Abstract

Carotid cavernous fistulae are an uncommon disease. They are classified as direct or indirect. In direct fistulas there is an abnormal communication between the internal carotid artery and the cavernous sinus. Indirect forms have an abnormal bypass between the meningeal branches of the internal and/or external carotid arteries and the same sinus. The purpose of this article is to provide an overview of the anatomy of the envolved area and the clinical findings, diagnostic evaluation and treatment.

Keywords: Carotid-cavernous sinus fistula; Carotid artery; Cavernous sinus

Resumo

Fístulas carotídeo-cavernosas são raras. São classificadas nos tipos direto e indireto. Fistulas directas têm uma comunicação anormal entre a artéria carótida interna e o seio cavernoso. Nas formas indiretas a conexão se faz entre os ramos meningeos da carótida interna e/ou externa e o mesmo seio. O propósito deste artigo é o de atualizar os conceitos anatômicos, clínicos, diagnósticos e terapêuticos desta situação.

Descritores: Fístula carotídeo-cavernosa; Artéria carótida interna; Seio cavernoso
INTRODUCTION

Anomalous communication between the internal carotid artery (ICA) or its branches and/or branches of the external carotid artery (ECA) with the cavernous sinus causes an abrupt change in the direction and distribution of brain and orbital blood flow — an uncommon condition of varying severity.

The condition typically presents with pulsating proptosis with murmur, and most cases can mimic conjunctivitis, unilateral glaucoma or Graves’ disease.

The anatomical complexity of the region can be assessed by increasingly sophisticated, high-resolution neuroimaging techniques that significantly improve the accuracy of topographic diagnosis and therapeutic access.

The aim of this review is to update the anatomical, clinical, and therapeutic knowledge related to carotid-cavernous fistula (CCF).

Anatomy of the carvenous

The cavernous sinuses (CSs), like all other cerebral sinuses, are venous channels (or extra-dural plexuses) formed by the inner and outer layers of the dura mater (DM). Also called the pachymeninx, the DM consists of a thick, resistant tissue rich in collagen fibres, blood vessels and nerves.

The CS occupies a small territory in the middle cranial fossa (parasellar location, lateral to the sphenoid sinus). It is 2-cm long and 1-cm wide, extending from the orbit to the petrous apex. Its osseous boundaries include the body and wings (greater and lesser) of the sphenoid, the tuberculum and dorsal part of the sella, the carotid groove, and the clinoid processes.

The DM covers the superior, lateral (with the sheaths of nerves III, IV, V1 [first branch of V], and possibly V2) and medial (fused with the periosteum of the sella) surfaces; the middle cranial fossa forms the lower surface.

The CS is a venous plexus that receives the blood returning from the eyes and orbits through the superior orbital fissure, individually or in a common trunk, via the superior orbital vein (SOV) and the inferior orbital vein (IOV, which is connected with the facial vein and may flow to the pterygoid plexus through the inferior orbital fissure), as well as the superficial middle cerebral vein, the inferior cerebral vein (including the uncal vein, temporal lobe), the sphenoparietal (vein or sinus, receiving the flow from the middle cerebral vein and variable contributions from the inferior frontal, anteromedial temporal, orbital, and meningeal veins), and pituitary veins. The SOV is formed by the junction of the angular and frontal veins in the anterior orbit, with a diameter of approximately 2 to 3.5 mm, which can change with head position or the Vasalva manoeuvre.

CS drainage flows to the superior petrosal sinus (SPS, which empties into the junction of the sigmoid and transverse sinuses) and the inferior petrosal sinus (IPS, with empties into the jugular bulb), communicating with the contralateral CS at the clivus (intercavernous plexus or circular sinus). The basilar venous plexus connects the CS to the epidural vertebral plexus; multiple emissary veins interconnect the CS inferiorly to the pterygoid plexus through the foramen ovale.

Cranial nerves III, IV, VI, and V1 run along the CS, as well as sympathetic and parasympathetic fibres and the ICA. The ICA is subdivided into seven segments: cervical (C1), petrous (C2), lacerum (C3), cavernous (C4), clinoïd (C5), ophthalmic (C6), and communicans (C7). The branches emerging at the CS comprise: (a) the meningohypophyseal trunk (the origin of the inferior hypophyseal, the marginal and basal tentorial [the Bernasconi-Cassinari branch, which anastomoses with the ophthalmic], and lateral clival and dorsal meningeal branches), (b) the posterior and inferior hypophyseal arteries, (c) the inferolateral trunk (or inferior artery of the CS, which subdivides into the superior, anteromedial, anterolateral [which anastomoses with branches of the internal maxillary], and posterior branches, (d) McConnell’s capsular artery, and, less frequently, (e) the ophthalmic artery. The ECA reaches the CS through the accessory meningeal artery (a branch of the middle meningeal or maxillary artery) which connects to the branches of the inferolateral trunk and the ascending branch of the pharyngeal.

