Streptococcus milleri
An Organism for Head and Neck Infections and Abscess

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Background: Streptococcus milleri, a commensal organism, has the potential to cause significant morbidity. There is a paucity of published data regarding this organism in the head and neck.

Objectives: To identify and assess the presentation, treatment, and outcomes of pediatric patients affected by this pathogen.

Study Design: Review of the Department of Pathology database at Children's Hospital of Wisconsin, Milwaukee, between 1997 and 1999 identified 26 patients with cultures positive for S milleri group (SMG) bacteria. Retrospective chart analysis examined the demographic data, site of origin of infection, additional organisms cultured, symptoms, treatments, and complications.

Results: Sixteen patients had SMG infections involving the head and neck region. Sites of origin included the paranasal sinuses, dental, facial soft tissues, deep neck spaces, peritonsillar region, and a tracheostomy site. The paranasal sinuses were the most common site in 37% (6/16). Streptococcus milleri was the only isolate in 69% (11) of the infections. Significant local extension occurred in 56% (9/16) of the patients and included the orbit, skull base, cranium, and deep neck spaces. All patients had surgical drainage and 15 also received intravenous antibiotic treatment. One complication of osteomyelitis of the frontal bone occurred with resolution after surgical debridement and intravenous antibiotic treatment.

Conclusions: Streptococcus milleri can be an aggressive pathogen in the head and neck with a propensity for abscess formation and local extension of the infection in a pediatric population. Surgical drainage with antibiotics is generally successful in management of the condition. However, emerging penicillin resistance and the ability for local extension require suspicion of incomplete treatment if clinical symptoms persist.


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The name Streptococcus milleri was first proposed by Guthof in 1956 to describe gamma hemolytic streptococcus found in an oral cavity infection. Streptococcus milleri group (SMG) bacteria are microaerophilic bacteria categorized with viridans streptococci. Although different classifications have been used in referring to S milleri group (SMG) bacteria, recently in the United States SMG bacteria have been divided into 3 different species: Streptococcus intermedius, Streptococcus anginosus, and Streptococcus constellatus. The lack of uniformity in classifying these organisms, varying phenotypic traits, and the difficulty in culturing them have contributed to the lack of reports and relative unfamiliarity with SMG bacteria.

Streptococcus milleri are organisms commonly found on the mucous membrane of the oral cavity, oral pharynx, gastrointestinal tract, and genitourinary tract. Although they are commensal organisms, they can become pathogenic and lead to an infection to the surrounding or distant sites after mucosal disruption caused by trauma.

When pathogenic, SMG bacteria commonly form abscesses, have local extension to surrounding tissues, and have been associated with suppurative metastatic complications. Because of the aggressive behavior of these organisms, and the lack of reports concerning SMG bacteria, a study was performed to examine the presentation, response to therapy, and complications associated with SMG infections in the head and neck.

RESULTS

In the 16 patients with SMG bacterial infections involving the head and neck, the average age was 10.4 years (age range, 2-17
METHODS

A retrospective review of patients diagnosed as having SMG bacterial infections at Children’s Hospital of Wisconsin (CHW), Milwaukee, was performed between years 1997 and 1999. These patients were identified using the Department of Pathology database at CHW, which catalogues all the cultures performed for every specimen at CHW. Twenty-six patients were identified from the database and 16 had infections in the head and neck area. Demographic data, presenting symptoms, site of origin of the infection, additional organisms cultured, treatment, and complications were reviewed. Preexisting factors and the specialties of the providers who treated the patients were also gathered.

Correlations between the sites of the infection and local extension, pure vs mixed culture, abscess formation, and complications were analyzed. The use of radiographic studies prior to treatment was examined. The type of antibiotic, mode of antibiotic delivery (oral or intravenous [IV]), preoperative vs postoperative antibiotic therapy, and length of medical treatments were studied. With regard to the surgical treatment, the type of approach and details of the procedure were examined. The charts were reviewed from the day of service to at least 3 months after the initial treatment. All the complications that occurred during the follow-up were documented. Complications were defined as additional morbidity associated with the SMG infection due to infectious spread or persistence despite appropriate initial surgical and medical intervention.

The origins of infections were paranasal sinuses, dental, facial soft tissue, deep neck spaces, peritonsillar region, and a tracheostomy site (Table 1). The most common site of infection was the paranasal sinus (n=6), followed by dental origin (n=5). Eleven (69%) of the 16 cultures had an isolated growth of SMG bacteria. The polymicrobial cultures grew aerobic and anaerobic organisms detailed in Table 1. Pure SMG bacterial cultures demonstrated a 64% local extension of the infection to surrounding structures compared with 40% in the polymicrobial cultures. All dental infections demonstrated pure SMG cultures.

