A Case of Pediatric Garré Osteomyelitis Caused by Infected Dentigerous Cyst

NINA WAKIMOTO, KEIICHI UCHIDA*, TAKANAGA OCHIAI**,
EMI OKI, NORIYUKI SUGINO*, TAKEO FUJII,
ATUSHI SHINOHARA*** AND AKIRA TAGUCHI*

含歯性囊胞の感染に起因した小児の Garré 骨髄炎の 1 例

脇 本 仁 奈 内 田 啓 一* 落 合 隆 永**
大 木 絵 美 杉 野 紀 幸* 藤 井 健 男
篠 原   淳*** 田 口   明*

要約: 今回われわれは、含歯性囊胞の感染に起因した小児の Garré 骨髄炎と診断された 1 例について報告した。患者は 4 歳、男児で右側下顎臼歯部の腫脹部の精査を主訴として来院した。受診時、左側顜頸部から頬下部に圧痛と開口障害を伴う腫脹を認め、顔貌は左右非対称であり、左側頜下大臼歯部の頬側歯槽粘膜部に圧痛を伴う腫脹を認めた。画像所見では第二乳臼歯部は歯根吸収を認め、変変内部に一部含まれ、頬側皮質骨外側には層状の骨膜反応を認めた。全身麻下にて口腔内から左側下顎第二乳臼歯を抜去し腫瘍摘出術を行った。病理学的所見では非角化性重層扁平上皮に裏装されて囊胞様構造を認め、上皮下結合組織は浮腫性の炎症細胞浸潤を伴っていた。臨床症状、画像所見および病理組織学的所見からの総合的診断により、含歯性囊胞の感染に起因した Garré 骨髄炎と診断した。小児期における顎骨骨髄炎に対しては、消炎処置後に原因歯の抜去と囊胞摘出を行うことにより良好な治癒経過が得られ、早期の診断と治療が重要であることが示唆された。

Abstract: We herein report a child with Garré osteomyelitis caused by an infected dentigerous cyst. The patient was a 4-year-old boy in whom detailed examination showed swelling of the right mandibular molar region. The swelling was accompanied by tenderness and trismus between the left cheek and submandibular region, the face was asymmetric, and there was diffuse swelling accompanied by tenderness in the buccal alveolar mucosa of the left mandibular molar region. Imaging findings revealed root resorption in the second deciduous molar that was partially encompassed by the swelling, and a laminar periosteal reaction on the lateral side of the buccal cortex. The patient underwent cystectomy under general anesthesia with extraction of the second deciduous molar in the left lower jaw via an intraoral approach. Pathologically, a cystic structure, lined with non-keratinized stratified squamous epithelium and subepithelial connective tissues accompanied by edematous inflammatory cell infiltrates, was observed. Garré osteomyelitis caused by an infected dentigerous cyst was diagnosed based on clinical symptoms and both imaging and pathological findings. Early diagnosis and treatments are suggested to be important, as osteomyelitis of the jaw in childhood may fully resolve with extraction of the culprit tooth and cyst after anti-inflammatory treatments.

Key words: Garre's Osteomyelitis（ガレーの骨髄炎）、dentigerous cyst（含歯性囊胞）、child（小児）、mandible（下顎骨）

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Introduction

Garré osteomyelitis is a rare type of osteomyelitis occurring in the long bones of young adults. In the stomatognathic region, it usually affects the mandible in children around 10 years of age, and does not produce
significant clinical symptoms except for swelling. Pathologically, this disease is characterized by gross thickening of the periosteum with peripheral reactive bone formation (i.e., periosteal reaction). The common causes of Garré osteomyelitis are infections resulting from periapical lesions or tooth extraction; however, the occurrence of this form of osteomyelitis due to an infected dentigerous cyst is rare. We herein report a case with Garré osteomyelitis due to an infected dentigerous cyst with imaging findings and a discussion of the relevant literature.

