



Review Article

Deciphering Neuro-Ophthalmic Presentations of Carotid Cavernous Fistulas: A Comprehensive Analysis of Venous Flow Dynamics and Clinical Implications

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ABSTRACT

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Background: Carotid cavernous fistulas (CCFs) are abnormal arteriovenous connections between the carotid arterial system and the cavernous sinus, presenting with complex neuro-ophthalmic manifestations due to the redirection of arterial blood into the venous system. This study systematically reviews the diverse neuro-ophthalmic presentations of CCFs, emphasizing the influence of venous flow dynamics.

Subjects and Methods: A comprehensive literature search was conducted in PubMed, Scopus, and Web of Science, focusing on keywords such as "carotid cavernous fistula," "neuro-ophthalmic presentations," and "optic nerve compression." Recent and historical studies were analyzed to assess the neuro-anatomical impacts on neuro-ophthalmic symptoms from CCFs. This review aimed to consolidate knowledge and refine diagnostic and therapeutic strategies for CCF management.

Results: The findings demonstrated that the neuro-ophthalmic presentations were quite distinctive, depending on the direction of venous flow. Anterior flow, overall, was associated with proptosis, conjunctival arterialization, and red, dilated vessels. In contrast, posterior flow was associated with cranial nerve complications, most notably abducens nerve palsy and trigeminal neuralgia, manifesting as double vision and facial pain, respectively. It therefore seems that the symptomatology and severity of CCFs is heavily dependent on the direction of blood flow.

Conclusions: The flow direction through the veins is of significant importance in the clinical presentation and prognosis of CCFs. These dynamics must be appreciated to improve diagnosis and allow for optimal treatment, thus averting the risk of fatal complications. In this review, the need for tailored therapeutic strategies through detailed vascular and neuro-ophthalmologic analysis is outlined.

Introduction

Carotid cavernous fistulas represent an abnormal arteriovenous connection between the carotid arterial system and the cavernous sinus with a host of neuro-ophthalmic manifestations (1,2). In essence, this was an excellent transcript on how this condition

significantly impacts ocular and cranial structures through the shunting of arterial blood into the venous system. Symptoms may vary from proptosis and conjunctival arterialization to vision loss and ophthalmoplegia, depending on the flow dynamics and the particular venous drainage (1,3). Precise diagnosis is essential in view of the

numerous presentations of the condition and the critical importance of appropriate management based on diagnosis; often it is necessary to use classifications such as the Barrow system (4). In spite of the great technical and material progress of imaging and intervention methods, there is a continuing critical need that, to our best knowledge, no one else provides: a comprehensive review of the extant literature, which consolidates the current status with regard to the neurophthalmic presentations of this clinical entity: the carotid cavernous fistula. Such a review is pivotal for refining diagnostic accuracy and optimizing treatment strategies, thereby enhancing patient outcomes. This article aims to address this gap by systematically examining and synthesizing the wealth of information available.

Subjects and Methods

A literature search was conducted through PubMed, Scopus, and Web of Science using the relevant keywords "carotid cavernous fistula," "neuro-ophthalmic presentations," and "optic nerve compression". This review will focus on contemporary research and will be substantiated by the relevant key articles of the past, which will act as critical foundational information on carotid cavernous fistulae and their neuro-ophthalmic implications. The selection of articles for this review was based on inclusion criteria for those studies that impact the neuro-anatomical symptoms caused by the carotid cavernous fistulas. Included articles have been qualitatively analyzed to describe and discuss the information they provided on the advances made on both diagnosis and treatment. This review will create a scaffold and will indicate potential areas for further research regarding the neuro-ophthalmic management of carotid cavernous fistulas and the concomitant development of diagnostic criteria and treatment modalities.

Results

According to the identified neuro-ophthalmic manifestations of CCFs and as organized in Table 1 (1-8), the characteristic clinical manifestations are related to the venous flow direction across the anatomical structures of question. For example, anterior flow is mainly the cause of proptosis and the characteristic "red eye" since it leads to arterialization across the superior and inferior ophthalmic veins (1).

In contrast, posterior flow mainly compromises the cranial function and is the chief cause of the double vision that results from the abducens nerve palsy (2) and the trigeminal neuralgia-associated facial pain or headache (3). Therefore, depending on the venous flow direction, the CCF symptoms in the patients will be dependent and varied.

Table 2 presents a comprehensive summary of the clinical characteristics and venous flow dynamics observed in patients with carotid cavernous fistulas (CCFs) across various studies (Table 2) (12-27).

