

Significance of *Streptococcus milleri* in acute rhinosinusitis with complications

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Abstract

Objectives: To assess the significance of *Streptococcus milleri* in acute rhinosinusitis with complications.

Methods: A retrospective case note review was undertaken of in-patients at both the Red Cross Children's Hospital and the Groote Schuur Hospital (for adults), Cape Town, South Africa, between 1999 and 2003, with a diagnosis of acute rhinosinusitis with complications. The following were documented: age, gender, complications, organisms cultured and their sensitivity, type and number of operations, and length of hospital stay.

Results: Seventy-one case notes were reviewed, for 30 female and 41 male patients, representing 38 adults and 33 children. *Streptococcus milleri* was the most commonly implicated organism (52.1 per cent; 37/71). Patients from whom this organism was isolated tended to require more than one operative procedure, and had a protracted hospital stay.

Key words: Sinusitis; Complications; *Streptococcus Milleri*

Introduction

Acute rhinosinusitis represents acute infection of the nose and paranasal sinuses. The commonly implicated pathogenic organisms are *Haemophilus influenzae*, *Streptococcus pneumoniae* and *B Moraxella catarrhalis*, and, less commonly, *Streptococcus pyogenes* and *Staphylococcus aureus*. Complications occur as a result of spread of infection from within the sinuses to adjacent tissues: anteriorly, to cause Pott's puffy tumour; laterally, to cause orbital cellulitis, associated intraorbital abscesses and blindness; and superiorly, to cause a variety of intracranial infections and abscesses.

However, in our geographic area (Cape Town, South Africa), *Streptococcus milleri* has in recent years been isolated in a number of patients, both adults and children, suffering from acute rhinosinusitis with orbital and intracranial complications. It has been noted that these patients tend to require more than one operative procedure and have a significantly longer hospital stay.

The *Streptococcus milleri* group comprise anaerobic bacteria of the Lancefield group F classification, subdivided into three species: *Streptococcus anginosus*, *Streptococcus constellatus* and *Streptococcus intermedius*. These bacteria are known to cause pyogenic abscesses in many parts of the body. It is, however, unclear if all strains are similarly virulent. The Lancefield group F antigen is associated with

beta-haemolysis, an important pathogenic factor. Another pathogenic factor is production of the enzyme hyaluronidase, which destroys tissue planes. Other pathogenic factors, not exclusive to beta-haemolytic bacteria, are the production of nucleases, bacteriocins, proteolytic enzymes, antiphagocytic capsular materials and surface proteins. Recurrence of abscesses could be due to some of these pathogenic factors.¹

This study of our recent experience of acute sinusitis with complications was undertaken to assess the frequency with which *S milleri* was implicated and its effects on the course and duration of disease.

Methods

A retrospective study was undertaken at both the Red Cross Children's Hospital and the Groote Schuur Hospital (for adults), reviewing all records for patients admitted from 1999 to 2003 with complicated acute rhinosinusitis (i.e. orbital and/or intracranial complications), diagnosed both clinically and on computed tomography (CT) scan. Data analysed included: age; gender; duration of hospital stay; complications (orbital (lid abscess, subperiosteal abscess and blindness), intracranial (meningitis, subdural abscess, extradural abscess, brain abscess and cavernous sinus thrombosis) and presence of Pott's puffy tumour); type and number of surgical procedures performed (either ENT or

neurosurgical); and the organisms isolated and their sensitivities.

The statistical methods used in the analysis included: chi-square test, to test for association between two categorical variables; Fisher's exact test, to test for association between two categorical variables; Cochran–Maentel–Haezel test, to test whether the association between two categorical variables remains strong after adjusting for a third variable; and Wilcoxon rank sums test, to test for group differences in continuous variables (non-parametric data).

The level of statistical significance considered in all the analyses was 5 per cent. Analyses were performed using the statistical software packages Sas V9.1 and Systat 6.0 for Windows.

Results

Data were collected for 71 consecutive patients (30 females and 41 males). Thirty-three patients were children from the Red Cross Children's Hospital (i.e. zero to 12 years) and 38 were adolescents or adults from the Groote Schuur Hospital (i.e. 13 years and older). Patients' ages ranged from 16 months to 58 years. Clinically, all patients had suffered acute rhinosinusitis, with orbital signs ranging from periorbital cellulitis to overt proptosis. Intraorbital and intracranial complications were detected on CT scans of the sinuses and brain, usually performed on admission. Patients' complications and the corresponding frequency of *S milleri* isolation are listed in Table I.

Table II lists all organisms isolated.

