Otolaryngology–Head and Neck Surgery (2010) 143, 392-396

ORIGINAL RESEARCH–SINONASAL DISORDERS

Sinogenic orbital and subperiosteal abscesses: Microbiology and methicillin-resistant *Staphylococcus aureus* incidence

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No sponsorships or competing interests have been disclosed for this article.

ABSTRACT

OBJECTIVE: To assess the current bacteriology and the incidence of methicillin-resistant *Staphylococcus aureus* in orbital and subperiosteal abscesses of paranasal sinus disease origin.
STUDY DESIGN: Case series with chart review.
SETTING: An otolaryngology and ophthalmology specialty hospital.
SUBJECTS AND METHODS: Fifty-three patients were treated between 1994 and 2008 for orbital or subperiosteal abscess and paranasal sinusitis, confirmed by imaging and surgical intervention; 46 had operative culture specimens and comprise the study cohort.
RESULTS: The mean patient age was 28 years; one third were younger than 18. Nearly twice as many patients had subperiosteal (n = 30) as had orbital abscesses (n = 16). In 12 patients (26%), cultures were negative or grew only skin flora contaminants (coagulase-negative staphylococci, diphtheroids, and *Propionibacterium acnes*). Fifteen patients (33%) grew more than one pathogen. Streptococci were isolated in 17 of the 46 cases (37%), *S. aureus* in 13 (28.3%), gram-negative bacilli in eight (17.4%), and anaerobes in nine (19.6%). Methicillin-resistant *S. aureus* accounted for three (23.1%) of the *S. aureus* isolates and 6.5 percent of the total cases.
CONCLUSION: Abscess cultures grew a mixture of bacteria, including gram-positive cocci, gram-negative bacilli, and anaerobes. Although streptococci were the most common genus of bacteria isolated, *S. aureus* was the single most common pathogen recovered and one fourth of these cases were methicillin-resistant *S. aureus*. Given the significant morbidity that may result from inadequate treatment, an antibiotic active against methicillin-resistant *S. aureus* should be included in the initial broad-spectrum antimicrobial treatment regimen of orbital and subperiosteal abscesses of sinusitis origin until culture results are available.

Methicillin-resistant *Staphylococcus aureus* (MRSA), defined as having a minimum inhibitory concentration for oxacillin of 4 μg/mL or greater, was first described in 1961. MRSA isolates have resistance to all beta-lactam agents, conferred by an abnormal low-affinity binding protein, PBP-2a. Historically, MRSA has been a nosocomial infection typically acquired by inpatients exposed to a clonal isolate. In the last decade, however, community-acquired MRSA (CA-MRSA) infections have been increasingly reported.[1] Such has been true in the otolaryngology literature as well, with documentation of increased rates of MRSA in neck abscesses,[2,3] chronic otitis media,[4] and both acute and chronic rhinosinusitis.[5-7] CA-MRSA has been associated with increased severity of disease, abscess formation, and treatment failure. Much of this virulence has been attributed to the production of Panton-Valentine leukocidin, a leukocyte-lysing cytotoxin that has been increasingly found in some MRSA strains.[8,9] A five-year (2001-2006) analysis of a national microbiologic database identified 21,009 pediatric *S. aureus* head and neck infections, of which 21.6 percent were MRSA in etiology.[10] This same study also found that nearly 60 percent of the MRSA infections were probably attributable to CA-MRSA.

The potential ophthalmologic complications of sinusitis are well known and include periorbital inflammatory edema (preseptal cellulitis), orbital (postseptal) cellulitis, subperiosteal abscess, orbital abscess, and cavernous sinus thrombosis.[11] With the exception of preseptal cellulitis, patients with such complications clinically manifest proptosis, chemosis, ophthalmoplegia, and visual impairment. Contrast-enhanced computed tomography contributes significantly to the differential diagnosis by demonstrating the paranasal sinuses involved and demarcating the location and extent of the inflammatory process within the orbit.[12] Therapeutic management includes the immediate initiation of intravenous antibiotic therapy and possible surgical drainage as dictated by the severity of orbital manifestations. The morbidity of these complicated sinus infections can be quite

Received March 6, 2010; revised May 25, 2010; accepted June 8, 2010.

0194-5998/$36.00
doi:10.1016/j.otohns.2010.06.818

severe, with progression to blindness or intracranial involvement if not properly treated.

A recent study from the Texas Children's Hospital found MRSA to be the cause of orbital cellulitis or abscess secondary to sinusitis in 21 percent of their pediatric cases; 73 percent of the *S. aureus* cultures in their study were MRSA.[13] A childhood case of subperiosteal ophthalmologic abscess secondary to acute sinusitis of CA-MRSA etiology at our institution prompted us to investigate whether the incidence of MRSA in such complicated rhinosinusitis cases was also increasing in our geographic location.

