Status Epilepticus with Fever in a Toddler with Pyogenic Meningitis Due to Complicated Acute Sphenoid Sinusitis

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We present a toddler with acute sphenoid sinusitis presenting as status epilepticus with fever, intracranial abscess and meningitis. Cerebrospinal fluid analysis suggested bacterial meningitis, but polymerase chain reaction test was positive for human herpes virus 6. We highlight diagnosis and treatment of this uncommon condition. *(J Pediatr 2024;14:200123).*

Case Report

A previously healthy, fully immunized, 2-year-old girl was transported via emergency medical services to our community emergency department campus on a winter evening, in status epilepticus. The mother reported a 3-day prodrome of coryza and cough, 2 weeks before presentation. On arrival, she was obtunded with tonic extension of her extremities and gaze deviation to the right. Her initial temperature was 36.8°C, obtained via an axillary thermometer. Convulsive seizures were controlled with 2 doses of midazolam and a loading dose of levetiracetam. The total duration of seizure activity was approximately 15 minutes. Point-of-care electrolytes showed hyponatremia of 125 mEq/L and she received a 5-mL/kg 3% hypertonic saline bolus for persistent altered mental status. The repeat serum sodium was 130 mEq/L. A cranial noncontrast computed tomography (CT) scan, shortly after arrival, showed no intracranial pathology, except for partial opacification of the maxillary, ethmoid, and sphenoid sinuses.

Approximately 45 minutes later, she remained somnolent and tachycardic and a repeat temperature, obtained via rectal route was 40.5°C. She underwent a lumbar puncture, and cloudy cerebrospinal fluid (CSF) was obtained. She received a dose of vancomycin, ceftriaxone, and dexamethasone. CSF showed 2800 white blood cells and 85% neutrophils. The Gram stain was negative. CSF glucose was 52 and protein was 148. Serum glucose obtained was 140 mg/dL. This preliminary CSF profile suggested bacterial meningitis.[1,2] CSF polymerase chain reaction (PCR) test was positive for human herpes virus 6 (HHV-6). Our laboratory uses a syndromic multiplex PCR panel that can detect 14 pathogens, including bacteria, viruses, and yeast in the CSF. Acyclovir was started empirically owing to concern for herpes simplex virus encephalitis, given the presentation of seizure, fever, and altered mental status, before knowing that HHV-6 was detected on the PCR panel. It was subsequently discontinued in the intensive care unit.

Urine sodium and osmolarity were high, serum osmolality was low, and hyponatremia was attributed to syndrome of inappropriate antidiuretic hormone. Her parenteral fluids were restricted before transport. She was transferred to the pediatric intensive care unit of the Children's Hospital, where magnetic resonance imaging (MRI), MR angiography, and MR venography were obtained owing to her persistent altered level of consciousness, concern for bacterial meningitis, and associated cerebrovascular complications. It confirmed sphenoid sinusitis with skull base osteomyelitis and intracranial micro abscess measuring 18 mm at the tuberculum sellae (**Figure**, A-C) In addition, it showed enhancement along the intracranial arteries along the anterior circle of Willis and narrowing of the carotid bifurcations bilaterally. The vascular narrowing worsened on repeat imaging, hence aspirin and nimodipine were started prophylactically. There was no evidence of venous sinus thrombosis on MRI or MRV.

She underwent endoscopic sinus drainage by our consulting otolaryngologist. Pediatric infectious diseases and neurology services were also consulted early in her intensive care course. The patient was maintained on vancomycin and ceftriaxone to cover the most common causes of bacterial meningitis in this age group. The etiology of her meningitis was deemed to be related to contiguous spread from the sinuses, and metronidazole was added to cover for anaerobic flora. Vancomycin was ultimately discontinued, once cultures from the CSF were sterile, and her sinus cultures grew *Staphylococcus intermedius*, susceptible to ceftriaxone. She

CSF	Cerebrospinal fluid
CT	Computerized tomography
MRI	Magnetic resonance imaging
HHV	Human herpe

