Case report

Septic cavernous sinus thrombosis in a paediatric patient with undiagnosed thrombophilia

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SUMMARY

A previously healthy 8-year-old girl presented to the hospital with right periorbital and forehead swelling in the setting of a 1-week history of upper respiratory symptoms. Contrast-enhanced CT revealed pansinusitis with orbital and frontal abscesses and thrombosis of the anterior portion of the superior sagittal sinus. She was treated with surgical drainage, antibiotics and anticoagulants. After 2 days she developed cranial nerve (CN) VI palsy. Contrast-enhanced MRI revealed small epidural abscess, right-sided thrombi of the cavernous sinus, internal carotid artery and internal jugular vein, in addition to the superior sagittal sinus. Thrombophilia workup revealed heterozygosity for factor V Leiden. She underwent 6 weeks of parental antibiotic therapy, 3 months of anticoagulation therapy and 7 days of steroids. With treatment, her visual acuity returned to baseline, CN VI palsy resolved and repeat imaging showed resolution of thrombi and epidural abscess, but persistent narrowing of the internal carotid artery.

BACKGROUND

Septic cavernous sinus thrombosis (CST) is a rare life-threatening condition which results mainly from sinusitis (sinogenic) and facial infections. Paediatricians must maintain a high index of suspicion for CST in cases of orbital cellulitis, especially when ocular nerve palsies are out of proportion to the degree of orbital swelling. Contrast-enhanced CT and MRI are the imaging modalities of choice for diagnosis.

Accepted medical management includes broad spectrum antibiotics and anticoagulation therapies, but steroids are controversial. Also, early surgical drainage of abscesses is essential. Complications include cranial nerve (CN) palsies, meningitis and abscesses of the brain, subdural and epidural spaces. CN VI palsy is common due to its course in the cavernous sinus lumen. Recent mortality rates were reported at 8%.

Case presentation

A previously healthy 8-year-old girl presented to the hospital with right periorbital and forehead swelling in the setting of a 1-week history of upper respiratory symptoms. She was also complaining of right eye pain and blurred vision which started on the day of presentation. There was no known family history of clotting disorder. The initial examination revealed a temperature of 38.1°C, right periorbital and forehead swelling, reactive pupils, normal extraocular muscles, no papilloedema and

visual acuity on admission was 20/30 in the right eye and 20/40 in the left eye.

INVESTIGATIONS

On presentation, she had a normal white blood cell count ($6.9 \times 10^9/L$), electrolytes and renal function. C-reactive protein was elevated at 4.5 mg/dL (normal range is <0.3). The cultures obtained during forehead and orbital abscesses drainage grew microaerophilic *Streptococci* and *Eikenella corrodens*. Prothrombin time, partial thromboplastin time, international normalized ratio (INR), prothrombin G20210A, protein C activity, free protein S, total protein S, antithrombin III and plasminogen levels were all normal. Factor V Leiden genotype was heterozygous (R506Q/N). CT on admission revealed pansinusitis, orbital and frontal abscesses and superior sagittal sinus thrombosis (figures 1 and 2). Later, her MRI revealed small epidural abscess, right-sided thrombi of the cavernous sinus, internal carotid artery and internal jugular vein, in addition to the superior sagittal sinus (figures 3–5).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of periorbital and forehead swelling include sinusitis, orbital cellulitis, abscess and Pott's Puffy tumour. Complications of these conditions include dural sinus thrombosis, including CST, intracranial abscess and meningitis. The later was unlikely based on the absence of meningeal signs on physical examination. CT on admission confirmed the diagnoses of sinusitis with orbital cellulitis and abscess in addition to superior sagittal sinus thrombosis. MRI later revealed multiple thrombi and tiny epidural abscess.

