CASE REPORT

The Spectrum of Cavernous Sinus and Orbital Venous Thrombosis: A Case and a Review

Paul F.S. Lai, M.D.,
and Michael D. Cusimano, M.D., M.H.P.E., F.R.C.S.(C)

Abstract—Orbital venous pathologies encompass a broad range of entities including tumors, shunts, congenital anomalies, aneurysms, and obstructive lesions. Patients may present with a variety of clinical findings which may include a combination of tumefaction, vascular engorgement, orbital pulsation, and exophthalmos, depending on the relationship between the lesion and the vascular system. Clinical findings may be unreliable in excluding serious underlying disorders, and so an extensive clinical and radiologic evaluation is necessary. This article presents a rare case of spontaneous aseptic cavernous sinus-superior ophthalmic vein thrombosis in a woman on hormone replacement therapy, and illustrates the multidisciplinary approach in diagnosis and management. The literature on issues surrounding this case is reviewed. (*Skull Base Surgery*, 6(1):53–59, 1996)

Apart from retinal vein occlusion, venous disease of the orbit is a rare occurrence. It can manifest as arteriovenous malformation or fistula, cavernous sinus or superior ophthalmic vein thrombosis, or an orbital varix with or without thrombosis. It may lead to temporary or permanent cosmetic deficit and/or ophthalmologic findings such as proptosis, chemosis, impaired extraocular movement, impaired visual acuity, defective color vision, and secondary glaucoma. In the case of cavernous sinus thrombosis, the thrombosis can spread to other dural venous sinuses, and death, hemiparesis, epilepsy, or spread of infection in septic cases can result. Cases of pituitary insufficiency and the syndrome of inappropriate antidiuretic hormone secretion have been reported following thrombosis of cavernous sinus.^{1,2} Thrombosis of orbital veins without associated cavernous sinus thrombosis is rare. We present a case of cavernous sinus-orbital vein thrombosis in a previously healthy woman, illustrating this rare condition and its management.

CASE REPORT

One month prior to presentation this 45-year-old perimenopausal woman experienced severe left thigh pain while on menopausal hormonal replacement with minestrin. This eventually resolved without significant abnormalities revealed by Doppler studies and venograms. Ten days prior to presentation she experienced right-sided temporal/frontal headache with periorbital swelling and subconjunctival hemorrhage in the right eye. The headache started in the morning as a sharp and excruciating pain which was accompanied by nausea, slight vomiting, and diaphoresis; by afternoon, she developed marked right-sided visual loss, proptosis and chemosis of the right eye to the extent that she was unable to voluntarily open her right eye. An ophthalmologist prescribed prednisone, and a CT scan done 2 days later failed to reveal significant intracranial abnormalities. There

was no dizziness, loss of consciousness, diplopia, aura, nor audible bruit. Within the next several days, much of the periorbital swelling and chemosis subsided, and the patient regained most of her vision, although she still complained of intermittent headache, fatigue, and blurred vision.

At presentation, the patient had residual right subconjunctival hemorrhage and a relative afferent pupillary defect with reduced color vision in the right eye. Her pupils were equal and reactive to light. Visual acuity of the patient was 20/30 + 2 bilaterally and her visual fields were normal. The rest of the exam was unremarkable.

During her admission, an MRI was performed but showed no dural malformation and no asymmetry in the dimensions of the cavernous sinus. However, cerebral angiography revealed asymmetry of filling of the cavernous sinus due to markedly diminished opacification of the right cavernous sinus, suggesting the diagnosis of cavernous sinus-superior ophthalmic vein thrombosis. Given her normal coagulation profile, it was felt that her thrombosis was due to the effect of minestrin. Her perimenopausal symptoms were treated with clonidine. She was hydrated, given analgesics, and after 5 days she had returned to normal completely. At 18 months follow-up, she has remained well off minestrin.

DISCUSSION

Pathophysiology

Given that dural venous sinuses and the cerebral veins they drain have no valves, flow is determined by pressure gradients. Venous blood may thus stagnate in the head and orbital regions as a result of venous obstruction. The pathogenesis of thrombosis can be attributed to three predisposing factors: 1) stasis of blood flow (pooling or obstruction); 2) injury to the vessel wall; and 3) hypercoagulability of blood.³ Thrombosis may occur in association with orbital varix, arteriovenous malformation, dural-sinus fistula, and neoplastic processes. In most cases, isolated thrombosis of orbital veins are uncommon, as they are usually associated with cavernous sinus thrombosis.

