Pediatric Mediastinitis as a Complication of Methicillin-Resistant *Staphylococcus aureus* Retropharyngeal Abscess

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**Objective:** To examine changes in the incidence, bacteriology, and complications of retropharyngeal infection (RPI) over an 8-year period.

**Design:** Retrospective medical record review.

**Setting:** Tertiary children's hospital.

**Patients:** The study population comprised 108 patients younger than 18 years old.

**Intervention:** Medical record review of patients with a discharge diagnosis of RPI (International Classification of Diseases, Ninth Revision code 478.24).

**Main Outcome Measures:** Cases from June 1997 to May 2001 were compared with those from June 2001 to May 2005 to examine changes in the incidence, bacteriology, and complications of RPI.

**Results:** The number of RPI cases doubled from 36 to 72 in the final 4 years. In the first 4 years, no isolates of methicillin-resistant *S. aureus* (MRSA) were found, and 1 patient developed mediastinitis. In the last 4 years, 8 of 25 patients (32%) with positive cultures had MRSA isolated, and 7 cases of mediastinitis occurred. Of the 8 children with cultures positive for MRSA, 6 developed mediastinitis. The median age for all children with RPI was 32.5 months (n=108). The median age for children with MRSA and mediastinitis was 6.5 months (n=8) and 5.5 months (n=8), respectively.

**Conclusions:** An alarming increase in the number of RPI cases occurred over the final 4 years. Methicillin-resistant *S. aureus* is now a significant pathogen in patients with RPI at our institution. Documented local increases in community-associated MRSA infections and universal sensitivity to clindamycin suggest that community-associated MRSA is responsible for the change in bacteriology. A high correlation exists between MRSA infection and mediastinitis. Patients with MRSA infections are younger and may be vulnerable to developing mediastinitis because of immature immune systems. A higher index of suspicion is needed for MRSA, especially in patients younger than 1 year.


**Methods**

Following institutional review board approval, a retrospective medical record review of patients treated for RPI at LeBonheur Children's Medical Center in Memphis, Tennes-
A total of 108 patients were identified. Thirty-six cases of RPI were encountered during the first 48 months of the study. During the last 48 months of the study, 72 cases of RPI were identified. From June 1997 to May 2001, 13 of 36 RPI cases (36%) required operative intervention. The percentage of RPI incised and drained increased to 44% (32/72) between June 2001 and May 2005 (Table 1).

Purulent fluid was obtained from 39 of the 45 cases in which operative intervention was deemed necessary. Of the 39 samples collected, bacterial growth occurred in 35 (90%). Between June 1997 and May 2001, 10 positive cultures yielded 17 bacterial isolates. Polymicrobial normal oropharyngeal flora (7 of 17 isolates) and group A streptococcus (5 of 17 isolates) were the only organisms isolated from multiple patients. Single isolates of a viridans streptococcus, Staphylococcus epidermidis, Proteus species, Citrobacter species, and group C streptococcus accounted for the other 5 bacterial isolates. Between June 2001 and May 2005, 25 positive cultures yielded 32 bacterial isolates. Ten patients had polymicrobial normal oropharyngeal flora isolated (10 of 32 isolates), 9 patients had cultures positive for S. aureus (9 of 32 isolates), and 7 patients had cultures positive for group A streptococcus (7 of 32 isolates). Two isolates of a viridans streptococcus and single isolates of Klebsiella pneumonia, Enterobacter species, and Klebsiella oxytoca were also recovered. In addition, yeast was isolated in 1 culture (Table 2).

Staphylococcus aureus was not isolated in the cultures during the first 4 years of the study. In contrast, 9 patients had cultures positive for S. aureus during the final 4 years (P = .04 by the Fisher exact test). Sensitivities demonstrated that MRSA accounted for 8 of the 9 S. aureus isolates (89%). Of the 25 patients with positive cultures during the final 4 years of the study, 8 (32%) had MRSA isolated (Table 2). All 8 of the MRSA isolates were sensitive to clindamycin, gentamicin, rifampin, and vancomycin, and 7 of the 8 isolates displayed erythromycin resistance.

One case of mediastinitis occurred as a complication of RPI during the first half of the study period. Interestingly, cultures sent after needle aspiration did not reveal growth of a pathogenic organism. During the final half of the study, there were 7 cases of mediastinitis. All 6 surgically managed cases of mediastinitis occurred in children with positive MRSA cultures. All surgically managed cases had computed tomographic evidence of extensive fluid level attenuation in the neck (Figure, A) and superior mediastinum (Figure, B). One medically managed case of mediastinitis had radiographic evidence of a retropharyngeal phlegmon with slight extension into the superior mediastinum but no obvious radiographic evidence of fluid collection. Cultures were not obtained, but the antibiotic therapy was directed to cover MRSA. Among all patients with a culture taken, mediastinitis was more common in patients
with a documented staphylococcal infection ($P < .001$ by the $\chi^2$ test) (Table 3). In addition, children with MRSA mediastinitis often required additional surgical interventions, admission to the intensive care unit, intubation, serial computed tomographic scans, treatment with multiple intravenous antibiotics, and assistance of consultation services for additional operative procedures (Table 4).