All 16 patients had surgical drainage and 15 patients were treated with IV antibiotics postoperatively. The only patient who did not receive postoperative IV antibiotics was a patient who underwent endoscopic sinus surgery for presumed allergic fungal sinusitis; he had his SMG infection identified on follow-up and had an unexpected postoperative course. One patient with cystic fibrosis received preoperative clindamycin phosphate for 3 weeks, underwent endoscopic sinus surgery for chronic sinusitis, and was discharged without complications after 14 days of IV antibiotic therapy. The remaining 14 patients presented with surgical indications for intervention due to abscess formation (n=10) or pyogenic sinusitis (n=4) with infectious extension of the sinusitis to surrounding structures.

Computed tomography was used as a preoperative tool to identify the pyogenic infection and plan surgical drainage for all 6 patients with sinusitis and the 1 patient with a deep neck space abscess. In the remaining 9 patients, abscess formation was evident from clinical examination findings, and additional radiographic studies were not necessary for surgical planning. Drainage of sinusitis (n=6) was the most common surgical treatment. Four patients had incision and drainage: 2 for subcutaneous abscesses and 2 for deep neck abscess. Four patients had dental extraction and the remaining 2 underwent quinsy tonsillectomy (this procedure is a tonsillectomy performed on a patient with peritonsillar abscess).

Postoperatively, the average length for IV antibiotic therapy was 9.9 days, with a range of 1 to 42 days. Additional oral antibiotics were prescribed at the time of discharge for 11 patients for a mean of 12.3 days, with a range of 4 to 21 days. The average length of total antibiotic treatment was 18.9 days. The most common antibiotics were oral amoxicillin with clavulanate and IV ampicillin with sulbactam. Therapy with multiple IV antibiotics was used in 9 patients.

There were 9 patients (56%) with significant local extension of the infection at the time of presentation (Table 1). The sites of extension were to the cranium, orbit, skull base, maxillary sinus, and deep neck space. The paranasal sinuses were the most common origin for local extension. Two of the paranasal sinus infections extended from the ethmoid sinus to the orbit and the other 2 spread from the frontal sinus to the cranium. Infections of dental origin were the next most common site to present with extension; 1 to the submandibular space, 1 to the buccal space, and 1 to the maxillary sinus. There was no documented distal seeding of these infections to areas such as the heart or lungs.

There was only 1 complication that occurred after initial surgical drainage and postoperative antibiotic therapy. This patient presented with a frontal sinusitis with intracranial extension that led to the formation of an epidural abscess. The patient initially underwent a craniotomy with evacuation of an epidural abscess and obliteration of the frontal sinus. Subsequently the patient developed osteomyelitis of the anterior wall of the frontal sinus, which required surgical debridement and treatment with IV antibiotics for 12 days. The patient did not have any further complication at 6-months follow-up.

COMMENT

Head and neck infections have varying presentations and outcomes depending on the offending organism and its
site of origin. Organisms with the potential for abscess formation and local extension in the head and neck region warrant special attention owing to the proximity of many vital structures. One such pathogen is *S milleri*. Despite these characteristics, SMG bacteria have been relatively neglected in the literature. This has occurred, at least in part, because of some difficulties in categorizing and identifying these organisms in culture.

*Streptococcus milleri* belong to the *Streptococcus viridans* organisms. The SMG bacteria consist of 3 species, *anginosus*, *constellatus*, and *intermedius* that are grouped together based on similarities in their 16S ribosomal RNA subunit.² There are a total of 98 strains for the 3 species. They are alpha-, beta-, or gamma-hemolytic and belong to Lancefield groups A, C, F, H, or nontypable. *Streptococcus anginosus* is mostly nonhemolytic and *S constellatus* is usually beta-hemolytic. Most Lancefield F streptococci are *S milleri*. Culturing these organisms can be difficult because of the requirement of up to 10% carbon dioxide in the culture environment to grow effectively, which is not standard in most laboratories.

*Streptococcus milleri* was initially described as an oral cavity organism causing periodontal abscess. However, each SMG species has a predilection for specific anatomic sites.³ *Streptococcus anginosus* is more commonly isolated from gastrointestinal and genitourinary tract infections. *Streptococcus constellatus* has a propensity for the respiratory and gastrointestinal tracts. *Streptococcus intermedius* is responsible for most head and neck infections, such as suppurative otitis media, pyogenic sinusitis, and intracranial abscesses.¹⁹ As a group, the most common site of infection is the abdomen, followed by head and neck area.¹⁹ Although endocarditis, metastatic liver abscesses, and bacteremia by SMG bacteria have been reported, distal spread of the infection is less common than local extension. However, if bacteremia does occur, the mortality rate has been reported to be 26.3%.⁷

*Streptococcus milleri* has a higher incidence of infections among males.⁵ This was further demonstrated in our series, with 81% (13/16) of the patients being male. Although these organisms have been identified in all age groups with a documented age range of 9 months to 93 years, they are less common in neonates or infants.¹⁰,¹¹ The youngest patient identified in this series was 2 years old. Transmission to an unborn fetus or neonate is possible when SMG bacteria are part of the cervical or vaginal flora.⁶,¹¹ This is the first series to concentrate on SMG presentation and treatment in an exclusively pediatric population.