This table includes data from selected case reports and original research studies, highlighting key parameters such as sample size, patient age, sex distribution, study design, clinical manifestations, and venous flow dynamics.

The analysis reveals that the clinical manifestations of CCFs vary significantly based on the direction of venous flow. Anterior venous

flow is primarily associated with ocular symptoms such as proptosis, conjunctival arterialization, and red dilated vessels. In contrast, posterior venous flow is more frequently linked to cranial nerve complications, including abducens nerve palsy, resulting in double vision, and trigeminal neuralgia, presenting as facial pain or headache. This differentiation underscores the importance of understanding venous flow dynamics in diagnosing and managing CCFs effectively. Overall, the data emphasize the necessity of tailored diagnostic and therapeutic approaches based on the specific venous flow patterns in CCF patients. This targeted approach can help optimize patient outcomes and mitigate potential complications associated with CCFs (Table 2) (12-27).

Table 1. Neuro-Ophthalmic Presentations of Carotid Cavernous Fistulas by Venous Flow Direction

Flow Direction & Anatomical Impact	Clinical Presentation	Explanation
Anterior Flow: Superior and Inferior Ophthalmic Veins	Proptosis, "red eye," and potential vision loss due to increased venous pressure.	Arterialized blood flows into the ophthalmic veins, causing dilation and congestion, visible as red, dilated vessels.
Anterior Flow: Conjunctiva and Episclera	Arterialization visible as squiggly, dilated, tortuous vessels on the conjunctiva and episclera.	The direct arterial blood into these areas causes distinct redness and vessel tortuosity.
Posterior Flow: Cranial Nerve VI (Abducens)	Double vision due to inability to move the eye laterally, typically presenting as abducens nerve palsy.	Increased pressure or compression within the cavernous sinus impacts the abducens nerve.
Posterior Flow: Cranial Nerve V (Trigeminal)	Facial pain or headache, indicative of trigeminal neuralgia.	The trigeminal nerve is affected by altered venous drainage patterns or direct compression in the cavernous sinus.

Discussion

The literature review related to CCFs underlines the fact that their neuro-ophthalmic presentations must be well understood. Abnormal communications between the carotid arterial system and the cavernous sinus create different signs and symptoms due to unusual arterial blood flow into the venous system. This paper nicely outlines the various clinical presentations, the Barrow classification, which subdivides fistulas according to the source of the blood flow: from the internal carotid artery itself (Type A) and its branches (Types B, C, and D) (4). Understanding this classification and the associated clinical presentations helps to develop an excellent management approach to CCFs.

It is through this pathophysiological understanding that allows CCFs' clinical manifestations to be explained. The pathophysiology is based on a redirection of arterial blood into the venous system through the cavernous sinus, which affects the superior and inferior ophthalmic veins. Clinical symptoms are best described by the flow, either

anterior or posterior. Anterior flow leads to “red eye shunts.” These include proptosis of the eyes with a visible arterIALIZATION phenomenon of the conjunctiva and episclera, described as squiggly, dilated, and tortuous vessels (1). Presentation may also include symptoms of optic neuropathy or ocular ischemia due to the pressure exerted by the sudden increase in venous return (2,3).

On the other hand, posterior flow affects the cranial nerves within the cavernous sinus. It affects the abducens and trigeminal nerves. When the abducens nerve is affected, there is diplopia and lateral gaze palsy, while involvement of the trigeminal nerve leads causes facial pain or headache sometimes associated with venous congestion or even direct nerve compression (3). The diseases generally present as “red eye shunts,” but as it progresses, so does the pressure in the vein. Initially, they can be “white eye shunts,” where there are not very many findings on the face, but there is significant cranial nerve involvement. The management of CCFs relies heavily on understanding the nature of the fistula, with the Barrow classification guiding treatment decisions. For instance, direct high-flow fistulas (Type A) typically require more aggressive and immediate intervention to prevent irreversible damage due to high arterial pressure within the ocular and cranial structures. In contrast, the lower-flow fistulas (Types B, C, and D) might be managed conservatively depending on the symptoms and the risk of progression to cortical venous drainage, which can be life-threatening (4).

Management is further complicated by the possible long-term complications of neglected or poorly managed CCFs. These may lead to chronic ocular symptoms, unrelenting cranial nerve palsy, and even increased susceptibility to stroke because of cortical venous reflux. In this context, this is the exact importance of early and proper intervention, for which detailed angiographic studies and classifications are needed in the mitigation of the risks and the improvement of the outcomes for these patients.

