Cavernous Sinus Thrombosis as a Result of a Fungal Infection: A Case Report

Andrew Horowitz, DMD, MD, Dylan Spendel, DMD,† Richard Kraut, DDS,‡ and Gary Orentlicher, DMD§*

Cavernous sinus thrombosis (CST) is a rare disease with the potential for significant morbidity and even death. Rapid diagnosis and aggressive medical and surgical management are imperative for patients with CST. The cause may be aseptic or infectious. When the cause is infectious in nature, it is most commonly from a bacterial origin. However, we present the case of a 57-year-old man with a fungally related CST that ultimately led to his death.

J Oral Maxillofac Surg 71:1899.e1-1899.e5, 2013

Cavernous sinus thrombosis (CST) is a rare disease with the potential for significant morbidity and even death. Rapid diagnosis and aggressive medical and surgical management are imperative for patients with CST. The cause may be aseptic or infectious. When the cause is infectious in nature, it is most commonly from a bacterial origin.[1] However, we present the case of a 57-year-old man with a fungally related CST that ultimately led to his death.

Case Presentation

The patient was a 57-year-old man, with a history of diabetes mellitus, coronary artery disease, and hypertension, who initially presented on January 1, 2008, to the emergency department at White Plains Hospital Center (WPHC) with a diagnosed sinus infection of 2 weeks' duration, which was being treated with levofloxacin. During his initial presentation, he complained of a 2-day history of left facial pain and pressure, as well as nasal congestion. His emergency room examination was relatively unremarkable, with some mention of tenderness over the left maxillary sinus, poor dentition, and gingival bleeding. He was discharged by the emergency department physician with a diagnosis of facial pain and a dental abscess, with instructions to follow up with his primary care physician.

On January 3, 2008, initial treatment for a dental infection was instituted, and the patient began a course of clindamycin. On January 5, 2008, he flew to India for a family affair. Immediately after his arrival, he was taken to a hospital with a left facial droop and sialorrhea. He was diagnosed with progression of the sinus infection, and intravenous antibiotic and steroid therapy was instituted. On January 10, 2008, left-sided blindness ensued. His workup consisted of carotid Doppler examination, lumbar puncture, and a magnetic resonance imaging (MRI) scan, which suggested orbital cellulitis.

The patient returned to the United States and was readmitted on January 19, 2008, to WPHC. On admission, the patient was somnolent but arousable. His left eye was proptotic with no light perception and no extraocular movement. He had left facial paresis and cellulitis. Computed tomography (CT) and MRI examination at the time indicated a left CST with orbital cellulitis and dural enhancement (Figs 1-3). He was empirically treated with vancomycin, imipenem, and amphotericin B.

On hospital day 4, he was taken to the operating room (OR) for endoscopic sinus surgery. The intraoperative

*Attending, White Plains Hospital Center, White Plains, NY; and Private Practice, Scarsdale, NY.

†Resident, Department of Oral and Maxillofacial Surgery, Montefiore Medical Center, Bronx, NY.

‡Chairman, Department of Dentistry, Director, Oral and Maxillofacial Surgery, Montefiore Medical Center, Bronx, NY.

§Chief, Department of Oral and Maxillofacial Surgery, White Plains Hospital Center, White Plains, NY; and Private Practice, Scarsdale, NY.

Address correspondence and reprint requests to Dr Horowitz: 495 Central Park Ave, Ste 201, Scarsdale, NY 10583; e-mail: horowitz.drew@nyomis.com

