Transarterial Embolization of an Indirect Carotid-Cavernous Fistula with N-Butyl Cyanoacrylate: Case Report

Embolización Transarterial de Fistula Carótido-Cavernosa Indirecta con N-Butyl

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ABSTRACT
Carotid-cavernous fistulas are vascular shunts that allow blood to flow from the carotid artery into the cavernous sinus. Some fistulas are characterized by a direct connection between the cavernous segment of the internal carotid artery and the cavernous sinus. Other carotid-cavernous fistulas are dural, consisting of a communication between the cavernous sinus and one or more meningeal branches of the internal carotid artery, the external carotid artery, or both. Endovascular management is the treatment modality of choice in these cases. We report the use of N-butyl cyanoacrylate in a successful transarterial embolization of a dural carotid-cavernous fistula fed by arterial branches of the internal -and mainly- external carotid arteries (Barrow type D).

Key words: Carotid-cavernous fistula; Transarterial embolization; N-Butyl Cyanoacrylate

INTRODUCTION
Carotid-cavernous fistulas are abnormal connections between the internal, external, or both carotid arteries and the cavernous sinus. According to Barrow et al.4, carotid-cavernous fistulas (CCF) are classified into direct (type A) and indirect (types B–D) types. Direct CCF are high flow shunts between the cavernous portion of the internal carotid artery and the cavernous sinus and usually caused by traumatic laceration of the internal carotid artery or rupture of an intracavernous carotid aneurysm14,36.

Indirect CCF are dural fistulas between the cavernous sinus and extradural branches of the internal carotid artery, the external carotid artery, or both. Most indirect CCF are idiopathic and occurs spontaneously, they may be associated with pregnancy, trauma, sinusitis, surgical procedures, or cavernous sinus thrombosis5,18,34. Type B are fistulas between meningeal branches of the internal carotid artery and the cavernous sinus. Type C are dural shunts between meningeal branches of the external carotid artery and the cavernous sinus. Type D are fistulas between meningeal branches of both the internal carotid artery and external carotid artery and the cavernous sinus5,34. This shunting of blood can lead to ocular venous hypertension and explains the presence of orbital symptoms and ophthalmoscopic findings. Direct and indirect CCFs most commonly cause the classic triad of proptosis, conjunctival chemosis and cranial bruit but can masquerade as chronic conjunctivitis, meaning that ophthalmologists may be the first physicians to encounter a patient with clinical manifestations of CCF5,10,46.

Arterialized conjunctival and episcleral vessels in association with N-Butyl Cyanoacrylate: Case Report

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with conjunctival chemosis, pulsating proptosis, thrill and bruit should raise the possibility of a diagnosis of an arteriovenous fistula. Other less common associated symptoms include diplopia, decreased visual acuity and elevated intraocular pressure (IOP). Symptoms are related to the degree of arteriovenous shunting and the route of venous drainage. Indirect fistulas usually result in less severe symptoms, with insidious onset, mild orbital congestion, proptosis and low or no bruit. Patients with spontaneous indirect CCF may present with pulsatile tinnitus, temporal headache and ptosis.

Most CCFs are not life threatening, but the compromised eye is at risk. Main indications for treatment include glaucoma, diplopia, intolerable bruit or headache, and severe proptosis causing exposure keratopathy. Indirect CCF can be treated by manual extracranial compression or transarterial and/or transvenous endovascular techniques, with endovascular approaches demonstrated as safe and effective in the treatment of CCFs.

In this report, we describe the treatment of a CCF type D, focusing on transarterial endovascular treatment with NBCA via dural shunts between meningeal branches of the external carotid artery and the cavernous sinus.

CASE REPORT

A 83-year-old man presented with a 3-month history of left ocular congestion, left pulsatile retro-orbital headaches, decreased vision and diplopia. There was no history of head trauma, the patient did not smoke and had no hypertension. Physical examination revealed conjunctival chemosis and exophthalmos. There were no oculomotor nerves palsies and pupillary light reflexes were normal.

Magnetic resonance imaging (MRI) of the brain was performed, showing left eye proptosis and slight dilatation of the superior ophthalmic vein.

