Mandibular osteomyelitis is one of the most common infectious diseases and is usually odontogenic or traumatic in origin. Meanwhile, mandibular osteomyelitis caused by a process of unknown etiology is known to develop during the clinical course. In 1987, Chamot et al described a syndrome associated with synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO syndrome), which is characterized by osteoarticular and dermatologic symptoms. The most prevalent site of bone lesions is the anterior chest wall with involvement of other locations including the sternum, clavicles, ribs, spine, and peripheral long and flat bones. Bone lesions in SAPHO syndrome demonstrate clinical and radiologic features similar to diffuse sclerosing osteomyelitis. Clinical diagnosis of SAPHO syndrome is defined as the presence of any one of the following: 1) multifocal osteitis with or without skin manifestations; 2) sterile acute or chronic joint inflammation associated with pustules or psoriasis of palms and soles, or acne, or hidradenitis; or 3) sterile osteitis in the presence of one of the skin manifestations. Other investigators have suggested that early diagnosis of this condition is crucial to avoid repeated examinations and invasive procedures; however, the etiology of SAPHO syndrome remains unknown. Treatment has therefore been difficult and focuses on symptoms only.

This report presents the long-term follow-up of a case of SAPHO syndrome in the mandible of a patient who received nonsteroid anti-inflammatory drugs (NSAIDs) and long-term administration of macrolides in combination with surgical procedures.

Report of a Case

A 51-year-old woman was referred to the Department of Oral and Maxillofacial Surgery, Nagasaki University Graduate School of Biomedical Sciences (Nagasaki, Japan) in November 1998 because of a painful swelling of the right
cheek associated with limited mouth opening for at least 3 weeks. She did not have weakness or fever. At that time, the patient reported no use of medications or previous treatment for these conditions. Her medical history was unremarkable. There was no history of trauma to the maxillofacial complex.

Clinical examination showed a bony hard swelling in the region of the right parotid-masseter and the right temporomandibular joint (TMJ) without suppuration and cervical lymphadenopathy (Fig 1). Intraorally, no alterations were seen in the oral mucosa. Fever did not increase during the course. In laboratory data, C-reactive protein was slightly elevated (2.3 mg/dL); however, blood counts and other laboratory tests were within normal limits.

Panoramic radiogram and coronal TMJ tomogram showed destruction of the condyle and reactive sclerosis of the articular process of the mandible (Figs 2A,B). Coronal contrast-enhanced T1-weighted magnetic resonance image showed a low intensity signal of the bone marrow of the condyle and ascending ramus (Figs 3A,B). Based on a diagnosis of mandibular osteomyelitis, antibiotic and NSAID therapy was given for 1 week, but it failed to improve the symptoms. Partial resection of the condyle with an open biopsy was performed under general anesthesia. The histopathologic examination showed fibrous granulation tissue and mature lamellate cellular bone (Fig 4). Microbiologic culture from the biopsy specimen was negative.

Two years later, the patient also experienced pain and swelling in the right mandibular body, but no evidence of recurrence of the mouth-opening limitation. At that time, panorama radiogram showed bone sclerosis with scattered osteolyses of the ascending ramus (Fig 5A). Coronal TMJ tomogram showed cortex formation of the condyle; however, the progressive sclerotic change and periosteal reaction were predominant in the ascending ramus (Fig 5B). Coronal contrast-enhanced T1-weighted magnetic resonance image demonstrated extension of the low intensity

**FIGURE 1.** Extraoral photograph shows a bony hard swelling in the region of the right parotid masseter.


**FIGURE 2.** Panoramic radiogram (A) and coronal TMJ tomogram (B) show destruction of the condyle and reactive sclerosis of the articular process of the mandible.

signal of the bone marrow to the mandibular angle, and the periosteal reaction was observed outside the original cortex (Fig 6). Bone scintigram (technetium 99m) showed enhanced uptake in the right ascending ramus and sternoclavicular joint (Fig 7). In laboratory data, as in the first examinations, C-reactive protein was slightly increased (0.55 mg/dL); however, other laboratory test results were within normal limits. In addition, she was negative for rheumatoid factor and antinuclear antibody. Serum immunoglobulin levels and immunoglobulin G subclasses were normal. HLA antigen typing was positive for A11, A24, B55, B52, and Cw1. Based on the clinical manifestations, laboratory examinations, and radiologic findings, a diagnosis of SAPHO syndrome was established.

Extensive decortication of the ramus was performed to decrease swelling of the mandible. Histopathologic findings showed fibrous granulation tissue and bone fragments, as in the first surgical treatment. Microbiologic culture of the biopsy specimen was also negative. The patient subsequently received long-term administration of clarithromycin (400 mg/d) and etodolac (200 mg/d) for at least 3 months. During that time, she had a long symptom-free period. At this point, the antibiotic and NSAID treatments were stopped.