TREATMENT

At the time of admission, the patient was started on broad-spectrum intravenous antibiotics including vancomycin (15 mg/kg every 6 hours), ceftriaxone (50 mg/kg daily) and metronidazole (10 mg/kg every 8 hours). On day 2 of her hospitalisation, the patient underwent functional endoscopic sinus surgery (FESS) and incision and drainage of the abscesses. Dexamethasone (0.5 mg/kg every 12 hours) was started after surgery to decrease the orbital swelling. She developed CN VI palsy on day 2 of hospitalisation, which prompted obtaining an MRI on the next day. Due to the extensive thrombi seen on the MRI, a thrombophilia workup was obtained and the patient was then started on

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Figure 1 Coronal reformatted contrast-enhanced CT of the sinuses demonstrating a triangular-shaped low attenuation filling defect in the superior sagittal sinus (black open arrow). A small collection of fluid attenuation is present along the medial wall of the right orbit consistent with orbital abscess (white open arrow). It is adjacent to the right ethmoid sinuses which are opacified.

low-molecular-weight heparin (LMWH) 1 mg/kg every 12 hours. An antifactor Xa activity was used for dosage adjustments. The antibiotics were narrowed on hospital day 5 based on culture sensitivities to ceftriaxone and metronidazole. Dexamethasone was continued due to concern for thrombosis-associated vasculitis. The patient received a total of 6 weeks of parental antibiotic therapy, 3 months of LMWH treatment and 7 days of dexamethasone. No neurosurgical intervention was required for the epidural abscess.

OUTCOME AND FOLLOW-UP

The patient was discharged home after 10 days to complete her antibiotics and anticoagulation therapies. At her 3-month follow-up, visual acuity was normal and CN VI palsy had resolved. Follow-up imaging at 3 months showed resolution of the cavernous sinus, superior sagittal sinus and internal jugular vein thrombi, but persistent narrowing of the right internal carotid artery.

DISCUSSION

Septic CST is a rare and life-threatening condition that results most commonly from sinusitis and facial infections, and less

Figure 2 Sagittal reformatted contrast-enhanced CT of the sinuses demonstrating soft tissue swelling over the right frontal sinus and a small area of water attenuation adjacent to the outer table of the skull, consistent with a small subperiosteal abscess and adjacent soft tissue oedema (white open arrow). The fluid level in the right frontal sinus is consistent with acute sinusitis (black open arrow).

Figure 3 Coronal contrast-enhanced T1 weighted image through the sella turcica demonstrating abnormal expansion of the right cavernous sinus with absent enhancement of a large portion of the cavernous sinus, consistent with cavernous sinus thrombosis (white open arrow).

common from otogenic, odontogenic and distal infections.^{1–3} Patients with CST will often exhibit periorbital oedema, chemosis, orbital pain, proptosis, diplopia and visual impairment. Tenderness over the sinuses and nasal discharge might be present in sinogenic CST.^{1–3} Approximately 3%–4% of children hospitalised with sinusitis develop intracranial complications.⁴ In one study, CST was reported in 2 of 50 (4%) paediatric patients with intracranial complications due to sinusitis.⁴ In another study of 21 children with intracranial complications due to sinusitis, epidural abscess was reported as the most common complication in 10 patients (48%) but there were no CST cases.⁵ A spread of infection into the cavernous sinus is possible through multiple mechanisms, including direct penetration through the thin, bony plates lining the frontal, maxillary and ethmoid sinuses. The infection can also spread via haematogenous extension through the valveless venous system connecting the face, orbit and sinuses.⁶ Contrast-enhanced CT and MRI are considered the imaging modalities of choice for CST diagnosis.⁷ There are many complications of CST and any one of the contents within the cavernous sinus may be affected. This includes CNs III, IV, V1, V2 and VI. However, CN VI is more susceptible to irritation as it courses directly through the cavernous sinus lumen and is not protected by arachnoid mater, in contrast to the other nerves in the sinus. CN IV is the least susceptible.^{1,2} Septic CST can

Figure 4 Transverse diffusion weighted image at the level of the frontal sinuses reveals abnormal restricted diffusion along the medial surface of the right frontal lobe. This was not T2 shine-through when compared with the accompanying apparent diffusion coefficient map (figure 5). The finding is consistent with a small intracranial abscess.

