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【 CASE REPORT 】

Multiple Deep-seated Dentofacial Abscesses Caused by Multidrug-resistant Viridans Group Streptococci

Shinnosuke Fukushima[1], Hideharu Hagiya[1], Yuki Mizuta[1], Yasuhiro Nakano[1], Masahiro Takahara[1], Kayo Okamoto[2], Yuko Hayashi[2], Kiyoshi Yamada[2], Kou Hasegawa[1] and Fumio Otsuka[1]

Abstract:
Odontogenic infections, generally caused by dental caries and periodontal disease, can result in fatal illness. We herein report a 71-year-old Japanese woman with type 2 diabetes and hemodialysis who suffered from multiple dentofacial abscesses mainly caused by multidrug-resistant *Streptococcus oralis*. She complained of pain and swelling of her face, with an extraoral fistula from the left cheek. Following 3 surgical debridement procedures and partial mandibulectomy, in addition to 12 weeks of antimicrobial therapy, the multiple dentofacial abscesses were ameliorated. A combination of surgical and antimicrobial treatments following an early diagnosis is essential for reducing further complications.

Key words: dentofacial abscesses, odontogenic infection, osteomyelitis, multidrug resistance, viridans, *Streptococcus*

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Introduction

Odontogenic infections are one of the most common diseases in humans, usually being caused by dental caries and periodontal disease. If untreated, the dental-origin illness may spread into the contiguous facial and neck spaces, even reaching anatomically distant locations (1, 2) and causing multiple severe complications, such as airway obstruction, necrotizing fasciitis, descending mediastinitis, pericarditis, and cerebral abscess (3). Without appropriate dental procedures and antimicrobial treatment, the disease can result in a fatal outcome (4, 5). With the development of modern antibiotics, fatality rates have been reduced significantly. However, a majority of severe head and neck infections, especially in the maxillofacial space (2), still stem from odontogenic infections.

Major causative organisms of odontogenic infections include streptococci and anaerobic bacteria, which constitute the normal oral flora (6). Among various streptococci, the viridans group *Streptococcus* (VGS) is the most common organism involved in odontogenic infection. VGS is usually reported to be highly sensitive to penicillin (7, 8); therefore, penicillin remains the drug of choice in the management of maxillofacial infections. However, VGS strains with reduced susceptibility to multiple drugs are now emerging in clinical settings (7-10).

We herein report a refractory case of multiple deep-seated dentofacial abscesses caused mainly by multidrug-resistant VGS.

Case Report

A 71-year-old Japanese woman visited our dental clinic presenting with pain and swelling of her face as well as an extraoral fistula of the left cheek (Fig. 1). Her medical history included insulin-treated type 2 diabetes and hemodialysis for 10 years. There was no clear history of antimicrobial

[1]Department of General Medicine, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Japan and [2]Department of Plastic and Reconstructive Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Japan

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Correspondence to Dr. Hideharu Hagiya, hagiya@okayama-u.ac.jp

exposure. Dental inspection found suppurative discharge from the left mandibular molar residual root, and the patient was referred to our medical clinic for a further investigation and treatment.

On admission, the patient was alert and her vital signs were as follows: blood pressure, 133/51 mmHg; heart rate, 67 beats per minute; respiratory rate, 16 per minute; and body temperature, 37.0℃. A physical examination revealed swelling and tenderness ranging from her left forehead to the anterior neck. She had trismus and left-sided facial palsy. Laboratory tests showed an elevated white blood cell count (29,110/μL), C-reactive protein level (41.6 mg/dL), and hemoglobin A1C level (9.0%). Contrast-enhanced computed tomography showed multiple dentofacial abscesses of her left face, reaching the left temporal and masseter muscles, as well as the submandibular, submental, and parapharyngeal spaces (Fig. 2). Additional magnetic resonance imaging showed left mandibular osteomyelitis. Blood culture on admission was negative.

