Fever, Frontal Sinus Mass, and CSF Pleocytosis
in a 44-Year-Old Man

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Intracranial complications arising from frontal sinusitis occur infrequently. However, they can progress with such rapidity that the clinical situation becomes far advanced before they are recognized. Radiographic imaging techniques may not be definitive early in the course of these complications.

The infectious disease service was asked to evaluate a middle-aged man with acute global headache and nasal discharge for two weeks. CSF pleocytosis (3,600 WBC/mm³) was documented on lumbar puncture, and a dense mass was noted on sinus radiographs. At surgery, a large bony lesion was found extending from the right frontal sinus into the adjacent ethmoid sinus and nasal-frontal duct. The authors discuss the bacteriology, pathogenesis, and potentially serious intracranial and extracranial complications of frontal sinusitis which were considered during their evaluation of this patient.

CASE PRESENTATION

DR. CHARLES BERENSON (Infectious Disease Fellow): A 44-year-old Algerian man had been in generally good health until presenting to Yale–New Haven Hospital with the sudden onset of severe global headaches. One and one-half days prior to admission, a localized right frontal headache was noted, followed by photophobia, chills, malaise, and a stiff neck. He admitted to about two weeks of straw-colored nasal discharge and a two-month history of occasional bronchitis, nonproductive cough, and nonseasonal intermittent sinus congestion. He had experienced transient hearing difficulties during his late teens, secondary to multiple ear infections that were no longer problematic. On the day of admission, he had gone to a clinic for evaluation of his worsening headaches. Sinus films showed a mass within the right frontal sinus.

The patient’s past medical history was remarkable for alcohol abuse, from which he had reformed two years earlier, and a two-pack-per-day smoking history. There was no history of diabetes, tuberculosis, or known tuberculosis exposure. He had emigrated to the United States from Algeria twenty years previously and married an American woman. They had two children and kept no pets. The patient was employed as an auto mechanic and had done no recent foreign traveling. On physical examination the patient appeared to be toxic and in considerable distress, making a great effort to shield his eyes from any light. Temperature was 102.6°F. Pupils were reactive, and extraocular movements were intact. Both fundi and tympanic membranes appeared normal. Frontal and maxillary sinuses were quite tender, but no erythema, warmth, or
periorbital swelling was apparent. Chest, heart, and abdominal examinations were unremarkable. Meningismus was present, but his neurological exam was otherwise normal.

Laboratory evaluation revealed a white blood cell (WBC) count of 16.7 cells/µl with 78 polymorphonuclear leukocytes, 6 bands, 7 lymphocytes, and 9 monocytes. Some toxic granulations were noted. Hemoglobin concentration and hematocrit were 14.4 gm/dl and 47.1 percent, respectively. Serum electrolytes, glucose, blood coagulation profile, and urinalysis were normal. A chest radiograph was also normal. Sinus films, taken at the referring clinic, accompanied him. Would anyone care to comment on them (Fig. 1)?

DR. J. DAVID GAINES (Clinical Associate Professor of Medicine; Chief of Infectious Disease, Waterbury Hospital): It appears that the patient has a large calcified mass in the right frontal sinus. Both maxillary sinuses appear hazy as well.

DR. FRANK BIA (Associate Professor of Medicine; Infectious Disease Section): In addition, both frontal sinuses are completely opaque. Maxillary sinus haziness is more pronounced on the left.

A PHYSICIAN: What about the ethmoid sinuses?

DR. GEORGE THORNTON (Clinical Professor of Medicine; Chief of Medicine, Waterbury Hospital): Ethmoid sinusitis is a potentially devastating disease. It can present with an unusual headache, occasionally located at the vertex of the skull [1]. In neither my experience nor in my reading have I ever heard it described as global.

DR. BERENSON: The radiologist felt this represented pansinusitis, which included ethmoid involvement. On admission, a computerized tomographic (CT) head scan was obtained, both with and without contrast administration. It was read as normal, without any evidence of brain abscess. The ventricles were of normal size with no shift of midline structures. Additional radiologic evaluation of the sinuses was not immediately undertaken.

A lumbar puncture was then performed. Cerebrospinal fluid (CSF) contained 81 red blood cells/mm³ and 3,600 white blood cells/mm³—65 polymorphonuclear leukocytes, 14 lymphocytes, and 21 monocytes. The CSF protein concentration was 100 mg/dl; the glucose concentration was 62 mg/dl. A serum glucose of 119 mg/dl had been noted on admission. CSF VDRL and cryptococcal antigen determinations were negative. A Gram stain of CSF revealed many white blood cells but no organisms. Counterimmunoelectrophoresis (CIE) of the CSF was negative for the following antigens: H. influenza type b, Klebsiella pneumonia, pneumococci, group B streptococci, and meningococci.