Figure 5 Accompanying apparent diffusion coefficient map for figure 4.

be complicated by intracranial infections including meningitis, epidural, subdural and brain abscesses. CST should always be in the differential diagnosis of postseptal or orbital cellulitis, especially in patients who fail to respond to medical treatment or develop seizures or neurological deficits.¹⁻³ Narrowing or occlusion of the intracavernous segment of the internal carotid artery is frequently reported (83%) in CST, likely due to arteritis or thrombosis.^{1,7} No large arterial strokes were found in one study despite significant narrowing.⁷ An increased intracranial pressure is usually seen more with superior sagittal and lateral sinus thrombosis than CST.¹ Lemierre syndrome due to septic thrombophlebitis of the internal jugular vein was reported in 2 of 12 children with CST (17%) in one study.⁷ Septic emboli are rare, but when they occur, the lungs are the most common site.¹ Morbidity and mortality of paediatric CST have improved dramatically due to early recognition and aggressive therapy with antibiotics, anticoagulants and surgical intervention. The mortality rate is recently reported at 8% and most patients have no long-term lasting morbidity compared with the mortality rate of 15%–30% reported in earlier studies.⁷⁻⁹ High dose, broad spectrum parental antibiotic therapy should initially be directed towards the most common pathogens including *Staphylococcus aureus*, *Streptococcus* sp, *Haemophilus influenzae*, and anaerobic bacteria and should have good blood–brain barrier penetration. A common regimen includes third generation cephalosporin, metronidazole and antistaphylococcal antibiotic. The recommended duration of parental antibiotic therapy is between 4 and 6 weeks.¹⁻³ If the paediatric patient has comorbidities, such as immunosuppression, diabetes or chronic steroid use or if the said patient fails to improve on initial antibiotic regimen, antifungal agents should be added. Fungal infections are associated with a worse outcome.^{7,9} Surgical intervention is critical and should include incision and drainage of the primary source of infection,

Patient's perspective

Our daughter had increased symptoms of headache, eye pain and fever leading up to her admission. On the morning of admission, we noted swelling in her forehead and a high (104.6) persistent fever. Once we were at the hospital, she reported having double vision. Prior to this illness, she never had any visual issues. Despite immediate treatment, the swelling in her forehead continued and required two separate surgical drainages, one during her admission and the other as an outpatient after discharge. The swelling settled over her eyes and placed pressure over the left eyelid which made it difficult for her to open her left eye. The swelling eventually led to cellulitis in the left eyelid that was surgically drained. Subsequent MRI showed left superior ophthalmic vein thrombosis, which was resolved on the following MRI. Early in her admission, she had paralysis of her abducens muscle which resulted in double vision when she had both eyes open. The double vision lasted for about 3 months at which time she slowly gained abduction back of her right eye. We feel that the immediate treatment of her illness prevented her from having more severe effects. With the cavernous sinus thrombosis, she was at risk of having a 'frozen' eye, which would have involved CNs III and IV in addition to VI. The periorbital abscess was managed surgically without any further effects. With the immediate treatment, the epidural abscess resolved without need for surgical intervention. Our daughter's case was complicated by a genetic clotting factor that we were unaware of prior to this illness. We were fortunate to have a team of doctors that recognised her condition and began treatment right away. After 4 months, she is slowly getting back to her previously energetic self.

