**Summary:**

**Community acquired Methicillin resistant Staphylococcus aureus (MRSA) infections in children had been on the rise for the last decade. Atypical presentations of orbital cellulitis caused by this pathogen were previously recognized. To our best knowledge this is the first report of a healthy girl presenting with fulminant community acquired MRSA causing bilateral Cavernous sinus thrombosis and brain infarcts. This case emphasizes the aggressiveness of such infections and the enhanced awareness required in healthy pediatric population, as well as the need for early multimodal imaging and multidisciplinary treatment.**

**Case Report:**

A healthy 14-year-old girl had localized swelling and redness of the right lower eyelid 3 days prior to her admission (presumed to be a sty). She was referred to the emergency room with 39.40C temperature and bilateral eyelids swelling. Leukocytosis (9,000 cells/mcL) and elevated CRP (11.68 mg/L) were measured. Ophthalmologic examination demonstrated visual acuity (VA) of 6/9 bilaterally, 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 examination. The Patient was admitted for IV Amoxicillin Clavulonate 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.

Computed tomography venogram (figure 1) demonstrated filling defects of the cavernous sinus (CS) and of the superior ophthalmic veins (SOV) bilaterally consistent with cavernous sinus thrombosis (CST). MRI (figure 2) demonstrated cavernous sinus filling defects as well as cavernous internal carotid artery (ICA) and medial cerebral artery (MCA) narrowing and arterial wall enhancement with brain infarcts.

No subperiosteal, periorbital or orbital abscess or sinusitis were evident in different imaging modalities, although preseptal swelling with right more than left orbital fat involvement were evident.

Lumbar puncture revealed a cloudy cerebrospinal fluid, with a cell count of 4,050, elevated protein 196.5mg/dl, decreased glucose 28.8 mg/dl and gram-positive Cocci.

Vancomycin, Ceftriaxone, Metronidazole and anticoagulation were initiated. At this stage due to her rapidly deteriorating consciousness, the patient was transferred to the pediatric intensive care unit (PICU). Given the Blood and CSF, MRSA isolates and the imaging findings of bilateral CST, Rifampin was added (per susceptibilities) and Methylprednisolone and anticoagulation were initiated.

During her PICU stay, mild right hemiparesis was noted without cerebral hemorrhage in imaging. Ocular motility was significant for a bilateral abduction deficit with bilateral esotropia.

Hemodynamically stable and after MRSA eradication, Rifampin was stopped, and steroids were further tapered. The patient was discharged after a total of 47 days with persisting mild right hemiparesis. The patient was referred to rehabilitation at daycare and to continued neurologic and ophthalmic follow ups.

ophthalmic examination on her latest follow up, 4 months after her discharge demonstrated bilateral VA of 6/6, normal optic nerves functions, normal optic discs, and mild esotropia with mild bilateral abducens paresis without diplopia.

Follow Up MRI demonstrated severe bilateral ICA narrowing at the CS without permanent new neurologic morbidity.

**Discussion:**

SepticCavernous Sinus Thrombosis (CST) is a rare, frequently blinding and potentially fatal disease, usually associated with sinusitis, orbital cellulitis or less commonly with various midfacial infections1. CST also has the potential of inflicting extensive cerebrovascular morbidity as demonstrated in our case report.

Some of the largest series concerning pediatric CST published in the last few years1,2, stated the main causes for CST to be Sinusitis (mainly Sphenoid) and the main pathogens involved to be Streptococcus Angiunous with a frequency of MRSA cases of up to 10%.

In the last decade or so, there has been an increasing amount of evidence concerning the increasing incidence of community acquired MRSA infections3 and of community acquired MRSA orbital cellulitis4,5,6. Nevertheless, New reports are now indicating a reversal of this trend7.

The first report of a community acquired MRSA orbital cellulitis in a non-immunocompromised child was reported by Vazan et al8, in 2007 in a 16-month-old male who exhibited ethmoidal and maxillary sinusitis.