DR. JOHN MELLORS (Assistant Professor of Medicine, Infectious Disease Section): Diagnoses worth considering should include Pott’s puffy tumor, an osteomyelitis of the frontal bone which spreads subcutaneously, and also epidural abscess, subdural empyema, or possibly brain abscess. While this patient’s CSF white blood cell count is higher than that usually found in the last three entities, it is still within the reported range of experience [2]. In addition, CT scans have been reported occasionally to miss a subdural empyema early in its course [3].

DR. FRANK BIA: Keep in mind that this patient did not present with pansinusitis and CSF pleocytosis alone. He had a potentially invasive mass lesion which could have allowed infection to spread beyond usual boundaries. If one wishes to evaluate the nasal sinuses adequately, special CT views of the sinuses are often needed [10].
COMPLICATIONS OF FRONTAL SINUSITIS

DR. BERENSON: CT views were taken through the nasal sinuses in the frontal plane (Fig. 2). They demonstrate pansinusitis, with either opacification or air-fluid levels present in each frontal and ethmoid sinus, and the sphenoid sinus as well. The dense calcified mass seems to have actually eroded through the inferior and posterior walls of the frontal sinus. We still could not determine if it had invaded the dura mater. A technetium bone scan (Fig. 3) was obtained on the first hospital day. There is an area of intense uptake that corresponds to the right frontal mass lesion. Other areas of his frontal sinuses and calvarium did not appear involved.

A gallium scan was obtained to see if the uptake on the bone scan represented a focus of acute osteomyelitis and to localize any abscesses that might have been missed. The gallium scan did not display intense uptake in the right frontal region. Taken together, the bone and gallium scans were not felt to indicate an acute osteomyelitis or abscess collection.

DR. VINCENT T. ANDRIOLE (Professor of Medicine, Chief, Infectious Disease Section): The most logical move would be to obtain a diagnostic sinus aspirate at this point.

DR. BERENSON: His right maxillary sinus had been aspirated. The fluid had fewer white blood cells than were present in CSF, and no organisms were noted on Gram stain. Unfortunately, the remainder of the specimen was disposed of, and bacterial cultures were not obtained.

DR. GAINES: Since the maxillary sinus fluid was never cultured, it would be reasonable to repeat the procedure, especially since this patient would likely require a long course of therapy.

DR. BERENSON: A second maxillary aspirate was performed through the right naris after empiric antibiotic treatment had already been started. No organisms were seen.
on Gram stain. Aerobic and anaerobic bacterial cultures yielded no growth of organisms.

A PHYSICIAN: If you felt that the infection originated from the right frontal region, why wasn’t the right frontal sinus drained?

DR. ANDRIOLE: The complications associated with aspiration of the frontal sinuses often prompt some otolaryngologists to institute empiric antimicrobial therapy for a period of 48 hours before attempting it. If no improvement is noted, draining the frontal sinuses becomes somewhat more urgent. Also, with pansinusitis, the bacteriology of each sinus is likely to be similar.

DR. BIA: As an infectious disease consultant, one might have preferred to obtain material from the right frontal sinus before initiating antibiotic treatment. However, our ENT consultants pointed out that an open procedure would likely be necessary to
investigate adequately the calcified sinus lesion. They did not want to open that frontal sinus until superimposed infection could be largely eliminated.

DR. BERENSON: Under these circumstances, a decision in favor of empiric antibiotic coverage was made. The patient was begun on an antibiotic regimen consisting of ampicillin, to cover streptococci and Hemophilus species [9], metronidazole for anaerobic coverage, and oxacillin for Staphylococcus aureus coverage.

DR. ROBERT BALTIMORE (Associate Professor of Pediatrics): There are some single agents that might have provided adequate coverage of organisms that we encounter in the nasal sinuses. Some of the newer cephalosporins, such as cefuroxime, provide coverage against Hemophilus influenzae and anaerobes. Why didn’t you choose one of these?

DR. BIA: Among anaerobes, consideration must be given to Bacteroides fragilis coverage, for which metronidazole is superior [11]. In fact, we thought about second and third generation cephalosporins, particularly because the latter penetrate the CSF rather well. Frontal osteomyelitis was still a serious consideration; coverage had to include Staphylococcus aureus [11]. Without having benefit of sensitivities or minimum inhibitory concentrations, an antistaphylococcal penicillin provides more reliable coverage for S. aureus than second or third generation cephalosporins. Empiric decongestant therapy may also be of use in this setting, and it was begun [11].

