**Abstract**

Septic cavernous sinus thrombosis (CST) associated with community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA), a rising pathogen in the healthy pediatric population, may have atypical presentation and a fulminant course, including significant cerebral arterial involvement.

A 14-year-old healthy girl presented with fever and bilateral eyelid edema. Within a few hours she developed deterioration in consciousness and bilateral proptosis with conjunctival chemosis. CT excluded sinusitis and revealed filling defects of the cavernous sinus and the superior ophthalmic vein bilaterally, consistent with bilateral CST. MRI demonstrated internal carotid and middle cerebral arteries narrowing with watershed brain infarcts. Her blood cultures grew MRSA. The patient gradually improved with a combination of antibiotics, anticoagulation, and steroids, although some neurologic deficits were noted.

This case emphasizes the need for enhanced awareness, early multimodal neuroimaging, and multidisciplinary treatment to achieve a better outcome. A potential new treatment modality may be considered in future CST cases.

**Introduction**

Septiccavernous sinus thrombosis (CST) is a rare, frequently blinding, and potentially fatal disease, usually associated with sinusitis and orbital cellulitis or less commonly with various midfacial infections1. Septic CST may have a vague initial presentation and rapid deterioration with the potential of inflicting significant cerebrovascular damage. This is a unique and important report of a healthy patient presenting with fulminant community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) infection causing bilateral CST and brain infarcts.

**Case Report**

A healthy 14-year-old girl had had localized swelling and redness of the right lower eyelid (presumed to be a sty) 3 days prior to her admission. She was referred to the emergency room with a temperature of 39.4°C and bilateral swelling of the eyelids. Leukocytosis (9,000 cells/mcL) and elevated CRP (11.68 mg/L) were measured. Ophthalmologic examination demonstrated bilateral visual acuity of 6/9, significant right more than left lid edema, mild conjunctival chemosis, equal round reactive pupils with no afferent pupillary defect, normal eye movements and a normal dilated fundus. The patient was admitted for intravenous amoxicillin clavulanate treatment for presumed periorbital cellulitis.

Several hours later, a rapid deterioration in consciousness had occurred, with the appearance of meningeal signs and bilateral proptosis with significant chemosis. Consequently, the patient was transferred to the pediatric intensive care unit.

A computed tomography venogram (figure 1) demonstrated filling defects of the cavernous sinus and, bilaterally, of the superior ophthalmic veins, consistent with CST. MRI demonstrated cavernous sinus filling defects (figure 2A) and narrowing with arterial wall enhancement of the internal carotid artery (in its cavernous part) and middle cerebral artery (figure 2B) and brain infarcts (figure 2C). No subperiosteal, periorbital, or orbital abscess or sinusitis were evident using different imaging modalities, although preseptal swelling was evident with orbital fat involvement more on the right than the left.

Lumbar puncture revealed a cloudy cerebrospinal fluid, with a cell count of 4,050, elevated protein (196.5 mg/dL), decreased glucose (28.8 mg/dL), and Gram-positive cocci.

Following these findings, a diagnosis of septic CST with cerebral ischemia was made. Intravenous vancomycin, ceftriaxone, and metronidazole were initiated, as well as anticoagulation and methylprednisolone. The patient’s blood cultures grew MRSA and rifampin was added, according to the bacterial sensitivity results.

During her stay in the pediatric intensive care unit, following an improvement in her consciousness, she was noted to have mild right hemiparesis and bilateral restriction in abduction with bilateral esotropia. No cerebral hemorrhage was located on repeated imaging and her neurologic deficits were attributed to cerebral ischemia. Gradually the patient improved, MRSA was eradicated, rifampin was discontinued, and steroids were further tapered. The patient was discharged after a total of 47 days.

The patient was referred to ambulatory daycare rehabilitation and continued neurologic and ophthalmic follow ups. She gradually returned to her normal daily routine including walking. Ophthalmic examination on her latest follow up, 4 months after her discharge, demonstrated a bilateral visual acuity of 6/6, normal optic nerve functions, normal optic discs, and mild esotropia with mild bilateral abducens paresis without diplopia. Follow-up MRI demonstrated residual bilateral internal carotid arteries narrowing at the cavernous sinuses, without new neurologic morbidity.