Methods

Institutional review board approval was obtained for a retrospective chart review of patients admitted to the Massachusetts Eye and Ear Infirmary between 1994 and 2008. A case list was generated from discharge data of all adult and pediatric patients with the dual diagnoses of sinusitis (keywords: sinusitis, chronic sinusitis, acute sinusitis, pansinusitis) and an orbital complication (keywords: periorbital, orbital, retro-orbital, periosteal, subperiosteal, abscess, cellulitis, cavernous sinus thrombosis); 159 charts were reviewed. Fifty-three patients met the inclusion criteria of an acute sinusitis episode or an acute exacerbation of chronic sinusitis with a concurrent orbital or subperiosteal abscess requiring surgical drainage. Of these, seven were excluded because of insufficient microbiologic data. The remaining 46 patients constitute the subjects of this article. Data collected from these charts included patient demographics (date of birth and gender), admission date, primary and secondary diagnoses, surgical interventions performed, bacterial cultures and sensitivities, and antibiotic treatment at the time of surgery. The method of culture collection was not uniformly specified in the operative records, but use of sterile "culturette" swabs is standard practice at this institution. Where a separate entry in the microbiology record indicated that an anaerobic culture was submitted, this refers to a specimen obtained with the use of a swab placed in a specific anaerobic collection tube.

For comparative purposes, nationwide data also were obtained from The Surveillance Network database maintained by Eurofins-Medinet. The Surveillance Network is an electronic national database that collects antimicrobial resistance test results from more than 300 healthcare institutions.[14] Susceptibility or resistance to oxacillin for all *S. aureus* cultures obtained from sites labeled either "eye" or "sinus" was requested for the years between 1997 and 2008 (1997 was the earliest date for which such data were available). These data were further categorized by geographic region and by pediatric versus adult age. Specifics as to how the cultures in the "eye" and "sinus" categories were obtained were not available.

Results

As outlined previously, a total of 46 patients were identified with 1) the dual diagnoses of sinusitis and an ophthalmologic abscess complication requiring acute surgical intervention and 2) operative sinus or orbital/subperiosteal abscess culture data. The entire patient cohort had a mean age of 28.4 years, with a range of two to 69 years. There were 17 pediatric (age < 18 years) cases and 29 adult (age ≥ 18 years) cases. The mean pediatric age was 11.3 years, and the mean adult age was 38.3 years. A male predominance was present across all age groups (36 of 46, 78% overall; 16 of 17, 94% pediatric; 20 of 29, 69% adult).

All patients had acute sinusitis or an acute exacerbation of chronic sinusitis. Sixteen patients (16 of 46, 34.8%) had an orbital abscess, and 30 (30 of 46, 65.2%) had a subperiosteal abscess (Table 1). Among the pediatric age group, six patients (6 of 17, 35.3%) had an orbital abscess, and 11 (11 of 17, 64.7%) had a subperiosteal abscess.

Abscess cultures were obtained in 27 patients, including 10 with concurrent sinus cultures; the remaining 19 patients had sinus cultures only. Whereas aerobic culture results were available for all patients, anaerobic cultures were not uniformly performed.

Coagulase-negative staphylococci, diphtheroids, and *Propionibacterium acnes* grew from 15 abscess and 20 sinus cultures. These organisms were considered skin flora contaminants and not sinus or subperiosteal/orbital abscess pathogens. Nearly one fourth of the patients (12 of 46) had cultures that grew solely these contaminants or had no growth.

In the remaining 34 patients, pathogenic organisms grew from abscess (17 cases) and sinus cultures (22 cases) (Table 2). The major pathogens included streptococci (17 patients), *S. aureus* (n = 13), gram-negative bacilli (n = 8), and anaerobes (n = 9). Fifteen patients had cultures that grew two or more pathogens. Streptococci were the most common genus among pathogens. *Streptococcus anginosis* (*milleri*) was identified in six of the alpha-hemolytic streptococcal isolates, whereas Group C (n = 3) or Group A (n = 1) streptococci were identified in four of the five beta-hemolytic streptococcal isolates; identification to the species level was unavailable in seven cases. *Haemophilus influenzae* was present in one isolate, *Haemophilus aphrophilus* in another. Enterobacteriaceae (*Klebsiella*, *Morganella, Serratia*) were isolated in four patients, including one who had both *Klebsiella* and *Morganella*. Anaerobic cultures were not sent in all cases, but anaerobes were present in nine

