Pneumococcal Facial Cellulitis in Children

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ABSTRACT. *Objective.* **To review the epidemiology and clinical course of facial cellulitis attributable to *Streptococcus pneumoniae* in children.**

Design. **Cases were reviewed retrospectively at 8 children's hospitals in the United States for the period of September 1993 through December 1998.**

Results. **We identified 52 cases of pneumococcal facial cellulitis (45 periorbital and 7 buccal). Ninety-two percent of patients were <36 months old. Most were previously healthy; among the 6 with underlying disease were the only 2 patients with bilateral facial cellulitis. Fever (temperature: ≥100.5°F) and leukocytosis (white blood cell count: >15 000/mm³) were noted at presentation in 78% and 82%, respectively. Two of 15 patients who underwent lumbar puncture had cerebrospinal fluid with mild pleocytosis, which was culture-negative. All patients had blood cultures positive for *S pneumoniae*. Serotypes 14 and 6B accounted for 53% and 27% of isolates, respectively. Overall, 16% and 4% were nonsusceptible to penicillin and ceftriaxone, respectively. Such isolates did not seem to cause disease that was either more severe or more refractory to therapy than that attributable to penicillin-susceptible isolates. Overall, the patients did well; one third were treated as outpatients.**

Conclusions. **Pneumococcal facial cellulitis occurs primarily in young children (<36 months of age) who are at risk for pneumococcal bacteremia. They present with fever and leukocytosis. Response to therapy is generally good in those with disease attributable to penicillin-susceptible or -nonsusceptible *S pneumoniae*. Ninety-six percent of the serotypes causing facial cellulitis in this series are included in the heptavalent-conjugated pneumococcal vaccine recently licensed in the United States.** *Pediatrics* **2000;106(5). URL: http://www.pediatrics.org/ cgi/content/full/106/5/e61;** *Streptococcus pneumoniae, cellulitis, antibiotic resistance.*

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ABBREVIATION. CSF, cerebrospinal fluid.

Facial cellulitis includes both periorbital (preseptal) and buccal cellulitis. When associated with trauma or contiguous infection (eg, stye), *Staphylococcus aureus* or *Streptococcus pyogenes* are likely causes.[1,2] In the absence of trauma or contiguous infection, historically *Haemophilus influenzae* type b was the most common cause followed by *Streptococcus pneumoniae*.[3,4] Since the virtual eradication of invasive disease caused by *H influenzae* type b in the United States through the use of conjugated vaccines, *S pneumoniae* now likely predominates in such cases. In view of this and the dramatic increase in antibiotic resistance noted among *S pneumoniae* isolates beginning in the early 1990s,[5] we reviewed the epidemiology and clinical course of facial cellulitis attributable to *S pneumoniae* among children seen in recent years at 8 children's hospitals in the United States.

METHODS

The US Pediatric Multicenter Pneumococcal Surveillance Group consists of investigators from 8 children's hospitals. Since 1993, these investigators have prospectively identified children seen at their centers with invasive disease attributable to *S pneumoniae* (documented by isolation from a normally sterile body site).[5] For the current study, further information was gathered retrospectively for each case of facial cellulitis identified from September 1, 1993 through December 31, 1998.

The pneumococcal isolates from each center were sent to a central laboratory (Infectious Disease Research Laboratory, Texas Children's Hospital, Houston, TX) where serotyping and susceptibility testing for penicillin and ceftriaxone were peformed. Isolates were serotyped by the capsular swelling method using commercially available antisera (Statens Seruminstitut, Copenhagen, Denmark; Daco, Inc, Carpinteria, CA).[6] Susceptibility testing was performed by standard microbroth dilution with Mueller-Hinton media supplemented with 3% lysed horse blood.[7] Susceptibility was defined according to the 1999 National Committee for Clinical Laboratory Standards guidelines for minimal inhibitory concentrations[8]: for penicillin, ≤.06 μg/mL, susceptible; .1–1.0 μg/mL, intermediate; ≥2.0 μg/mL, resistant: for ceftriaxone, ≤.5 μg/mL, susceptible; 1.0 μg/mL, intermediate; and ≥2.0 μg/mL, resistant. Isolates that were intermediate or resistant were considered nonsusceptible.

