

15. Raibley SO, Beckett RP, Nowakowski A: Multiple traumatic bone cysts of the mandible. *J Oral Surg* 37:335, 1979
16. Magliocca KR, Edwards SP, Helman JI: Traumatic bone cyst of the condylar region: Report of 2 cases. *J Oral Maxillofac Surg* 65:1247, 2007
17. Wright JG, Yandow S, Donaldson S, et al: A randomized clinical trial comparing intralesional bone marrow and steroid injections for simple bone cysts. *J Bone Joint Surg Am* 90:722, 2008
18. Capanna R, Dal Monte A, Gitelis S, et al: The natural history of unicameral bone cyst after steroid injection. *Clin Orthop Relat Res* 166:204, 1982
19. Scaglietti O, Marchetti PG, Bartolozzi P: Final results obtained in the treatment of bone cysts with methylprednisolone acetate (depo-medrol) and a discussion of results achieved in other bone lesions. *Clin Orthop Relat Res* 165:33, 1982
20. Hansen LS, Scapone J, Sprout C: Traumatic bone cysts of jaws: Report of sixty-six cases. *Oral Surg Oral Med Oral Pathol* 37: 899, 1974
21. Wilkins R: Unicameral bone cysts. *J Am Acad Orthop Surg* 8:217, 2000
22. Oppenheim WL, Galleno H: Operative treatment versus steroid injection in the management of unicameral bone cysts. *J Ped Orthop* 4:1, 1984
23. Yu CL, D'Astous J, Finnegan M: Simple bone cysts. The effects of methylprednisolone on synovial cells in culture. *Clin Orthop Relat Res* 34, 1991

J Oral Maxillofac Surg
68:212-217, 2010

Diffuse Chronic Sclerosing Osteomyelitis of the Mandible With Synovitis, Acne, Pustulosis, Hyperostosis, and Osteitis: Report of a Long-Term Follow-Up Case

Souichi Yanamoto, DDS, PhD, Goro Kawasaki, DDS, PhD,†
Izumi Yoshitomi, DDS, PhD,‡ and Akio Mizuno, DDS, PhD§*

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 al¹ described a syndrome associated with synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO syndrome), which is characterized by osteoarticular and dermatologic symptoms.² The most prevalent site of bone lesions is the anterior chest wall with involvement of other locations including the sternum, clavi-

cles, ribs, spine, and peripheral long and flat bones.¹⁻⁴ Bone lesions in SAPHO syndrome demonstrate clinical and radiologic features similar to diffuse sclerosing osteomyelitis.⁵ 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.⁶ 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.^{1,2,5-7} Treatment has therefore been difficult and focuses on symptoms only.^{3,5,7}

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

Received from the Department of Oral and Maxillofacial Surgery, Unit of Translational Medicine, Course of Medical and Dental Sciences, Nagasaki University Graduate School of Biomedical Sciences, Sakamoto, Nagasaki, Japan.

*Senior Assistant Professor.

†Associate Professor.

‡Assistant Professor.

§Professor and Chairman.

Address correspondence and reprint requests to Dr Yanamoto: Department of Oral and Maxillofacial Surgery, Unit of Translational Medicine, Course of Medical and Dental Sciences, Nagasaki University Graduate School of Biomedical Sciences, 1-7-1 Sakamoto, Nagasaki, 852-8588, Japan; e-mail: syana@nagasaki-u.ac.jp