Received March 1 2013

Accepted May 23 2013

0278-2391/13/00527-2$36.00/0

http://dx.doi.org/10.1016/j.joms.2013.05.021

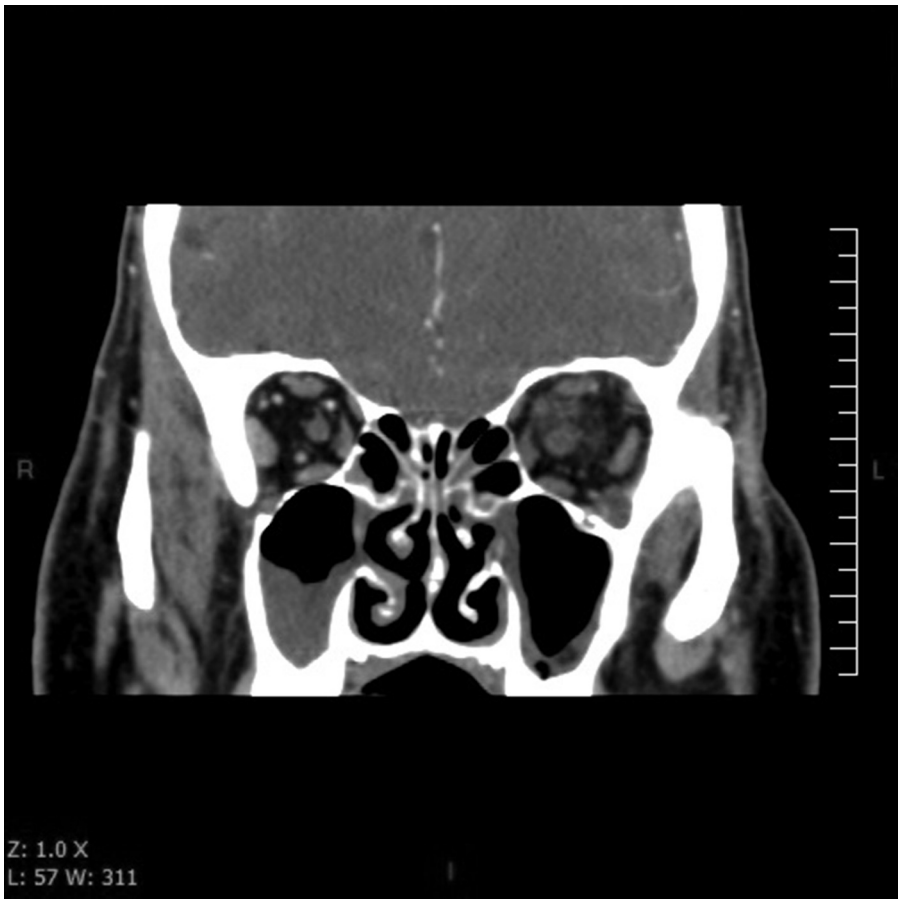

FIGURE 1. Enhancement of retrobulbar tissues including superior ophthalmic vein as evident in CST, seen on CT.

Horowitz et al. Cavernous Sinus Thrombosis. J Oral Maxillofac Surg 2013.

findings showed a necrotic area on the hard palate (Fig 4) and necrotic left inferior turbinate and septum. No purulence was noted, and minimal bleeding was present. Cultures grew *Escherichia coli* and *Klebsiella pneumonia*, which were sensitive to imipenem. The biopsy specimens showed fungal forms consistent with *Aspergillus* (Fig 5). Despite aggressive medical management and an additional surgical debridement, consisting of partial maxillectomy, the patient's condition continued to worsen (Fig 6). He was subsequently transferred to Montefiore Medical Center on February 3, 2008.

Initial therapy at the larger hospital included anticoagulation with heparin and a change of antifungals to voriconazole. The patient was subsequently taken back to the OR for an ethmoidectomy, sphenoidectomy, maxillary antrostomy, and orbital decompression. His postoperative course waxed and waned and was subsequently complicated by acute renal failure and heart failure. He became hemodynamically unstable, requiring vasopressors. He then developed acute respiratory distress syndrome (ARDS) and multiorgan failure, and ultimately, he died.