Although they are commensal organisms, and can be routinely cultured more than 50% of the time in the oral cavity and more than 25% of the time in the oro-pharynx,² mucosal barrier disruption can allow for invasion into the underlying tissue. Thick pus and abscess formation are the common features of these infections, which can lead to local extension or suppurative metastatic complications.⁶,⁷,¹²,¹³ A report from the 1977 Centers for Disease Control showed that *S milleri* was the most common organism associated with abscess formation among the *S viridans* group, accounting for 71% of brain abscess, 40% for abdominal abscess, and 34% for extra-abdominal abscess.¹³ The Central Public Health Laboratory in London, England, also published that *S milleri* was the most common organism (28.3%) among 152 streptococci isolates for purulent disease.¹⁴

Formation of abscesses with SMG bacteria is both pure and polymicrobial. Most abdominal cultures are polymicrobial while most head and neck cultures grow only SMG bacteria.² In our study 69% (11/16) of the head and neck cultures had an isolated growth of SMG bacteria. Although a higher percentage (64% [7/11]) of the pure cultures had local extension than the mixed cultures (40% [2/5]), these data do not necessarily demonstrate decreased pathogenicity of mixed cultures. Rather, the SMG

### Table 1. Characteristics of the Infections

<table>
<thead>
<tr>
<th>Origin of Infection</th>
<th>Organisms Cultured Other Than <em>Streptococcus milleri</em></th>
<th>Local Extension</th>
<th>Surgical Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dental</td>
<td>None</td>
<td>No</td>
<td>Abscess</td>
</tr>
<tr>
<td>Dental</td>
<td>None</td>
<td>No</td>
<td>Abscess</td>
</tr>
<tr>
<td>Dental</td>
<td>None</td>
<td>Yes</td>
<td>Abscess with submandibular space extension</td>
</tr>
<tr>
<td>Dental</td>
<td>None</td>
<td>Yes</td>
<td>Abscess with maxillary sinus extension</td>
</tr>
<tr>
<td>Dental</td>
<td>None</td>
<td>Yes</td>
<td>Abscess with buccal space extension</td>
</tr>
<tr>
<td>Facial soft tissue</td>
<td><em>Eikenella corrodens</em></td>
<td>Yes</td>
<td>Abscess with skull base extension</td>
</tr>
<tr>
<td>Frontal sinus</td>
<td><em>Staphylococcus epidermidis</em></td>
<td>Yes</td>
<td>Pyogenic sinusitis with intracranial extension</td>
</tr>
<tr>
<td>Frontal sinus</td>
<td><em>Peptostreptococcus</em></td>
<td>Yes</td>
<td>Pyogenic sinusitis with intracranial extension</td>
</tr>
<tr>
<td>Ethmoid sinus</td>
<td>None</td>
<td>Yes</td>
<td>Pyogenic sinusitis with orbital extension</td>
</tr>
<tr>
<td>Ethmoid sinus</td>
<td>None</td>
<td>Yes</td>
<td>Pyogenic sinusitis with orbital extension</td>
</tr>
<tr>
<td>Maxillary sinus</td>
<td><em>Proteus mirabilis</em></td>
<td>No</td>
<td>Chronic sinusitis</td>
</tr>
<tr>
<td>Maxillary sinus</td>
<td><em>Pseudomonas aeruginosa</em></td>
<td>No</td>
<td>Allergic fungal sinusitis</td>
</tr>
<tr>
<td>Peritonsillar space</td>
<td>None</td>
<td>No</td>
<td>Abscess</td>
</tr>
<tr>
<td>Peritonsillar space</td>
<td><em>E corrodens</em></td>
<td>No</td>
<td>Abscess</td>
</tr>
<tr>
<td>Retropharyngeal space</td>
<td>None</td>
<td>Yes</td>
<td>Abscess with prevertebral space extension</td>
</tr>
<tr>
<td>Tracheostomy site</td>
<td>None</td>
<td>No</td>
<td>Abscess</td>
</tr>
</tbody>
</table>

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bacteria in the mixed culture may represent growth from normal flora, as shown by Poole and Wilson.15

The awareness and understanding of the potential morbidity associated with SMG infections has been rising. With increased efforts to identify these organisms, recent articles have documented the infectious morbidity of this pathogen in the head and neck. Several studies have reported intracranial extension from sinogenic sources.6,13,16 In addition, Jousimies-Somer et al recently identified SMG as a potential pathogen in 38 of 143 peritonsillar abscesses. The difficulty in cultivating and identifying these organisms may mean that their true incidence as a tonsillar pathogen may be underrepresented. It should be mentioned that this series as well as most others identify patients based on surgical cases, which may bias the population toward a greater number of complicated infections.

