The Significance of Streptococcus anginosus Group in Intracranial Complications of Pediatric Rhinosinusitis

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Objective: To assess the significance of the Streptococcus anginosus group in intracranial complications of pediatric patients with rhinosinusitis.

Design: Retrospective cohort study.

Setting: Tertiary pediatric hospital.

Patients: A 20-year review of medical records identified patients with intracranial complications resulting from rhinosinusitis. In the 50 cases identified, S anginosus was the most commonly implicated bacterial pathogen in 14 (28%). Documented data included demographics, cultured bacteria, immune status, sinuses involved, type of intracranial complication, otolaryngologic surgical and neurosurgical intervention, type and duration of antibiotics used, and resulting neurologic deficits. Complications and outcomes of cases of S anginosus group–associated rhinosinusitis were compared with those of other bacteria.

Main Outcome Measures: The severity and outcomes of intracranial complications of pediatric rhinosinusitis due to S anginosus group bacteria compared with other bacteria.

Results: Infection caused by the S anginosus group resulted in more severe intracranial complications (P < .001). In addition, patients with S anginosus group–associated infections were more likely to require neurosurgical intervention (P < .001) and develop long-term neurologic deficits (P = .02). Intravenous antibiotics were administered for a longer duration (P < .001) for S anginosus group–associated infections.

Conclusions: Rhinosinusitis associated with the S anginosus group should be considered a more serious infection relative to those caused by other pathogens. Streptococcus anginosus group bacteria are significantly more likely than other bacteria to cause more severe intracranial complications and neurologic deficits and to require neurosurgical intervention. A low threshold for intervention should be used for infection caused by this pathogen.

PEDiATRIC RHINOSINUSITIS IS relatively common. Most cases are caused by Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, and, less commonly, Staphylococcus aureus and Streptococcus pyogenes.\(^1\) The increasing number of children attending day care facilities has led to an increasing incidence of this disease.\(^2\) Complications associated with rhinosinusitis, although potentially devastating, are rare. Intracranial and orbital complications occur via direct extension from the sinuses or hematogenous spread. Approximately 3% of pediatric patients hospitalized with rhinosinusitis develop an intracranial complication.\(^3\) These infections include meningitis, epidural abscess, subdural abscess, brain abscess, and cavernous sinus thrombosis.\(^4\) Streptococcus and Staphylococcus are frequently associated with these diseases.\(^5\)

The Streptococcus anginosus group, previously known as the Streptococcus milleri group, is from the Streptococcus family, which is known to be a cause of serious infections.\(^6\) This group includes S anginosus, S intermedius, and S constellatus. The S anginosus group has been shown\(^7\) to be a major causative factor of intracranial infections in adults, particularly those in which acute bacterial rhinosinusitis is the inciting infection. The Streptococcus family produces many enzymes and works synergistically with anaerobic bacteria to cause tissue necrosis and abscess formation.\(^7\)

At the Alberta Children’s Hospital, Calgary, we have observed several severe intracranial complications from rhinosinusitis caused by the S anginosus
group. We reviewed the medical records of all patients who had an intracranial complication of rhinosinusitis to determine whether the disease severity and outcomes were worse when the *S. anginosus* group was the causative organism.

**METHODS**

A review of medical records from patients at the Alberta Children’s Hospital was conducted. Ethics approval was received from the Conjoint Health Research Ethics Board of the University of Calgary. Demographic and personal health information was collected from hospital records and health records, including data regarding intracranial complications of pediatric rhinosinusitis as well as the medical and surgical interventions undertaken to treat the infection in each patient.

Children aged 1 day to less than 18 years were included. All patients must have been admitted to Alberta Children’s Hospital between January 1, 1991, and December 31, 2010, with an intracranial complication of acute bacterial rhinosinusitis. Patients who were immunocompromised when they developed the infection were excluded from analysis.

In all statistical analyses, variables and outcomes of patients with rhinosinusitis caused by the *S. anginosus* group were compared with those caused by other organisms. Primary outcome variables included age, sex, type of intracranial complication, duration of hospital stay, duration of antibiotic use, surgical intervention requirement, and permanent neurologic deficits due to intracranial complications of the infection.