Streptococcus milleri was the commonest organism isolated, being found in 37 of the 71 patients (52.1 per cent; $p = 0.0456$).

Notably, no bacteria were cultured for 10 patients. This may be related to antibiotic treatment prior to admission.

All patients underwent a surgical procedure; some had combined ENT and neurosurgical procedures. Five patients underwent dental extractions, suggesting dental caries to be the source of infection.

A total of 84 ENT surgical procedures was performed in the 71 patients, an average of 1.2 procedures per patient. The ENT procedures included antral

washout, incision and drainage of lid abscess, drainage of subperiosteal abscess, drainage of pus associated with Pott's puffy tumour, and trephination of the frontal sinus(es). The 30 neurosurgical procedures performed, on 14 patients, essentially involved evacuation of pus via either burr holes or craniotomy. Redrainage of pus via the original operative site was frequently required, and the average number of operations per patient was 2.14.

Patients' lengths of hospital stay ranged from two to 50 days (average 9.8 days). Patients from whom *S milleri* was isolated stayed an average of seven days, while those with other organisms stayed an average of five days, a marginally significant difference ($p = 0.055$). Patients with intracranial complications, who required multiple operative procedures, stayed longest in hospital, particularly paediatric patients. One adult male patient was admitted twice in two months with orbital cellulitis. One female paediatric patient was admitted twice, a year apart, with acute rhinosinusitis. *Streptococcus milleri* was isolated in both patients.

Discussion

Acute rhinosinusitis comprises acute bacterial infection of the nose and sinuses. It is commonly associated with upper respiratory tract infection due to viruses such as adenovirus, rhinovirus, influenza virus and parainfluenza virus. It is not known for certain whether the viral infection precedes or is concurrent with the bacterial infection. The mechanisms whereby virus infection predisposes to sinusitis may involve: microbial synergy; induction of local inflammation that blocks the sinus ostia; increase of bacterial attachment to the epithelial cells; and disruption of local immune defences.^{2,3} Sinusitis can be precipitated by apicitis of maxillary teeth, with infection first involving the maxillary sinus and then spreading to other sinuses if not controlled. The common symptoms are headache, purulent nasal discharge, fever, and facial pain with or without swelling. The common clinical signs are pyrexia, facial tenderness with or without periorbital cellulitis, fetor, and identification of pus in the middle meatus.

TABLE I
COMPLICATIONS AND FREQUENCY OF ISOLATION OF *STREPTOCOCCUS MILLERI*

Complications	Patients (n (%))	<i>S milleri</i> isolated (n (%))	<i>p</i>
Orbital	48 (67.6)	32/48 (66.7)	
Lid abscess	15 (21.1)	13/15 (86.7)	0.026
Subperiosteal abscess	33 (46.5)	19/33 (57.6)	0.390
Blindness	0	0	
Pott's puffy tumour	11 (15.5)	4/11 (36.4)	0.244
Intracranial	14 (19.7)	9/14 (64.3)	0.309
Meningitis	5		
Subdural abscess	7		
Extradural abscess	6		
Brain abscess	2		
Cavernous sinus thrombosis + CN VI palsy	1		

CN = cranial nerve

TABLE II
ORGANISMS ISOLATED

Organism	Isolates (n (%))
<i>S milleri</i>	37 (52.1)
<i>H influenzae</i>	15 (21.1)
<i>S aureus</i>	9 (12.7)
Anaerobes	10 (14.1)
<i>S pneumoniae</i>	3 (4.2)
Streptococcus sp	4 (5.6)
<i>S pyogenes</i>	4 (5.6)
<i>B catarrhalis</i>	2 (2.8)
No growth	10 (14.1)

In recent articles by Brook² and Brook and Frazier,³ the causative organisms usually implicated in acute rhinosinusitis were *H influenzae*, *S pneumoniae*, *Moraxella catarrhalis*, *S aureus* and *S pyogenes*, and in recurrent acute rhinosinusitis were *S pneumoniae*, followed by *H influenzae*, then *M catarrhalis*. In these reports, *S milleri* was not mentioned.

In a 1997 review of sinusitis complications by Giannoni *et al.*,⁴ of 203 patients seen over a 10-year period, 19 suffered intracranial complications: cerebral abscess (five patients), epidural abscess (five), meningitis (five) and subdural abscess (four). The organisms isolated were streptococcus sp, *S aureus*, *H influenzae*, *Escherichia coli*, *Proteus mirabilis*, enterobacter and anaerobes. *Streptococcus milleri* was not isolated, but the streptococcus species were not differentiated, and four patients with these as the isolated organism had recurrence of intracranial abscesses.

