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Head and neck infections caused by *Streptococcus milleri* group: An analysis of 17 cases

Tomohisa Hirai [a,*], Shinji Kimura [b], Naoki Mori [b]

[a] *Department of Otorhinolaryngology, Head and neck surgery, Hiroshima Prefectural Hospital, 1-5-54 Ujinakanda, Hiroshima 734-8530, Japan*
[b] *Department of Otorhinolaryngology, Onomichi General Hospital 7-19 Kohama-cho, Onomichi 722-8508, Japan*

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Abstract

Backgrounds: *Streptococcus milleri* group (SMG) is a common inhabitant of the mouth and gastrointestinal tract, and can be an aggressive pathogen causing abscess formation at various sites in the body. However, it has rarely been listed as a cause of head and neck infections.
Objectives: The present study was performed to evaluate the clinical significance of SMG by reviewing the microbiology and clinical records of patients with SMG in head and neck infections retrospectively.
Study design: A retrospective review of all patients diagnosed as having SMG bacterial infections at Onomichi General Hospital, Hiroshima, between the years 2001 and 2002 was performed; 17 patients developed head and neck infections with SMG. Here, we describe the clinical features and management of SMG in head and neck infection.
Results: The patient population consisted of 12 males and 5 females with a median age of 62 years (age range, 8–78 years). The sites of infection were as follows: maxillary sinus ($n = 6$), peritonsillar region ($n = 4$), subcutaneous ($n = 3$), submandibular space–retropharyngeal space ($n = 1$), deep neck–mediastinum ($n = 1$), parapharyngeal space ($n = 1$), submandibular space ($n = 1$), tonsil ($n = 1$), parotid gland ($n = 1$), and masseter muscle ($n = 1$). Ten cases (59%) were of suppurative diseases. Six cases (35%) had mixed SMG with anaerobe infection. Three cases showed deteriorating clinical courses, and all three of these cases were culture-positive for SMG with anaerobes. In addition, one deteriorating case showed gas gangrene regardless of repeated surgical debridement and intravenous antibiotic therapy; hyperbaric oxygen therapy improved this patient's condition.
Conclusion: It is important to recognize SMG as a pathogen in head and neck infection. In addition, the care should be taken with infectious diseases caused by SMG with anaerobes as the patient's clinical course can deteriorate rapidly.

Keywords: *Streptococcus milleri* group; Head and neck infections; Clinical features; Treatment; Hyperbaric oxygen therapy

1. Introduction

The nomenclature of *Streptococcus milleri* group (SMG) remains controversial. At the present time, *Streptococcus intermedius*, *Streptococcus anginosus*, and *Streptococcus constellatus* are collectively referred to as the "*Streptococcus milleri*" group [1].

SMG is a common commensal in the mouth and gastrointestinal tract [2]. It can be an aggressive pathogen and causes brain abscess [3], subperiosteal abscess of the orbit [4], lung abscess, pleural empyema, and intra-abdominal abscess [5]. On the other hand, there is a paucity of published data regarding this organism as a serious pathogen in head and neck infections.

We report 17 patients who developed head and neck infections with SMG during a 2-year period at Onomichi General Hospital. Here, we describe the clinical features and management of SMG in head and neck infection.

2. Materials and methods

A retrospective review of all patients diagnosed as having SMG bacterial infections at Onomichi General Hospital, Hiroshima, between the years 2001 and 2002 was

* Corresponding author. Tel.: +81 82 254 1818; fax: +81 82 253 8274.
E-mail address: t-hirai@hph.pref.hiroshima.com (T. Hirai).

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performed. Organisms were isolated with a conventional biphasic aerobic/anaerobic blood culture system. Samples were cultured on sheep blood agar and incubated in a CO_2-enriched atmosphere for 24 h. Microorganisms recovered from blood cultures were identified using BBL CRYSTAL GP and RGP (BECTON DICKINSON, Mountain View, CA).

3. Results

SMG was isolated from 77 patients over a period of 2 years. The sites of infection were as follows: head and neck ($n = 17$), abdominal cavity ($n = 12$), sputum ($n = 10$), lachrymal sac ($n = 8$), trachea ($n = 4$), thoracic cavity ($n = 4$), anus ($n = 4$), limbs ($n = 3$), urine ($n = 2$) and others ($n = 13$). Nineteen cases (26%) had abscess formation in the brain, spinal epidural cavity, bladder, anus, or subcutaneously. The strains were identified in 10 of the 77 cases (13%): *S. anginosus* ($n = 3$), *S. constellatus* ($n = 4$), *S. intermedius* ($n = 3$).