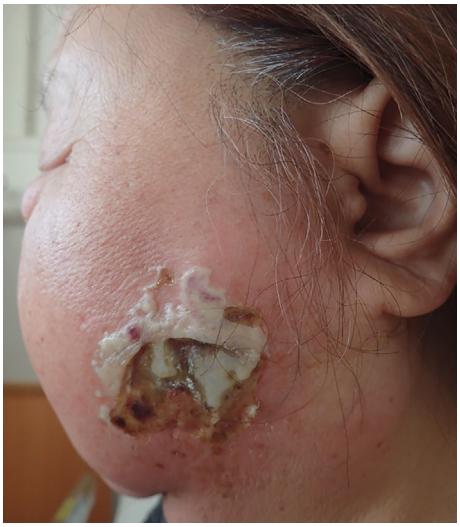

Figure 1. **Extraoral fistula from the left cheek.**

After receiving a diagnosis of left-sided multiple deep-seated abscesses originating from an odontogenic infection, she was administered intravenous treatment with 3 g of ampicillin/sulbactam daily. The patient also underwent intraoral and extraoral drainage by oral surgeons and dermatologists. Despite these efforts, the massive abscesses did not improve, and comprehensive debridement with partial mandibulectomy was performed under general anesthesia 15 days after the initial admission.

Bacterial culture of the purulent discharge detected *Streptococcus oralis* as well as *Candida albicans* and *Actinomyces naeslundii*. Antimicrobial susceptibility testing of *S. oralis* showed resistance to multiple antimicrobials, including beta-lactams (Table). Antibiotic therapy was appropriately adjusted to a combination of ampicillin/sulbactam (3 g every 24 hours), clindamycin (600 mg every 8 hours), and micafungin (100 mg every 24 hours). Postoperatively, the resected portion was managed with negative pressure wound therapy. With a good clinical course, the patient underwent additional debridement and a cutaneous flap using the left anterolateral thigh on day 45. Subsequently, two more local debridement surgeries were performed, along with prolonged antimicrobial therapy of ampicillin/sulbactam for 12 weeks, clindamycin for 8 weeks, and micafungin for 2 weeks.

Discussion

We described a refractory case of multiple dentofacial abscesses that required several intensive surgical treatments and prolonged antimicrobial therapy. The head and neck region has a complex anatomy with relatively loose connections. The superficial fascia of the retropharyngeal space extends from this region to the mediastinum and prevertebral zone, known as the danger space (11), which is often invaded by odontogenic infections (12). This case highlights the involvement of multidrug-resistant VGS strains and risk

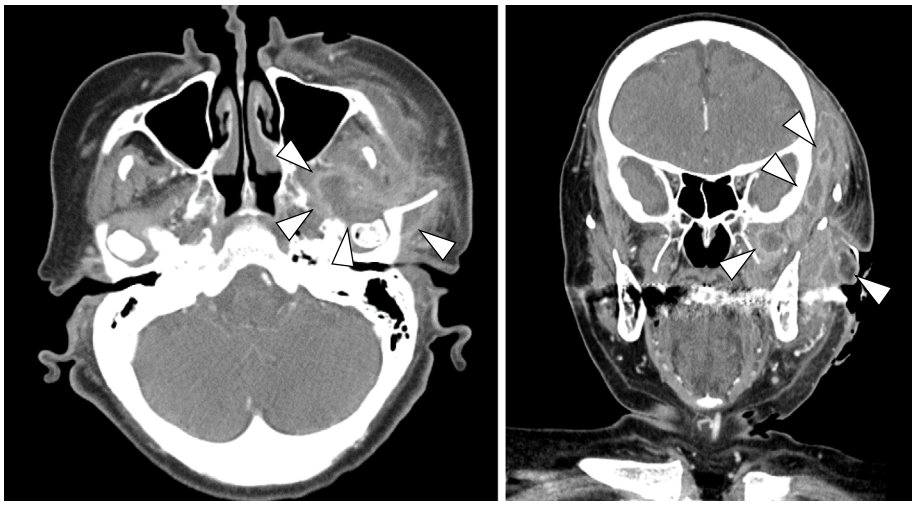

Figure 2. **Contrast-enhanced computed tomography of the face. Axial (A) and coronal (B) views demonstrating multiple deep-seated abscesses.**

Table. Antimicrobial Susceptibility Testing of *Streptococcus oralis*.