Cerebral angiography showed a left Barrow Type D indirect CCF supplied by meningeal branches of the right internal carotid artery via the infraorbital branch and left external carotid artery via the accessorius and anterior meningeal branches. The CCF drained from the cavernous sinus into a dilated left supraorbital vein (SOV), a large vein into the superior sagittal sinus, and via a large facial vein into left subclavian vein. The left jugular vein could not be identified.

Endovascular treatment was decided. Transarterial embolization with NBCA glue via the external carotid arterial feeders was performed. A 5.5F sheath was introduced into the right femoral artery and a micro catheter with a micro guide wire was navigated through the left external carotid artery into the accessory and anterior meningeal branches. NBCA glue mixed with Ethyl-esters of the iodized fatty acids of poppyseed oil (20% NBCA) was injected as the embolic agent into many little, tortuous branches of the accessory and anterior meningeal arteries. Post-embolization angiography revealed no fistulous filling through indirect branches of external carotid artery. The ophthalmic vein and the large anterior facial vein had reduced their flow and size. No complications occurred during the procedure.

At one month follow-up clinical examination, chemosis and proptosis had almost disappeared. The patient did not have headaches, and vision and diplopia had improved considerably.

DISCUSSION

A CCF is an abnormal communication between the carotid arterial system and the cavernous sinus. CCFs can be classified by cause (traumatic vs spontaneous), velocity of blood flow (high vs low flow), and anatomy according to fistulous supply to the cavernous sinus (type A: internal carotid artery [ICA]; type B: dural branches of the ICA; type C: dural branches of external carotid artery [ECA]; type D: combined ICA-ECA).

Direct CCFs (type A) are characterized by a direct connection between the cavernous segment of the internal carotid artery and the cavernous sinus. These fistulas are usually high-flow, and are most often caused by a single, traumatic tear in the arterial wall or by the rupture of an intracavernous aneurysm. Other CCFs are indirect or dural with many of these lesions actually congenital arteriovenous fistulas that develop spontaneously, or in the setting of atherosclerosis, systemic hypertension, connective tissue disease, and during or after childbirth. Dural CCFs consist of a communication between the cavernous sinus and one or more meningeal branches of the internal carotid artery (type B), the external carotid artery (type C), or both (type D). Of these, fistulas involving branches from both the
internal and external carotid arteries are the most common, as in the case presented above.

Pathogenesis

Indirect CCFs usually become symptomatic spontaneously, and although many patients who develop an indirect CCF are otherwise healthy, certain conditions seem to predispose to the development of this lesion, including pregnancy, systemic hypertension, atherosclerotic disease, connective tissue diseases (e.g. Ehlers-Danlos syndrome type IV), and minor trauma. Proptosis, episceral and conjunctival arterializations may be due to the resistance from the retrograde venous drainage into the ophthalmic vein. One may expect restricted ocular motility and diplopia as a result of enlargement of extracocular muscles; and exposure keratopathy as a result of proptosis. The occurrence of glaucoma (which may be of several types) is in most cases due to increased episceral venous pressure, yet some are due to angle closure or iris neovascularization.

Clinical Manifestations

Carotid-cavernous fistula is an abnormal communication between the internal or external carotid arteries and the cavernous sinus. Indirect or dural carotid-cavernous fistulas are characterized by a communication between the cavernous sinus and one or more meningeal branches of the internal carotid artery, external carotid or both. In this type of fistula the intracavernous portion of internal carotid artery remains intact. Arterial blood flows through the meningeal branches of external or internal carotid arteries indirectly into cavernous sinus. Due to the slow blood flow, the clinical features are more subtle than in a direct fistula.

Dural CCFs usually occur in middle-aged or elderly women, but may produce symptoms in either gender and at any age, such as the case we report (83 years). Symptoms and signs produced by these lesions are influenced by several factors, including the size of the fistula, the location within the cavernous sinus, the rate of flow, and especially the drainage pattern.

When dural CCFs drain posteriorly into the superior and inferior petrosal sinuses, they are usually asymptomatic. In some cases, however, such fistulas produce cranial neuropathies, such as trigeminal neuropathy, facial nerve palsy, or oculomotor palsies. In most of these cases, there is no evidence of orbital congestion. In most cases of oculomotor paresis caused by a posteriorly-draining dural CCF, the onset of the paresis is sudden, and only one of the nerves is affected being the oculomotor nerve the most commonly affected. Other manifestations of posteriorly-draining CCFs include brainstem congestion that may be associated with neurologic deficits, and rarely, intracranial hemorrhages.