such as FESS.^{1-3,7} Ideally, surgical intervention should take place early in the disease process before clinical signs develop. The American Stroke Association (ASA) recommends treating children with cerebral venous thrombosis with LMWH, even in the presence of intracranial haemorrhage. The ASA also recommends thrombophilia testing in these cases in order to identify underlying coagulation defects.¹⁰ Factor V Leiden is the most common inherited thrombophilia. Heterozygosity occurs in approximately 3%–8% of the US and European population, while homozygosity occurs in approximately 1:5000. A meta analysis by Kenet *et al* showed a Leiden variant significantly increased risk of cerebral venous thrombosis in children with an OR of 2.74.¹¹ The treatment guidelines for children generally follow adult guidelines with anticoagulation recommended for at least 3 months following a venous thrombosis provoked by a clinical risk factor that has since resolved.¹² Finally, corticosteroid use is controversial and if used, should only be done so for a short duration. Proposed benefits are decrease in orbital inflammation, CN oedema and thrombosis-associated vasculitis. However, there are no randomised controlled trials investigating these benefits, mainly due to the rarity of this condition. The previously mentioned benefits should be weighed against the risks of immune suppression and hypercoagulability caused by steroids.^{1,2,10} Our patient developed CST following extension of infection from an orbital abscess, which was the primary site of infection. Another possible risk factor included the patient's heterozygous factor V Leiden. While heterozygous factor V Leiden does not often cause spontaneous thrombosis in paediatric patients, given the right circumstances it can contribute to thrombotic events, as in our patient's case. Patients with factor V

Learning points

- Cavernous sinus thrombosis (CST) is a rare, life-threatening complication of sinusitis or nearby facial infection.
- Early, aggressive therapy for sinogenic CST should include broad spectrum parental antibiotics, anticoagulants and surgical intervention.
- Corticosteroids are controversial but may be warranted in certain cases.
- Hypercoagulability workup is recommended in children with cerebral sinus thrombosis including CST.

Leiden should know the signs and symptoms of thrombosis and avoid other risk factors such as obesity, smoking and estrogen-containing medications.¹² She also had complications including CN VI palsy on day 2 of her hospitalisation, despite draining of the orbital abscess and being on antibiotics for 2 days. This illustrates that these findings can occur even after proper treatment is initiated and should be monitored for facial infections. Overall, if patients are diagnosed quickly and appropriate therapy is initiated, most will do well, just as our patient has done.

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REFERENCES

- 1 Bhatia K, Jones NS. Septic cavernous sinus thrombosis secondary to sinusitis: are anticoagulants indicated? A review of the literature. *J Laryngol Otol* 2002;116:667–76.
- 2 Desa V, Green R. Cavernous sinus thrombosis: current therapy. *J Oral Maxillofac Surg* 2012;70:2085–91.
- 3 Lizé F, Verillaud B, Vironneau P, et al. Septic cavernous sinus thrombosis secondary to acute bacterial sinusitis: a retrospective study of seven cases. *Am J Rhinol Allergy* 2015;29:e7–12.
- 4 Deutschmann MW, Livingstone D, Cho JJ, et al. The significance of Streptococcus anginosus group in intracranial complications of pediatric rhinosinusitis. *JAMA Otolaryngol Head Neck Surg* 2013;139:157–60.
- 5 Glickstein JS, Chandra RK, Thompson JW. Intracranial complications of pediatric sinusitis. *Otolaryngol Head Neck Surg* 2006;134:733–6.
- 6 Brook I. Microbiology and choice of antimicrobial therapy for acute sinusitis complicated by subperiosteal abscess in children. *Int J Pediatr Otorhinolaryngol* 2016;84:21–6.
- 7 Smith DM, Vossough A, Vorona GA, et al. Pediatric cavernous sinus thrombosis: a case series and review of the literature. *Neurology* 2015;85:763–9.
- 8 Yarrington CT. Cavernous sinus thrombosis revisited. *Proc R Soc Med* 1977;70:456–9.
- 9 Frank GS, Smith JM, Davies BW, et al. Ophthalmic manifestations and outcomes after cavernous sinus thrombosis in children. *J Aapos* 2015;19:358–62.
- 10 Saposnik G, Barinagarrementeria F, Brown RD, et al. Diagnosis and management of cerebral venous thrombosis: a statement for healthcare professionals from the American heart Association/American stroke association. *Stroke* 2011;42:1158–92.
- 11 Kenet G, Lütkehoff LK, Albierti M, et al. Impact of thrombophilia on risk of arterial ischemic stroke or cerebral sinovenous thrombosis in neonates and children: a systematic review and meta-analysis of observational studies. *Circulation* 2010;121:1838–47.
- 12 Kujovich JL. Factor V Leiden thrombophilia. *Genet Med* 2011;13:1–16.

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