The spread of diagnostic imaging, particularly through computed tomography (CT), magnetic resonance imaging (MRI), and digital subtraction angiography (DSA), has greatly increased the detection and characterization of carotid cavernous fistulas (CCFs). Additionally, such diagnostic tools were not only essential for confirmation but also provided crucial information on the anatomy of the fistula, the course, and flow characteristics thereof, and the neighboring structures in the anticipated therapeutic procedures (1, 4, 5).

The variety of clinical presentations and outcomes of CCFs demonstrates the complexity of the condition. According to Williams (2018) (2), therapy diversified substantially, and case-tailored treatment was being constantly emphasized at different clinical representations. Sunit Das et al. (2006) (5) demonstrated that, following a posterior approach, transarterial coiling led to stabilization of vision of a CCF patient and, if appropriate interventions are taken, significant recovery may be expected. Additionally, E. Klevtsova et al. (2015) (6) presented a case of acquired posttraumatic CCF with seizures and focal neurological findings. Such studies or reviews show the scale of possible neuronal manifestations of CCFs.

Spontaneous resolution without surgery might also occur in CCF. Accordingly, M. Bujak et al. (2010) (7) reported two cases of spontaneous closure of dural carotid-cavernous fistula. Findings suggest that a natural occlusion mechanism may be present in some dural CCFs. On the other hand, post-embolization, N. Bonnin et al. (2013) (8) also displayed changes in signs as well as neuroradiological features that pointed toward recovery. W. Spencer et al. (1973) (9), on the other hand, reported extreme cases as well as those of ischemic ocular necrosis secondary to untreated CCFs, which reiterated the need for management on time and at all levels.

These studies collectively emphasize the necessity of a comprehensive diagnostic and therapeutic approach. A. Eswar et al. (2014) (10) reported on a case of CCF mimicking myasthenia gravis, posing a diagnostic challenge and necessitating advanced diagnostic strategies to differentiate CCF from other neurological disorders. Furthermore, collaborative efforts described by E. Zanaty et al. (2005) (11) between neuro-ophthalmologists and interventional neuroradiologists exemplify the multidisciplinary approach required to effectively manage these complex cases.

The findings of this study align with previous research on CCFs which underscores the significance of understanding venous flow dynamics in managing CCFs. Clinical and angiographic characteristics of dural arteriovenous fistulas, as highlighted by Suh et al. (2013) and Miller et al. (1995), demonstrate the complexity and variability of these conditions. The endovascular treatment of CCFs, particularly through transvenous embolization, has been shown to be effective in numerous studies, including those by Gupta et al. (2006) and Alexander et al. (2010), further validating our approach to patient management (28-31).

Moreover, the pathophysiological understanding of CCFs and their clinical manifestations, as described by Tsai et al. (2016) and Miller et al. (2015), emphasizes the role of detailed imaging and angiographic studies in diagnosis and treatment planning. Studies by Halbach et al. (1987) and Suet al. (2014) have shown that the direction of venous drainage significantly influences clinical outcomes, reinforcing the need for tailored therapeutic strategies based on individual venous flow patterns. The varied clinical presentations and outcomes reported by Biondi et al. (2003) and Ellis et al. (2012) further highlight the importance of a personalized approach to CCF management (32-40).

This critical review on CCF has a number of limitations: the lack of consistency in reporting standards and reliance on historical data mean that potential bias can be introduced into the results; hence, it affects both the final result and generalizability. Besides, rapid improvement of diagnostic and treatment approaches makes data from the past hardly having a clear impact on present practices. In addition, these events are very rare, with difficulty in collection of large and diverse groups, thus limiting the strength of the results. These gaps need prospective research with standard reporting to upgrade our understanding and management of CCFs.

Table 2. Clinical Findings and Venous Flow Dynamics of A number of Case Reports and Original Research Studies Associated with Carotid Cavernous Fistulas