The cranial nerves (except VI) are situated along the lateral wall of the sinus, in the following order from top to bottom: III, IV (which appears in the orbit outside the annulus of Zinn) and V1. The abducens nerve runs medially to the ophthalmic and laterally to the ICA. The sympathetic fibres run along the surface of the ICA, join the VI nerve and are distributed with V1, with which they reach — through the long ciliary nerves — the pupil dilator muscle. Some sympathetic fibres run directly from the carotid plexus to the ciliary ganglion; others travel directly with the ophthalmic artery to the eyeball.

Manifestations

Given its variable severity, CCF has been classified according to different parameters with the ultimate goal of indicating the best therapeutic approach. Thus it is common to find descriptions based on aetiology (spontaneous or traumatic) or flow conditions (high or low). However, these classifications are incomplete, as they do not relate to prognosis or management. The most used classification has been proposed by Barrow et al. and is based on the arterial supply of these communications (Table 1).

CCF type A is the only type with direct communication between the ICA and the CS, therefore high flow is usually present (in 5% of cases, the entire flow moves through this connection). A compilation of different series shows that brain

<table>
<thead>
<tr>
<th>Type</th>
<th>Features</th>
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<tbody>
<tr>
<td>A</td>
<td>Direct communication between the ICA and the CS (high flow, more common after trauma)</td>
</tr>
<tr>
<td>B</td>
<td>Communication between branches of the ICA and the CS (rare)</td>
</tr>
<tr>
<td>C</td>
<td>Communication between branches of the ECA and the CS</td>
</tr>
<tr>
<td>D</td>
<td>Communication between branches of both the ICA and ECA and the SC (low flow; most frequent)</td>
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trauma (including iatrogenic trauma) is responsible for up to 80% of cases, the others occurring spontaneously (aneurysm rupture, or weakness of the vascular wall in cases of collagen deficiency, such as Ehlers-Danlos syndrome (49), fibromuscular dysplasia, pseudoxanthoma elasticum, osteogenesis imperfecta, or atherosclerosis (20). While acute forms occur more often in young men, spontaneous forms tend to occur in middle-aged women (3,8,9,12,23-25).

There is much disagreement regarding how direct trauma (especially blunt trauma) causes damage to the ICA wall, and particularly on bone fracture as a precondition (26). Gobin et al. (26) detected trauma in 95% of cases. In 42 cases of CCF type A presented by Helmeke et al. (26) there was no evidence of trauma. The authors then suggested that the distension of the vascular wall caused by a sudden increase in intraluminal pressure can explain many of these cases. In fact, several features of this vascular segment make it prone to shunting, among them the amount and direction of ligaments in relation to the adventitia, the conformation and mobility of the siphon (horizontal segment), the inextensibility of the dura, and adjacent bones (8,14,26). Iatrogenic causes in CCF type A include perforation by catheters or balloons during endovascular procedures, post-septoplasty, transphenoidal surgery, LeFort type 1 maxillary osteotomy, and access to the Gasserian ganglion in trigeminal diseases (21,22,23,27,28).

Direct fistulas can cause acute symptoms or manifest after days or months. They are usually 1-5 mm in size and 1-2% are bilateral, or even contralateral to the ophthalmic signs (8,29). Indirect CCF, also called dural shunt, is typically a low-flow condition which may be congenital or occur spontaneously, and which causes or results from venous thrombosis. Predisposing factors include hypertension, pregnancy, head trauma and stretching, post-menopause, thromboembolic disease, atherosclerosis, and collagen disease (10,30,31). Indirect spontaneous forms are much more frequent than direct forms (32). Spontaneous resolution in direct CCF occurs in 10-60% of cases, before or after angiography, possibly due to CS thrombosis, usually within 6-94 months (8,20,23,34).

Different subtypes of CCF cause different clinical signs, with varying speeds of onset and severity, which is usually higher in direct forms. Pathogenesis involves CS dilation and retrograde drainage (cortex and orbit), with increased vascular volume and enlarged orbital muscles, increased capillary transudation, elevated episcleral venous pressure, and impairment of the optic nerve and retina due to stasis. In direct CCF, these events lead to a more acute presentation with more abundant signs and symptoms (8,23,26-31). Indirect forms, however, have a milder or minimal presentation. This is possibly due to the fact that in many cases, drainage of dural shunts often occurs to the basal and petrosal sinus, and only in the presence of thrombosis there is flow back into the orbit (8,12,32,38-40).

