Fulminant Bacterial Meningitis Complicating Sphenoid Sinusitis

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Intracranial complications of sinusitis, including meningitis, are uncommon in childhood. Among pediatric patients admitted for treatment of sinusitis, 3.2% were found to have an intracranial complication.[1] Conversely, among pediatric patients with intracranial infections, only 2.4% had infections secondary to sinusitis.[2] Infection of the sphenoid sinuses, however, merits particular concern. These thin-walled sinuses develop late in childhood, and their deep location places them adjacent to the dura mater and other critical structures. Here we describe 2 previously healthy adolescent boys who developed fulminant bacterial meningitis as a complication of sphenoid sinusitis.

CASES

Patient 1 is a previously healthy 14-year-old African-American male with sickle trait who presented to an outside emergency department after 5 days of headache and fatigue, 2 days of fever and nasal congestion, and sudden worsening of headache with decreased level of consciousness. On arrival, he was disoriented and agitated with Glasgow Coma Scale (GCS) = 6 and marked hypertension (180/120 mm Hg). Lumbar puncture found an elevated opening pressure = 52 cm H_2O and yielded turbid fluid with a leukocyte count of 14,000/mm^3 (95% neutrophils, 2% lymphocytes, 3% monocytes), glucose < 20 mg/dL, protein 1,293 mg/dL, and abundant Gram-positive diplococci. The patient was intubated, treated with antihypertensives, and transported to our ICU. Vancomycin (60 mg/kg/d) and ceftriaxone (100 mg/kg/d) were begun. Admission CBC revealed WBC 23,700/mm^3 (46% neutrophils, 39% bands), normal hemoglobin, and platelets. Serum electrolytes, blood urea nitrogen, creatinine, and serum aminotransferases were normal. Computerized tomography scan of head showed fluid and mucoper-

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iosteal thickening in the left ethmoid sinus and both sphenoid sinuses (Fig. 1A). CSF culture and blood cultures grew *Streptococcus pneumoniae* sensitive to penicillin (MIC ≤ 0.03 µg/mL); vancomycin was discontinued. The initial hypertension quickly resolved and the patient remained hemodynamically stable throughout the hospitalization. He experienced steady improvement in his level of consciousness and was extubated on hospital day 6. Audiogram was normal. The patient was discharged in good condition upon completing 10 days of ceftriaxone therapy.

Patient 2 is a previously healthy 12-year-old African-American male who presented to our emergency department following 3 days of productive cough, greenish nasal discharge and headache, 2 days of fever, nausea and vomiting, then sudden worsening of headache with photophobia and neck discomfort. He had normal vital signs and clear mental status, but meningismus was appreciated on examination. A lumbar puncture found opening pressure of 41 cm H_2O, and yielded clear fluid with a leukocyte count of 144/mm^3 (88% neutrophils, 5% lymphocytes, and 7% monocytes), glucose 88 mg/dL, protein 32 mg/dL, and negative Gram stain. CBC showed WBC 14,700/mm^3 (40% neutrophils, 51% bands), normal hemoglobin, and platelets. Serum electrolytes, blood urea nitrogen, creatinine, and serum aminotransferases on admission were normal. Within a 3-hour observation period in the emergency department, he rapidly deteriorated with GCS dropping to 6, and then suffered a right-sided focal seizure with periodic breathing. Blood pressure and pulse remained stable. The patient was intubated and admitted to the ICU, vancomycin and ceftriaxone treatment initiated, and an intracranial pressure monitor was placed. Computerized tomography scan of head revealed total opacification of right ethmoid, maxillary and sphenoid sinuses (Figure 1B). CSF culture yielded *Streptococcus pyogenes* while blood culture was sterile; vancomycin therapy was discontinued. On hospital day 3, the patient's condition worsened, with development of adult respiratory distress syndrome, inotropic support requirements, and appearance of a scarletiniform rash over the entire body. Clindamycin therapy was added and he ultimately experienced widespread epidermal desquamation. The patient received prolonged ventilatory support and intracranial pressure monitoring, but was ultimately discharged in good condition following 2 weeks of antibiotic therapy and an additional 3 weeks of rehabilitative care. Audiogram was normal.