**Case Report**

A four-year-old boy presented with swelling in the left facial region which had first been noted in early October in 201X. A pediatrician prescribed medication only and followed him up, because the patient had no significant symptoms except for the swelling. The patient subsequently experienced pyrexia and swelling in the left cheek accompanied by pain and was thus brought to a dentist. X-ray at the time showed an area of opacity in the left mandibular first molar region. In October 201X, the patient was referred to our university hospital for further detailed examinations and treatment. At the time of the initial examination, clinical findings outside the oral cavity included a temperature of 37.8°C, swelling in the area between the left cheek and submandibular region accompanied by tenderness and trismus, and facial asymmetry. There was neither fluctuation nor dysphagia. Clinical findings within oral cavity included diffuse swelling of the buccal alveolar mucosa of the left mandibular region and accompanying tenderness. His blood tests revealed a white blood cell count of $143 \times 10^3/\text{UL}$ and a C-reactive protein (CRP) level of $1.7\text{mg/d}$, both of which indicated inflammation. Intra-oral X-ray showed widening of the periodontal membrane space and poor root canal filling in the left mandibular first and the second deciduous molar region and the left mandibular region (Fig. 1). Panoramic X-ray showed an oval-shaped well-defined cyst-like lucency located around the impacted left mandibular first molar with incomplete root development, and the left mandibular second deciduous molar located adjacent to the cyst-like lesion (Fig. 2). CT and CBCT examinations were further performed to closely observe inflammation by informing the necessity of imaging tests to and obtaining approval from the child’s parents. Cone-Beam computed tomography (CT) showed the impacted left mandibular molar with incomplete root development, an oval-shaped opacity with buccolingual bone expansion located on the upper external side of the dental cyst, root resorption in the second deciduous molar partially encompassed by the swelling, laminar periosteal reaction and the presence of a fistula on the external side of the buccal cortical bone, and thickening of the cortical bone (Fig. 3 A, B). CT showed a well-defined opacity with buccolingual bone formation near the impacted left mandibular first molar, periosteal reaction in the cheek, marked swelling of the soft tissues in the left cheek and the masseter muscle, and a high density area in the left subcutaneous fat layer (Fig. 4 A, B). Based on clinical symptoms and imaging findings, Garré osteomyelitis with cellulitis in the buccal region,
due to an infected dentigerous cyst, was diagnosed.

Then, swelling was not reduced despite treatment for resolution at the outpatient, and the patient was admitted to our hospital for the purpose of treating inflammation and surgery in November 201X. On the first hospital day, he underwent incisional drainage from the gingival mucosa in the cheek mucosa and was started on intravenous antibiotic treatment with rocephin™ (CTRX), a cephem antibiotic agent, 1 g daily for 12 days, along with oral administration of flomox tablets™ 100mg (CFPN-PI), an antimicrobial agent, 300mg daily for 13 days, because he had cellulitis in the cheek accompanied by pyrexia and the swelling was increasing. The swelling in the area between the left cheek and submandibular region accom-
panied by tenderness as well as that of the buccal alveolar mucosa of the left mandibular molar region then resolved, indicating amelioration of the inflammation. On the 13th hospital day, we performed infected root canal treatment, considering that the left deciduous molar was the causative agent of infection based on imaging studies. We performed root canal filling again in lesion D of the left mandible. Although we did not perform root canal filling in lesion E of the left mandible, there was no pus discharge from the root canal. A repeat blood test showed a white blood cell count of \(83 \times 10^2/\mu l\) and a CRP level of 0.7 mg/dl, indicating amelioration of the inflammation. In December 201X, the patient underwent cystectomy under general anesthesia using an intraoral approach. An incision was made in the left buccal mucosa. After mucoperiosteal elevation, the cortical bone was removed. Cystectomy was then performed by extracting lesion E from the left mandible. The left mandibular first molar was in a developmental stage and there was a tooth crown within the jawbone. A tumorous lesion was observed on the periphery and the upper part of the first molar. The anterior part of the tumorous lesion was continuous with the distal part of lesion E of the left mandibular first molar. The left mandibular first molar was preserved because it was still undergoing developmental processes. Gauze drain impregnated with achromycin ointment was used for impaction, and a brace was applied. Pathological findings showed a cystoid structure lined with non-keratinized stratified squamous epithelium and subepithelial connective tissues accompanied by edematous inflammatory cell infiltrates. The pathological diagnosis was dentigerous cyst (Fig. 5 A, B). Intraoral observation was regularly performed at the oral surgery outpatient postoperatively, and no specific abnormal findings were observed around the surgical site after 2 years and 5 months post-operation with well course. The patient is currently followed up at the outpatient of a dental clinic for children.

Discussion

Incidence of osteomyelitis of the jaw is lower in young population than in adults, and the number of children who have osteomyelitis also decreases because of development of antibiotics or reduction in rampant caries. However, mild inflammation is often chronic and may be caused by infection from periodontal diseases or pericoronitis of wisdom tooth, and it is obvious that the osteomyelitis is caused by chronic inflammation\(^1\). Garré osteomyelitis is a rare disease among children and has a wide range of clinical presentations including new bone formation, bone destruction, and multiple swollen lymph nodes\(^2\). Typically, Garré osteomyelitis occurs in the mandibles of children around 10 years of age. This disease is often chronic, producing no pain and few other significant clinical symptoms. It is characterized by gross thickening of the periosteum with peripheral reactive bone formation\(^3\) Garré osteomyelitis was first described in the maxillofacial region by Pell et al.\(^4\) as an osteomyelitis of the mandible in young adults. They reported that Garré osteomyelitis produced no or mild pain and was accompanied by hardened, bone-like, swelling.