© 2010 American Association of Oral and Maxillofacial Surgeons

0278-2391/10/6801-0036\$36.00/0

doi:10.1016/j.joms.2009.04.121

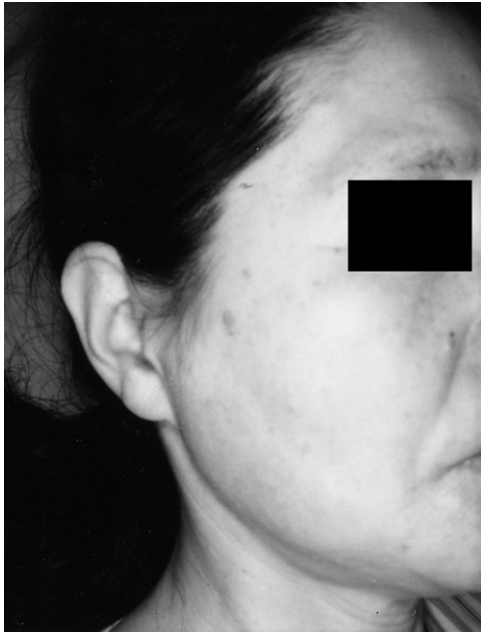


FIGURE 1. Extraoral photograph shows a bony hard swelling in the region of the right parotid masseter.

Yanamoto et al. Mandibular Osteomyelitis in SAPHO Syndrome. J Oral Maxillofac Surg 2010.

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 unre-

markable. 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

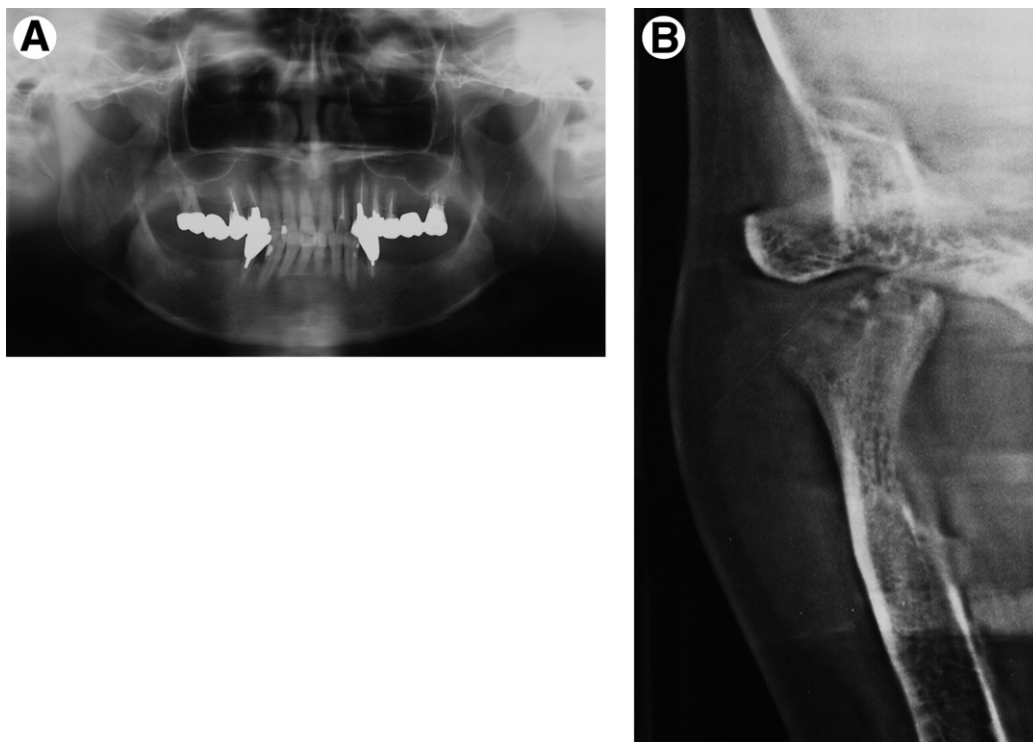


FIGURE 2. Panoramic radiogram (A) and coronal TMJ tomogram (B) show destruction of the condyle and reactive sclerosis of the articular process of the mandible.

Yanamoto et al. Mandibular Osteomyelitis in SAPHO Syndrome. J Oral Maxillofac Surg 2010.



FIGURE 3. Coronal contrast-enhanced T1-weighted magnetic resonance image shows a low intensity signal of the bone marrow of the condyle (A) and ascending ramus (B).

Yanamoto et al. Mandibular Osteomyelitis in SAPHO Syndrome. *J Oral Maxillofac Surg* 2010.