The major venous drainage of the orbit is posterior through the superior ophthalmic vein (SOV) and the inferior ophthalmic vein (IOV). The IOV, which is formed inferolaterally as a plexus, passes posteriorly adjacent to the inferior rectus muscle and drains into the superior ophthalmic and the pterygoid plexus. The SOV, the larger of the two veins, is formed by the confluence of the angular, nasofrontal, and supraorbital veins of the face. The SOV first extends posteriolaterally to the medial border of the superior rectus muscle in the anterior third of the orbit. In the second segment, the SOV enters the muscle cone and passes laterally beneath the superior rectus. The last segment begins when the vein extends

posteromedially along the lateral border of the superior rectus into the superior orbital fissure where it drains into the cavernous sinus.⁴ Hence, pathology in the cavernous sinus can mimic the superior orbital fissure syndrome causing ophthalmoplegia, ptosis, and involvement of VI.⁵

The optic nerve can be vulnerable within the bony confines of the orbit, especially at the apex where the nerve is tethered to bone or in the bony canal of the optic nerve, although this rarely occurs in isolated cavernous sinus thrombosis. The marked acute decrease in vision in our patient, the subsequent persistence of a relative afferent pupillary defect, and the decreased color vision in the right eye could be the result of damage to the optic nerve and ocular ischemia attributed to the mass effect from orbital edema associated with venous congestion. Raised intraocular pressure and elevated venous pressure in the cavernous sinus and tributaries can cause retinal ischemia and anterior ischemic optic neuropathy due to decreased retinal perfusion pressure even without occlusion of the central retinal artery.^{6,7}

Etiologies

Cavernous sinus thrombosis (CST) may be aseptic or septic. Septic CST may be associated with contiguous or venous spread of infection in orbital cellulitis, boils in the face, and chronic bacterial infection of the sinuses (usually the ethmoid air sinuses).⁸⁻¹¹ Besides being associated with carotid aneurysms and surgical treatment of trigeminal neuralgia, the usual aseptic cases occur in debilitated patients (marasmic phlebothrombosis) at the extremes of age, with the etiologic factors being anemia, hypercoagulability (eg, polycythemia, antithrombin III deficiency acquired from nephrotic syndrome, SLE, or L-asparaginase therapy), dehydration (from chemotherapy, malignancy, gastrointestinal disturbance, or diabetic ketoacidosis), and hypotension allowing stagnation of blood (Table 1).¹²⁻¹⁴ Also, aseptic thrombosis of the posterior part of the ophthalmic vein and of the cavernous sinus has been described secondary to compression or obstruction by malignant tumors of the skull base or nasopharynx.¹⁵ Spontaneous aseptic thrombosis in a healthy individual is extremely rare.

The only etiologic factor for thromboembolic disease in our patient was her minestrin therapy (norethindrone acetate 1 mg and ethinyl estradiol 20 µg) and possibly perimenopausal hormonal changes. Numerous retrospective and prospective studies have concluded that the incidence of thrombophlebitis and thromboembolism is increased with the use of oral contraceptives, with the incidence increasing with higher dosages of estrogen.^{16,17} In general, the risk returns to normal within approximately 1 month of discontinuation. The increase in incidence of thromboembolism is also supported by studies that have shown that patients taking estrogens or combined oral contraceptives have increased platelet aggrega-

Table 1. Literature Review of Cavernous Sinus Thrombosis: 1976–1994
(72 English articles; ref. 1,2,7,28,30,33–99) Causes in brackets [] were reported in older literature

