Staphylococcus aureus cavernous sinus thrombosis mimicking complicated fungal sinusitis

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Abstract

Septic cavernous sinus thrombosis is a rare and potentially life-threatening complication of infections involving the paranasal sinuses or the middle one-third of the face. We report a challenging case of cavernous sinus thrombosis to familiarize otolaryngologists with its clinical features, diagnosis, and management. The patient was a 45-year-old diabetic woman whose signs and symptoms mimicked those of complicated fungal sinusitis. She presented with fever, nausea without vomiting, frontal headache, bilateral ptosis and swelling, double vision, a partial loss of visual acuity in the left eye, and restricted lateral ocular movements. Her Snellen visual acuity had been reduced to 8/10 on the right and 6/10 on the left. Radiologic investigation revealed cavernous sinus extension of sphenoid sinusitis and a fungus-ball appearance in the sphenoid sinus. On the second day of her admission, the patient's vision was further reduced to 6/10 on the right and 2/10 on the left. She then underwent urgent bilateral anterior and posterior ethmoidectomy and sphenoidectomy. At postoperative follow-up, her vision had stabilized at 10/10 bilaterally. At 2 months after discharge, she exhibited no evidence of abducens nerve palsy, and her ocular function had returned to normal. The diagnosis of cavernous sinus thrombosis requires a high index of suspicion and confirmation by imaging. The favorable outcome in our case was attributable to early diagnosis, prompt initiation of appropriate intravenous antibiotic therapy, and surgical drainage by the skillful surgical team.

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Introduction

Acute rhinosinusitis is an inflammation or infection of the mucosa of the nasal passages and at least one of the paranasal sinuses. It is most often caused by a community-acquired viral infection; other causes include bacterial and fungal infections.[1] Reported rates of morbidity and mortality in patients with complications of sinusitis range from 5 to 40%.[2] With the institution of appropriate antibiotics, better imaging modalities, and advancements in surgical interventions, the incidence of both intra- and extracranial complications has steadily decreased.[3,4] Still, morbidity and mortality remain a concern.[5]

The two most common sequelae of sinusitis are orbital infections and intracranial complications.[6] Orbital infections have been classified into five stages: *periorbital cellulitis, orbital cellulitis, subperiosteal abscess, orbital abscess,* and *cavernous sinus thrombosis* (CST), with the latter being the most devastating.[7,8] Septic CST was first described by Dease in 1778.[9] It was frequently encountered in the preantibiotic era, but since then it has become rare.[10] We describe a new case of septic CST that mimicked complicated fungal sinusitis. Our aim is to familiarize otolaryngologists with the clinical features, diagnosis, and management of this serious condition.

Case report

A 45-year-old diabetic woman presented for medical treatment to our ophthalmology outpatient clinic. Her signs and symptoms included fever, nausea without vomiting, frontal headache, bilateral ptosis and swelling, double vision, and a partial loss of visual acuity. Also, her lateral ocular movement on the left was restricted, indicating a complete paralysis of the abducens nerve. Her Snellen visual acuity had been reduced to 8/10 on the right and 6/10 on the left. An ENT examination confirmed the findings of the initial ophthalmologic

examination. The patient was an ill-looking woman with a temperature of 38.7°C. No signs of meningitis were evident.

Nasal endoscopic examination detected bilateral purulent rhinorrhea and pus in the nasal cavities, and the patient was admitted to the Department of Oto-rhinolaryngology. Laboratory testing revealed a blood glucose level of 190 mg/dl and a glycosylated hemoglobin (HbA_{1c}) level of 8.5%. The white blood cell count was 10,500/mm^3. Other hematologic parameters were within the range of normal.

Investigations for a systemic cause of infection other than sinusitis were carried out. Findings on chest radiography, echocardiography, testing for human deficiency virus, and IgG, IgE, and autoantibody measurements were normal. Screenings for thrombophilia and vasculitis were negative, and the erythrocyte sedimentation rate (Westergren method) was 96 mm/hr. The patient's hyperglycemia was controlled with immediate insulin therapy, and blood cultures were taken.

Computed tomography (CT) and magnetic resonance imaging (MRI) were performed. CT showed sphenoid sinus opacification and a defect in the lateral wall of the left sphenoid sinus secondary to lysis (figure 1). Paranasal and orbital CT revealed sphenoid and ethmoid sinusitis together with an asymmetrical dilation of the left superior ophthalmic vein and orbital cellulitis on the left side, which gave an impression of an early phase of CST.

Figure 1. Coronal CT demonstrates the sphenoid sinus opacification and the lysis of the left sphenoid sinus wall (arrow).