A PHYSICIAN: Would anyone consider giving chloramphenicol as single drug therapy in this setting?

DR. BIA: Chloramphenicol, as a single agent, can be useful for coverage of H. influenzae, streptococci, pneumococci, and anaerobes. The problem, in this setting, is
the possibility of staphylococcal osteomyelitis. Chloramphenicol's coverage of *S. aureus* is not reliable. One might make a case for use of an antibiotic combination including chloramphenicol and a more reliable antistaphylococcal agent.

**DR. ANDRIOLE:** In 1964 members of our otolaryngology department described a patient who had a similar problem involving a sphenoid sinus mucocele. The inflammatory mass originated in the sinus epithelium and eroded the sinus walls, as might a malignancy [4]. While the lesion we are considering today most resembles a benign osteoma radiographically, it might be a malignancy or a mucopyocele, either of which could have eroded posteriorly. A CT scan would not distinguish these.

**DR. BERENSON:** After less than 24 hours of antibiotic therapy, a second lumbar puncture showed a CSF white blood cell count that had risen to 5,600/mm³, with 67 percent polymorphonuclear leukocytes, 14 percent lymphocytes, and 19 percent monocytes. The CSF protein concentration was 50 mg/dl and the glucose was 73 mg/dl. However, by the third hospital day, the patient had clinically improved, despite seemingly worse CSF parameters. By the fourth hospital day, he had defervesced and remained afebrile from that point onward. On that day, a third lumbar puncture was performed. The CSF white blood cell count had dropped to 480 cells/mm³. The protein and glucose concentrations were unchanged.

**A PHYSICIAN:** How well does the microbiology laboratory culture spinal fluid anaerobically?

**DR. STEPHEN EDBERG (Associate Professor of Laboratory Medicine):** We do culture it anaerobically. However, problems may arise in transporting CSF samples. Exposing large surface areas to air can significantly decrease the yield of anaerobes. Adequate cultures should grow most Bacteroides species and other anaerobes commonly seen in brain abscesses, but they could fail to grow some of the more fastidious anaerobes if CSF is not transported in anaerobic medium.

**DR. BERENSON:** Our differential diagnosis included anaerobic infection underlying a right frontal mucopyocele, a malignancy, or osteoma formation. Whatever the causative lesion, a tear in the dura mater could have led to the high CSF WBC count. Such a lesion would require surgical repair. At the request of the surgical consultants, a definitive procedure was deferred to allow for several weeks of antibiotic treatment. The patient did well and a bifrontal craniotomy was performed. Intraoperatively, a small amount of purulent material was found in the right frontal sinus. Gram stains, acid-fast stains, and KOH preparations of that material showed no bacterial or fungal organisms. The bony lesion, which extended from the right frontal sinus into the adjacent ethmoid sinus and nasal-frontal duct, was removed. Where the mass impinged upon the dura mater, the dura was notably thinned. With most of the lesion removed, a definite rent in the dura was exposed, requiring repair with a single suture. All exposed surfaces were covered with temporalis muscle. The patient received intravenous antibiotics for another ten days post-operatively, and was discharged to receive oral antibiotics for an additional week. All intraoperative cultures were negative, including aerobic, anaerobic, mycobacterial, and fungal cultures of bone and purulent sinus material. A lumbar puncture prior to discharge showed complete resolution of CSF pleocytosis. Histopathological examination of the bony lesion, including special stains for microorganisms, demonstrated a benign osteoma with no evidence of malignancy or osteomyelitis.
TABLE 1
Complications of Frontal Sinusitis

| Intracranial                          | Extracranial/Bony                      |
|---------------------------------------|----------------------------------------|
| Extradural or subdural abscess        | Localized subperiosteal abscess        |
| Brain abscess                         | Spreading osteomyelitis                |
| Meningitis                            | Orbital cellulitis                     |
| Cavernous sinus thrombosis            |                                        |

DR. MELLORS: Why did he develop pansinusitis in the first place? Was it allergic in origin?

DR. BERENSON: We did not obtain a history of allergies, but the pathologist identified a sinus polyp. An unrecognized allergy could have been his predisposition for sinusitis.

A PHYSICIAN: Is an osteoma a known consequence of chronic sinusitis?

DR. BERENSON: I have not found this described as a consequence of, or in association with, sinusitis. It seemed to be a coincidental lesion that clearly contributed to morbidity in this case.