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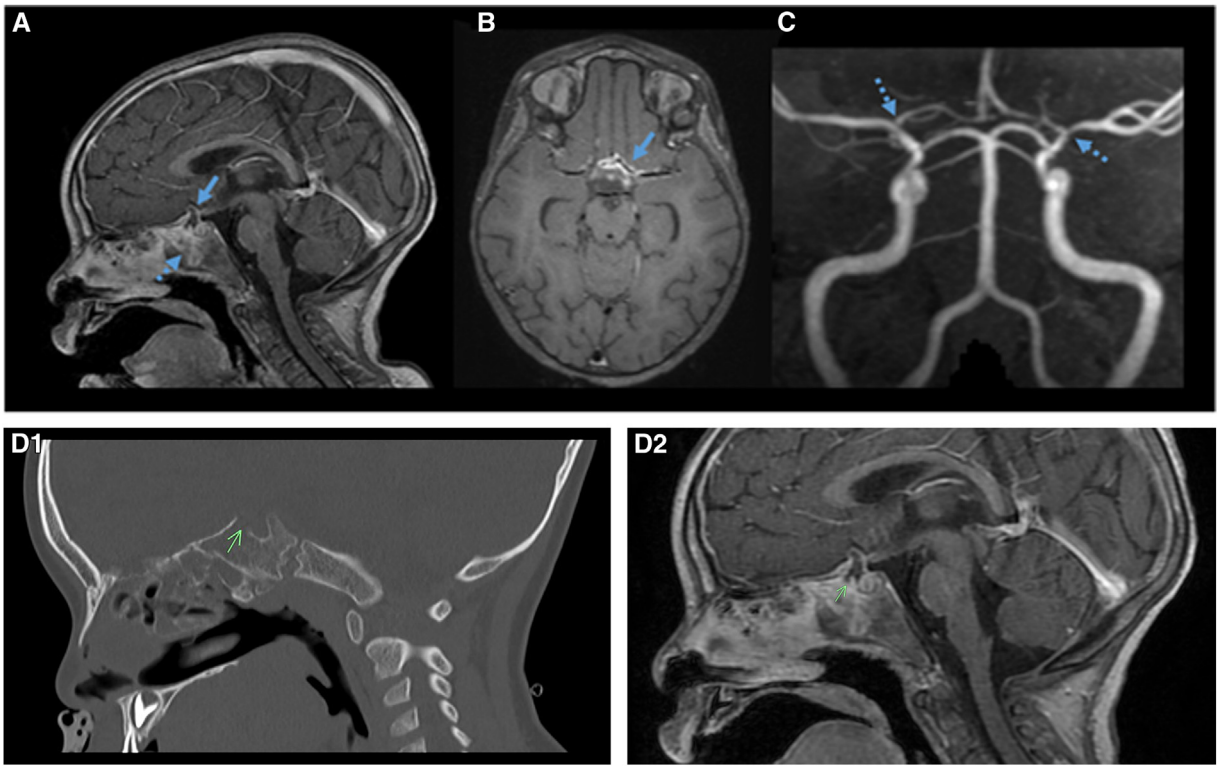

Figure. MR images of basisphenoid osteomyelitis with intracranial abscess and vasculitis. **A,** The small abscess (*solid arrow*) adjacent to sella turcica and bone marrow enhancement of the basisphenoid. **B,** Enhancement along the intracranial arteries of the anterior circle of Willis in keeping with vasculitis. **C,** Corresponding MR angiography showing stenoses at the distal intracranial internal carotid artery (ICA), ICA bifurcations, and A1 segments of the ACAs. **D,** CT images clearly show that the bone defect on CT correlates with location of the extra parenchymal abscess. Note that the abscess has a small finger like projection superiorly. This could represent a trans dural component extending into the subarachnoid space, but still extra parenchymal.

completed 6 weeks of parenteral antimicrobial therapy for epidural abscess. She had an uneventful clinical course, with no further seizure activity and a normal neurological examination at discharge.