MRI confirmed extension of the sinusitis into the left cavernous sinus, and it demonstrated a fungus-ball appearance accompanied by lysis on the lateral wall of the right sphenoid sinus (figure 2). Fluid-attenuated inversion recovery (FLAIR) MRI sequences showed lysis

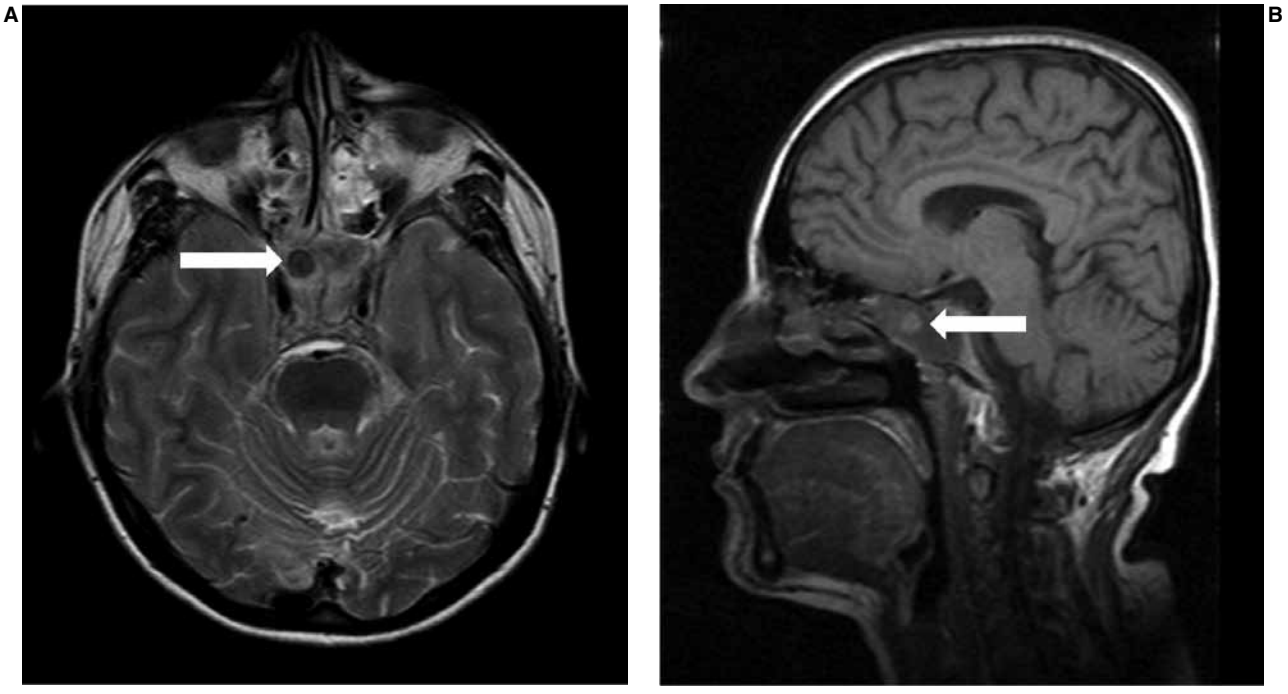

*Figure 2. Axial T2-weighted MRI (**A**) and sagittal T1-weighted MRI (**B**) show the fungus-ball appearance (arrow) in the right sphenoid sinus.*

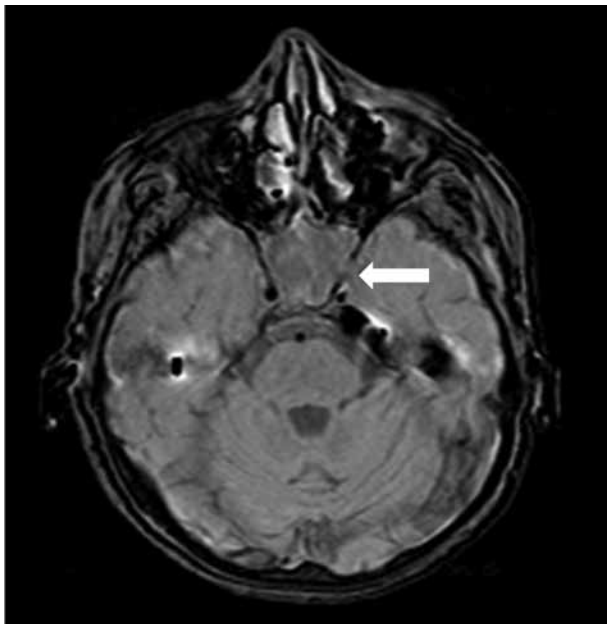

Figure 3. Axial FLAIR MRI shows the lysis (arrow) in the lateral wall of the left sphenoid sinus.

in the lateral wall of the left sphenoid sinus (figure 3).