The clinical features of 17 patients with head and neck infections identified as having SMG are shown in Table 1. The median age of the patients was 62 years (age range, 8–78 years). The patients consisted of 12 males and 5 females. Three patients (18%) had a systemic underlying condition, i.e., diabetic mellitus, heart failure, and HIV infection. The sites of infection were as follows: maxillary sinus ($n = 6$), peritonsillar region ($n = 4$), subcutaneous ($n = 3$), submandibular space–retropharyngeal space ($n = 1$), deep neck–mediastinum ($n = 1$), parapharyngeal space ($n = 1$), submandibular space ($n = 1$), tonsil ($n = 1$), parotid gland ($n = 1$), and masseter muscle ($n = 1$). There were seven cases of inflammatory disease (non-suppurative), consisting of six cases of sinusitis and one case of tonsillitis. The remaining 10 cases (59%) were all of suppurative disease. Table 2 shows the antibiotic susceptibilities of the 17 cases. Antibiotics that showed 100% efficacy against SMG were cefaclor, ceftizoxim, cefpirome, sultamicillin, flomoxef, imipenem/cilastatin, clindamycin, and levofloxacin. On the other hand, ampicillin showed poor efficacy against SMG; five cases (29%) were resistant to ampicillin. With regard to coexistent species, eight cases (47%) had a single bacterial culture-positive for SMG, eight other cases (47%) had two positive bacterial cultures, and the remaining one case (6%) had three positive cultures. Six cases (35%) had mixed

Table 1
Clinical features of 17 cases of SMG in head and neck infections

Case No.	Age(y)/ Sex	Associated site of infection	Type of infection	Coexistent species	Surgical treatment	Underlying condition
1	41/M	retropharyngeal space	abscess	anaerobes	tonsillectomy, intraoral drainage	None
2	70/F	cheek ~ submandibular space ~ retropharyngeal space	abscess	*Prevotella intermedia* *Fusobacterium species*	Percutaneous drainage, submandibulectomy	None
3	76/F	retropharyngeal space ~ deep neck ~ mediastinum	abscess	*Peptostreptococcus*	multiple percutaneous drainage	None
4	72/M	parotid gland	abscess		none	heart failure
5	65/F	subctaneous of face	abscess		Percutaneous drainage	None
6	77/M	submandibular space	abscess	*Haemophilus species*	Percutaneous drainage,	None
7	78/M	masseter muscle	abscess		none	None
8	55/M	peritonsillar lesion	abscess	anaerobes	intraoral drainage	None
9	35/F	peritonsillar lesion	abscess	*Haemophilus influenzae*	intraoral drainage	None
10	70/M	peritonsillar lesion	abscess		intraoral drainage	diabetic mellitus
11	49/F	tonsil	inflammation		none	None
12	28/M	maxillary sinus	inflammation	MSSA	intranasal drainage	None
13	33/M	maxillary sinus	inflammation		none	None
14	34/M	maxillary sinus	inflammation		none	HIV-infecion
15	62/M	maxillary sinus	inflammation	MSSA	intranasal drainage	None
16	62/M	maxillary sinus	inflammation	*Prevotella species*	none	None
17	67/M	maxillary sinus	inflammation		intranasal drainage	None

Table 2
Antivicrobial susceptibility of SMG isolated from 17 cases in head and neck infections

Antimicrobial agent	Sensitive (n)	Intermediary (n)	Resistant (n)
Ampicillin	12	1	5
Cefaclor	17	0	0
Ceftizoxime	17	0	0
Cefpirome	17	0	0
Sultamicillin	17	0	0
Flomoxef	17	0	0
Imipenem / Cilastatin	17	0	0
Minocycline	15	2	0
Clindamycin	15	0	2
Levofloxacin	17	0	0

SMG with anaerobe infection. The associated cultures were *Staphylococcus aureus*, *Haemophilus* species, *Prevotella intermedia*, *Fusobacterium* species, *Peptostreptococcus*, etc.

Three cases (cases 1–3) in Table 1 showed a deteriorating clinical course.

A 41-year-old man (case 1) was admitted with pharyngeal pain, dyspnea, and trismus. He had a left peritonsillar abscess and severe retropharyngeal mucosal swelling. The airspace was almost occlusive due to pharyngeal edema. Emergent endotracheal intubation and subsequent intraoral drainage with tonsillectomy were performed. Postoperatively, he was treated with meropenem and clindamycin. The patient made a gradual recovery after the operation. SMG and anaerobic Gram-negative bacillus were isolated from the pus of the retropharyngeal space.