Discussion

Winslow erroneously coined the term "sinus cavernosi" in the 18th century.[2] The cavernous sinus is not a dural sinus nor is it cavernous; it is an extradural compartment.[3] Several vital structures are contained within the sinus: the internal carotid artery and its sympathetic plexus; the oculomotor (cranial nerve [CN] III), trochlear (CN IV), and abducens nerves (CN VI); the ophthalmic and maxillary divisions of the trigeminal nerve; and the superior and inferior ophthalmic veins.[4]

CST was first described by Bright in 1831.[5] The cause may be aseptic or as a result of infections involving the paranasal sinuses, face, orbits, oral cavity, and middle ear.[1,6] These infections may spread to the cavernous sinus through direct extension or, most commonly, from the facial vein through the ophthalmic veins or pterygoid plexus. Given the complex anatomy contained within the sinus, any involvement may lead to ptosis, ophthalmoplegia, facial paresthesias, proptosis, chemosis, and papilledema.[7]

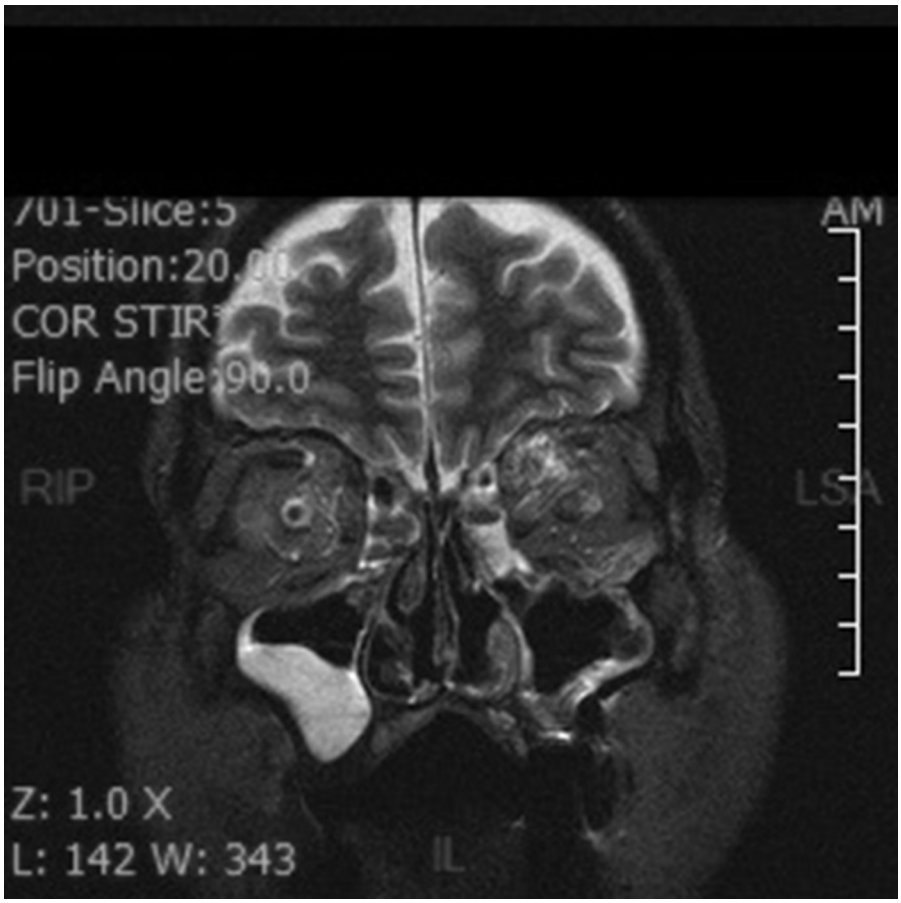

FIGURE 2. Enhancement of retrobulbar tissues including superior ophthalmic vein as evident in CST, seen on MRI.

Horowitz et al. Cavernous Sinus Thrombosis. J Oral Maxillofac Surg 2013.