**Discussion**

Septic CST in children without sinusitis is rare1,2. Infection spread occurs through valveless veins draining the midfacial region to the cavernous sinus2. Involvement of MRSA, a less typical and more aggressive infection, without abscess formation, can further complicate and rapidly deteriorate a case of CST, presenting a known diagnostic and therapeutic challenge. Mathias et al. found sinusitis in only 17% of pediatric orbital cellulitis induced by MRSA4. They demonstrated that MRSA-related pediatric orbital cellulitis is an infection with possible atypical presentation, which frequently lacks accompanying sinusitis, but rather is associated with eyelid infections4.

Some case series concerning pediatric CST have been published in the past few years1,2. These series found that the main cause for CST was sinusitis (mainly sphenoid) and that the main pathogen involved was *Streptococcus anginosus*. The reported frequency of MRSA as the causative agent was up to 10%.

The first report of community-acquired MRSA orbital cellulitis in a non-immunocompromised child was made by Vazan et al8 in 2007, in a 16-month-old boy who exhibited ethmoidal and maxillary sinusitis. Further case series demonstrated MRSA to be the causative infectious agent in pediatric orbital cellulitis in between 36%9 and 44% of cases6.

There have recently been 2 large series reporting pediatric CST: included within the series were a 5-year-old girl with unilateral MRSA-related CST with no sinusitis2 and a 10-year-old girl with bilateral MRSA-related CST with sinusitis3. These MRSA cases represented 9% and 12% of all pediatric CST reported in those series, which is significantly lower than the reported MRSA frequency of 36%–44% in the pediatric orbital cellulitis series cited above9,6.

In the past decade, studies have shown an increasing incidence of community-acquired MRSA infections in general3 and specifically of community-acquired MRSA-related orbital cellulitis4,5,6. Nevertheless, new reports are now indicating a reversal of this trend7. Whether the frequency of MRSA infections will rise or decline is yet to be determined. Either way, these trends, which may be population and geography dependent, should be taken into consideration when pediatricians and ophthalmologists approach pediatric septic CST patients.

To the best of our knowledge this is the first pediatric case report of a fulminant community-acquired MRSA infection that began with a presumed sty and rapidly evolved to bilateral CST with accompanying meningitis and cerebral infarcts in the absence of sinusitis.

As reported by Frank et al2, CST is often associated with internal carotid artery and middle cerebral artery narrowing with possible neurologic sequel. Our patient suffered from significant bilateral internal carotid artery narrowing and watershed cerebral infarcts in the anterior cerebral and middle cerebral arteries’ territories. She has had a rather favorable outcome to date, but cerebral vasculature changes and damage are evident.

Residual narrowing of the cavernous part of the internal carotid arteries was noted in a follow-up MRI nearly half a year after her initial presentation. This phenomenon was previously described by Press et al., who studied the MRI findings of 10 pediatric CST cases, 3 of whom demonstrated residual carotid artery narrowing lasting 1–10 years from presentation10. These findings may represent inflammatory and later fibrotic changes in the previously thrombosed cavernous sinuses.

Diagnosing and treating these patients is a considerable challenge, due to the initially vague clinical presentation and the rapid deterioration that follows11. Quick recognition of the signs, which include fever, periorbital swelling, proptosis, simultaneous dysfunction of cranial nerves 3,4,5 and 6, which may become bilateral, and a toxemic patient, could possibly prevent further patient deterioration12. It is, therefore, critical to perform early neuroimaging to establish a rapid and definitive diagnosis, and to orchestrate a multidisciplinary team involvement. Treatment should be based on broad-spectrum antibiotics (including those effective against MRSA), anticoagulation, and surgical evacuation of abscesses when appropriate1,2.

A recent article13 concerning transfemoral catheterization of thrombosed cavernous sinus and superior ophthalmic veins in a 7-year-old child reported a significant improvement following recanalization achieved by microcatheter mechanical thrombectomy. This report raises a question about the future role of interventional neuroradiology procedures in CST. Especially interesting is to consider whether timely recanalization by mechanical thrombectomy will be able to prevent the ocular and cerebral complications that occur with septic CST. Additional case series of thrombectomy in CST are required to further establish the safety and efficacy of this new treatment modality in different CST scenarios. Nevertheless, in view of this report and the rarity and severity of CST, ophthalmologists along with the multidisciplinary management team should consider such interventions in CST patients when appropriate.