A 70-year-old woman (case 2) was admitted with right cheek swelling and trismus. Computed tomography (CT) showed a subcutaneous abscess of the left cheek. Surgical drainage through the canine fossa was performed on the first day of admission. Subsequently, she was treated with antibiotic therapy (cefozopran and clindamycin). However, the abscess spread over adjacent structures, i.e., the submandibular space and parapharyngeal space. A second drainage was performed percutaneously on the fifth day after admission, and the patient made a gradual recovery after the second operation. SMG, *P. intermedia*, and *Fusobacterium* species were isolated from the pus from the submandibular space.

A 76-year-old woman (case 3) was admitted with face and neck swelling, dyspnea, and pharyngeal pain. She had bilateral neck swelling and severe retropharyngeal mucosa swelling. The airspace was almost occlusive due to pharyngeal edema. A CT scan showed the presence of gas gangrene deep within the neck. She underwent emergent tracheotomy and extensive surgical debridement of the necrotic tissue was performed twice. Despite repeated debridement and administration of several antibiotics (meropenem, clindamycin, and sultamicillin), a subsequent CT scan showed that the abscess had spread to the mediastinum. The patient then underwent hyperbaric oxygen therapy (2.8 atm, 60 min/day) 15 times and she made gradual recovery. SMG and *Peptostreptococcus* were isolated from the pus of the deep neck space.

4. Discussion

SMG has been reported by some researchers to be an aggressive pathogen in the head and neck [6–8]. However, SMG is not well recognized as an important pathogen in head and neck infections. There are two factors responsible for this. First, culture of SMG requires some special methods; incubation must be performed in air containing carbon dioxide or in an anaerobic atmosphere [6,9]. Second, SMG is a common inhabitant of the mouth and gastrointestinal tract, and so might be not recognized as a pathogenic organism and may be reported generically as *Viridan streptococci*, anaerobic *Streptococcus*, or β-hemolytic *Streptococcus* [4,9]. In the respiratory tract, Shinzato and Saito [10] reported that SMG caused pulmonary infection more often than had been reported previously. We also found that SMG was closely associated with pyogenic infection in various sites throughout the whole body, especially the head and neck.

The precise pathogenic role of the SMG is as follows: (1) a structural component of the organism suppresses the phagocytic activity of polymorphonuclear neutrophils [11]; (2) extracellular products from SMG have immunosuppressive activity [12]; and (3) the co-existence of SMG with anaerobes accelerates inflammation [8,13]. In a mouse model of pneumonia, the mortality rates were significantly high when infected with both SMG and *P. intermedia* as compared with infection with each organism separately [13]. In addition, abscess forming ability was enhanced by co-inoculation of SMG and *Fusobacterium nucleatum* in comparison with either organism alone in vitro; this was suggested to be because the supernatant of *F. nucleatum* might maintain the SMG bacterial number in the abscess by both enhancing bacterial growth and suppressing phagocytic killing of SMG by polymorphonuclear leukocytes [14]. In the present study, the cultures from the three serious cases were all mixtures of SMG and anaerobes. Therefore, the care must be taken in the treatment of patients with infectious diseases caused by SMG with anaerobes as their clinical course can deteriorated rapidly.

The antimicrobial susceptibility patterns of the strains in the present study conformed to those reported previously [7,15]. Several strains of SMG have been shown to have acquired tolerance to antibiotics. In the present study, some strains showed poor susceptibility to ampicillin or clindamycin. In the management of suppurative disease caused

by SMG, adequate drainage and vigorous antibiotic therapy continue to be important [16]. However, we experienced a deteriorating case with gas gangrene despite repeated surgical debridement and intravenous antibiotic therapy; hyperbaric oxygen therapy eventually improved the patient's condition. Hyperbaric oxygen therapy increases microcirculation in the affected tissues and promotes tissue repair by augmenting collagen deposition, angiogenesis, and re-epithelialization [17,18]. Brogan et al. [19] reported a case of necrotizing fasciitis caused by Group A *Streptococci* that was cured by a multidisciplinary therapeutic approach, including thorough surgical debridement, antibiotic therapy, and hyperbaric oxygen therapy. Patients with gas gangrene caused by SMG should be treated by combination therapy with surgical debridement, antibiotic therapy, and hyperbaric oxygen.

5. Conclusions

The key points in the management of head and neck abscess are early diagnosis, adequate drainage, and control of infection by appropriate agents. It is important to recognize SMG as a pathogen in head and neck infection and to be aware of its predisposing factors, especially the co-existence of anaerobes. In cases with gas gangrene caused by SMG, combination therapy consisting of surgical debridement, antibiotic therapy, and hyperbaric oxygen should be considered.

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