Author	Publication year	Sample size	Mean age±SD	Sex (N,%)	Study Design	Origin of the Study	Clinical Manifestations of patients	Venous Flow Dynamics
Pérez Sempere et al. ⁽¹²⁾	1991	2	66.5 ± 3.5	Female (2, 100%)	Case Report	Spain	Case 1 presents with right-sided ptosis, impaired right-eye adduction, a dilated nonreactive right pupil, headache, and diplopia. Case 2 presents with left-sided ptosis, impaired left-eye adduction, headache, and diplopia.	Posteriorly draining dural fistula
Aciermoe t al. ⁽¹³⁾	1995	2	63.5 ± 2.5	Female (2, 100%)	Case Report	USA	Case 1 presents with left abduction deficit, periocular pain, and horizontal diplopia. Case 2 exhibits persistent headache, horizontal diplopia, right upper eyelid ptosis, and impaired ocular movement in the right eye.	Posterior drainage into inferior petrosal sinus
Loré et al. ⁽¹⁴⁾	2003	1	67 (Single patient)	Female (1, 100%)	Case Report	Italy	The patient presents with moderate swelling around both eyes, redness of the sclera, swelling of the conjunctiva, slight bulging of the eyes, eye pain, excessive tears, and diplopia.	Dural carotid cavernous fistula draining into the ipsilateral superior ophthalmic vein
Peng et al. ⁽¹⁵⁾	2004	1	42 (Single patient)	Female (1, 100%)	Case Report	Taiwan	The right eye exhibits pain, protrusion, and limited movement. Elevated intraocular pressure of 30 mmHg in the right eye. Proptosis and abduction restriction. The right eye exhibits dilated conjunctival and episcleral vessels, as well as a hyperemic disc.	Using color Doppler ultrasonography, retrograde pulsatile flow in the right superior ophthalmic vein was seen.
Ikeda et al. ⁽¹⁶⁾	2005	1	55 (Single patient)	Female (1, 100%)	Case Report	Japan	The patient is experiencing a severe and persistent headache in the right orbitofrontal region, as well as diplopia caused by paralysis of the right abducens nerve. No symptoms of orbito-ocular involvement were found during the entire clinical course.	In the arterial phase, the dural carotid-cavernous sinus fistula has three directional drainage pathways. significant outflow into the vein of the eyes (SOV), High-rate outflow into the angular facial vein that stops the SOV from being enhanced for an extended period of time during the venous phase
Rooij et al. ⁽¹⁷⁾	2006	11	61.6 ± 15.2 (ranging from 27 to 77 years)	Female (8, 72.7%), Male (3, 27.3%)	Original Research	Netherlands	The presence of a clearly audible pulsatile bruit is observed in 100% of cases. There is a condition called bilateral exophthalmus with ophthalmoplegia, which occurred in 63.6% of cases. Reduced visual acuity (8, 72.7%), Hemiplegia with aphasia occurred in 9.1% of cases. The occurrence of cerebral bleeding is related with significant cortical venous drainage in a majority of cases (2, 18.2%).	High-flow CCFs: 5 cases, Intermediate-flow CCFs: 3 cases, Low-flow CCFs: 3 cases, Venous drainage to superior ophthalmic veins, minor cortical venous drainage
Das et al., ⁽¹⁸⁾	2006	1	58 (Single patient)	Male (1, 100%)	Case Report	USA	The patient experienced a gradual deterioration of vision in the right eye, leading to total blindness within a period of 5 weeks after undergoing carotid artery angioplasty and stenting. The patient presents with symptoms including right proptosis (bulging of the eye), retro-orbital discomfort (pain behind the eye), right facial numbness, pulsatile proptosis impaired visual acuity, and intermittent diplopia. The individual experiences total loss of vision in the right eye, including the inability to perceive light, and paralysis of the muscles that control eye movement.	Angiography verified high-flow direct CCF, and the cavernous region was reached with dissection of the proximal right ICA. Superior and inferior ophthalmic vein engorgement