Descriptive statistics were tabulated for all variables in the presence and absence of *S. anginosus* group rhinosinusitis. A 2-sided Fisher exact test was conducted on all categorical variables (sex, adenoidectomy, sinus involvement, intracranial complication, concurrent orbital complication, otolaryngologic surgical intervention, neurosurgical intervention, and neurologic deficits). Frequency distribution tables were created for continuous variables (length of hospital stay, age, and duration of antibiotic use) including analysis of variance, skew, and kurtosis. A 2-sample unpaired *t* test was conducted to determine the statistical significance of relationships between *S. anginosus* group-associated infection and continuous primary outcome variables. Ninety-five percent confidence intervals were calculated on the basis of binomial distribution. Simple logistic regression analysis was performed to assess variables that may have confounded a significant outcome on univariate analysis.

**RESULTS**

Fifty-five patients meeting the inclusion criteria were identified; 4 patients were excluded because they were immunocompromised, and 1 patient was excluded because of death during admission to the hospital. There were no significant differences in sex, age, duration of hospitalization, or location of rhinosinusitis between the *S. anginosus* group and the comparative group. Fourteen patients had rhinosinusitis due to the *S. anginosus* group (Table 1). It was the most commonly implicated bacterial pathogen, accounting for 14 of the 50 cases (28%).

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**Table 1. Patient Demographics and Characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Streptococcus anginosus (n = 14)</th>
<th>Other Organisms (n = 36)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>10.8 (3.6)</td>
<td>9.1 (5.4)</td>
<td>.28</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>8 (57)</td>
<td>28 (78)</td>
<td>.17</td>
</tr>
<tr>
<td>Female</td>
<td>6 (43)</td>
<td>8 (22)</td>
<td></td>
</tr>
<tr>
<td>Previous adenoidectomy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>14 (100)</td>
<td>32 (89)</td>
<td>.55</td>
</tr>
<tr>
<td>Yes</td>
<td>0</td>
<td>3 (8)</td>
<td></td>
</tr>
<tr>
<td>Sinus involvement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frontal</td>
<td>9/14 (64)</td>
<td>14/24 (58)</td>
<td>.13</td>
</tr>
<tr>
<td>Maxillary</td>
<td>9/14 (64)</td>
<td>26/36 (72)</td>
<td>.73</td>
</tr>
<tr>
<td>Sphenoid</td>
<td>6/14 (42)</td>
<td>13/26 (50)</td>
<td>.75</td>
</tr>
<tr>
<td>Ethmoid</td>
<td>10/14 (71)</td>
<td>27/36 (75)</td>
<td>&gt;.99</td>
</tr>
</tbody>
</table>

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Note: One patient was excluded because of death from intracranial complications of sinusitis upon admission, and 4 were excluded because of a compromised immune system. Some patients' cultures grew multiple organisms. Patients with rhinosinusitis localization information unavailable, those younger than 5 years (sphenoid), and those younger than 7 years (frontal) were excluded.
of acute rhinosinusitis with intracranial complication. Table 1 reports the descriptive statistics of patient demographics and characteristics analyzed.

Rhinosinusitis with intracranial complications of all cause was significantly more common in males (36 patients [72%]) than in females (14 [28%]) (P = .03). Streptococcus pneumoniae was the second most common bacterial cause of rhinosinusitis with intracranial complications, accounting for 10 cases (20%). A descriptive statistical analysis of the neurosurgical, otolaryngologic surgical, and antibiotic interventions is reported in Table 2.

Patients with S anginosus group–associated rhinosinusitis were more likely to require neurosurgical intervention compared with patients with infections caused by other organisms (9 patients [64%] vs 5 [14%]; P < .001). There was no significant difference between the groups for otolaryngologic surgical intervention. Intravenous antibiotics were administered a mean of 20 days longer in the S anginosus group (95% CI, 11-28 days; t48 = 4.53; P < .001). There was no significant difference between the groups for oral antibiotic administration.

The complications and sequelae resulting from rhinosinusitis are listed in Table 3. All patients had intracranial complications; however, those with S anginosus group–associated infections were more likely to develop complications other than meningitis (P = .001) (Table 3). Only 2 of 14 intracranial complications (14%) resulting from rhinosinusitis due to the S anginosus group were meningitis compared with 21 of 36 patients (58%) when the complications were caused by other organisms. Patients with S anginosus group–associated rhinosinusitis were also more likely to develop permanent neurologic deficits (P = .02) (Table 3). There was no significant difference between the groups for concurrent orbital infection.