In a recent report of intracranial complications of rhinosinusitis by Jones *et al.*,⁵ *S milleri* was the most common organism, being implicated in 33 of 47 patients. In 11 patients, it was found in association with other organisms: bacteroides and anaerobes (five patients), eikenella and bacteroides (one), *S epidermidis* (one), Gram-positive cocci (two), *S aureus* (one), and a microaerophilic streptococcus (one). No organisms were cultured in eight cases.

In the present series, the most commonly isolated organism was *S milleri* (37/71; 52.1 per cent; $p = 0.046$, i.e. marginally significant), followed by *H influenzae* and then *S aureus*. In the two patients with recurrent sinusitis, *S milleri* was isolated on both occasions. Anaerobes were isolated in 10 patients (14 per cent), being commonly found together with other organisms.

- Although *Streptococcus milleri* has been known to cause sepsis in other parts of the body, it has infrequently been reported as a cause of sinus infection
- *Streptococcus milleri* was a significant pathogen in this series of patients with acute rhinosinusitis with complications, being isolated in 52.1 per cent of cases
- These patients tended to require multiple surgical procedures, both ENT and neurosurgical

The intracranial complications occurring in this series (see Table II) are comparable with those reported by Giannoni *et al.*⁴ *Streptococcus milleri* was isolated in nine of the 14 patients, both from the sinuses and the intracranial sepsis. *Streptococcus milleri* was found significantly more frequently than other organisms ($p = 0.0144$). For three of the four remaining patients, the organisms isolated were *H influenzae* with *S pyogenes* (one patient), group C streptococcus with an anaerobic bacillus (one) and *S aureus* with *S pyogenes* (one); in the fourth patient (with meningitis), lumbar puncture results were suggestive of tuberculous meningitis. Culture from the sinuses of this patient showed no growth; however, the patient had received empirical antibiotics.

It is not clear why *S milleri* was the commonest organism isolated in this series of patients. Factors may have included previous antibiotic treatment, immunisation against *H influenzae*, improved laboratory techniques (with speciation of streptococcus) or a change in the pathogens involved in acute rhinosinusitis.

Despite *in vitro* *S milleri* sensitivity to the antibiotics given, pus tended to recollect, especially intracranially. The reasons for this are not clear. Possibly, it may be due to the virulence of *S milleri* in relation to intracranial tissues; at present, the degree of such virulence is unknown. On admission, all our patients were commenced on empirical antibiotics (ampicillin, cloxacillin and metronidazole); if intracranial sepsis was present, a third generation cephalosporin (cefuroxime) was added. Antibiotics were altered according to culture and sensitivity results.

Five of our patients required dental extractions as part of their sinusitis treatment; in these cases, dental sepsis may have been the origin of the sinusitis. In dental caries, enamel is affected first; infection then spreads to the pulp, resulting in damage to the pulp vessels. If this remains untreated, infection extends through the roots of decayed teeth into the alveolar bone, then into the sinus. These infections can extend to the orbit, but spread to the buccal area is more common.⁶

Conclusion

Although *S milleri* has been known to cause sepsis in other parts of the body, it has infrequently been reported as a cause of sinus infection. *Streptococcus milleri* was a significant pathogen in our series of patients with acute rhinosinusitis with complications, being isolated in 52.1 per cent of cases. Such patients were significantly more likely to require multiple surgical procedures, both ENT ($p = 0.0176$) and neurosurgical ($p = 0.0144$). Patients with intracranial complications required longer hospitalisation (up to 50 days); hospital stay was longest in those who required multiple surgical procedures.

References

- 1 Schauman NJ, Turner JE. clinical significance of beta hemolytic Streptococci of milleri group in oral abscesses. *J Clin Paediatr Dent* 1999;23:137-42

- 2 Brook I. Microbiology and antimicrobial management of sinusitis. *Otolaryngol Clin North Am* 2004;**37**: 253–66
- 3 Brook I, Frazier EH. Microbiology of recurrent acute rhinosinusitis. *Laryngoscope* 2004;**114**:129–31
- 4 Giannoni CM, Stewart MG, Alfred EL. Intracranial complications of sinusitis. *Laryngoscope* 1997;**107**: 863–7
- 5 Jones NS, Walker JL, Bassi S, Jones T, Punt J. The intracranial complications of rhinosinusitis. *Laryngoscope* 2002;**112**: 59–63
- 6 Mehra P, Murad H. Maxillary sinus disease of odontogenic origin. *Otolaryngol Clin North Am* 2004;**37**:347–64

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