Théaudin et al. ⁽¹⁹⁾	2008	1	75 (Single patient)	Female (1, 100%)	Case Report	France	The patient experienced frontal headache of severe extent, temporary and recurrent diplopia, bilateral conjunctival injection, episcleral and conjunctival hyperemia on both eyes, vertical paresis of the left eye, ptosis and complete ophthalmoplegia of the right eye, partial motor seizures, facial palsy on the right side, and aphasia.	DCCF draining into leptomeningeal veins; Outflow veins: right inferior petrosal sinus occluded; left superficial sylvian vein draining into left temporal and parietal lobe cortical veins; left inferior petrosal sinus draining into the internal jugular vein
Kim et al. ⁽²⁰⁾	2013	1	32 (Single patient)	Female (1, 100%)	Case Report	Republic of Korea	Blowout fractures on both sides, Diplopia characterized by impaired abduction of the left eye, No orbito-ocular indications, including chemosis, ptosis, or exophthalmos.	Posteriorly draining CCF with isolated abducens nerve palsy
Erickson et al. ⁽²¹⁾	2014	1	32 (Single patient)	Male (1, 100%)	Case Report	USA	The patient demonstrated proptosis, ocular motility deficits, decreased vision in the right eye, orbital bruit, minor right exotropia, moderate motility deficits in all cardinal gaze directions, dilated conjunctival blood vessels, and 3 mm of proptosis in the right eye.	Profound dilatation of the right superior ophthalmic vein
Leishangthem et al. ⁽²²⁾	2017	1	71 (Single patient)	Female (1, 100%)	Case Report	USA	Progressive left-sided monocular diplopia and ptosis were initially diagnosed as monocular myasthenia gravis. The patient also exhibited left-sided proptosis, ocular bruit, partial third and fourth nerve palsies, chemosis of the left eye inferiorly, and corkscrewing of conjunctival blood vessels.	Indirect high-flow left CCF, type D (supply from both ICA/ECA meningeal branches)
Lin et al. ⁽²³⁾	2019	1	32 (Single patient)	Male (1, 100%)	Case Report	Taiwan	The patient demonstrated progressive double vision for four months, right-sided headache and periocular pain, right-side partial ptosis with a mid-dilated right pupil and a poor reaction to light, limited right-side extraocular movement with impaired adduction, no chemosis, proptosis, conjunctival injection, swollen eyelids, or ocular bruits, normal best-corrected visual acuity and intraocular pressure in both eyes, and normal other cranial nerve functions.	Right-sided CCF is mostly fed by the right inferior petrosal sinus via venous drainage from the dural branch of the right middle meningeal artery.
Azzam et al. ⁽²⁴⁾	2021	1	29 (Single patient)	Male (1, 100%)	Case Report	USA	The patient exhibited progressive proptosis, diplopia, right-sided proptosis, periorbital edema, and conjunctival injection. Generalized ophthalmoplegia of the right eye was most pronounced during abduction. The patient also exhibited tortuous episcleral vessels and blood in Schlemm's canal, as well as dilated, tortuous retinal vessels.	Low-flow indirect carotid-cavernous fistula (CCF) with flow reversal into the right superior ophthalmic vein and Cavernous sinus enhancement on CT
Cavasin et al. ⁽²⁵⁾	2021	1	68 (Single patient)	Female (1, 100%)	Case Report	Italy	The patient demonstrated lacrimation, visual disturbance, redness and edema of the conjunctiva, spontaneous retrobulbar pain, and pain on horizontal or vertical gaze. Additionally, the patient experienced subjective intermittent diplopia due to eye motility impairment. The patient did not exhibit any signs of optic nerve involvement, such as visual acuity loss, and no significant	Exophthalmos on the left Without a discernible hypertrophic superior or inferior ophthalmic vein, the size of the global left extrinsic ocular muscles increases.

hypertrophic superior or inferior ophthalmic vein.

Pellegrini et al. ⁽²⁶⁾	2022	1	92 (Single patient)	Female (1, 100%)	Case Report	USA	The patient displayed redness in both eyes, swelling of the eyelids, inflammation of the conjunctiva, paralysis of eye movements, drooping of the eyelids, protrusion of both eyes, severe inflammation and congestion of the conjunctiva, almost complete paralysis of eye movements in both eyes, complete drooping of the right upper eyelid, visual acuity of 20/200 with corrective lenses in both eyes, intraocular pressure of 21 mmHg in both eyes, and mild enlargement of retinal veins with no swelling of the optic disc.	Dilation of the superior ophthalmic veins on both sides. High-flow carotid-cavernous fistula in direct alignment with subsequent expansion of the extraocular muscles
Krothapalli et al. ⁽²⁷⁾	2023	1	56 (Single patient)	Male (1, 100%)	Case Report	USA	Progressive right eye proptosis, congestion, reduced visual acuity (20/40), limited duction, exophthalmos, pulsatile tinnitus, elevated intraocular pressure, and no optic disc swelling were all present in the patient. However, there was a significant amount of inflammation in the right orbit, as well as unusual enhancement of the basal frontal lobe next to the orbit.	Superior ophthalmic vein enlargement enlarged frontal vein Right carotid cavernous fistula (CCF) in indirect form Right internal jugular vein stenosis combined with right sigmoid sinus thrombosis

Conclusion

Neuro-ophthalmological examination of patients with carotid-cavernous fistulas shows that the venous flow direction determines the clinical manifestation. Anterior fistula flow results in the appearance of visible symptoms like proptosis and red eye, due to arterialization, while the posterior fistula flow impinges on the functioning of the cranial nerves with the symptoms that carry the potential of the worst eventualities, like diplopia and facial pain. Appropriate management of CCFs relies on correct classification and understanding of the flow dynamics in a manner that can prevent serious complications and improve outcomes.

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Conflict of Interest

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