Eight of the 10 S pneumoniae cases occurred after 2002, when the 7-valent pneumococcal conjugate vaccine was introduced in Alberta. Interestingly, 10 of the 14 S anginosus cases occurred after 2002.

Multivariable analysis was performed to look at the risk of surgical intervention during infections caused by S anginosus compared with all other bacteria. A simple logistic regression controlled for severity of the infection (ie, abscess vs nonabscess) showed increased odds of surgical intervention when S anginosus was the pathogen (odds ratio, 5.5; 95% CI, 0.8-40.5; P = .09).

**COMMENT**

Streptococcus anginosus group is known to be particularly aggressive and is generally susceptible to penicillin, ampicillin, erythromycin, and tetracycline. Our study shows that intracranial complications resulting from pe-
diatric rhinosinusitis caused by \textit{S anginosus} are significantly more likely to require neurosurgical intervention and a longer duration of intravenous antibiotics. In addition, these infections are more likely to cause more severe intracranial complications and permanent neurologic deficits. Simple logistic regression analysis showed that the risk of requiring surgical intervention is higher in the \textit{S anginosus} group regardless of whether an abscess is present. To date, there have been no studies comparing the severity of \textit{S anginosus} with other bacteria in causing intracranial complications associated with pediatric rhinosinusitis. One study\textsuperscript{3} found that patients with \textit{S anginosus}–associated intracranial infections caused by rhinosinusitis were common; however, further variables associated with \textit{S anginosus} and other bacteria beyond the hospital length of stay were not analyzed.

Extracellular enzymes are generated by the bacteria and might be a factor in its potent virulence. It has been shown\textsuperscript{7,10} that this group is able to produce several enzymes, including hyaluronidase, deoxyribonuclease, and chondroitin sulfatase. These enzymes are capable of causing tissue liquefaction and leading to abscess formation. It also has been shown\textsuperscript{7,8} that \textit{S anginosus} group organisms can act synergistically with anaerobic bacteria to cause worse abscesses. This may explain why the \textit{S anginosus} group caused significantly worse intracranial infections compared with other organisms. A recent study\textsuperscript{12} has shown that brain abscesses caused by the \textit{S anginosus} group can be treated successfully with cefotaxime and metronidazole, as well as rifampin, if the Glasgow Coma Scale score is less than 11.

A likely explanation for \textit{S anginosus}–associated infections requiring a longer duration of intravenous antibiotic therapy is the increased likelihood of abscesses. At our institution, patients with abscesses routinely receive 4 to 6 weeks of intravenous antibiotics compared with only 2 weeks for those with meningitis. This variability makes the type of infection a confounding factor in determining whether the duration of intravenous antibiotic therapy is significantly different between the \textit{S anginosus} group and other organisms.

The \textit{H influenzae} type b vaccine has dramatically reduced the incidence of meningitis caused by this organism. Our study did not have any such cases, so we cannot comment on whether the vaccine has changed the incidence of \textit{H influenzae}–associated meningitis resulting from rhinosinusitis.

The widespread use of the multivalent pneumococcal vaccine has dramatically changed the bacteriology of rhinosinusitis.\textsuperscript{13,14} This could explain the recent prominence of \textit{S anginosus} as a cause of intracranial infections secondary to rhinosinusitis. However, these studies did not comment on the \textit{S anginosus} group. Interestingly, our study had more cases of \textit{S pneumoniae} and \textit{S anginosus} after the introduction of the 7-valent pneumococcal conjugate vaccine. It is possible these more recent \textit{S pneumoniae} cases were caused by subtypes that do not express the antigens found in the vaccine. Studies would be necessary to determine this.

In conclusion, \textit{S anginosus}–group–associated rhinosinusitis should be considered a serious infection in children because of its prevalence in severe intracranial complications, with more neurologic deficits, greater likelihood of neurosurgical intervention, and longer durations of intravenous antibiotic therapy compared with other bacteria. Early and aggressive interventions are required when treating these virulent infections.

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