Clinical signs range from mild paresis and dysfunctions (nerves III, V, VI - the latter involved in up to 85% of cases (8)) without orbital congestion to pulsatile proptosis (milder in indirect forms). When CCF drainage flows to petrosal sinus, the SOV can have normal dimensions with a quiet eye (with some paresis, a condition called “white-eyed cavernous shunt”) (44). Signs and symptoms include: Chemosis (90% in type A), pain (25-40%), diplopia (50-68%), episcleral venous dilation with arterialisation, glaucoma (50-83%, with pulse asymmetry on tonometry (41)), murmur in the orbital region and surroundings (less dramatic or absent in dural forms; in order to assess it, the patient should be instructed to look down with the opposite eye, reducing involuntary movements and blinking), intracranial haemorrhage (5%, type A (44), and epistaxis (1-2%, type A) (1,3,20,26,40,45-49).

Characteristic symptoms include pulsatile exophthalmos, murrmur and venular dilation with chemosis (Dandy’s triad) (42). A change in the nature of the murmur may indicate improvement or a change in the drainage pattern (32,39). Children often have orbital murmurs, therefore the isolated presence of this finding after head trauma does not necessarily indicate fistula (30,39).

Increased muscle volume together with paresis produced in the CS cause diplopia and ophthalmoplegia (11,23). Ocular and orbital venous stasis causes circulatory distress of the optic nerve and retina, leading to papilledema, venular engorgement, retinalchoroidal, or retinal capillary disease (ischemia, oedema, haemorrhage) (31). A chronic lack of adequate perfusion in these sites can cause venous occlusion, proliferative retinopathy, vitreous haemorrhage, choroidal detachment, and neovascular glaucoma (32,33). Severe proptosis, eyelid cyanosis, and chemosis (possibly with spontaneous bleeding or after minimal trauma, and sometimes affecting the corneal surface [exposure keratopathy]) are associated with increased blood flow (6,13,18). Visual loss (90% in direct forms; rarely mild or bilateral) can be acute (associated with damage to II nerve) or gradual (1,22,24,48,54).

Glucoma can be caused by episcleral hypertension (20-25% present with blood in Schlemm’s canal), neovascularisation, or anterior displacement of the iris-lens diaphragm (52,53,58).

**Diagnosis and differential diagnosis**

Diagnostic suspicion is stronger in cases with a variety of characteristic signs. However, the gold standard for any type of CCF is cerebral angiography. It identifies the type, location and size of the connection, examines the vascular surroundings (aneurysms, pseudo-varices), and co-existing alterations, especially ischemic effects on the cortex. The main complications of the procedure include cerebral infarction (0.1-0.5%), adverse effects related to the contrast material, and death (0.1%) (8,20,23,32,57). Initial evaluation is done with Doppler ultrasound (50,58), computed tomography (CT), and magnetic resonance imaging (MRI). Note that normal results in these tests do not exclude the diagnosis (11,12). Additional techniques such as image subtraction or CT angiography can be used (42). CT can assess proptosis, CS and SOV dilation, enlargement of the extrinsic muscles (without predominance of specific muscles, such as the inferior and middle recti in Graves’ ophthalmopathy (39)), and bone fractures. Richer details are obtained with MRI, which shows the condition of the other brain sinuses, signs of hypertension, oedema, and cortical, cerebellar or brainstem involvement (42-44). This method and its improvements can achieve 83% sensitivity and 100% specificity (45). The SOV is increased in 75-100% of cases and may be the only imaging finding; it is rarely bilateral, and can even be contralateral (in cases with atypical drainage) (2,4,12). Occasionally remissions and exacerbations can occur, which is explained by SOV thrombosis, a differential diagnosis detected by MRI (42).

Ultrasound is useful in differentiating between dural and direct types, but also on follow-up. Increased flow turbulence in the ICA or ECA, inversion and arterialisation of vascular flow are characteristic signs (43).