The most common causes of an infectious CST are infections of the sphenoid, ethmoid sinusitis, and otitis media, followed by maxillary dental infections.[8,9] Before the advent of antibiotics, the mortality rate was as high as 100%, and it is now as low as 20%.[6,8,10] The most common organisms isolated from these patients are staphylococcal and streptococcal species.[1,5,7]

Our case presents an unusual finding of CST due to aspergillosis. *Aspergillus* species are highly aerobic and found in environments rich in oxygen. They are acquired through the inhalation of spores and are commonly isolated from soil, plant debris, and the indoor environment.[11] The most common species that cause disease in humans are *Aspergillus flavus*, *fumigatus*, and *clavatus*. Because of the mode of transmission, when infection develops, it likely involves the pulmonary system. Other less likely sites for infection are the central nervous system, kidneys, heart, liver, esophagus, skin, and respiratory sinuses.[12]

The most common cause of an infectious CST usually arises from sinusitis.[1] In this case biopsy specimens from the maxillary sinuses showed septate and branching hyphae on Periodic Acid-Schiff (PAS) and Grocott-Gomori's methenamine silver (GMS) stains that were consistent with *Aspergillus*. As a result of the histopathology, the likely source for the CST was due to fungal sinusitis.

With the advent of CT and MRI, the diagnosis of CST has improved, therefore reducing the morbidity and mortality rates of the disease. Determining the exact cause relies on identification of an organism, when possible, in culture or on histologic examination. Although these organisms typically will grow on standard media, the initiation of empiric antifungal therapy may lead to false-negative findings. In addition, in patients who may be too unstable to undergo invasive procedures to obtain clinical specimens, the presence of serum markers such as galactomannan and (1,3)–β-D-glucans may signify the presence of the fungus.[13]

The treatment for a fungally related CST involves a surgical component, with the majority of therapy directed medically. As with all infections, the basic surgical principles of removing the offending source, debridement of necrotic or involved tissue, and/or incision and drainage of involved sites must be applied.

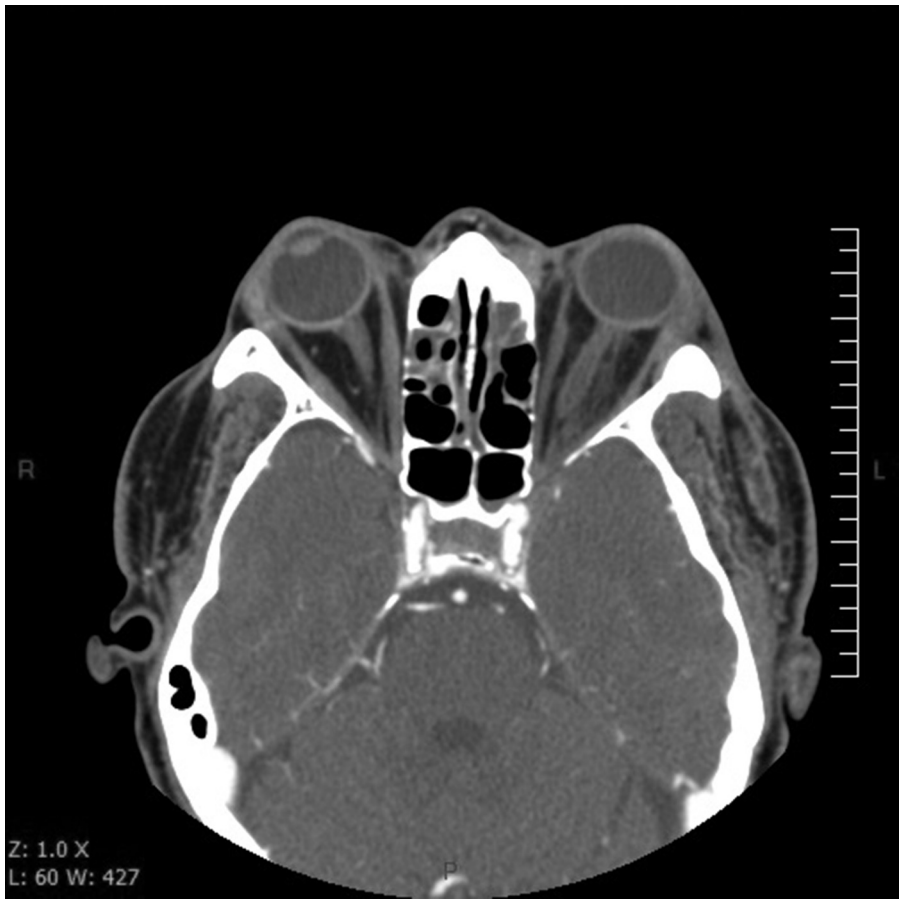

FIGURE 3. Enhancement of carotid arteries with suboptimal visualization of associated venous structures consistent with CST.