In reviewing the case reports by Eversole et al.\(^5\) (29 cases), Ohno et al.\(^6\) (15 cases), Lichty et al.\(^7\) (22 cases), and Maki et al.\(^8\) (15 cases), the average onset age of Garré osteomyelitis was found to be around 10 years. Our present patient was four years old, clearly younger than average. The reason for Garré osteomyelitis frequently occurring in children around age 10 might be that the mandibles of children around this age are highly proliferative and their teeth are being replaced by new teeth. In addition, the mandibular first molars are susceptible to dental caries. These factors may result in the formation of periapical lesions especially in children around age 10\(^8\). The mandible is more often affected than the maxilla. This might be attributable to the bone

Fig. 5 Pathological findings are consistent with a cystoid structure lined with non-keratinized stratified squamous epithelium. The subepithelial connective tissues surrounding the cystoid structure are accompanied by an edematous inflammatory cell infiltrate. (hematoxylin and eosin, \(\times 10\))
of the maxilla being more porous than that of the mandible and having a more abundant blood supply, whereas the cells in the mandible are more prone to bone formation due to an insufficient blood supply from the periosteum because of the thickened cortical bone\(^8\). In the present case, we considered the osteomyelitis to have been caused by the spread of chronic inflammation of the periapical lesion of the second deciduous molar into the cystic cavity. This assumption was based on the Cone Beam CT observation that root resorption in the second deciduous molar was partially encompassed within the swelling and on the intraoperative finding of the lesion being continuous with the distal part of lesion E of the left mandible.

With regard to the diagnostic criteria for Garré osteomyelitis, Eversole et al.\(^5\) proposed the following requirements: 1) facial asymmetry resulting from localized osseous enlargement; 2) histological findings of a benign fibro osseous lesion in the periosteum; 3) infection, trauma, or other source of irritation; and 4) complete or partial remodeling of excess bone after elimination of the cause. We applied these criteria to the present case: 1) the patient showed swelling in the area between the left cheek and submandibular region, producing facial asymmetry, at the time of the first examination; 3) there was a periapical lesion with chronic inflammation; and 4) partial resolution of the inflammation was observed after surgery. Although we did not confirm the deposit bone forming as periosteal reaction histopathologically in the periosteum, Garré osteomyelitis of the mandible was diagnosed based on clinical and imaging findings.

On imaging studies, Garré osteomyelitis is characterized by the formation of periosteal new bone in the lower margin of the mandible or the bone cortex, which can be classified into a solid periosteal reaction or an ‘onion peel’ periosteal reaction: the former represents a continuous bone formation attached to the external cortical surface, whereas the latter represents a multi-laminar periosteal reaction with an onion-skin appearance.\(^8,10\). Maki et al.\(^7\) reported that 13 of their 15 cases were classified as ‘onion peel’ type and the remaining two as solid type. Uneoka et al.\(^10\) classified four of five cases as ‘onion peel’ type and the other as solid type. They noted that Garré osteomyelitis of the mandible resulting from a periapical lesion had tended to present with the onion peel periosteal reaction.\(^8,10\). The presence of a fistula is another important radiographic characteristic of Garré osteomyelitis. As the disease develops, the fistula caused by a periapical lesion in the jawbone promotes lamellar bone formation in the periosteum. Therefore, the examination to detect the presence of a fistula is clinically important\(^11\). On Cone Beam CT, the present patient showed the typical ‘onion peel’ periosteal reaction and a belt-like X-ray opacity suggesting the presence of a fistula in the periosteum with peripheral reactive bone formation.

The differential diagnoses of Garré osteomyelitis include chronic osteomyelitis of the mandible and Ewing sarcoma. The chronic osteomyelitis of the mandible is frequently observed in middle-aged or elderly adults. This disease involves changes in the osteoblastic cells in the bone marrow cavity and is refractory to Conventional anti-inflammatory treatment.\(^8\). On the other hand, Garré osteomyelitis is frequently observed in children. The disease involves minor changes in osteoblastic cells in the bone marrow cavity and has a relatively good prognosis.\(^8\). However, clinical differentiation between these two diseases can on occasion be difficult. Therefore, detailed imaging studies as well as clinical evaluation are important for making the diagnosis. Ewing sarcoma shows an ‘onion peel’ periosteal reaction. Although the X-ray findings in Ewing sarcoma are similar to those in Garré osteomyelitis, clinical examination is useful for the differential diagnosis because Ewing sarcoma progresses more rapidly and is accompanied by paresthesia of the lips.\(^13\).

Garré osteomyelitis can be treated by removing infection origin including medical therapy of antibiotics, root canal therapy, or teeth removal. When a focus of infection or adding bone is extensive, surgical bone removal, removal of cortical bone, or jaw resection may be required.\(^14\). Our present patient received anti-inflammatory treatments and subsequently underwent extraction of both the culprit tooth and the cyst. Postoperative course is well and the surgical site is almost completely repaired with new bone without facial asymmetry or abnormal findings in growth status. No facial asymmetry or developmental delays have been observed, to date. We consider early diagnosis and treatment to be important for osteomyelitis of the mandible in children.

Acknowledgement, conflicts of interest, and ethical issues

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