 3D contrast-enhanced MRA (TR 3D MRA) offer significant improvements over 3D TOF MRA. TR 3D MRA introduces temporal resolution, allowing dynamic visualization of contrast material through cerebral vessels, which is crucial for assessing the dynamic characteristics of dural arteriovenous fistulas, such as venous flow patterns. In a comparative study, TR 3D MRA proved reliable in detecting dural arteriovenous fistulas, indicating its suitability for follow-up imaging, as it can address some of the limitations of 3D TOF MRA [30].

Three-dimensional TOF MRA is known to be very sensitive in detecting CCF, with some downsides in terms of the specificity [14]. The source images of 3D TOF MRA proved useful in identifying fistulas before an invasive DSA study was undertaken; if an abnormal flow is detected on these images, the patient is indicated for the DSA [6].

Whenever there is a suspicion of an orbital or intracranial abnormality that may affect the optic nerve or visual pathways, experienced neuroradiologists are needed to accurately detect indirect CCF due to these types of CCF not often demonstrating classic symptoms.

Conclusions

Regardless of the patient's history of trauma, a patient presenting with bilateral periorbital edema, conjunctival chemosis, ophthalmoplegia, diplopia, and diminished visual acuity should be tested for a spontaneous bilateral CCF, to prevent delayed treatment.

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Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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