The statistical significance of differences in the frequencies of categorical variables was tested with either Fisher's exact test or χ^2 test for trends. Two-tailed *P* values <.05 were considered significant.

RESULTS

During the study, 52 patients with facial cellulitis were identified. Forty-five had periorbital and 7 had buccal cellulitis. They ranged in age from 6 weeks to

6 years with a median age of 11.1 months. Forty-eight (92%) were <36 months old. Thirty-four patients (65%) were male. Thirty-two patients were white, 17 were black, and 3 were Hispanic. Ten patients attended day care, 38 did not, and this information was unknown in 4 cases.

Underlying illnesses included: cancer (4), human immunodeficiency virus type 1 infection (1), and facial cystic hygroma (1). Only 2 patients had bilateral facial cellulitis (both periorbital) and both had underlying disease: acute lymphocytic leukemia (1) and human immunodeficiency virus (1). Thus, both of the patients with bilateral cellulitis had an underlying disease/immunodeficiency versus 4 of 50 patients with unilateral infection ($P = .01$).

Recent previous trauma to the affected area was noted in 3 patients and contiguous infection in 2 (stye [1] and dacryocystitis [1]). The onset of cellulitis was preceded by symptoms of upper respiratory tract infection (rhinorrhea, cough, and/or congestion) in 28 children, while 20 lacked such symptoms, and in 4 this information was unknown. Such symptoms were present in 24 of 41 (59%) with periorbital cellulitis and 4 of 7 (57%) with buccal cellulitis. Fourteen patients had concomitant otitis media: 11 of 45 (24%) with periorbital and 3 of 7 (43%) with buccal cellulitis ($P = .36$). Six of these involved the ipsilateral ear, 3 the contralateral ear, and in 5 both ears were involved. The 3 patients with buccal cellulitis had otitis media in ipsilateral, contralateral, and bilateral ears, respectively.

All patients but 1 had a history of fever. Temperature was documented at the time of presentation for 50 patients: 39 (78%) were febrile ($\geq 100.5°F$); 29/50 (58%) and 22/50 (44%) had temperatures $\geq 102°F$ and $\geq 103°F$, respectively. The cellulitis was noted to have a violaceous hue in 6 cases.

White blood cell count was measured at the time of presentation in 51 patients: the mean was 22 998/mm^3, with a range of 500 (patient with acute lymphocytic leukemia) to 49 900/mm^3. The white blood cell count was >15 000/mm^3 in 42/51 (82%) and >20 000/mm^3 in 32/51 (63%). Fifty patients had white blood cell differential counts performed that revealed: mature neutrophils, mean 56% (range: 0% [patient with acute lymphocytic leukemia] to 84%); and immature neutrophils, mean 8% (range: 0%–30%). Eighteen patients (36%) had $\geq 10\%$ immature neutrophils.

Fifteen patients underwent lumbar puncture; 10 were <12 months old and 5 of these were noted to be irritable or lethargic. All cerebrospinal fluid (CSF)

test results were normal except for pleocytosis that was noted in 2 patients with periorbital cellulitis (Table 1). These 2 patients had blood cultures positive for penicillin- and ceftriaxone-susceptible pneumococci. All CSF Gram-stains and cultures were negative for bacteria.

Ten patients (all with periorbital cellulitis) had radiologic studies that included the paranasal sinuses (plain radiography, 5; computed tomography, 5). All studies showed abnormalities of the sinuses (thickened mucosa or opacification; no air-fluid levels were noted). The maxillary sinuses were abnormal in all, ethmoids in 8, and pansinusitis was noted in 3 patients. Abnormal findings were bilateral in 7 (including 1 patient with bilateral cellulitis) and unilateral in 3 (the cellulitis was ipsilateral in 2 of these and bilateral in 1).

All patients had blood cultures positive for *S pneumoniae*. One patient also had aspiration of the cellulitis performed, which was culture-positive. Among the 49 isolates submitted for serotyping, the predominant serotypes were 14 (53%) and 6B (27%; Table 2).