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,⁸ which is the most severe form of sterile bone inflammation in children.⁹ 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.⁸

A sternocostoclavicular lesion is the most frequent site of SAPHO syndrome, followed by the sacroiliac joint and the spine.^{10,11} Diffuse sclerosing osteomyelitis of the mandible is a well-known bone lesion of SAPHO syndrome. Hayem et al¹¹ 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%).⁶ Despite previous reports of SAPHO

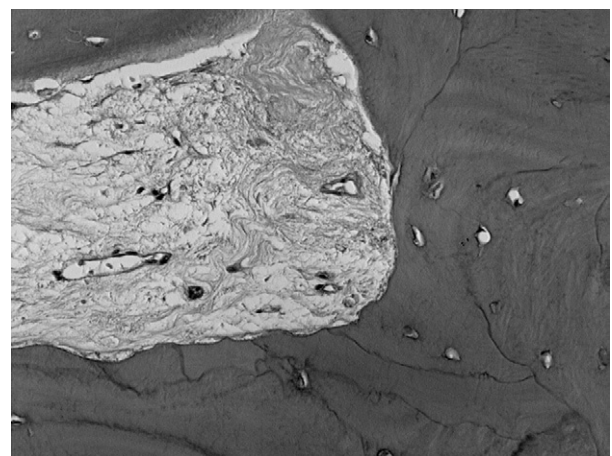


FIGURE 4. Histopathologic examination shows fibrous granulation tissue and mature lamellate cellular bone.

Yanamoto et al. Mandibular Osteomyelitis in SAPHO Syndrome. *J Oral Maxillofac Surg* 2010.

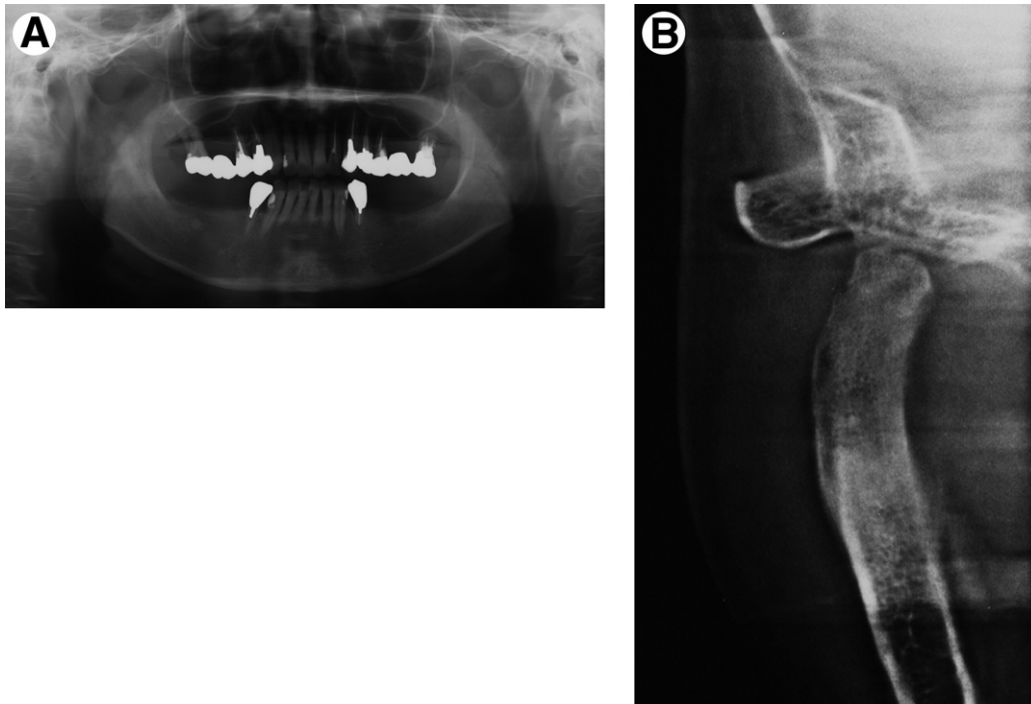


FIGURE 5. Two years after first surgical treatment. A, Panoramic radiogram shows bone sclerosis with scattered osteolyses of the ascending ramus. B, Coronal TMJ tomogram shows cortex formation of the condyle; however, progressive sclerotic change and periosteal reaction is predominant in the ascending ramus.