During the first 4 years of the study, the median age at presentation was 30 months, with an interquartile range (IQR) of 17.5 to 60.5. The median age at presentation rose to 34 months (IQR, 17.0-62.5 months) during the final 4 years. Among patients who underwent operative incision and drainage, the median age decreased from 45 months (IQR, 29-72 months) during the first half of the study period to 25 months (IQR, 11-44 months) during the last half of the study period ($P = .04$ by the Wilcoxon rank sum test). The age at presentation for cases of MRSA and mediastinitis ranged from 4 to 16 months, with a median age at presentation of 6.5 months ($n=8$) and 5.5 months ($n=8$), respectively. Patients with $S$ aureus infections were younger than patients with other pathogens or negative cultures ($P < .001$ by the Wilcoxon rank sum test).

The median duration of hospital stay for all patients with RPI was 30 days (IQR, 4-7 days). Patients with MRSA infections had a significantly longer median duration of stay (14 days [IQR, 9-19 days]) than those without a culture proven $S$ aureus infection ($P = .002$ by the Wilcoxon rank sum test).

### Table 3. Cases of Methicillin-Resistant *Staphylococcus aureus* (MRSA) and Mediastinitis

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Retropharyngeal infections, total No.</td>
<td>36</td>
<td>72</td>
</tr>
<tr>
<td>Cases surgically managed</td>
<td>13</td>
<td>32</td>
</tr>
<tr>
<td>Cases of MRSA</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Cases of mediastinitis</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Cases of MRSA and mediastinitis</td>
<td>0</td>
<td>6$^a$</td>
</tr>
</tbody>
</table>

$^a$Significant association between MRSA infection and mediastinitis ($P < .001$ by the $\chi^2$ test).

Numerous studies document the array of potential bacterial pathogens in pediatric RPA. Although variations in incidence exist across studies, viridans streptococcus, $S$ aureus, $\beta$-hemolytic streptococci, gram-negative rods, and anaerobic bacteria are all reported.$^1,7,8$ As depicted in Table 2, normal oropharyngeal flora ($n=17$ [49%]), group A streptococcus ($n=12$ [34%]), and $S$ aureus ($n=9$ [26%]) were the most frequently isolated organisms from the 35 positive cultures. This is similar to a 2004 study that found group A streptococcus (34% of cases), normal oropharyngeal flora (32%), and $S$ aureus (11%) as the 3 most common isolates in 73 patients with retropharyngeal or parapharyngeal abscesses.$^8$

To our knowledge, no prior large-scale studies focused on characterizing the bacteriology of pediatric RPA report a predominance of MRSA. As seen in Table 2, 8 of the 9 $S$ aureus isolates (89%) we report displayed methicillin resistance. During the last 4 years of our study, cultures grew MRSA in 8 of 25 patients (32%) with positive cultures compared with 0 of 10 patients in the initial portion of the study. This represents a notable change in the bacteriology of RPA at our institution during the 8-year study period.

*Staphylococcus aureus* is a successful pathogen known for its genetic plasticity. The bacterium is adept at acquiring genetic elements that mediate antibiotic resistance and virulence factor expression.$^{10}$ Historically, MRSA has been associated with the hospital environment, accounting for 30% to 40% of all $S$ aureus nosocomial infections.$^{11}$ However, during the 1990s, MRSA infection was observed in community-dwelling individuals without established risk factors.$^{13,14}$ Since that time, reports of community-associated MRSA (CA-MRSA) have continued to rise.$^{13,14}$ Numerous reports document alarming increases in the number CA-MRSA infections in the pediatric patient population.$^{10,13,17}$ A study performed at our institution between January

**Figure.** Computed tomographic scan of the neck, revealing extensive fluid attenuation in the retropharyngeal space that extends to the lateral neck and great vessels, (A) and of the chest, with extension of fluid into the mediastinum below the level of the carina (B).
Table 4. Overview of Patients With Methicillin-Resistant Staphylococcus aureus (MRSA) Mediastinitis