Table 1
Abscess type relative to age group

	Orbital abscess	Subperiosteal abscess
Pediatric	6	11
Adult	10	19
Total	16	30

Table 2
Bacterial isolates of all patients

Bacteria	Abscess*	Sinus*	Patients*
Gram-positive cocci			
Staphylococcus aureus			13
Methicillin-sensitive	3	8	10
Methicillin-resistant	2	2	3
Streptococcus species			17
S. anginosis (milleri)	2	5	6
Other alpha-hemolytic streptococci†	2	6	6
Group A Streptococcus	1	0	1
Group C Streptococcus	1	2	3
Other beta-hemolytic streptococci†	0	1	1
Gram-negative bacilli			8
Campylobacter	0	1	1
Haemophilus aphrophilus	1	1	1
Haemophilus influenzae	0	1	1
Klebsiella pneumoniae	1	1	2
Klebsiella oxytoca	0	1	1
Morganella morganii	1	1	1
Serratia liquifaciens	1	0	1
Other, not identified	0	1	1
Anaerobes			9
Bacteroides	1	0	1
Clostridia innocuum	0	1	1
Eikenella corrodens	1	0	1
Fusobacterium species	3	3	5
Peptostreptococcus	3	1	4
Porphyromonas	1	1	1
Prevotella intermedia	0	1	1
Prevotella oralis	0	1	1

*Categories are not mutually exclusive. Ten patients had cultures of both sites, and some cultures had multiple pathogens. Three patients had methicillin-resistant *Staphylococcus aureus* (MRSA) infections: one had MRSA in cultures of both orbit and sinus. Eight patients' cultures grew eight different gram-negative bacilli. Nine patients' cultures grew anaerobes, including four with more than one type of anaerobe.
†Alpha-hemolytic or beta-hemolytic streptococci not further identified.

patient samples. The specific anaerobes recovered are listed in Table 2 and primarily represent oral flora anaerobes (e.g., *Peptostreptococcus*, *Prevotella, Eikenella*, *Porphyromonas*, and *Fusobacterium*). Four patients had cultures that grew only anaerobes.

Of the 10 patients with both sinus and abscess cultures, five had a concordance of pathogenic organisms between culture sites; such organisms included *S. aureus*, alpha-hemolytic streptococci, *Morganella morganii, Fusobacterium*, and *Porphyromonas*. An additional three patients had concordance only of skin flora (*Propionibacterium acnes* and *Staphylococcus epidermidis*), and in two patients there was no concordance between culture sites.

S. aureus was the most common single organism and grew from the abscess (n = 5) and/or sinus cultures (n = 10) of 13 patients, representing 28.3 percent of the study population; three of these patients were of pediatric age. *S. aureus* alone was isolated in five of these 13 cases; in the other eight cases, pathogens such as anaerobes, alpha-hemolytic streptococci, and gram-negative bacilli also were cultured. In three patients (6.5%), orbital (n = 2) or sinus (n = 2) cultures grew MRSA: these patients were aged five, 18, and 53 years, and these cases were recorded in 1995, 2005, and 2006. The MRSA grew with gram-negative bacilli in one case, with alpha-hemolytic streptococci in another, and as the sole pathogen in the third. In five of these 13 *S. aureus* cases, both abscess and sinus cultures were obtained; *S. aureus* grew in the sinus cultures of all five (including two with MRSA) but in the concurrent abscess cultures of only two patients.

Data from The Surveillance Network (TSN) database is shown in Table 3. Cultures labeled "eye" in this database were not further specified, so the data reported are likely to include a variety of ophthalmologic sources. From 1997 to 2008, MRSA accounted for 36.1 percent of TSN *S. aureus* isolates from eye cultures and 21.6 percent of sinus *S. aureus* isolates. Further breakdown by region and age show that MRSA accounted for a substantial proportion of *S. aureus* isolates of eye and sinus cultures in New England and in the pediatric age group.