DISCUSSION

Sphenoid sinusitis is identified in approximately 3% of cases of acute sinusitis, typically in the context of pansinusitis.[3] Significant development of the sphenoid sinuses does not begin until age 4 to 6, thus, sphenoid sinusitis is restricted
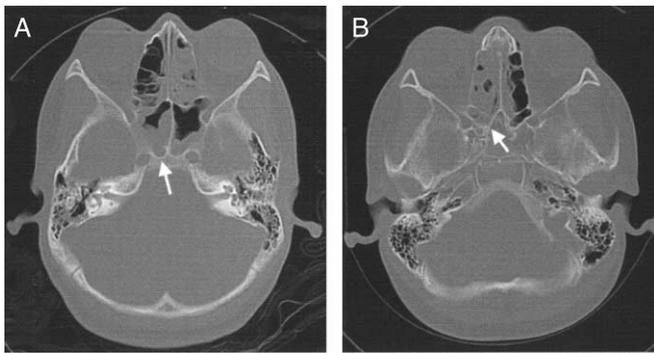
FIGURE 1. Computerized tomography of showing sphenoid sinus opacification (arrows) in two adolescent boys with fulminant meningitis.

to older children and adolescents. Likewise, intracranial complications of sinusitis appear predominantly in older children. Pooling 4 published pediatric series,[1,2,4,5] we calculated a median age of 13 years and a male proponderance of 3:1.

Approximately 80% of pediatric patients with intracranial complications of sinusitis have sphenoid involvement.[2,4–7] Table 1 summarizes the features of pediatric sphenoid sinusitis with intracranial complications from those cases in which sufficient clinical data were provided.[2,5–7]

The anatomic location of the sphenoid sinus places it adjacent to the optic canals, dura mater, cavernous sinuses, cranial nerves III to VI, and the internal carotid arteries. The bony walls of the sphenoid are thin or sometimes absent, leaving the sinus separated from intracranial structures by a narrow mucosal barrier. Diagnosis of sphenoid sinusitis is often difficult.[8] Located deep in the apex of the nasal cavity, the sphenoid sinuses are not amenable to percussion nor transillumination and may be indistinct on routine radiographs.[3] Early symptoms are usually nonspecific, including nasal congestion, fever, and poorly localized headache. Ultimately, the headache may become intractable and other symptoms such as photophobia, tearing or painful parasthesias in the distribution of the trigeminal nerve may develop. Delays

TABLE 1. Case Summaries of 18 Reported Cases of Pediatric Sphenoid Sinusitis With Intracranial Complications