Yanamoto et al. Mandibular Osteomyelitis in SAPHO Syndrome. J Oral Maxillofac Surg 2010.

syndrome in the literature,^{6,7,11-13} only 4 cases involving the TMJ have been reported.^{7,11-13} These cases presented various complications such as TMJ ankylosis⁷ and inflammatory spread to the temporal bone causing deafness.¹² Although our case also involved the TMJ and showed destruction of the condyle and reactive sclerosis of the articular process of the man-

dible, good progress was achieved by partial resection of the condyle as the initial surgical procedure.

Suei et al⁵ recommended that mandibular osteomyelitis lesions should be classified into bacterial osteomyelitis and osteomyelitis in SAPHO syndrome. Diagnos-

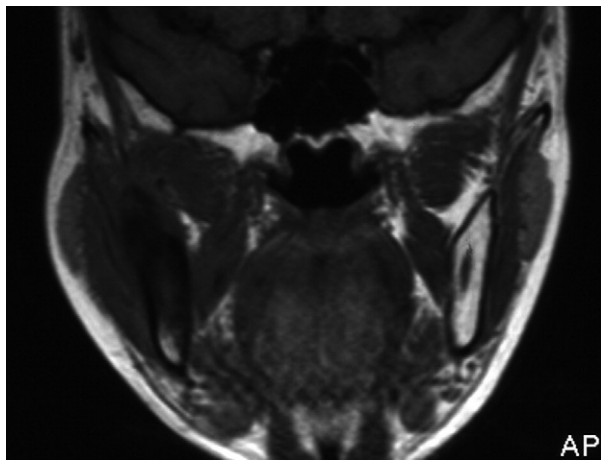


FIGURE 6. Coronal contrast-enhanced T1-weighted magnetic resonance image shows extension of the low intensity signal of the bone marrow to the mandibular angle, and the periosteal reaction is observed outside the original cortex.

Yanamoto et al. Mandibular Osteomyelitis in SAPHO Syndrome. J Oral Maxillofac Surg 2010.

FIGURE 7. Technetium 99m bone scintigram shows enhanced uptake in the right ascending ramus and sternoclavicular joint.

Yanamoto et al. Mandibular Osteomyelitis in SAPHO Syndrome. J Oral Maxillofac Surg 2010.