Not every post-traumatic exophthalmos is due to CCF. Fractures of the orbital floor produce pain and exophthalmos (brain herniation) without murrmur. Rarer types of fistula, such as a connection between the CS and the posterior communicating artery or the meningeal artery produce a similar presentation. Chronic conjunctivitis, orbital pseudotumor, Graves’ disease, inflammation (Tolosa-Hunt syndrome (46)), and thrombophlebitis of the CS are among possible differential diagnoses (2,23,25,27,30,43,58,62) (Table 2).
Table 2
Differential diagnosis of CCF

<table>
<thead>
<tr>
<th>Disease</th>
<th>Differential features</th>
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<tbody>
<tr>
<td>Orbital cellulitis</td>
<td>External or lacrimal infection, trauma, involvement of paranasal sinuses, fever, rhinorrhoea, malaise, leukocytosis</td>
</tr>
<tr>
<td>Graves exophthalmos</td>
<td>Evidence of systemic disease, slow progression with exacerbation, upper eyelid retraction, lid lag, T3-T4-TSH.</td>
</tr>
<tr>
<td>Orbital pseudotumour</td>
<td>Varying onset, muscle-tendon involvement, proptosis, isolated thickening of the lateral rectus, bilateral in 25%, pain on movement, variable loss of acuity, affects the anterior portion (palpable lacrimal gland), signs of uveitis, serous retinal detachment.</td>
</tr>
<tr>
<td>Tolosa-Hunt</td>
<td>Persistent retro-ocular pain (preceding paresis), variable loss of acuity, symptoms lasting days or weeks, recurring, responding to corticosteroids in 24-48h, anamolous tissue in the superior orbital fissure on CT</td>
</tr>
<tr>
<td>Cavernous sinus thrombophlebitis</td>
<td>Fever (30-90%), rapid progression (bilateral), foci of infection (sinusitis, face [25%], ear, teeth, gums), leukocytosis, affects the patient’s clinical condition (confusion, seizures, stupor, coma), death &lt;30%</td>
</tr>
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</table>

Management

Emergency endovascular treatment of CCF is indicated in the presence of pseudoaneurysm, large CS varix, venous drainage toward the cortex, thrombosis extending beyond the fistula, increased intracranial pressure, altered mental status, proptosis and/or progressive loss visual acuity, brain haemorrhage, and ischemic stroke(36,47,52). In other situations, the severity of the condition versus the possibility of spontaneous resolution should be taken into account, especially in dural forms(32,40). Neuro-endovascular treatment should be used only when conservative management proves ineffective, or before ocular surgical procedures(27,32,40,43).

The endovascular approach is the current procedure of choice, either through an arterial or venous access. Different natural or synthetic occlusive materials can be used: Absorbable gelatin (gelfoam), silastic, silicone, platinum coils, autologous blood or blood products, polyvinyl alcohol, ethanol, cyanoacrylate, concomitant radiosurgery(30,31,32,33,34,35,36,37,38,39). About 75% of cases have some permanent loss of visual acuity(41). Different studies found 85-90% success rates, and complications range from 5 to 8% (death in 1%)(38,39,40). Relapse is not uncommon(40). Indirect CCF is treated more conservatively, considering the lower severity, the chance of spontaneous resolution and the risks of interventions(32,40). Symptoms can often worsen after successful occlusion (intentional or accidental) of the fistula, but there seems to be no higher risk of death in this subgroup than in patients without dural fistula(32,33,34).

Manual compression of the ipsilateral carotid artery and jugular vein can help closing up to 30% of dural CCFs(31). This manoeuvre should be performed using the contralateral hand (thus any deficit in this arm acts as a warning and a safety mechanism to interrupt compression) for 10 seconds, 5-6 times every hour. Compression should be increased over a few weeks(20). There are some contraindications to compression. Absolute contraindications are: Hypersensitive carotid sinus syndrome, carotid stenosis due to atherosclerosis or carotid ulceration, vertebrobasilar insufficiency, syncope or hypotension, transient ischemic attack, cardiac arrhythmia, and previous haemorrhage around the CCF. Relative contraindications are: Eye pressure above 25 mmHg with severe visual field loss, and severe vision loss(31,32).

Propotosis, chemosis and keratopathy should be managed according to severity. Lubricants (eye drops, gels), forced nocturnal eyelid occlusion, and topical antibiotics (when appropriate) are often necessary(40).

For glaucoma, drugs that reduce the production of aqueous humour are indicated (beta-blockers, alpha-adrenergic agonists, carbonic anhydrase inhibitors), while drugs promoting drainage are ineffective (pilocarpine and prostaglandin analogues)(36). Fistulising surgery (trabeculectomy with or without mitomycin) may be necessary; care should be taken to leave some posterior sclerotomy for the management of possible choroidal effusion(50). Neovascular forms (glaucoma and retinopathy), when associated, require laser photocoagulation and/or drainage valves(38,52). Nonpolaritative retinal repercussions are managed conservatively(39).

A study by Ishijima et al (52), which included the largest number of CCF cases complicated with glaucoma, showed good general prognosis, largely related to primary occlusion. With CCF closure most signs disappear within varying times (eye pressure in 72 hours, on average), but visual damage and some paresis may persist.

REFERÊNCIAS