Cause	Presentation	Number of Cases	Frequency
Septic			
Facial infections ^{2,7,28,30,34–45}	Acute	66	0.398
Orbital infections ^{35,39,46–52} (Orbital/periorbital cellulitis, styes)	Acute	9	0.054
Sinusitis ^{30,33,43,53–63}			
Sphenothmoidal	Acute	14	0.084
Frontal	Acute/Chronic	4	0.024
Unspecified	Acute	13	0.078
Mucormycosis ^{30,64–74}			
Rhinocephal	Acute	8	0.048
Otocerebral	Acute	2	0.012
Otitis Media/mastoiditis ^{30,35,36,75,76}	Acute/Chronic	5	0.030
Petrositis ⁷⁷	Acute	1	0.006
Dental infections ^{33,43,59,78–84}	Acute/Chronic	11	0.066
Bacterial meningitis ³⁹	Acute	2	0.012
Sepsis from other sources ^{1,59}	Acute	2	0.012
Subtotal		137	0.825
Aseptic			
Trauma ^{35,59,61,85,86}			
Supraorbital	Acute	2	0.012
Mandible fracture	Acute	1	0.006
Penetrating orbital trauma (Basal skull fracture)	Acute	2	0.012
Postsurgery ^{87–94}			
Rhinoplasty	Acute	2	0.012
Cataract extraction	Acute	1	0.006
Basal skull (including maxillary)	Acute	2	0.012
Tooth extraction [Trigeminal neuralgia]	Acute/Chronic	3	0.018
Hematologic ^{14,59,95}			
Polycythemia rubra vera	Acute	2	0.012
Acute lymphocytic leukemia	Acute	1	0.006
Hypercoagulability unspecified [elevated IgM, antithrombin III deficient]	Acute	1	0.006
Malignancy			
[Rhabdomyosarcoma]			
[Nasopharyngeal tumor]			
Vascular ⁹⁶			
Dural fistula [carotid artery aneurysm]	Acute	1	0.006
Other ^{59,97,98}			
Ulcerative colitis	Acute	1	0.006
Dehydration	Acute	1	0.006
Heroin overdose	Acute	1	0.006
Idiopathic (no cause specified) ⁹⁹	Acute	8	0.048
Subtotal		29	0.175
Total		166	1.000

tion, accelerated blood clotting, altered blood concentrations of some clotting factors, and altered fibrinolytic activity related to decrease in antithrombin III.^{16–18} Pregnancy, the puerperium, and oral contraceptive pill have prominent associations with dural sinus thrombosis.^{19,20} A review of superior sagittal sinus thrombosis by Schell and Rathe found the oral contraceptive pill to be the most common association.²¹

Clinical Features and Differential Diagnosis

In the evaluation of patients suspected of having orbital vascular disease, the important information elicited in the history should include: onset, course, duration

of symptoms (eg, pain, diplopia) and signs, past disease (eg, sinus disease, hypercoagulability), trauma, and family history. On external examination a combination of any one of proptosis, hemorrhage, vascular engorgement (eg, chemosis or episcleral venous dilation), and pulsation or bruit may be present. Examination of the cranial nerves with emphasis on vision (including color and contrast), ocular motility, and the pupils are essential. Venous congestion may be evident on fundoscopic exam, and the intraocular pressure (IOP) may be elevated due to increase in episcleral pressure.

In superior orbital vein thrombosis and cavernous sinus thrombosis the findings can present suddenly, representing acute compromise to the venous drainage system. In cavernous sinus thrombosis there is

papilledema and massive edema of the orbit and eyelids, in addition to the findings of increased IOP, retinal venous congestion and conjunctival chemosis found in SOV thrombosis.²² However, cavernous sinus thrombosis and SOV thrombosis may be difficult to distinguish, as the two conditions may coexist. Acute CST may be confused with rhinocerebral mucormycosis and orbital cellulitis, which may also give rise to thrombosis of the cavernous sinus as mentioned above (Tables 1, 2). In more indolent forms of CST, usually those secondary to odontogenic or otogenic infections, when the cavernous sinus is slowly obliterated, the orbital manifestations are less impressive.¹¹ Sino-orbital aspergillosis (the indolent form of rhinocerebral mucormycosis), subperiosteal mucocoeles, and Tolosa-Hunt syndrome (granulomatous infiltration in the parasellar region), or other processes producing a superior orbital fissure syndrome (a complex of symptoms involving the ocular motor nerves and V1) or orbital apex syndrome, may resemble chronic CST (Table 2).¹¹ These latter two syndromes usually result from unilateral extension of infection from the adjacent sphenoid or posterior ethmoid air sinuses.⁷ The superior orbital fissure syndrome has also been described following trauma, neoplasms, and syphilitic, tuberculous or nonspecific lesions.²³ Visual impairment occurs when the orbital apex is involved, but not with lesions confined to the superior orbital fissure.⁵