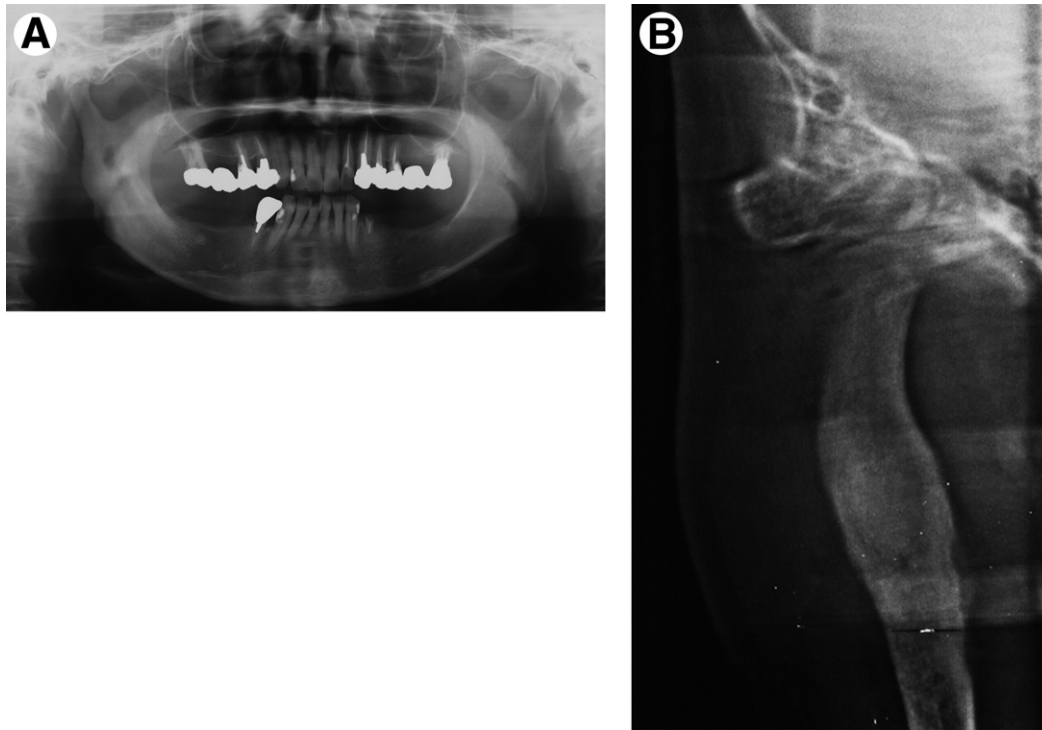


FIGURE 8. Eight years after second surgical treatment. A, At the last radiologic examination, panoramic radiogram showed slight enhancement of sclerosis of the ascending ramus. B, Coronal TMJ tomogram showed slight enlargement of the ascending ramus.

Yanamoto et al. Mandibular Osteomyelitis in SAPHO Syndrome. J Oral Maxillofac Surg 2010.

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 nonsup-

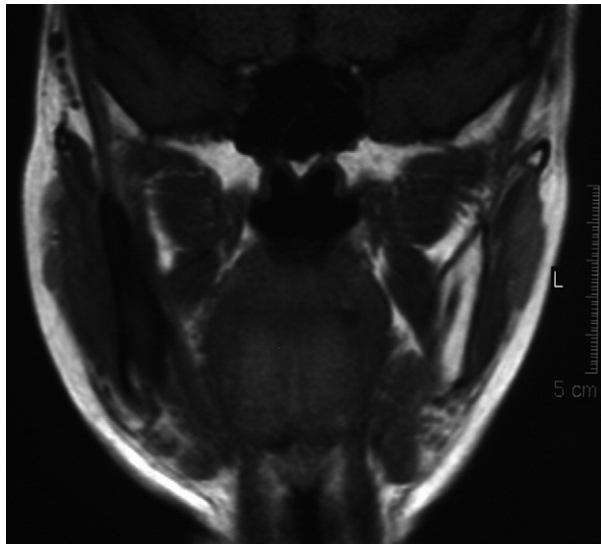


FIGURE 9. Eight years after second surgical treatment. Coronal contrast-enhanced T1-weighted magnetic resonance image remained almost unaltered from that seen in Figure 6 (2 yrs after first surgical treatment).

Yanamoto et al. Mandibular Osteomyelitis in SAPHO Syndrome. J Oral Maxillofac Surg 2010.

puration and a mixed radiographic pattern accompanied by solid-type periosteal reaction, external bone resorption, and bone enlargement.^{5,10,14} Moreover, in SAPHO syndrome, progressive bone sclerosis with scattered osteolyses (mixed type) is a common feature⁵; however, bone resorption may be prominent in the early stage, whereas sclerotic changes may be observed in a more quiescent chronic reaction.⁵ 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%.¹¹ Moreover, Kahn et al¹⁵ 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.¹⁶ Although some studies have suggested that antigen HLA B27 is associated with SAPHO syndrome,^{1,6} some recent reports have supported the idea that the HLA B27 phenotype could not be associ-

ated with the pathogenesis of SAPHO syndrome.^{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^{3,7,11,13}; however, these modalities have very limited efficacy and cannot cure the disease.^{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.^{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.^{3,7,11,13,18} Corticosteroid therapy is acceptable for patients with a poor clinical response to NSAIDs.^{11,13} In almost all cases, long-term administration of macrolides and conservative treatment with NSAIDs have been recommended.^{5,7,11,18} Recently, treatment with pamidronates or bisphosphonates has been reported to be effective¹¹; 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 nonsupuration 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.