<table>
<thead>
<tr>
<th>Age, mo</th>
<th>Surgical Interventions (Time to Operation)</th>
<th>Days in Hospital</th>
<th>Days in ICU</th>
<th>Days Intubated</th>
<th>CT Scans</th>
<th>IV Antibiotics (Days of Treatment)</th>
<th>Oral Antibiotics (Days of Treatment)</th>
<th>Additional Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>Transoral drainage (12 h); transcervical drainage (4 d)</td>
<td>19</td>
<td>9</td>
<td>9</td>
<td>4</td>
<td>Vancomycin (7); ceftriaxone (9); clindamycin (14)</td>
<td>None</td>
<td>Cardiopulmonary surgery consultation for transcervical drainage</td>
</tr>
<tr>
<td>6</td>
<td>Transoral drainage (6 h)</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>Clindamycin (5); clindamycin (7)</td>
<td>Clindamycin (10)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Transoral drainage (6 h); transthoracic drainage (24 h)</td>
<td>30</td>
<td>13</td>
<td>8</td>
<td>6</td>
<td>Vancomycin (14); ceftazidime (14); clindamycin (28)</td>
<td>Clindamycin (10)</td>
<td>Pediatric surgery consultation for transthoracic drainage and chest tube management</td>
</tr>
<tr>
<td>8</td>
<td>Transoral drainage (4 d)</td>
<td>15</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>Ampicillin-sulbactam (2); vancomycin (7); clindamycin (14)</td>
<td>Clindamycin (10)</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Transoral drainage (6 d)</td>
<td>11</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>Penicillin G (2); gentamicin (2); ceftriaxone (3); vancomycin (2); clindamycin (7)</td>
<td>Clindamycin (14)</td>
<td>Discharged with PICC for 7-day course of clindamycin</td>
</tr>
<tr>
<td>4</td>
<td>Transcervical drainage (3 d); thoracotomy (6 d)</td>
<td>24</td>
<td>14</td>
<td>10</td>
<td>3</td>
<td>Ceftriaxone (3); ampicillin-sulbactam (3); meropenem (6); tobramycin (3); clindamycin (3); vancomycin (20); rifampin (16)</td>
<td>None</td>
<td>Cardiopulmonary surgery consultation for thoracotomy, decortications of empyema, and chest tube management</td>
</tr>
</tbody>
</table>

| Abbreviations: CT, computed tomographic; ICU, intensive care unit; IV, intravenous; PICC, peripherally inserted central catheter. |

2000 and June 2002 revealed that 38% of all MRSA infections treated at our children’s hospital were community-associated during the first 18 months of the study. This percentage rose to 63% during the last 12 months of the study, affirming the exponential increases of CA-MRSA reported at pediatric institutions in other regions of the country.

Community-acquired MRSA has microbiological and clinical characteristics that distinguish it from hospital-associated MRSA (HA-MRSA). Community-acquired MRSA possesses different genetic elements (staphylococcal cassette chromosome mec type IV), virulence factors (Panton-Valentine leukocidin), and antibiotic susceptibility patterns. Community-acquired MRSA is characterized by increased sensitivity to clindamycin, trimethoprim-sulfamethoxazole, and rifampin, differentiating it from its hospital counterpart. Similar to sensitivity patterns reported in Texas and Illinois, strains of CA-MRSA at our institution are typically erythromycin resistant and clindamycin susceptible. However, there is a caveat to initial antibiotic sensitivity reports. Erythromycin-resistant strains could be expressing the type B macrolide-lincosamide-streptogramin, or MLSB, phenotype that is capable of inducing clindamycin resistance and causing treatment failure [10,16-19]. Therefore, clindamycin monotherapy should be avoided in critically ill children until inducible clindamycin resistance is excluded by double-disk diffusion testing (D test). Awareness of local resistance patterns is paramount in appropriate antibiotic choice.

Community-acquired MRSA is described in the context of otolaryngologic infections. In 1992, Gottlieb et al first reported 15 cases of CA-MRSA infections over a 3-year period, mainly in the context of otitis externa. More recently, one study from our institution in Memphis, Tennessee, and an additional study out of Houston, Texas, documented the occurrence of CA-MRSA in pediatric deep neck abscesses. An additional case series from our institution reported a case of RPA leading to mediastinitis.

To our knowledge, the 8 cases of MRSA RPA reported in the present study is the largest number reported in the literature to date. Interestingly, data from our institution between 2000 and 2003 documented 5 pediatric deep neck abscesses caused by CA-MRSA and no cases caused by HA-MRSA. This fact, coupled with the universal susceptibility of our MRSA isolates to clindamycin, suggest these RPA cases were caused by CA-MRSA. Although beyond the scope of this review, testing of our MRSA isolates for genetic elements and virulence factors unique to CA-MRSA would have provided valuable insights. Although none of the cases occurred in hospitalized patients or persons with ongoing medical illnesses, a limitation of this review is the lack of documentation of specific risk factors (such as prior admission to neonatal intensive care unit, hospitalization or surgery within the prior year, and close contact with health care workers) that would have placed these community-dwelling individuals at risk for hospital-acquired MRSA.