Further case series described an increasing portion of MRSA as a causative infectious agent in orbital cellulitis, in the pediatric population, with frequency of up to 36% of culture isolates9 and 44% of cases6.

In 2 large series reporting pediatric CST in the recent years there was a report of, a 5-year-old girl with unilateral MRSA related CST with no sinusitis2 and another report of, 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. To note, this portion is significantly lower than the reported MRSA frequency of 36%-44% in the pediatric orbital cellulitis series by Mckinley et al and Vaska et al respectively9,6. Mathias et al, had found sinusitis in only 17% of the pediatric orbital cellulitis induced by MRSA4 .He demonstrated MRSA related pediatric orbital cellulitis is an infection with possible atypical presentation, which frequently lacks accompanying sinusitis, but rather is associated with eyelid infections4.

To our best knowledge this is the first pediatric case report of a fulminant MRSA infection that presented as periorbital cellulitis rapidly evolving to bilateral cavernous sinus thrombosis, with accompanying meningitis and cerebral infarcts in the absence of sinusitis.

As reported by Frank et al2, CST is often associated with ICA and MCA narrowing with possible neurologic sequel. Our patient suffered from significant bilateral ICA narrowing and watershed cerebral infarcts in the right ACA and right MCA territories causing right hemiparesis (figures 2B and 2C). Our case had a rather favorable outcome to date, but extensive cerebral vasculature changes were evident.

This case emphasizes a serious condition in children, which may have an atypical presentation and a rapid deterioration with possible extensive cerebrovascular damage, secondary to MRSA septic CST. Whether pediatric community acquired MRSA infections, including pediatric orbital cellulitis infections will be rising or declining, and this maybe population and geography dependent, is yet to be determined. Clinicians must keep high index of suspicion of these atypical and potentially aggressive infections and perform early neuroimaging to achieve rapid diagnosis, and to orchestrate a multidisciplinary team treatment based on broad spectrum antibiotics (including those effective against MRSA), anticoagulation and possibly steroids alongside surgical evacuation of abscesses when appropriate.

A recent report10 concerning transfemoral catheterization of thrombosed Cavernous sinus and SOV’s in a 7-years-old, which improved dearly post treatment, raises the question about the future role of interventional neuroradiology treatments in CST and its ability to prevent the extensive ocular and cerebral complications that ensue once the CST causes ischemic and inflammatory wide spread cerebral damages. Given this report, ophthalmologists along with the multidisciplinary management team of CST patients should consider such interventions when appropriate.

**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 Sep 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 Aug;19(4):358-62.

3: Moran GJ, Krishnadasan A, Gorwitz RJ, Fosheim GE, McDougal LK, Carey RB, Talan DA; EMERGEncy ID Net Study Group. Methicillin-resistant S. aureus infections among patients in the emergency department. N Engl J Med. 2006 Aug 17;355(7):666-74.

4: Mathias MT, Horsley MB, Mawn LA, Laquis SJ, Cahill KV, Foster J, Amato MM, Durairaj VD. Atypical presentations of orbital cellulitis caused by methicillin-resistant Staphylococcus aureus. Ophthalmology. 2012 Jun;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 Nov;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 Apr;12(2):205-6. Epub 2007 Dec 26.

9: McKinley SH, Yen MT, Miller AM, Yen KG. Microbiology of pediatric orbital cellulitis. Am J Ophthalmol. 2007 Oct;144(4):497-501. Epub 2007 Aug 15.

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

**Cavernous Sinus Thrombosis Case Report Figures’ legends**

FIGURE 1

CTV demonstrated a filling defect of the cavernous sinus bilaterally (black arrows).

Figure 2A

MRI with Gadolinium revealed filling defects of the Cavernous sinuses (white arrow) and enhancement of the carotid artery in the cavernous part (black arrow).

Figure 2B

Diffusion Weighted MRI revealed Watershed infarcts between MCA and ACA territories (black arrows).

Figure 2C

MRA demonstrating Bilateral Cavernous ICA (white arrow) and MCA (black arrows) irregularity and narrowing.