Antibiotic susceptibility testing was performed at the central laboratory for 50 isolates, and at the local laboratory for 1 (which was penicillin- and ceftriaxone-susceptible). Of the 51 total isolates, 43 were susceptible (84%), 5 intermediate (10%), and 3 resistant to penicillin (6%), while 49 were susceptible (96%) and 2 intermediate (4%) to ceftriaxone. For each calendar year of study, the percent of pneumococci that were nonsusceptible to penicillin was 1994, 14.3; 1995, 7.1; 1996, 30.0; 1997, 14.3; and 1998, 20.0. During the study, there was not a statistically significant increase in the percent of cases each year attributable to penicillin-nonsusceptible isolates ($P = .56$). During the month before presentation with cellulitis, β-lactam antibiotics had been taken by significantly more patients with penicillin-nonsusceptible isolates (3/8, 38%) than by patients with penicillin-susceptible isolates (3/43; 7%; $P = .04$).

Overall, 17 patients (33%) were treated as outpatients. Among the 35 patients (67%) admitted, 16 (46%) had no fever after the day of admission and 23 (66%) had none after the next day. The median duration of hospitalization was 3 days with a range of 1 to 17 days (this latter patient had newly diagnosed acute lymphocytic leukemia). Eleven of the 35 patients (31%) were hospitalized ≤ 2 days, and 19 (54%) were hospitalized ≤ 3 days.

All patients were treated successfully. The clinical courses of the 3 patients with penicillin-resistant isolates (2 were intermediate and 1 susceptible to ceftri-

TABLE 1. Patients With Facial Cellulitis and Abnormal CSF Findings

Age	CNS Symptoms	Antibiotics Before LP	WBCs/mm^3 (% Neutrophils)	RBCs/mm^3	Glucose (mg/dL)	Protein (mg/dL)	Therapy
10 wk	Irritability	None	18 (52)	760	82	50	Ampicillin IV, 1 dose Ceftriaxone and vancomycin IV, 2 d Amoxicillin/clavulanate PO, 8 d
9 mo	None	Amoxicillin, 2 d Ceftriaxone, 1 dose	9 (91)	0	76	19	Cefotaxime IV, 8 d Nafcillin IV, 5 d Cefpodoxime proxetil PO, 11 d

CNS indicates central nervous system; LP, lumbar puncture; WBC, white blood cell; RBC, red blood cell; IV, intravenous; PO, oral.

TABLE 2. Pneumococcal Serotypes Isolated From Patients With Bacteremic Facial Cellulitis

Serotype	No. Isolates	Percent
4	2	4
6B	13	27
9V	2	4
14	26	53
18C	2	4
23F	2	4
33	1	2
Nontypeable	1	2
Totals	49	100

axone) are outlined in Table 3. All 3 of these patients had periorbital cellulitis. Their clinical courses seem to be similar to patients with penicillin-susceptible isolates.

DISCUSSION

Pneumococcus is now likely the most common cause of bacteremic facial cellulitis in children. Our series is by far the largest published to date of pneumococcal facial cellulitis. We have included both periorbital and buccal cellulitis in this series because although there has been much discussion regarding the pathogenesis of each, it is likely that both are associated with pneumococcal bacteremia.

Although proposed by some authors, it is unlikely that buccal cellulitis occurs via lymphatic spread from ipsilateral otitis media.[9] Our finding of otitis media in 43% (3 of 7 patients) with buccal cellulitis is similar to 38% noted in a previous series.[9] In our series, in 1 of these 3 only the contralateral ear was involved. In the above noted series[9] of cases accumulated before the eradication of disease attributable to *H influenzae* type b, 35 of 38 bacteremic patients with buccal cellulitis had disease attributable to *H influenzae* type b, while nontypeable *H influenzae* causes otitis media.

Similarly, although proposed by some authors, it is unlikely that sinusitis plays a major role in the pathogenesis of periorbital cellulitis.[3,10] In our series, radiologic studies of the sinuses were abnormal in all 10 patients who underwent such studies; however, these abnormalities may be attributable to overlying soft tissue swelling and/or mild upper respiratory tract illness.[3,11] Upper respiratory tract symptoms were noted in 59% of patients with periorbital cellulitis (and in 57% of those with buccal cellulitis). Further, before the eradication of disease attributable to

H influenzae type b, although this organism was commonly noted to cause bacteremic periorbital cellulitis, it is again nontypeable *H influenzae* that causes sinusitis.