Community-acquired MRSA tends to cause localized skin and soft tissue disease, although serious invasive
infections leading to death have occurred.10,12,13,16 At our pediatric hospital, Buckingham et al18 determined that invasive CA-MRSA infections occurred with the same frequency as invasive HA-MRSA infections. In addition, studies in the pediatric population report that CA-MRSA causes more severe infection with more serious complications, such as complicated pneumonia, than community-acquired methicillin-susceptible \textit{S. aureus}.16,19

Another finding in our study is the increasing incidence of MRSA mediastinitis as a complication of RPA. Although 1 case of mediastinitis was encountered between 1997 and 2001, an alarming 7 cases were documented during the final 4 years of the study (Table 3). Of the 8 patients with positive MRSA cultures, 6 (75%) developed mediastinitis as a complication. This high complication rate suggests that MRSA is a more invasive pathogen with a greater potential for complications than other bacteria implicated in RPI. If the cases of MRSA and complicating mediastinitis we report are indeed attributable to CA-MRSA, our results support the evidence that CA-MRSA is a more severe and potentially complicating infection than methicillin-susceptible \textit{S. aureus}.

A noteworthy finding was the concentration of MRSA mediastinitis cases in children younger than 1 year. In fact, all cases occurred in children younger than 16 months. In 2005, a large study evaluating CA-MRSA in 3 diverse geographic communities found that CA-MRSA infections were more frequent in those younger than 2 years and more commonly encountered in African Americans in one of the communities studied.13 In addition, Ochoa et al19 found that children with CA-MRSA were more likely to be younger (mean age, 1.6 years) and African American than those with methicillin-susceptible \textit{S. aureus} (mean age, 2.6 years). This study supports the evidence that those younger than 2 years are at greater risk. It is possible that infants’ relative states of immune system compromise during the first year of life predispose them to invasive retropharyngeal MRSA infection. Furthermore, infants appear to be at increased vulnerability to the complications of invasive MRSA infection such as mediastinitis. More investigation is needed into the various factors that may place African Americans and those younger than 2 years at risk. Nevertheless, a higher index of suspicion is needed for MRSA, especially in those younger than 2 years.

As observed in Table 4, children with MRSA mediastinitis often had prolonged and complicated hospital courses. Of the 6 cases of mediastinitis resulting from MRSA RPA, 3 resolved after incision and drainage of the RPA and appropriate antibiotic management. However, 3 patients required second surgical procedures and had especially tenuous hospital courses. We agree with reports in the literature that advocate broad-spectrum intravenous antibiotics along with aggressive surgical intervention of both cervical and mediastinal components.2,21 Fortunately, no fatalities were observed at our institution as a result of mediastinitis caused by RPA.

There has been an alarming increase in the number of RPI cases at our institution. The total number of RPI cases doubled during the last half of the study period. One of the driving forces behind this increase appears to be a shift in bacteriologic flora to drug-resistant pathogens such as MRSA. Based on documented evidence of increasing CA-MRSA infections in our pediatric patient population and universal susceptibility of our isolates to clindamycin, we believe that CA-MRSA infections are responsible for the observed change in bacteriology. Community-acquired MRSA is now considered a potential pathogen in all cases of RPI in our institution. As reports of CA-MRSA continue to increase in pediatric populations across geographic areas, clinicians must be mindful of the potential for CA-MRSA as a possible pathogen in serious and invasive disease, such as RPI.

As increasing numbers of MRSA and other drug-resistant pathogens become more common in RPI, it will become critical to obtain cultures and sensitivities of the bacteria to help direct further medical treatment. In addition, the high correlation between drug-resistant pathogens and complications such as mediastinitis suggests the need for early and aggressive surgical intervention in an attempt to reduce morbidity and mortality. Regardless of whether to intervene surgically, knowledge of local bacteriologic flora and resistance patterns is paramount to appropriate antibiotic selection.

Increased vigilance and a higher index of suspicion are needed for MRSA in RPI, especially in children younger than 2 years. As this age group appears to be at increased susceptibility to infection and increased vulnerability to the complications of infection, aggressive management is encouraged. More research is needed to better characterize the factors that place this group at risk.

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Author Contributions: Drs Wright and Stocks had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Stocks, Armstrong, and Gould. Acquisition of data: Wright and Armstrong. Analysis and interpretation of data: Wright, Armstrong, Arnold, and Gould. Drafting of the manuscript: Wright. Critical revision of the manuscript for important intellectual content: Wright, Stocks, Armstrong, Arnold, and Gould. Statistical analysis: Arnold and Gould. Administrative, technical, and material support: Stocks. Study supervision: Wright, Stocks, Armstrong, Arnold, and Gould.

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REFERENCES