Discussion

Status epilepticus is among the most common pediatric neurological emergencies, with significant morbidity and mortality, if not treated appropriately.[3] Febrile status epilepticus and complex febrile seizures have been commonly associated with HHV-6 and HHV-7 infections in young children.[4,5] However, detection of HHV-6 by PCR in the CSF in this immunocompetent child is almost certainly not a reflection of primary infection; rather, in light of the cellular profile of CSF, it represents reactivation or chromosomal integration of the virus.[6,7]

HHV-6 is a beta herpes virus that is often detected in CSF by multiplex PCR panels. Even in the presence of a positive PCR result, establishing HHV-6 as the cause of encephalitis or meningitis can be challenging, and its clinical significance is often questioned, especially in immunocompetent hosts.[6,7] Detection of HHV-6 viral nucleic acid often occurs outside of primary infection and may indicate viral latency, reactivation, or chromosomal integration (CiHHV-6), which is seen in approximately 1% of the population.[6,8]

Additionally, our case highlights that, even in young patients with incompletely developed sinuses, one must maintain a high index of suspicion for intracranial complications of sinusitis in the setting of fever with neurological symptoms. Pneumatization of the sphenoid sinus usually begins between the ages of 6 months and 4 years of age, but is not developed fully until 12-14 years of age.[9,10] Intracranial complications of sphenoid sinusitis are generally uncommon in children, and those requiring emergent operative intervention usually occur in older children.[11,12] Sphenoid sinusitis most often presents with headache and other generalized symptoms. Our patient may be the youngest reported case of a pyogenic complication associated with sphenoid sinusitis.[13,14] Of note, this child had an unusually large sphenoid sinus for a 2-year-old.[10] In general, in 1- to 2-year-old children, the average size of the sphenoid sinus is between 1 and 4 mm in greatest diameter and increases to 2-3 cm by adulthood.[10] We are not aware of any data to suggest that having a large sphenoid sinus for age portends greater risk of infections. Early operative management is reserved for either chronic symptoms or acute intracranial complications, as in our case.

CT with contrast is faster to accomplish, more readily available from the emergency department, and does not usually require sedation in children. It is especially useful to detect a large abscess or empyema with mass effect, or acute hydrocephalus, that may need urgent surgical intervention. CT scan is also usually needed to reveal bony details and abnormalities when planning surgical procedures. It does entail a small, long-term risk of radiation-induced malignancy in young children. Overall, MRI is a more sensitive imaging modality in the setting of intracranial infections. Restricted diffusion on MRI can confirm sinus disease and detect small abscesses, osteomyelitis, vascular complications, and inflammation of the extra-axial spaces or meningitis. Although a CT scan can detect bony lesions, MRI is a superior test in detecting early signs of osteomyelitis, such as bone marrow edema and inflammation, and in visualizing the brain parenchyma for evidence of cerebritis or infarction.

The intracranial abscess was located at the tuberculum sellae (**Figure**, B). The abscess was located under the dura, epidural in location. This location would be analogous to an osteomyelitis-related subperiosteal abscess in other parts of the body. The presence of a bone defect at the location of this abscess suggests that direct extension was the most likely pathophysiologic mechanism (**Figure**, D). Because there was no CSF leak, small bony defects are not considered a significant risk or entry point for future intracranial infection and are not repaired. Although colonization of the nasopharynx with hematogenous spread (valveless venous network) is the most common pathogenic mechanism for meningitis in children, caused by *Streptococcus pneumoniae* and *Neisseria meningitidis*, this case demonstrates that contiguous infection from the sinuses with bony defect is another possible mechanism. Venous sinus extension is another potential mechanism. However, neuroimaging in our case did not reveal intracranial venous sinus involvement. Our patient's sinus culture yielded *S intermedius*, which is a common pathogen associated with cases of intracranial extension owing to sinusitis.[12]

S intermedius belongs to a group of viridans Streptococci that are members of the normal flora of the oropharynx and sinuses. They are well-known to cause suppurative infections and can cross tissue planes leading to subperiosteal and intracranial complications from sinus disease. Although the CSF glucose was normal, it was <50% of the serum glucose. The hypoglycorrhachia and elevation of protein in CSF, in conjunction with degree of pleocytosis, was suggestive of pyogenic infection. Although it is possible that pleocytosis in the CSF was due to inflammation from the parameningeal infection, the other CSF indices and degree of complications led to treating this case as bacterial meningitis. The failure to isolate *S intermedius* from the CSF on culture or PCR suggests that the infection had not penetrated the CSF space; rather, the pleocytosis probably represented an inflammatory response to a parameningeal infection.