Acknowledgment

We thank the staff of the Department of Radiology and Cancer Biology and the Department of Oral Pathology and Bone Metabolism, Nagasaki University Graduate School of Biomedical Sciences.

References

1. Chamot AM, Benhamou CL, Kahn MF, et al: Acne-pustulosis-hyperostosis-osteitis syndrome. Results of a national survey. 85 Cases. *Rev Rhum Mal Osteoa-Articulaires* 54:187, 1987

2. Earwaker JWS, Cotton A: SAPHO: Syndrome or concept? Imaging findings. *Skeletal Radiol* 32:311, 2003
3. Roldan JC, Terheyden H, Dunsche A, et al: Acne with chronic recurrent multifocal osteomyelitis involving the mandible as part of the SAPHO syndrome: Case report. *Br J Oral Maxillofac Surg* 39:141, 2001
4. Sato T, Indo H, Kawabata Y, et al: Scintigraphic evaluation of chronic osteomyelitis of the mandible in SAPHO syndrome. *Dentomaxillofac Radiol* 30:293, 2001
5. Suei Y, Taguchi A, Tanimoto K: Diagnosis and classification of mandibular osteomyelitis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 100:207, 2005
6. Kahn MF, Hayem F, Hayem G, et al: Is diffuse sclerosing osteomyelitis of the mandible part of the synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO) syndrome? Analysis of seven cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 78:594, 1994
7. Utumi ER, Sales MAO, Shinohara EH, et al: SAPHO syndrome with temporomandibular joint ankylosis: Clinical, radiological, and therapeutical correlations. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 105:e67, 2008
8. Jansson A, Renner ED, Ramser J, et al: Classification of non-bacterial osteitis. *Rheumatology* 46:154, 2007
9. Girschick HJ, Raab P, Surbaum S, et al: Chronic non-bacterial osteomyelitis in children. *Ann Rheum Dis* 64:279, 2005
10. Maugars Y, Berthelot JM, Ducloux JM, et al: SAPHO syndrome: A follow up study of 19 cases with special emphasis on enthesitis involvement. *J Rheumatol* 22:2135, 1995
11. Hayem G, Bouchaud-Chabot A, Benali K, et al: SAPHO syndrome: A long-term follow-up study of 120 cases. *Semin Arthritis Rheum* 29:159, 1999
12. Marsot-Dupuch K, Doyen JE, Grauer WO, et al: SAPHO syndrome of the temporomandibular joint associated with sudden deafness. *AJNR* 20:902, 1999
13. Eyrich GK, Langenegger T, Bruder E, et al: Diffuse chronic sclerosing osteomyelitis and the synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO) syndrome in two sisters. *Int J Oral Maxillofac Surg* 29:49, 2000
14. Suei Y, Taguchi A, Tanimoto K: Diagnostic points and possible origin of osteomyelitis in synovitis, acne, pustulosis, hyperostosis and osteitis (SAPHO) syndrome: A radiographic study of 77 mandibular osteomyelitis cases. *Rheumatology* 42:1398, 2003
15. Kahn MF, Bouvier M, Palazzo E, et al: Sternoclavicular pustulotic osteitis (SAPHO). 20-Year interval between skin and bone lesions. *J Rheumatol* 18:1104, 1991
16. Queiro R, Moreno P, Sarasqueta C, et al: Synovitis-acne-pustulosis-hyperostosis-osteitis syndrome and psoriatic arthritis exhibit a different immunogenetic profile. *Clin Exp Rheumatol* 26:125, 2008
17. Suei Y, Tanimoto K, Miyauchi M, Ishikawa T: Partial resection of the mandible for the treatment of diffuse sclerosing osteomyelitis: Report of four cases. *J Oral Maxillofac Surg* 55:410, 1997
18. Baltensperger M, Gratz K, Bruder E, et al: Is primary chronic osteomyelitis a uniform disease? Proposal of a classification based on a retrospective analysis of patients treated in the past 30 years. *J Craniomaxillofac Surg* 32:43, 2004