Antibiotics	MIC (μg/mL)	Susceptibility
Penicillin G	>2	R
Ampicillin	>8	R
Ampicillin/Sulbactam	>8	R
Cefotiam	>8	n.d.
Cefotaxime	>8	R
Cefepime	4	n.d.
Imipenem	1	n.d.
Meropenem	2	n.d.
Gentamicin	16	n.d.
Clarithromycin	1	R
Clindamycin	≤0.25	S
Minocycline	16	n.d.
Levofloxacin	1	S

MIC: minimum inhibitory concentration, n.d.: not determined. Susceptibility testing was performed using Dry Plate Eiken (Eiken, Tokyo, Japan) based on the Clinical and Laboratory Standards Institute M100-S29.

factors for the incidence and exacerbation of the odontogenic maxillofacial infections.

VGS form the normal flora of oropharyngeal microbiota (13), which are currently classified into six distinct groups: *S. mutans, S. salivarius, S. anginosus, S. mitis, S. sanguinis,* and *S. bovis* (14). Of these, *S. oralis* belongs to the *S. mitis* group. VGS bacteria are generally susceptible to a wide variety of antimicrobials (15), including penicillin; however, the increasing number of cases of multidrug-resistant VGS poses a threat to patients (16-18). Molecular alterations in penicillin-binding proteins create high-level penicillin resistance in VGS (19), which has presumably been accelerated by the excessive use of oral beta-lactams (20).

Various studies have discussed the emergence of penicillin-resistant VGS, but the resistance rate seems to be situationally dependent. One Spanish study between 1988 and 1993 suggested that one-third of clinically-isolated VGS showed no susceptibility to penicillin (21). Another study in 1996 from the United State revealed that 16% of 219 *S. mitis* isolates showed resistance to penicillin (10). VGS species collected in a Korean hospital from 2011 to 2013 showed no susceptibility to penicillin in 40% of 1,448 isolates (9). In addition, a Turkish survey supported an increasing tendency of toward penicillin resistance; notably, more than half of viridans isolates in 2015 were resistant to penicillin (22). However, several studies have detected relatively few penicillin-resistant isolates, including 4% in a Swedish study between 1998 and 2003 (23) and 4% in a study from the United States from 1994 and 2002 (15). A recent retrospective surveillance in Taiwan based on the disk diffusion method reported a penicillin resistance rate of blood-origin VGS of 12.5% (39/312 isolates) (24).

In Japan, there are no comprehensive data regarding antimicrobial susceptibility of VGS. A nationwide questionnaire survey performed between 2000 and 2001 showed that 6.6% of VGS isolated from patients with endocarditis were resistant to penicillin (25). According to laboratory surveillance in our hospital, the susceptibility rate of penicillin G for *S. anginosus* group was 99.5% in 2018, while that of *S. mitis* was not calculated and is unavailable. Notably, the antimicrobial resistance rates of the *S. mitis* group are reportedly higher than those of other Streptococcal groups (9). A previous Japanese study showed that the penicillin susceptibility rate for *S. mitis* was only 41.7%, which was far lower than that of the *S. anginosus* group (97.1%) (26). Accordingly, clinicians should be aware that a growing number of penicillin-resistant VGS species may be involved in severe infections.

According to a study using the Taiwan National Health Insurance Database (27), facial infections that were attributed to odontogenic infections occurred more frequently in patients with diabetes than in those without diabetes (1,000-fold greater risk). Hyperglycemia can impair the leukocyte function, which can exacerbate infection (28). A retrospective study from China indicated that an older age (≥65 years) was also a potential factor for developing life-threatening complications following odontogenic infections (2). Other case-series study support the notion that risk factors for the development of odontogenic infections include diabetes, alcoholism, and immunosuppressed conditions, such as liver, renal, and heart failure (29). In the present case, uncontrolled diabetes, a history of long-term renal failure, and an advanced age were responsible for the progression of multiple facial abscesses.

In conclusion, we encountered a case of multiple deep-seated dentofacial abscesses caused by multidrug-resistant *S. oralis.* Odontogenic infections have the potential to develop lethal complications, especially in immunocompromised patients. The early diagnosis followed by a combination of surgical and antimicrobial treatments is imperative for successful patient care.

The authors state that they have no Conflict of Interest (COI).

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