The patient reported above had a dural CCF that drained mainly from the cavernous sinus into a dilated left SOV and a large vein into the superior sagittal sinus. Ocular signs of CCFs are related to two main pathogenesis; venous congestion and reduced arterial blood flow to the orbit. Typically, arterialization of conjunctival veins is associated with other ophthalmologic manifestations, particularly with proptosis and can be found in 82% to 100% of patients with orbital symptoms.

In mild cases, there is redness of one or, rarely, both eyes caused by dilation and arterialization of both conjunctival and episcleral veins. In these cases, the appearance may suggest a primary ocular disorder, such as conjunctivitis or episcleritis. However, a careful examination of dilated vessels usually demonstrates a typical tortuous corkscrew appearance that is virtually pathognomonic of a dural CCF. There also may be minimal eyelid swelling, conjunctival chemosis, proptosis, or a combination of these findings. Diplopia from abducens nerve palsy may be present.

In more severe dural CCFs, particularly those with a high flow rate, the symptoms and signs are identical with those of a direct CCF. In these cases, signs of orbital congestion, including proptosis, chemosis, and the dilation of conjunctival vessels, are obvious and severe.

Diplopia may result from ophthalmoparesis caused by ocular motor nerve palsies, orbital congestion, or both mechanisms, and there may be significant periorbital or retro-ocular discomfort or pain. Increased episcleral pressure and vortex venous pressure may result in elevated intraocular pressure and secondary glaucoma. Secondary glaucoma is a frequently observed ocular manifestation of CCF. Angle-closure glaucoma may develop from increased orbital venous pressure, congestion of the iris and choroid, and forward displacement of the iris-lens diaphragm.

Venous and arterial stasis could result in decreased ocular and retinal perfusion. Retinal and choroidal changes may include venous dilatation, retinal hemorrhage, central retinal vein occlusion, central retinal artery occlusion, cotton-wool
patches, serous retinal detachment, choroidal detachment and papilledema\textsuperscript{20,46}.

Visual loss, although less frequent than in patients with direct CCFs, occurs in up to 30\% of patients with indirect CCFs\textsuperscript{24,25,37}. It may be caused by ischemic optic neuropathy, chorioretinal dysfunction, or uncontrolled glaucoma\textsuperscript{9}.

The ocular manifestations of unilateral dural CCFs are almost always ipsilateral to the fistula, but they may be solely contralateral or bilateral\textsuperscript{34}.

**Diagnosis**

While cerebral angiography is the gold-standard imaging modality in the diagnosis of CCFs, patients typically undergo noninvasive cerebral imaging with Computed Tomography (CT), MRI, or CT/MR angiography first. Evidence of cavernous sinus enlargement, proptosis, extraocular muscle enlargement, superior ophthalmic vein dilation, or dilation of cortical or leptomeningeal vessels, as well as associated skull fractures, may be seen on CT or MRI and are suggestive of CCF\textsuperscript{2,14}. However, the absence of abnormalities on noninvasive imaging studies does not exclude the diagnosis of CCF.

If there is a high degree of clinical suspicion and/or imaging studies are consistent with the presence of CCF, the patient should be referred for diagnostic cerebral angiography. Typically, this will be performed using transfemoral arterial catheterization with imaging of the bilateral internal carotid arteries, and external carotid arteries, as well as the vertebral arteries\textsuperscript{12,14}.

**Differential Diagnosis of CCF**

Direct and indirect CCFs most commonly cause the classic triad of proptosis, conjunctival chemosis and cranial bruit but can masquerade as chronic conjunctivitis\textsuperscript{10,46}.

Some of the differential diagnoses for CCF include vascular lesions such as arteriovenous malformations, cavernous sinus thrombosis, cavernous sinus tumors, orbital tumors, skull base tumors, and mucoceles. Infections such as orbital cellulitis, mucormycosis and tuberculosis may also present as a CCF. Thyroid eye disease, orbital pseudotumor, Miasenia Gravis\textsuperscript{15} and orbital vasculitis resulting from Wegener’s granulomatosis, polyarteritis nodosa, intracranial sarcoidosis and Tolosa-Hunt syndrome may present like CCF. Therefore, a CCF should be included in the differential diagnosis of an “atypical” red eye.