Our study identified 6 sites of infection in the head and neck region: paranasal sinuses, dental, facial soft tissue, deep neck space, peritonsillar region, and a tracheostomy site. Fifty-six percent of these infections had significant local extension to the orbit, skull base, cranium, paranasal sinuses, and deep neck spaces. Owing to their proximity to the orbit and central nervous system, it is particularly important that a sinogenic source represented the greatest number of cases in this series and that 67% (4/6) of the sinus infections had extension to these vital areas. Although a limited number of patients with sinogenic abscesses by SMG are available in the literature, the potential for spread from the paranasal sinuses warrants further investigation and documentation.

All the patients in this study were surgically treated. Computed tomography was used in 7 patients (paranasal sinuses [6] and deep neck space [1]) that were difficult to diagnose with infection by examination alone. As is the case with most infectious processes that lead to abscess formation, surgical drainage is essential to allow for resolution.7,12

With the variable and overlapping phenotypic traits of SMG bacteria, they are often misdiagnosed.18 In the past, SMG bacteria have been mislabeled as nonhemolytic streptococcus, group F streptococcus, or streptococcus pyogenes.2,13,18 This has also contributed to an underappreciation and recognition of this organism as a pathogen. In addition, the need to further isolate S viridans into different species has only recently become more important. In the past, virtually all members of this family were highly sensitive to treatment with penicillin. However, recent reports have documented an increasing resistance by SMG bacteria against a number of antibiotics.19-21 This increasing resistance to several antibiotics cannot be ignored when treating patients with head and neck infections with close proximity to vital structures.

All but one patient in this review was given therapy with IV antibiotics, with the most common antibiotic being ampicillin with sulbactam. Duration of total antibiotic treatment in this series was 18.9 days, which is between the 7 and 30 days reported in the literature.7,10 Fortunately, most of the S milleri group remain sensitive to penicillin,19-21 although the susceptibility is decreasing. In 1994 Gomez-Garces et al1 reported no resistance to penicillin by SMG. Reviewing susceptibilities in studies from 1996 and 1999, there has been decreasing susceptibility to penicillin, cephalosporins, macrolides, ciprofloxacin, and clindamycin.18-21 (Table 2). Current susceptibilities for IV third-generation cephalosporins, cefotaxime and cefepime, are reported at 97% to 98%.20,22 Gentamicin and streptomycin have poor activities against SMG bacteria1,19,21; however, aminoglycosides have been shown to be synergistic with penicillin.7 Antibiotics that have consistently demonstrated 100% susceptibility to SMG bacteria are vancomycin, imipenem, and teicoplanin.19-21 Use of a non–β-lactam antibiotic, such as vancomycin, may be warranted in patients with an abscess near vital structures or with central nervous system infection. This is especially true if susceptibility testing is unable to be performed on the culture specimen. Since SMG bacteria are difficult to grow, sensitivities are not always available. The difficulty in obtaining antibiotic sensitivities, due to the fastidious growth of these organisms, was demonstrated in this study. The CHW microbiology laboratory was not able to universally provide sensitivities for the patients in this study. Streptococcus milleri group bacterial resistance should also be considered with lack of clinical resolution after surgical drainage if sensitivities are pending or unobtainable.

Despite surgical and appropriate IV antibiotic therapy, 1 patient in this series developed osteomyelitis of the frontal bone flap and required surgical debridement of the bone and another course of antibiotics. With persistence of symp-
Streptococcus milleri can be an aggressive pathogen in the head and neck region of pediatric populations with a propensity for abscess formation and local extension. Although no uniform treatments have been adopted, surgical drainage with antibiotics is generally successful in management. However, emerging antibiotic resistance and the ability for local extension, suspicion of incomplete treatment, or other abscess sites should be evaluated if clinical symptoms persist.

Educating the medical community about their existence, characteristics, and invasive nature could help health care providers become more aware of these organisms and properly treat these infections. Further studies detailing the presentation, treatment, and outcomes of these infections in the head and neck region are warranted with close attention to microbial sensitivities.

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