Horowitz et al. Cavernous Sinus Thrombosis. J Oral Maxillofac Surg 2013.

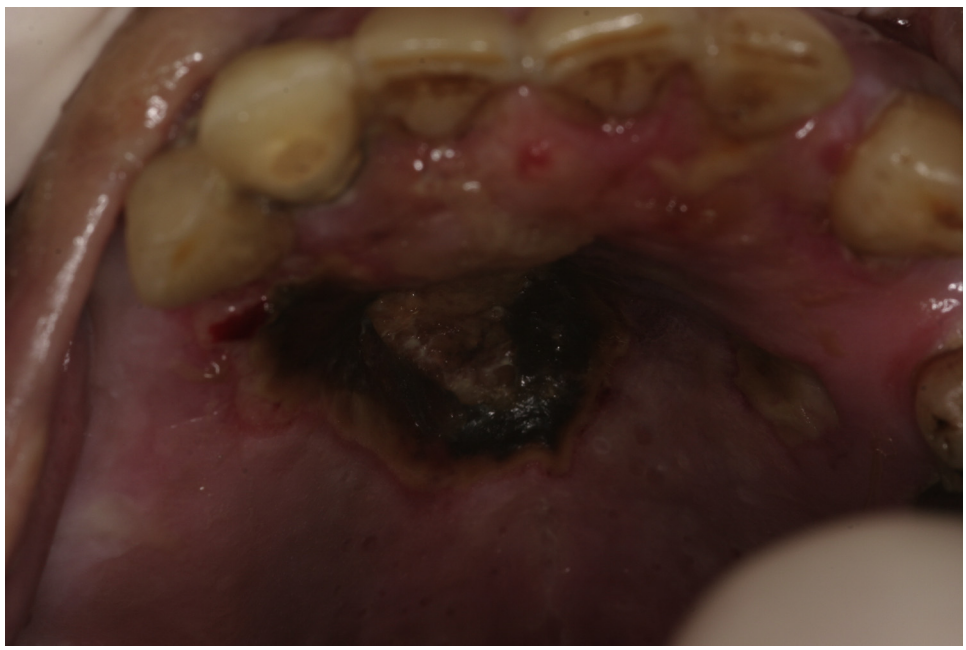

FIGURE 4. Large necrotic ulcer noted on hard palate.

Horowitz et al. Cavernous Sinus Thrombosis. J Oral Maxillofac Surg 2013.

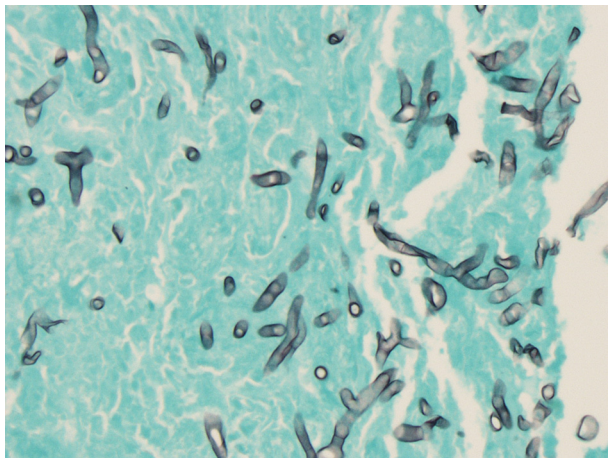

FIGURE 5. Branching hyphae as seen on Grocott-Gomori's methenamine silver (GMS) stain (magnification 40x).

Horowitz et al. Cavernous Sinus Thrombosis. J Oral Maxillofac Surg 2013.