Pneumococcal facial cellulitis occurs in patients at high risk for pneumococcal bacteremia, ie, children younger than 36 months of age (92% of our patients) who present with fever and leukocytosis.[12] Of interest, both of the patients in our series with bilateral periorbital cellulitis had underlying immunodeficiency. In patients who present with bilateral facial cellulitis, if an underlying immunodeficiency has not already been diagnosed, an evaluation for such might be considered. Also of interest, a violaceous hue was noted in 6 of our patients with pneumococcal facial cellulitis. Although once thought to be indicative of cellulitis attributable to *H influenzae* type b, others have noted the occurrence of a violaceous hue with pneumococcal disease as well.[4]

There is controversy regarding the need for lumbar puncture in the evaluation of infants and young children with facial cellulitis. In one series[13] among 73 children with bacteremic facial cellulitis who underwent lumbar puncture, 7 had culture-positive CSF (1 attribuable to *S pneumoniae*); some of these 7 had minimal or no meningeal signs (or abnormalities noted in CSF). These 7 patients ranged in age from 7 weeks to 14 months. Since that series was published, others have commented on the subsequent overuse of lumbar puncture in the evaluation of patients with facial cellulitis.[14] In our series of 15 patients who underwent lumbar puncture, 2 (including a 9-month-old with no meningeal signs) were found to have mild CSF pleocytosis (Table 1). The significance of the pleocytosis is not clear. The CSFs of these patients were culture-negative, although one had been pretreated. The 10-week-old received only 2 days of parenteral therapy and did well. Lumbar puncture should be considered carefully for patients with facial cellulitis who are <15 to 18 months of age and possibly bacteremic (ie, those presenting with signs of systemic illness including fever or leukocytosis[4,12]).

During the years of this study, among the 51 isolates from patients with bacteremic facial cellulitis, we did not demonstrate a statistically significant increase in the percent of cases due to penicillin-nonsusceptible pneumococci. However, in the years 1994–1995, 3 of 28 isolates (11%) were nonsusceptible to penicillin while in the years 1996–1998, 5 of 22

TABLE 3. Clinical Courses of Patients With Penicillin-Resistant Pneumococci

Age (Months)	Serotype	MIC (µg/mL) Penicillin/ Ceftiaxone	Hospitalized? No. Days Fever	No. Days Hospitalized	Therapy
12	6B	2/1	No		Ceftriaxone, 1 d
			—	—	Amoxicillin/clavulanate, 10 d
21	NT	2/1	Yes		Ceftriaxone, 3 d
			3	4	Oxacillin, <1 d
					Amoxicillin, 7 d
8	6B	2/.5	Yes		Cefotaxime, 3 d
			1	3	Clindamycin, 10 d

MIC indicates minimal inhibitory concentration; NT, nontypeable.

(23%) were nonsusceptible ($P = .27$). Previously, our group did note a significant increase in the percent of pneumococcal isolates nonsusceptible to penicillin during the years 1993–1996 when evaluating 1283 isolates from children with systemic pneumococcal infection.[5] In the current series, patients who had received β-lactam antibiotics in the previous 30 days were more likely to have disease due to pneumococcus that was nonsusceptible to penicillin. Such an association with recent prior antibiotic use was noted in our previous series and by others.[5]

Our patients with facial cellulitis generally responded well to therapy. One-third were treated as outpatients. Those admitted generally had short durations of fever and hospitalization as has been noted in other series of children with facial cellulitis.[2,15] Isolates of S pneumoniae that were nonsusceptible to penicillin (including 3 resistant to penicillin) did not seem to cause disease that was either more severe or more refractory to therapy than did penicillin-susceptible isolates.

The heptavalent-conjugated pneumococcal vaccine recently licensed in the United States includes pneumococcal serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F.[16] These 7 serotypes accounted for 47 of 49 isolates (96%) from our patients with facial cellulitis (Table 2). Continued surveillance of invasive disease attributable to S pneumoniae, including facial cellulitis, will, of course, be especially important as conjugated pneumococcal vaccines become widely used.

ACKNOWLEDGMENT

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