Age	Gender	Symptoms (Duration, days)	Sinus involvement*	Intracranial complications	Bacteriologic Isolate(s)	Reference
3	N/A	N/A	S, E	Meningitis	N/A	2
7	N/A	N/A	S, E, M	Meningitis	N/A	2
7	M	headache (90), vomiting (3)	S, M	Meningitis	*Staphylococcus aureus*	6
9	N/A	N/A	S, E, M	Frontal lobe abscess	No growth	2
10	N/A	N/A	S, F, E, M	Meningitis	N/A	2
10	M	fever (3), headache (3), nasal obstruction (3)	S, E	Meningitis, Septal abscess	*Streptococcus pneumoniae*	6
12	M	headache (4), nausea (1), anorexia (1), fever (1)	S, E	Meningitis	*S. pneumoniae*	7
12	M	headache (2), vomiting (2), fever (2), photophobia (2)	S, F, E, M	Meningitis	Group A *Streptococcus*	This study
13	N/A	N/A	S, F, E, M	Epidural abscess, Subdural abscess	*Staphylococcus epidermidis, Propionibacterium*	5
13	M	fever (14), rhinorrhea (10)	S, F, E, M	Subdural abscess	No growth	5
13	F	headache (3)	S	Meningitis	No growth	6
14	N/A	N/A	S, F, E, M	Frontal lobe abscess, Subdural abscess	*S. epidermidis*	2
14	N/A	N/A	S, F, E, M	Temporal lobe abscess, Subdural abscess	*S. epidermidis Streptococcus* sp.	2
14	F	fever (10), rhinorrhea (10), headache (10), periorbital edema (10)	S, F, E, M	Epidural abscess	*S. pneumoniae S. epidermidis*	5
14	M	headache (5), fever (1)	S, E, M	Meningitis	*S. pneumoniae*	This study
15	N/A	N/A	S, F, E, M	Subdural abscess	*Streptococcus* sp.	2
15	M	fever (21), headache (21), nausea/vomiting (21), ophthalmoplegia (21)	S, E, M	Cerebropontine abscess, Transverse sinus thrombosis	*S. aureus S. epidermidis Bacteroides* sp.	5
16	M	fever (3), seizure (3), cranial nerve palsy (3), hemiparesis (3)	S, F, E, M	Subdural abscess, Frontal osteomyelitis, Arteritis	*S. epidermidis* Group C *Streptococcus S. aureus, Bacteroides* sp., *Corynebacterium* sp.	5

*S = Sphenoid, E = Ethmoid, M = Maxillary, F = Frontal, N/A = Not Available

in appropriate therapy for acute sphenoid sinusitis are associated with a significant rate of morbidity.[3,9,10] Potential complications include orbital cellulitis and ophthalmoplegia, cortical vein or cavernous sinus thrombosis, intracranial empyema or abscess, and meningitis.

Sphenoid sinus infection is hypothesized to spread to the meninges by direct penetration of the sinus wall or by retrograde extension along the valveless diploic veins. Alternatively, a systemic bacteremia could be established with subsequent penetration of the blood-brain barrier. Following antecedent symptoms of sinusitis in our patients, rapid neurologic deterioration and increased intracranial pressure developed without accompanying signs of the sepsis syndrome, such as tachycardia and hypotension. Consequently, we hypothesize that direct CNS penetration from the infected sinuses was a primary event in each case.

The most common organisms identified in sphenoid sinusitis are *Staphylococcus aureus*, *S. pneumoniae*, and other aerobic or anaerobic streptococci.[3,11] *S. pneumoniae* appears to be the pathogen most frequently associated with development of meningitis as a complication. CSF culture from patient no. 1 yielded *S. pneumoniae* serotype 10A. Serotype 10 strains are only the 15th most common cause of invasive childhood *S. pneumoniae* infections in the United States and Canada, accounting for approximately 0.5% of sterile site isolates,[12] and represent only 2% of *S. pneumoniae* isolated from sinus cultures.[13,14] The serotype 10A capsule is not included in the recently licensed 7-valent conjugate *S. pneumoniae* vaccine (Prevnar, Wyeth Lederle). CSF culture from patient no. 2 yielded *S. pyogenes* serotype. Serotype M2 (*emm*2) strains are an infrequent cause of invasive human *S. pyogenes* infection, accounting for 34/2,234 (1.5%) of consecutively typed invasive isolates, and 0/27 meningitis cases in the 1995 to 2001 Centers for Disease Control Active Bacterial Core Surveillance program (Beall, personal communication). The rare association of these 2 bacterial strains with bacteremic infections lends further circumstantial support to meningitis developing in our patients as a complication of an untreated deep mucosal infection.

Both patients in this report had rapid progression of neurologic symptoms upon presentation, with elevated intracranial pressure, unresponsiveness, and the requirement for mechanical ventilation. The hospital course of patient no. 2 was further complicated when he developed characteristic signs of *S. pyogenes* toxic shock syndrome, including hypotension, multiple organ dysfunction, and a diffuse scarletiniform skin eruption with subsequent desquamation. These complications developed on hospital day 3 while on intravenous antibiotic therapy and in the absence of positive blood cultures.