**Treatment**

Indirect CCFs are rarely life threatening. Indirect CCFs are only treated if symptoms are intractable or intolerable or if vision is threatened. Main indications for treatment include glaucoma, diplopia, intolerable bruit or headache, and severe proptosis causing exposure keratopathy\textsuperscript{8,10}. The goal is to interrupt the fistulous communications and decrease the pressure in the cavernous sinus.

Spontaneous regression of indirect CCFs is not uncommon, with reported incidence ranging from 9.4\% to 46\%\textsuperscript{26}. Because of the usually benign nature of this disease, attempted conservative treatment by means of carotid/jugular compression is initially recommended. In cases with rapidly deteriorating ocular symptoms as in our patient, and/or cortical venous drainage, more urgent interventional therapy is necessary.

Transarterial or transvenous embolization is the main treatment modality for the treatment of most CCFs\textsuperscript{17,39}. Metallic coils and/or liquid embolic agents are now most commonly used for this purpose after the withdrawal of detachable balloons from the US market in 2003\textsuperscript{28,45}. Transarterial access is often used when the CCF originates from branches of the external carotid artery, as well as in selected cases of direct fistulas. When the CCF originates from branches of the internal carotid artery, transarterial embolization is significantly more difficult and carries an increased risk of stroke due to embolic reflux into the internal carotid artery. In those cases, a transvenous approach is used, and the fistula is occluded using either a coil or liquid embolization of the cavernous sinus\textsuperscript{14}.

Transvenous embolization of dural fistulas including indirect CCF allows preservation of the internal carotid artery. The specific approach depends on the venous drainage route from the cavernous sinus and the location of the distended part of the cavernous sinus. The cavernous sinus is most easily accessed through the inferior petrosal sinus (IPS) via the femoral or internal jugular vein. If the IPS approach is not possible or has failed, an anterior transvenous approach to the cavernous sinus through the SOV is a good alternative. Current statements favor the use of the surgical SOV approach only when transfemoral venous access has failed\textsuperscript{2,3}. The embolic agents for transarterial embolization can be ethylene vinyl alcohol copolymer (Onyx\textsuperscript{®}).
copolymers) (EV3, Irvine-CA) 6 or N-butyl cyanoacrylate.

When the fistula is fed by meningeal branches from both the external and internal carotid arteries, only the branches from the external carotid artery are usually embolized in hopes that the flow to the fistula will be sufficiently decreased as to result in its subsequent closure. The internal carotid artery is usually not embolized in this setting unless the endovascular surgeon can successfully catheterize the meningo-hypophyseal trunk or other meningeal feeders.

Complications from endovascular treatment of dural CCFs are uncommon except in patients with connective-tissue disorders, such as Ehlers-Danlos syndrome. However significant complications have been reported, including hemorrhage at the catheter insertion site, in the orbit from perforation of the superior or inferior ophthalmic vein, or even intracranially; damage to orbital structures, such as the trochlea when the superior ophthalmic vein is used for access to the cavernous sinus; local infection; sepsis; ophthalmic artery occlusion; and both transient and permanent neurological deficits, particularly facial pain and ocular motor nerve paresis but also brainstem infarction. Using current available techniques, successful closure of dural CCFs can be achieved in 80% to 100%.

Resolution of preexisting symptoms is related to their duration and severity. Symptoms and signs usually begin to improve within hours to days after the successful closure of a dural CCF. Any preexisting bruit immediately disappears, and intraocular pressure immediately returns to normal. Proptosis, conjunctival chemosis, redness of the eye, and ophthalmoplegia (whether caused by orbital congestion or an ocular motor nerve paresis) usually resolve completely within weeks to months, and most patients have a normal or near-normal external appearance within six months.

The management, after resolution of CCF, may involve treatment of glaucoma, exposure keratopathy and correction of persistent diplopia.
Indirect CCFs are rarely life threatening. However, they can cause intractable or intolerable symptoms and may also produce visual loss. In these cases, interventional therapy is necessary. Cerebral angiography is the gold standard imaging modality for diagnosis and classification of CCFs. Transarterial or transvenous embolization is the main modality of treatment for most CCFs; with little or no morbidity and mortality, and with resolution of most clinical manifestations. Transarterial NBCA embolization could be a valuable option in treatment of CCFs when the fistula is mainly fed by external carotid arteries.

**REFERENCES**

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