Children with intracranial bacterial infections are at risk of cerebrovascular complications, with as many as-one third of patients suffering from cerebral infarction.[15] Bacterial meningitis can lead to vasculitis or inflammation of the arterial wall, which can affect the major vessels of the circle of Willis, as seen in this patient, as well as the smaller lentifromriate arteries that branch off of the major vessels.[16,17] This can lead to large territory arterial ischemic strokes, watershed infarcts, or small infarcts in the deep gray and white matter, depending on which vessels are involved. A subset of patients with bacterial meningitis and arterial narrowing have been found not to have inflammation at the site of narrowing, suggesting that vasospasm may also contribute to arterial pathology in these patients.[18,19] Moreover, some patients with meningitis have arterial thrombosis in the absence of vasculitis, suggesting that clotting may also contribute to cerebrovascular pathology in the setting of bacterial meningitis.[20] Given the concern for the possibility of vasospasm and to prevent clot formation, our patient was treated with both aspirin and nimodipine.[21] Patients with intracranial bacterial infections are also at risk of cerebral venous sinus thrombosis.[22,23] This can occur in venous sinuses proximate to the infection but can also occur more distally. In the most severe cases, this can lead to venous infarction, which can be hemorrhagic.

Our case exhibited arterial wall enhancement and thickening consistent with vasculitis along both internal carotid arteries, and proximal anterior cerebral arteries (ACAs), and middle cerebral arteries. Especially striking was the enhancement along the ACAs. The patient also had edema of the left olfactory bulb, which suggests contiguous spread of the infection via the olfactory nerves at the nasal cavity roof. Additionally, there was inflammation of the anterior fornices. This was probably the result of direct spread from the adjacent ACAs.

In a critically ill child, it is important for acute care clinicians to obtain a rectal temperature as axillary or tympanic thermometry may be inaccurate.[24,25] The role of dexamethasone in acute bacterial meningitis is controversial. Data from adults with pneumococcal meningitis suggests that, when administered before or with antibiotics, it decreases neurological morbidity and deafness.[26,27] The Committee on Infectious Diseases of the American Academy of Pediatrics states that dexamethasone may be considered as adjunctive therapy, and its use is controversial because there are insufficient data to recommend its use in children.[28] Hyponatremia is the most common electrolyte disturbance seen in pediatric patients presenting with bacterial meningitis, with an incidence ranging between 30.3% and 66.4%, and is most often due to syndrome of inappropriate antidiuretic hormone.[29] It is important to correct severe, symptomatic hyponatremia promptly to avoid neurological complications. The rate of correction of serum sodium correction should not exceed 6-8 mEq/l per 24 hours.[30]

Our case highlights importance of maintaining a high index of suspicion for complicated sinusitis in a young child with status epilepticus and fever. CSF PCR results may be falsely positive for HHV-6 owing to ciHHV-6 virus in normal hosts, and in suspected pyogenic meningitis, MRI/MR angiography/MRV is a superior imaging test to a CT scan with contrast, for detection of intracranial infections and its complications. ■

CRediT authorship contribution statement

Jay Pershad: Writing – review & editing, Writing – original draft, Conceptualization. **Lexi Crawford:** Writing – review & editing, Validation. **Diego Preciado:** Writing – review & editing, Validation. **Dana Harrar:** Writing – review & editing, Validation, Conceptualization. **Jose Molto:** Writing – review & editing, Validation. **Craig Shapiro:** Writing – review & editing, Validation, Conceptualization.

Declaration of Competing Interest

The authors declare no conflicts of interest.

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