Computerized tomography of the brain, orbit, and sinuses is the diagnostic modality of choice for confirmation of sphenoid sinusitis and potential intracranial complications.[10] Findings could include mucosal thickening, sphenoid opacification, and bony erosions or sclerosis. Contrast enhancement should be performed to rule out epidural or brain parenchymal abscess formation. Antibiotic therapy directed at staphylococcal and streptococcal etiologies is indicated (eg, penicillinase-resistant β-lactam agents), and should be delivered parenterally to those patients who have any clinical or radiologic findings worrisome for intracranial extension. Surgical drainage and culture of the sphenoid sinus should be performed in those patients with delays in clinical response. Likewise, antibiotic therapy alone is usually inadequate for intracranial abscesses developing as a complication of sinusitis in children.[4,5]

CONCLUSIONS

A low index of suspicion is necessary for early diagnosis and treatment of sphenoid sinusitis and prevention of intracranial complications including meningitis. This is especially the case in pediatric patients who are more likely to have acute not chronic symptoms of sinusitis and to present only after advanced symptoms of the intracranial process.[2,5] A diagnosis of sphenoid sinusitis should be strongly considered in older children and adolescents, particularly males, who develop symptoms of fever and progressive poorly localized headache.

REFERENCES

1. Lerner DN, Choi SS, Zalzal GH, et al. Intracranial complications of sinusitis in childhood. *Ann Otol Rhinol Laryngol*. 1995;104:288–293.
2. Giannoni C, Sulek M, Friedman EM. Intracranial complications of sinusitis: a pediatric series. *Am J Rhinol*. 1998;12:173–178.
3. Lew D, Southwick FS, Montgomery WW, et al. Sphenoid sinusitis. A review of 30 cases. *N Engl J Med*. 1983;309:1149–1154.
4. Johnson DL, Markle BM, Wiedermann BL, et al. Treatment of intracranial abscesses associated with sinusitis in children and adolescents. *J Pediatr*. 1988;113:15–23.
5. Rosenfeld EA, Rowley AH. Infectious intracranial complications of sinusitis, other than meningitis, in children: 12-year review. *Clin Infect Dis*. 1994;18:750–754.
6. Leiberman A, Tovi F, Hirsch M. Pachymeningitis presenting feature of posterior sinus infection. *Eur J Pediatr*. 1986;144:583–585.
7. Maxwell FC, Couper RTL, Morris LL, et al. Meningitis and sphenoid sinusitis associated with free gas in the suprasellar cistern. *Pediatr Radiol*. 1994;24:594–595.
8. Levine H. The sphenoid sinus, the neglected nasal sinus. *Arch Otolaryngol*. 1978;104:585–587.
9. Macdonald RL, Findlay JM, Tator CH. Sphenoethmoidal sinusitis complicated by cavernous sinus thrombosis and pontocerebellar infarction. *Can J Neurol Sci*. 1988;15:310–313.
10. Xenos C, Rosenfeld JV, Kleid SM. Intracranial extension of sphenoid sinusitis. *Head Neck*. 1995;17:346–350.
11. Wyllie JW, 3rd, Kern EB, Djalilian M. Isolated sphenoid sinus lesions. *Laryngoscope*. 1973;83:1252–1265.
12. Hausdorff WP, Bryant J, Paradiso PR, et al. Which pneumococcal serogroups cause the most invasive disease: implications for conjugate vaccine formulation and use, part I. *Clin Infect Dis*. 2000;30:100–121.
13. Hansman D. Serotypes in Pneumococcal disease. A ten year study in Australia 1970 through 1979. *Aust NJ J Med*. 1983;13:359–364.
14. Tahkokallio O, Carlson P, Kaijalainen T, et al. Capsular polysaccharide types of *Streptococcus pneumoniae* isolated from maxillary sinus effusion. *Scand J Infect Dis*. 2001;33:393–394.