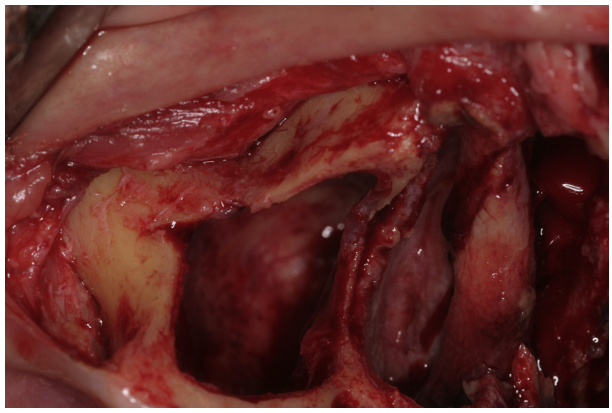

FIGURE 6. Healthy-looking bone and mucosa noted after partial maxillectomy.

Horowitz et al. Cavernous Sinus Thrombosis. J Oral Maxillofac Surg 2013.

Medically, these patients need to be treated with antifungal drugs, such as voriconazole, deoxycholate Amphotericin B, itraconazole, posaconazole, and caspofungin.[13] In addition, the role of anticoagulation therapy and steroids has been debated, with no clear evidence supporting either.[1,14,15]

Although this case presents the unusual finding of a CST due to invasive aspergillosis, the medical and surgical treatments were overwhelmed by the aggressive nature of the infection. As such, it is not entirely clear from the patient's medical record whether the symptoms began as a result of an odontogenic infection or as a sinus infection; regardless, clinicians must be reminded of the severe outcomes that could potentially evolve as a result of a CST.

References

1. Desa V, Green R: Cavernous sinus thrombosis: Current therapy. J Oral Maxillofac Surg 70:2085, 2012
2. Thakur JD, Sonig A, Khan IS, et al: Jacques Benigne Winslow (1669-1760) and the misnomer cavernous sinus. World Neurosurg. In press. doi:10.1016/j.wneu.2012.06.030
3. Parkinson D: Lateral sellar compartment O.T. (cavernous sinus): History, anatomy, terminology. Anat Rec 25:486, 1998
4. Zelenak M, Doval M, Gorscak J, Cuscela D: Acute cavernous sinus syndrome from metastasis of lung cancer to sphenoid bone. Case Rep Oncol 5:35, 2012
5. Watkins LM, Pasternack MS, Kousoubris P, Rubin PA: Bilateral cavernous sinus thrombosis and intraorbital abscesses secondary to streptococcus milleri. Ophthalmology 110:569, 2003
6. Cheung EJ, Scurry WC, Isaacson JE, McGinn JD: Cavernous sinus thrombosis secondary to allergic fungal sinusitis. Rhinology 47:105, 2009
7. Colbert S, Cameron M, Williams J: Septic thrombosis of the cavernous sinus and dental infection. Brit J Oral Maxillofac Surg 49:e25, 2011
8. Feldman DP, Picerno NA, Porubsky ES: Cavernous sinus thrombosis complicating odontogenic parapharyngeal space neck abscess: A case report and discussion. Otolaryngol Head Neck 123:744, 2000
9. Ahmmed A, Camilleri A, Small M: Cavernous sinus thrombosis following manipulation of fractured nasal bones. J Laryngol Otol 220:69, 1996
10. Kriss T, Kriss V, Warf B: Cavernous sinus thrombophlebitis: Case report. Neurosurgery 39:2, 1996
11. Zmeili OS, Soubani AO: Pulmonary aspergillosis: A clinical update. Q J Med 100:317, 2007
12. Denning DW: Invasive aspergillosis. Clin Infect Dis 26:781, 1998
13. Walsh TJ, Anaissie EJ, Denning DW, et al: Treatment of aspergillosis: Clinical practice guidelines of the Infectious Diseases Society of America. Clin Infect Dis 46:327, 2008
14. Ebright JR, Pace MT, Niazi AF: Septic thrombosis of the cavernous sinuses. Arch Intern Med 161:2671, 2001
15. Schuknecht B, Simmen D, Yüksel C, et al: Tributary venosinus occlusion and septic cavernous sinus thrombosis: CT and MR findings. Am J Neuroradiol 19:617, 1998