DISCUSSION

DR. BERENSON: Frontal sinusitis, whether acute or chronic, can lead to several potentially serious problems. These can be divided into intracranial and extracranial, or bony, complications (Table 1). Intracranial complications comprise most of the entities just discussed, including purulent extradural or subdural collections, brain abscesses, meningitis, and cavernous sinus thrombosis. The bony complications may include acute localized osteomyelitis, which may be associated with adjacent soft tissue infections such as orbital cellulitis [5]. Meningitis is unusual, but when it occurs it is most often caused by pneumococci, other streptococci, *Staphylococcus aureus*, or *Hemophilus influenzae* [2].

Extradural and subdural abscesses may occur, and they are usually located near the frontal lobes. They may cause focal motor or sensory deficits, decreased consciousness, and occasionally seizures. The most commonly associated organisms are streptococci, of which 50 percent were anaerobic in one series [2]. Other organisms include Bacteroides species, pneumococci, *Staphylococcus aureus*, and, less often, Proteus species.

When secondary to sinusitis, osteomyelitis of the skull is usually confined to the frontal bone. A localized subperiosteal abscess (Pott's puffy tumor) may form, or a diffusely spreading bony infection may extend via localized thrombophlebitis [2,8].

When sinusitis spreads to intracranial spaces, it generally does so by way of venous communications. Rarely, the posterior wall of the sinus and the dura itself are eroded by direct extension of infection. Sinuses are drained by small diploic veins that extend through the bony sinus wall. These veins communicate with the venous plexuses of the dura, the periorbital region, and the cranial periosteum. Septic thrombi can spread along any of these routes, even beyond the dural sinus to the sagittal sinus. When retrograde septic thrombophlebitis allows organisms to enter the subdural space, subdural empyema may occur. Brain abscesses can also result from retrograde embolization. Infrequently, a fistula between bone and dura forms, but this is more commonly seen with frontal sinus fractures or malignancies [6].
Pus spreads within the subdural space and, aided by gravity in the bedridden patient, it spreads along the frontal pole. It is curtailed from reaching the CSF by the arachnoid, which acts as a natural barrier. However, meningeal inflammation can occur with CSF parameters suggesting aseptic meningitis.

This course differs from that in our patient, who had pansinusitis and an intact neurologic exam without a decreased level of consciousness. His CSF white blood cell count was 3,600 cell/mm³, which is rather high and somewhat atypical for a subdural empyema [7]. This inflammatory response suggested bacterial meningitis; however, the absence of organisms on either culture or Gram stain, and the normal CSF glucose concentration did not support this diagnosis. A right frontal osteomyelitis, involving the bony lesion, could not be documented with combined technetium and gallium scans and was not evident on histopathological examination.

Finally, this bony lesion could have represented a malignancy eroding the dura. This was not the case. The occurrence of a benign osteoma associated with a sinus-dural fistula stands as a unique event among the complications of frontal sinusitis. This is how we were best able to explain the pathogenesis of events in our patient.

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REFERENCES

1. Morgan PR, Morrison WV: Complications of frontal and ethmoid sinusitis. Laryngoscope 90:661-666, 1980
2. Kaplan RJ: Neurological complications of infections of the head and neck. Otolaryngol Clin North Am 9:729-749, 1976
3. Kaufman DM, Litman N, Miller MH: Sinusitis: induced subdural empyema. Neurology (NY) 33:123-132, 1983
4. Norman PS, Yanagisawa E: Mucocele of sphenoid sinus. Arch Otolaryngol 79:646-652, 1964
5. Kutnick SL, Kerth JD: Acute sinusitis and otitis: their complications and surgical treatment. Otolaryngol Clin North Am 9:689-701, 1976
6. Remmler D, Boles R: Intracranial complications of frontal sinusitis. Laryngoscope 90:1814-1824, 1980
7. Kaufman DM, Miller MH, Steigbigel NH: Subdural empyema: Analysis of 17 recent cases and review of the literature. Medicine 54:485-498, 1975
8. Gil-Carcedo LM, Izquierdo JM, Gonzalez M: Intracranial complications of frontal sinusitis. J Laryngol Otol 98:941-945, 1984
9. Gwaltney JM, Syndor A, Sande MA: Etiology and antimicrobial treatment of acute sinusitis. Ann Otol Rhinol Laryngol 90:68-71, 1981
10. Hesselink JR, Weber AL, New PF, et al: Evaluation of mucoceles of the paranasal sinuses with computed tomography. Radiology 133:397-400, 1979
11. Baker AS: Sinusitis. Medical Grand Rounds 3:154-165, 1984