Discussion

Otolaryngologic infections attributable to community acquired MRSA isolates have become increasingly prevalent. This is particularly true of acute and chronic sinusitis, where a significant increase in the rate of recovery of MRSA has been documented in recent years.[7]

With respect to periorbital infections, *Haemophilus influenzae* was the most common etiology until the introduction of the HiB vaccine in 1985; subsequent studies in the late 1990s documented *Streptococcus pneumoniae* to be the predominant pathogen.[15] A recent study from the Texas Children's Hospital of 38 pediatric orbital cellulitis cases associated with sinusitis, however, found *S. pneumoniae* to be the etiologic organism in only one case.[13] Similarly, none

Table 3
Comparison of "The Surveillance Network" national and regional MRSA rates (1997-2008)

		Oxacillin resistance			
	S. aureus cultures	National		New England	
Specimen source	Total	n	%	n	%
All					
Eye:Eye	21,559	7785	36.1	130	30.7
Resp-U:Sinus	17,160	3708	21.6	95	21.6
Pediatric					
Eye:Eye	21,559	1659	22.2	12	13.5
Resp-U:Sinus	17,160	310	18.1	23	37.7

Resp-U, upper respiratory.

of the ophthalmologic abscesses in our study were caused by *S. pneumoniae*, but *Streptococcus anginosis* (*milleri*) accounted for six cases. *S. anginosis* (*milleri*) is an alpha-hemolytic streptococcus that, although part of the normal oral flora, is notorious for causing abscesses in the head and neck region.

S. aureus was the etiology of 28.9 percent (11 of 38) of the cases in the Texas study, with MRSA accounting for 72.7 percent (8 of 11) of those *S. aureus* isolates. In our study, *S. aureus* was likewise cultured in 28.3 percent of cases (13 of 46), but only three of these were attributable to MRSA. Our rate of MRSA relative to all *S. aureus* cases was 23.1 percent (3 of 13). This figure is significantly lower than in the Texas study but in agreement with regional New England data from TSN for sinus specimens, and approximates the 21.6 percent rate found in the study by Naseri et al[10] for all head and neck *S. aureus* cultures.

We did not find a difference between pediatric and adult rates of MRSA, with virtually equal values of 5.9 percent (1 of 17) and 6.9 percent (2 of 29), respectively. These numbers, however, are too small to make any definitive statements with respect to age group predisposition. There is no additional published data to our knowledge that similarly compares pediatric and adult MRSA or methicillin-resistant *S. aureus* sinus or orbital abscess culture rates.

A mixture of bacterial pathogens grew in 15 (33%) of the 46 cases, from either abscess or concurrent sinus cultures. This was true of the *S. aureus* cases as well, as eight (62%) of the 13 cases, including two of the three MRSA cases, also grew other pathogens.

Our study has several limitations. Such a retrospective review is dependent upon the accuracy of data acquisition, and seven of 53 possible patients were excluded from this study because culture results were not reported. More than one fourth of patients had cultures that grew only skin contaminants or were no growth. Because methods of culture collection were not specified in the operative records, some of these cases with negative cultures might have yielded pathogens had culture collection methods been optimal. Likewise, the incidence of anaerobic organisms is potentially underestimated because anaerobic cultures were not obtained in all cases. One additional concern is that sinus cultures obtained intraoperatively by endoscopic means may be contaminated by *S. aureus* colonization of the nasal cavity. *S. aureus* colonizes the nasal vestibules in at least 25 percent of the general population.[16] In our study, *S. aureus* grew from direct orbital or subperiosteal abscess cultures in five patients (including two with MRSA); therefore, these cases clearly did not reflect nasal contamination. In the remaining eight cases, the sinus culture was the source of the *S. aureus*, and seven of these cases also grew other pathogens, such as *Klebsiella*, anaerobes, and *S. anginosis* (*milleri*). Neither our study nor similar studies that include endoscopically obtained sinus cultures can absolutely exclude the possibility that the *S. aureus* in some of the cases may reflect nasal contamination. Such seems unlikely, however, given the clinical virulence of this organism in these cases and the associated pathogens.

Conclusion

Whereas national data suggest that MRSA accounts for between 20 and 30 percent of all *S. aureus* isolates cultured from a variety of head and neck sites, there is still a relative paucity of data specifically addressing the role of this organism in acute sinusitis cases with secondary orbital complications. Sinogenic orbital and subperiosteal abscesses at our institution proved to be attributable to a variety of bacteria including gram-positive cocci, gram-negative bacilli, and anaerobes. *S. aureus* was the sole or contributing pathogen in 28.3 percent of the cases, and nearly one fourth of these were MRSA. Given the significant morbidity that may result from inadequately treated subperiosteal and orbital abscesses of sinusitis etiology, a broad-spectrum antibiotic regimen, including vancomycin or another MRSA-active agent, is recommended as the initial therapy for these infections until culture results become known.

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Selena Liao, acquisition of the data, initial drafting of the manuscript, and final approval; **Marlene L. Durand,** analysis of the data, multiple revisions of the manuscript, and final approval; and **Michael J. Cunningham,** initial study planning and design, multiple revisions of the manuscript, and final approval.

Disclosures

Competing interests: None.

Sponsorships: None.

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