Contrast-enhanced T2-weighted MRI showed a heterogeneous signal hyperintensity (clots) within thrombosed vascular sinuses on all pulse sequences, as well as a narrowing of the carotid artery within the cavernous sinus (figure 4, A). It also showed an increased dural enhancement around the left cavernous sinus and along the floor of the middle cranial fossa, which raised suspicion of a pyogenic pachymeningitis. Contrast-enhanced T1-weighted MRI showed left cavernous sinus extension with heterogeneous contrast enhancement and infiltration of the sphenoid sinus infection into the adjacent dura mater (figure 4, B).

Empiric intravenous treatment was begun with 2 g of meropenem three times daily and 600 mg of linezolid twice daily. On hospital day 2, the patient's vision was reduced to 6/10 on the right and 2/10 on the left, and her lateral ocular movement on the left remained restricted (figure 5, A). She underwent a bilateral anterior and posterior ethmoidectomy and sphenoidectomy. The fungus-ball–like soft tissue was aspirated, and direct microscopic evaluation found no fungal hyphae.

Histopathologic analyses with hematoxylin and eosin, periodic acid–Schiff, and Gomori methenamine silver stains were negative. Gram staining and culture of the sphenoid collections revealed methicillin-susceptible *Staphylococcus aureus.*

On postoperative day 1, the patient's vision had improved to 9/10 bilaterally, and the severity of the abducens nerve palsy had lessened (figure 5, B). The operated area was assessed daily. MRI was performed on postoperative day 15 to look for progression of the infection, and none was found. The lesions in the cavernous sinus regressed over 3 weeks. Medical treatment was continued with the same dosages of meropenem and linezolid. At follow-up on postoperative day 22, the patient's vision stabilized at 10/10 bilaterally, and the movement of her left eye had returned to normal (figure 5, C). On postoperative day 24, she left the hospital.

Two months after discharge, the patient exhibited no evidence of abducens nerve palsy and no other signs or symptoms. She was followed up regularly in the outpatient clinic, and she remained free of disease as confirmed by MRI.

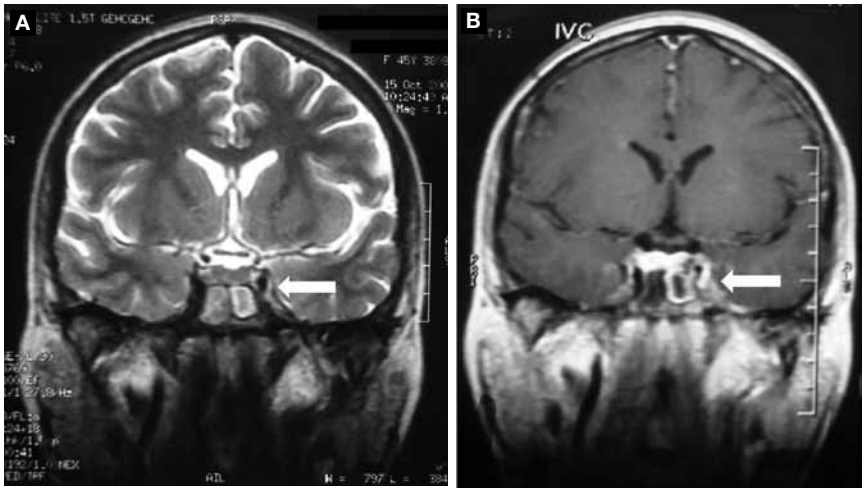

Figure 4. ***A:*** *Contrast-enhanced coronal T2-weighted MRI demonstrates the heterogeneous hyperintensity (arrow) secondary to the cavernous sinus thrombosis and the narrowing of the internal carotid artery within the cavernous sinus.* ***B:*** *Contrast-enhanced coronal T1-weighted MRI shows the cavernous sinus extension with heterogeneous contrast enhancement in the sinus (arrow) and infiltration and thickening in the adjacent dura mater.*

Discussion

The reported mortality rates among patients with CST are relatively high, ranging from 28 to 50%.[11] Among survivors, the incidence of permanent neurologic morbidity is approximately 50%.[11]

The freely anastomosing, valveless venous system of the paranasal sinuses allows infection to spread to the cavernous sinus in a retrograde fashion via the superior and inferior ophthalmic

*Figure 5. The patient's left lateral gaze is shown preoperatively (**A**) and during the early (**B**) and late (**C**) postoperative periods.*

veins. Because the right and left cavernous sinuses are connected via multiple venous sinuses, unilateral disease usually spreads quickly to the contralateral sinus. Our patient's CST was thought to have occurred secondary to her sphenoid sinusitis, although the imaging revealed a fungus-ball–like lesion.

