A Case of Cavernous Sinus Thrombosis with Meningitis Caused by Community Acquired Methicillin Resistant Staphylococcus Aureus

Manjunath Dinaker¹, Chandrahasa Sharabu², Sri Rama Surya Tez Kattula³, Varun Kommalapati³

Abstract
Septic cavernous sinus thrombosis is a rare clinical condition. Although Staphylococcus aureus is the most common pathogen causing septic cavernous sinus thrombosis (CST), it is an uncommon cause of meningitis. We report the first case of CST with meningitis in Hyderabad, Andhra Pradesh, caused by community acquired epidemic strain of Methicillin resistant staphylococcus aureus (MRSA), in a previously healthy individual with no risk factors. The patient recovered completely following treatment with Vancomycin. We consecutively reviewed all cases of community acquired staphylococcus aureus (CA-MRSA) with central nervous system involvement available in literature.

Introduction
Staph aureus accounts for 2-10% of cases of bacterial meningitis. Over 60% are nosocomial, while remaining are due to community acquired strains. The conditions that predispose to development of CST and meningitis are spread of infection from contiguous sites e.g. from sinusitis, neurosurgical interventions etc. This case is rare in that the infection had spread from post staphylococcal impetigo in the left pre-auricular region.

Case Report
A 16 year old female presented with complaints of high grade fever with chills and rigors and pain on left side of her face and headache for one week. She had a history of bathing in a community pool five days prior to her illness. No history of seizures, head injury, diabetes mellitus and any known immuno-compromised states. On examination, there was bilateral proptosis with features of orbital cellulitis. There were multiple pustules in the left pre-auricular area. The temperature was 100°F, pulse rate 100/min and BP was 120/90 mmHg. CNS examination showed neck rigidity, 1+deep tendon reflexes, flexor plantar response, positive Kernig’s sign and bilateral papilloedema.

Investigations
- CBP: Hb 8.1gms, WBC: 16,100/cumm (with shift to left), ESR 104 mm/hr.
- Urine analysis-Normal.
- Blood for malarial parasite was negative.
- HIV negative.
- Routine biochemistry showed mild hyponatraemia.
- Chest X-ray and Ultrasound abdomen was normal. Trans-oesophageal echo did
not reveal any vegetations.

A possibility of pyogenic meningitis versus cavernous sinus thrombosis was considered. CT scan of head and brain showed mild cerebral oedema with meningeal enhancement. CSF examination revealed 20 cells/cumm, differential count -100% lymphocytes, Glucose- 82 mg/dl, Protein- 58.6 mg/dl, ADA -2 IU/L. Staining for gram’s and AFB organisms were negative. She was started on IV Ceftriaxone and Vancomycin along with dexamethasone and Enoxaparin. Both blood and CSF samples isolated S. aureus which was confirmed by standard biochemical tests. Screening for methicillin resistance was done by Cefoxitin (30 g) disc diffusion test, and isolates were identified as MRSA which was resistant to Ampicillin, cephalosporins, erythromycin; intermediate sensitivity to Vancomycin and sensitive to Co-trimoxazole. The isolates from both blood and CSF were genotyped and the strain was identified as EMRSA-15 [Epidemic MRSA-15]. Panton valentine leukocidin [PVL] gene assay could not be done.

MRI of head and brain done on day two of hospitalisation showed:

1. Multiple acute infarcts in the left capsulo ganglionic region, left hippocampus, left corona radiata and left frontal white matter. (Figure 1, Blue arrow),
2. Thrombosis of superior ophthalmic veins and cavernous sinuses bilaterally with retrograde extension of the thrombus into right superior petrosal vein (Figure 2, Red arrows).
3. Dense enhancement of leptomeninges along the floor of middle cranial fossa with two small ring enhancing lesions along the right lobe convexity. The above findings suggest the possibility of septic cavernous sinus thrombosis with meningitis and post meningitis infarcts.

Based on the above culture report, rifampicin was added. Warfarin was overlapped with Enoxaparin on day 5. She responded rapidly to the above treatment, and her fever, headache and eye signs subsided. At discharge she was conscious, coherent and afebrile with mild residual right hemiparesis. On follow up at three months, she had recovered fully and oral anticoagulation was discontinued.

**Discussion**

S. aureus is a well-recognised but a rare cause of community acquired meningitis. However in septic CST and brain abscess, Staph aureus is the causative agent in 60-70% and 20% cases respectively.\(^1\)\(^,\)\(^2\) Septic CST is a lethal disease associated with high morbidity and mortality which was predominantly attributed to Hospital Acquired Methicillin Resistant Staphylococcus Aureus [HA-MRSA]. Of late increasing CST cases caused by CA-MRSA have been reported.\(^3\)\(^,\)\(^4\) EMRSA 15 and EMRSA 16 have caused outbreaks in the UK and the US. To the best of our knowledge in the last 4 years, only 11 cases of CNS disease caused by CA-MRSA have been published.\(^5\) Most of them were caused by USA 300 (ST8) and one by EMRSA 16. Clones in Europe are more diverse and heterogeneous. Four CST cases with meningitis and brain abscess, (3 by USA 300 and 1 by STG3) have been reported.\(^6\) Compared to Panton valentine leukocidin [PVL] negative strains, PVL positive strains are associated with more metastatic infection. The most common source of CST is spread from sinuses. Chronic sinusitis, complicated by CA-MRSA leads to haematogenous spread through valveless system of paranasal sinuses into cavernous sinus and brain.\(^7\)

To the best of our knowledge, this is the first case of septic CST (being reported from India), that spread from skin infection and caused meningitis due to CA-MRSA. This case highlights a culture proven case
of impetigo, meningitis and CST caused by CA-MRSA, acquired, probably from bathing in a community pool. Development of serious infection in a young person without predisposing conditions as in our case is typical of CA-MRSA. By imaging studies, CSF and blood cultures, the source of infection was traced to the pre auricular impetigo. We hypothesised that the infection seeded the meninges from pre auricular area, and later on spread to the cavernous sinus.

Because of the limited therapeutic options and difficulty in achieving therapeutic doses in CSF, treatment of MRSA infections in the CNS remains a challenge. Traditionally MRSA has been treated with vancomycin with or without rifampicin. However, Vancomycin has poor penetration in CSF (especially with concomitant steroid usage) with slow onset of action. (CSF to serum ratio of only 20% in patients with meningitis). Sporadic cases that responded to linezolid treatment have been reported which can be explained by its excellent CSF penetration (CSF to serum ratio of approximately 70%). It is interesting to note that all cases of CNS infection caused by CA-MRSA treated with Linezolid showed complete resolution and those treated with vancomycin without linezolid either died or had serious complications. Recently, Daptomycin has shown to be very effective in rat models, but USA 300 strain did not respond in-vitro. Dalbavancin can also be considered an alternative to vancomycin because of its good CSF penetration. In our patient, vancomycin along with rifampicin was used to achieve synergy. (Linezolid was not used due to anaemia). The role of antiocoagulation in CST is in debate, but haemorrhage due to antiocoagulation is rare and if started early, along with antibiotics, is beneficial.

Our experience throws light on the epidemiological spread of CA-MRSA, difficulties in diagnoses, increased anti-microbial resistance of community acquired strains and therapeutic challenges. Intensive laboratory surveillance, notification to the public health authorities and providing guidelines for healthcare professionals are important measures to contain the infection. Additional studies need to be done, to know the epidemiological spread and compare the therapeutic efficacy of Vancomycin with linezolid.

References