**Declaration of Interest:**

The authors report no conflicts of interest

**References**

1: Smith DM, Vossough A, Vorona GA, Beslow LA, Ichord RN, Licht DJ. Pediatric cavernous sinus thrombosis: A case series and review of the literature. Neurology. 2015 1;85(9):763-9.

2: Frank GS, Smith JM, Davies BW, Mirsky DM, Hink EM, Durairaj VD. Ophthalmic manifestations and outcomes after cavernous sinus thrombosis in children. JAAPOS. 2015;19(4):358-62.

3: Moran GJ, Krishnadasan A, Gorwitz RJ et al; EMERGEncy ID Net Study Group. Methicillin-resistant S. aureus infections among patients in the emergency department. N Engl J Med. 2006 17;355(7):666-74.

4: Mathias MT, Horsley MB, Mawn LA et al. Atypical presentations of orbital cellulitis caused by methicillin-resistant Staphylococcus aureus. Ophthalmology. 2012;119(6):1238-43.

5: Shome D, Jain V, Natarajan S, Agrawal S, Shah K. Community-acquired methicillin-resistant Staphylococcus aureus (CAMRSA)--a rare cause of fulminant orbital cellulitis. Orbit. 2008;27(3):179-81.

6: Vaska VL, Grimwood K, Gole GA, Nimmo GR, Paterson DL, Nissen MD. Community-associated methicillin-resistant Staphylococcus aureus causing orbital cellulitis in Australian children. Pediatr Infect Dis J. 2011;30(11):1003-6.

7: Sutter DE, Milburn E, Chukwuma U, et al. Changing susceptibility of Staphylococcus aureus in a US pediatric population. Pediatrics. 2016;137:1–3.

8: Vazan DF, Kodsi SR. Community-acquired methicillin-resistant Staphylococcus aureus orbital cellulitis in a non-immunocompromised child. J AAPOS. 2008;12(2):205-6.

9: McKinley SH, Yen MT, Miller AM, Yen KG. Microbiology of pediatric orbital cellulitis. Am J Ophthalmol. 2007;144(4):497-501.

10: Press CA, Lindsay A, Stence NV, Fenton LZ, Bernard TJ, Mirsky DM. Cavernous Sinus Thrombosis in Children: Imaging Characteristics and Clinical Outcomes. Stroke. 2015;46(9):2657-60.

11: Sethi P, Jones ST, Valenzuela AA. Septic cavernous sinus thrombosis with diffuse spread leading to cerebral ischemia. Orbit. 2013;32(5):330-2.

12: Pavlovich, Looi A, Rootman J. Septic thrombosis of the cavernous sinus: two different mechanisms. Orbit. 2006;25(1):39-43.

13: Bauer J, Kansagra K, Chao KH, Feng L. Transfemoral thrombectomy in the cavernous sinus and superior ophthalmic vein. BMJ Case Rep. 7;2018.

**Figure 1**

****

**Figure 2A**

****

**Figure 2B**

****

**Figure 2C**

****

**Figure Titles:**

**FIGURE 1**

Axial image of computed tomography venogram demonstrated a filling defect of the cavernous sinus bilaterally (black arrows), as opposed to the sigmoid sinus, which is completely filled with contrast (white arrow).

**Figure 2A**

T1 3D MRI with gadolinium at the venous phase revealed filling defects of the cavernous sinuses (white arrow), in contrast to complete opacification of other dural sinuses (asterisk). Enhancement of the carotid artery in the cavernous sinus is also noted (black arrow).

**Figure 2B**

MRI demonstrating bilateral cavernous irregularity and narrowing of the internal carotid artery (white arrow) and middle cerebral artery (black arrows).

**Figure 2C**

Diffusion-weighted MRI revealed watershed infarcts between middle cerebral artery and ACA territories (black arrows).