The clinical features of CST are related to the anatomic structures that are affected within the cavernous sinuses. Presenting symptoms can include headache, retro-orbital pain, deficits in visual acuity, and ophthalmoplegia. Common signs manifest as a result of a direct injury to cranial nerves III through VI and impaired venous drainage from the orbit and eye.[10,12] Examination may reveal ophthalmoplegia, a sluggish or dilated pupil, a decreased corneal reflex, and paresthesia over the distribution of the ophthalmic branch of the trigeminal nerve.

In nearly all patients, weakness of the extraocular muscle will be demonstrated at some point, usually shortly after chemosis and proptosis are first noted. Obstruction of venous drainage from the retina can result in vision loss. Our patient presented with bilateral ptosis and swelling, double vision, a partial loss of visual acuity, and restricted lateral movement in the left eye.

Proptosis, chemosis, and orbital edema are caused by the obstruction of the superior orbital vein. Lateral gaze palsy, as occurred in our patient, may be an isolated early neurologic finding. The VIth nerve, being the only cranial nerve that runs within the sinus, is located more medially, near the carotid artery, and it may be surrounded by blood.

Progression from unilateral orbital signs to bilateral involvement, as occurred in our patient, is a late and inconstant finding; when it does occur, it indicates that infection has (1) spread from its original side of the head through the intercavernous sinuses to the opposite cavernous sinus or (2) spread directly from the sphenoid air sinuses to both cavernous sinuses.[10,13]

Because septic CST is such a rare condition and its presenting features are nonspecific, it is often missed or diagnosed late. There are no pathognomonic signs or symptoms of septic CST. The diagnosis is best made through MRI or contrast-enhanced CT. MRI is considered superior to CT for diagnosing intracranial and intraorbital complications of inflammatory paranasal sinus disease.

In our case, paranasal and orbital CT revealed sphenoid and ethmoid sinusitis together with an asymmetrical dilation of the left superior ophthalmic vein and orbital cellulitis on the left side, which gave an impression of an early phase of CST. A fungus-ball appearance in the sphenoid sinus accompanied by lysis on the lateral sinus wall was seen on MRI. T2-weighted MRI showed an increased dural enhancement around the left cavernous sinus and along the floor of the middle cranial fossa; this raised suspicion of a pyogenic pachymeningitis, which was relevant to the medical condition of the patient.

The most common organisms reported in CST are *S aureus* and *Streptococcus* species.[14,15] *S aureus* is identified in about 60 to 70% of cases.[10] In our case, cultures taken from both of the sphenoid sinuses were positive for methicillin-susceptible *S aureus.* Contrary to what we expected, direct microscopic evaluation of the endoscopically excised tissue found no fungal hyphae, and cultures for fungi were negative.

Treatment of CST should be initiated with immediate administration of high-dose, broad-spectrum intravenous antibiotics with good blood-brain barrier penetration. Given the high morbidity and mortality associated with CST, clinicians should always include empiric antibiotic coverage with vancomycin or linezolid

for the most common pathogen, *S aureus*. Meropenem and linezolid provide broad polymicrobial coverage (gram-positive, gram-negative, and anaerobes), and thus they were the drugs of choice for our patient.

The role of anticoagulation in relieving venous congestion in the cavernous sinus and allowing for drainage through the superior ophthalmic vein is controversial because of the additional risk of intracranial hemorrhage.[16] Corticosteroid therapy is usually not recommended.[12]

Prompt drainage of the primary sites of infection is advisable in most circumstances.[12,17,18] Endoscopic sinus surgery is the procedure of choice for septic CST secondary to sphenoid and ethmoid infection. A timely operation may prevent permanent sequelae in patients with prolonged vision disturbances. Therefore, the interval between the onset of vision disturbance and surgical intervention should be less than 48 hours.[19] There is a high rate (75%) of complete recovery from abducens nerve palsy lasting more than 96 hours in patients with isolated sphenoid sinus disease.[20] In our case, the patient's visual acuity improved and gradually returned to normal in both eyes following surgery, and she ultimately experienced a complete ophthalmologic recovery.

In conclusion, the diagnosis of CST requires a high index of suspicion and confirmation by imaging. Intensive pharmacologic management combined with early surgical intervention is critical to prevent progression of CST and to reduce the risk of serious morbidity or death. The favorable outcome in our case was attributable to early diagnosis, prompt initiation of appropriate intravenous antibiotic therapy, and surgical drainage by the skillful surgical team. This case highlights the difficulty in differentiating between a fungus ball and sphenoid collections of acute bacterial rhinosinusitis on MRI in the presence of a clinically suspected CST.

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