After 6 months, she again experienced pain and swelling in the right mandibular body; however, the degree of pain and swelling were markedly decreased. Subsequently, these symptoms appeared every 3 months and the patient was discontinuously administered clarithromycin (400 mg/d) and etodolac (200 mg/d). This symptomatic treatment has been continuing for the past 8 years, resulting in sufficient relief of pain and swelling. At the last radiologic examination, panoramic radiogram showed slight enhancement of sclerosis of the ascending ramus (Fig 8A). Coronal TMJ tomogram showed slight enlargement of the ascending ramus (Fig 8B). Coronal contrast-enhanced T1-weighted magnetic resonance image remained almost unaltered (Fig 9).

Discussion

SAPHO syndrome is a rare disease of unknown infectious origin; however, its incidence is underestimated. A pediatric subset of SAPHO syndrome is referred to as chronic recurrent multifocal osteomyelitis, which is the most severe form of sterile bone inflammation in children. Moreover, SAPHO syndrome may be misdiagnosed if the location is atypical or if the clinical presentation is unusual. In fact, chronic recurrent multifocal osteomyelitis and SAPHO syndrome share several features: osteitis, unifocal or multifocal presentation, pustulosis, hyperostosis, and a good general state of health without spiking fevers, organomegaly, weight loss, or fatigue.

A sternocostoclavicular lesion is the most frequent site of SAPHO syndrome, followed by the sacroiliac joint and the spine. Diffuse sclerosing osteomyelitis of the mandible is a well-known bone lesion of SAPHO syndrome. Hayem et al reported 13 cases (10.8%) of mandibular osteomyelitis in 120 patients with SAPHO syndrome. Moreover, in a series of 85 patients with SAPHO syndrome, 7 had mandibular lesions (8.2%). Despite previous reports of SAPHO
syndrome in the literature, only 4 cases involving the TMJ have been reported. These cases presented various complications such as TMJ ankylosis and inflammatory spread to the temporal bone causing deafness. Although our case also involved the TMJ and showed destruction of the condyle and reactive sclerosis of the articular process of the mandible, good progress was achieved by partial resection of the condyle as the initial surgical procedure.

Suei et al recommended that mandibular osteomyelitis lesions should be classified into bacterial osteomyelitis and osteomyelitis in SAPHO syndrome. Diagnos-
tic features of bacterial osteomyelitis are suppuration and osteolytic radiographic change with lamellar-type periosteal reaction. In contrast, mandibular osteomyelitis in SAPHO syndrome is characterized by nonsuppurative and a mixed radiographic pattern accompanied by solid-type periosteal reaction, external bone resorption, and bone enlargement. Moreover, in SAPHO syndrome, progressive bone sclerosis with scattered osteolyses (mixed type) is a common feature; however, bone resorption may be prominent in the early stage, whereas sclerotic changes may be observed in a more quiescent chronic reaction. In accordance with these radiologic features, our case showed bone resorption of the condyle in the early stage, and sclerotic changes were observed with chronic inflammation in recent years.

Skin lesions typically seen in SAPHO syndrome are palmoplantar pustulosis and acne; however, not all of these manifestations necessarily occur. The incidence of skin lesions such as palmoplantar pustulosis and acne in patients with SAPHO syndrome has been reported as 84%. Moreover, Kahn et al reported the occurrence of long intervals between the development of skin and bone lesions; however, our case had no history of skin lesions.

SAPHO syndrome shows various immunogenetic backgrounds; however, its genetic basis remains unknown. Although some studies have suggested that antigen HLA B27 is associated with SAPHO syndrome, some recent reports have supported the idea that the HLA B27 phenotype could not be associ-
ated with the pathogenesis of SAPHO syndrome.\textsuperscript{11,16} Our patient did not have the HLA B27 phenotype.

In SAPHO syndrome, therapeutic modalities such as antibiotic administration, hyperbaric oxygen, curettage, saucerization, decortication, and partial resection of the affected bones have been reported by some investigators\textsuperscript{3,7,11,13}; however, these modalities have very limited efficacy and cannot cure the disease.\textsuperscript{5,13} Although surgical procedures such as decortication and removal of necrotic tissue may be useful in the early stages of the disease, it is well known that surgical treatment of osteomyelitis with SAPHO syndrome often has no or only short-term success.\textsuperscript{17,18}

Up to now, treatment for SAPHO syndrome has focused only on symptoms. NSAIDs seem to be the treatment of first choice, in combination with antibiotics.\textsuperscript{3,7,11,13,18} Corticosteroid therapy is acceptable for patients with a poor clinical response to NSAIDs.\textsuperscript{5,13} In almost all cases, long-term administration of macrolides and conservative treatment with NSAIDs have been recommended.\textsuperscript{3,7,11,18} Recently, treatment with pamidronates or bisphosphonates has been reported to be effective\textsuperscript{11}; however, the effects of these drugs have to be evaluated, because there are no long-term data on the outcome with these drugs. In our case, NSAIDs (etodolac 200 mg/d) and long-term macrolides (clarithromycin 400 mg/d) were administered. Moreover, surgical treatment in the early stage seemed effective to repress disease progression.

In conclusion, mandibular osteomyelitis in SAPHO syndrome is characterized by nonsuppuration and a mixed radiographic pattern accompanied by solid-type periosteal reaction, external bone resorption, and bone enlargement. SAPHO syndrome should be considered when a patient presents with osteomyelitis in other bones, arthritis, or skin diseases.

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References