Cavernous sinus thrombosis should be distinguished from carotid-cavernous sinus fistulas (CCF), as they may superficially resemble one another in acute presentations. Classically, septic CST presents with various combinations of fever, headache, sixth and occasionally third, fourth, and fifth nerve palsy, proptosis, decreased visual acuity, and chemosis and venous congestion. With the exception of pulsating exophthalmos with bruit behind the affected eye, which may not be present in low flow

fistulas, CCF may also present with any combination of venous congestion and chemosis, impaired eye movement, and reduced vision. Septic cavernous sinus thrombosis is a life-threatening emergency, while CCF is a hemodynamic event with long-range consequences for the orbit and globe. Arteriovenous communications involving the cavernous sinus can be classified as either direct shunts between cavernous sinus and the internal carotid or as dural shunts between the cavernous sinus and the meningeal branches of the internal and/or external carotid.²⁴ The majority of CCF are attributed to cerebral trauma involving basal skull fractures. However, similar fistulas can occur after rupture of an intracavernous carotid aneurysm or of an atherosclerotic internal carotid artery.^{25,26} Spontaneous fistulas as shown by arteriographic studies tend to be dural shunts. These shunts have a predilection for postmenopausal women, possibly due to alterations in blood coagulation associated with hormonal changes.²⁷ In direct CCF, high-pressure arterial flow fills the cavernous sinus and refluxes into the orbital veins producing pulsating exophthalmos, bruit, and episcleral, orbital, and intraocular venous congestion with increased IOP. In contrast, the relatively low-pressure arterial blood flow in dural shunts causes milder elevations of venous pressure leading to milder symptoms. Some authors have hypothesized that in dural shunts, orbital congestion may not occur until arterial flow is shifted from a posterior to an anterior direction into the orbit by the presence of intracranial venous thrombosis.²⁷ For pathologies such as carotid-cavernous sinus fistulas, neuroradiologic selective embolization techniques have become a routine, important part of management.²⁴

Imaging

In the past, orbital phlebography was considered to be the definitive radiologic procedure to demonstrate occlusion of the carotid sinus. However, phlebography is difficult and carries a significant risk of mobilization of the venous thrombus and dissemination of infection. Angiography can be extremely useful if nonfilling or asymmetry of filling of the carotid sinus/superior ophthalmic vein can be demonstrated. High-resolution CT provides good detail of the orbital soft tissues, bones, and adjacent intracranial structures, with good appreciation of calcification, bone erosion, fat replacement, and vascular dilation. Contrast enhancement will occur in most vasculogenic orbital disease. CT angiography also facilitates the study of the lateral wall of the cavernous sinus which frequently bulges out in thrombosis. MRI with fat suppression techniques increases orbital soft-tissue details. CT and, more recently, MRI have been recommended by different authorities as the methods of choice for the evaluation of a suspected cavernous sinus thrombosis.²⁸⁻³¹ Imaging studies may reveal enlarged superior ophthalmic vein with a nonenhancing internal clot and distended

Table 2. Differential Diagnosis of Cavernous Sinus Thrombosis

Conditions with acute presentations
Vascular abnormalities (including fistulas resulting from trauma, ruptured aneurysm)
Orbital/Periorbital (preseptal) cellulitis/abscess
Rhinocerebral mucormycosis
Ophthalmic migraine
Conditions usually with indolent or chronic presentation
Superior orbital fissure syndrome (including Tolosa-Hunt syndrome)
Orbital apex syndrome
Vascular malformations
Sino-orbital aspergillosis
Subperiosteal mucocoele
Allergic blepharitis
Nasopharyngeal tumor
Meningioma
Cogan syndrome* (polyarteritis nodosa associated with cerebral venous thrombosis)

ipsilateral cavernous sinus. Some have advocated the use of gadolinium enhanced MR if the thrombosis is relatively acute and sufficient methemoglobin is not present.³¹ Also, orbital echography with the real-time, dynamic nature of Color Doppler Flow Imaging (CDFI), may be useful in diagnosing CCF by demonstrating reversal of blood flow direction and arterial pulsations within the SOV.^{100,101} In cases of SOV thrombosis, CDFI may show enlarged collateral venous vessels and fail to demonstrate a patent SOV; however, the detection rate of SOV in normal subjects by CDFI is only somewhat above 90%.^{32,100,101}

Treatment

Treatment of cavernous sinus thrombosis is directed to the underlying cause, so an accurate diagnosis is essential. In the aseptic cases, this may include treatment of fractures and correction of metabolic abnormalities and vascular malformations. In the septic cases, high-dose broad spectrum intravenous antibiotic directed against *Staphylococcus*, other gram-positive bacteria, and anaerobes should be started without delay. In cases involving sinusitis, surgical drainage and debridement may be necessary. The use of heparin has not been supported by any randomized prospective trials, and anticoagulation carries a significant risk of hemorrhage if cortical venous infarction or necrosis of intracavernous portions of the carotid artery are present.³³

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