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# Diagnosis and classification of mandibular osteomyelitis

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To establish a unified classification system for mandibular osteomyelitis, various diagnostic terms were critically assessed and clinicopathologic findings of the lesions were carefully reviewed. We recommend classifying mandibular osteomyelitis into bacterial osteomyelitis and osteomyelitis associated with the synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome. Other diagnostic terms were excluded because they were not appropriate for classification. Diagnostic criteria for bacterial osteomyelitis are suppuration and osteolytic change. The lesions are easily cured by antibiotic treatments. Mandibular osteomyelitis in SAPHO syndrome is characterized by nonsuppuration and a mixed pattern on radiography, with solid type periosteal reaction, external bone resorption, and bone enlargement. The presence of osteomyelitis in other bones, arthritis, or skin diseases (palmoplantar pustulosis, pustular psoriasis, and acne) strongly suggests this syndrome. Antibiotic therapy is usually ineffective and the symptoms of SAPHO syndrome are often persistent. **(Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2005;100:207-14)**

Two continuing difficulties in the diagnosis and classification of mandibular osteomyelitis have prevented clinicians and researchers from developing an improved understanding of this inflammatory condition. One difficulty is that classification has been inconsistent and differs among the references,[1-6] as shown in Table I. This has resulted in dilemmas when deciding which classification system is most appropriate for planning treatment strategies, training students, and designing clinical research. The second difficulty is that synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome has not been clearly identified in existing classification systems. Mandibular osteomyelitis associated with this syndrome has been confounded with other forms of osteomyelitis of the mandible.[7-9]

In this study we address the difficulties associated with the nomenclature of mandibular osteomyelitis by evaluating the common diagnostic terms and presenting a proposed classification system for mandibular osteomyelitis with characteristic features and criteria for each diagnosis. Osteomyelitis in SAPHO syndrome has been included in this new classification system for mandibular osteomyelitis.

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## EVALUATION OF DIAGNOSTIC TERMS

In this section, we list the commonly used diagnostic terms and their definitions, followed by comments intended to clarify the problematic points in the current usage of diagnostic terms for diagnosis and classification.

### Acute and chronic

*Definitions*

Acute: (1) sharp, poignant; (2) having a short and relatively severe course.

Chronic: persisting over a long period of time.

*Comments*

"Acute" and "chronic" are frequently used to diagnose and classify osteomyelitis lesions. The sudden onset of severe symptoms with suppuration (abscess formation) leads clinicians to a diagnosis of acute suppurative osteomyelitis. If the symptoms continue, the diagnosis is changed to chronic (suppurative) osteomyelitis. Although an exact duration of symptoms

**Table I.** Existing classifications for mandibular osteomyelitis

| |
|---|
| 1: Osteomyelitis |
| Acute phase |
| Chronic phase |
| 2: Suppurative osteomyelitis |
| Chronic sclerosing osteomyelitis |
| focal sclerosing osteomyelitis |
| diffuse sclerosing osteomyelitis |
| Osteomyelitis with periosteitis (periosteitis ossificance) |
| 3: Acute suppurative osteomyelitis |
| Chronic suppurative osteomyelitis |
| Choric focal sclerosing osteomyelitis |
| Chronic diffuse sclerosing osteomyelitis |
| 4: Acute suppurative osteomyelitis |
| Chronic suppurative osteomyelitis |
| Chronic diffuse sclerosing osteomyelitis |
| Chronic osteomyelitis with proliferative periostitis (Garre's osteomyelitis) |
| 5: Acute osteomyelitis |
| Hematogenous osteomyelitis |
| Chronic sclerosing osteomyelitis |
| Garre's osteomyelitis |
| 6: Suppurative osteomyelitis |
| Osteomyelitis with periostitis |
| Tuberculous osteomyelitis |
| Sclerosing osteomyelitis |
| Focal type |
| Diffuse type |

qualifying as chronic has not been defined, several reports have identified lesions as chronic if symptoms continued 1 to 4 months after onset.[10-12] However, lesions with an insidious onset or without suppuration are frequently diagnosed as chronic osteomyelitis or primary chronic osteomyelitis, regardless of the duration of the symptoms. In the published literature, statements such as "chronic osteomyelitis may arise de novo" and "chronic osteomyelitis may arise without a preceding acute stage" appear. In these cases, the term "chronic" is erroneously interpreted and is being used to indicate the mildness of the symptoms rather than the chronicity. Furthermore, symptoms of acute exacerbation in chronic osteomyelitis are identical to those of acute osteomyelitis. "Acute" and "chronic" may thus be convenient and useful to indicate, respectively, the severity and the duration of the symptoms, but they cannot be used to classify osteomyelitis lesions appropriately. The 2 terms are not antonyms: "Acute" means severe and "chronic" indicates long duration.

## Focal and diffuse

*Definitions*

Focal: limited to 1 specific area.

Diffuse: not clearly limited or localized, widely distributed.

*Comments*

Focal sclerosing osteomyelitis (FSO) (also called condensing osteitis) and diffuse sclerosing osteomyelitis (DSO) may be differentiated by the extent of the lesion; FSO is localized and DSO extends diffusely, as the names suggest.[2,5] The 2 conditions, however, are quite different in nature and should not be differentiated on the basis of the extent of the sclerosis. DSO is a true osteomyelitis lesion with repeated pain and swelling, but FSO is merely an endosteal reactive hyperplasia to an infected focus such as periapical or marginal periodontitis. Neither swelling nor pain is observed at the site of FSO. Furthermore, FSO may extend widely (Fig 1). Diagnosis of osteomyelitis on the basis of bone sclerosis is difficult and causes misunderstanding. Infected florid cemento-osseous dysplasia and suppurative osteomyelitis with extensive sclerosis have been misdiagnosed as DSO, and the radiographic similarities between fibrous dysplasia and DSO also have been reported.[13-16]

## Primary and secondary

*Definitions*

Primary: first in order or in time of development.

Secondary: second or inferior in order of time, place, or importance; derived from or consequent to a primary event or thing.

*Comments*

Chronic osteomyelitis is often subdivided into secondary chronic osteomyelitis (SCO) and primary chronic osteomyelitis (PCO), depending on the severity of the initial symptoms.[17,18] SCO is defined as chronic osteomyelitis that develops secondary to acute symptoms and PCO is defined as chronic osteomyelitis that starts insidiously, with no acute phase. It is difficult, however, to differentiate existent lesions according to the severity of the initial symptoms. The borderline between SCO and PCO is vague and cannot be determined objectively. Furthermore, as the terms are currently used, PCO lesions may start with acute/subacute symptoms and SCO may start insidiously. After examination of the reports in the literature,[19-22] we have the impression that the 2 conditions have been and should be defined on the basis of the presence or absence of suppuration, rather than on the basis of the severity of the initial symptoms. Our review of the literature revealed that long-standing osteomyelitis with suppuration is SCO, and that without suppuration is PCO.

## Suppurative

*Definitions*

Suppurative: tending to suppurate; promoting suppuration.

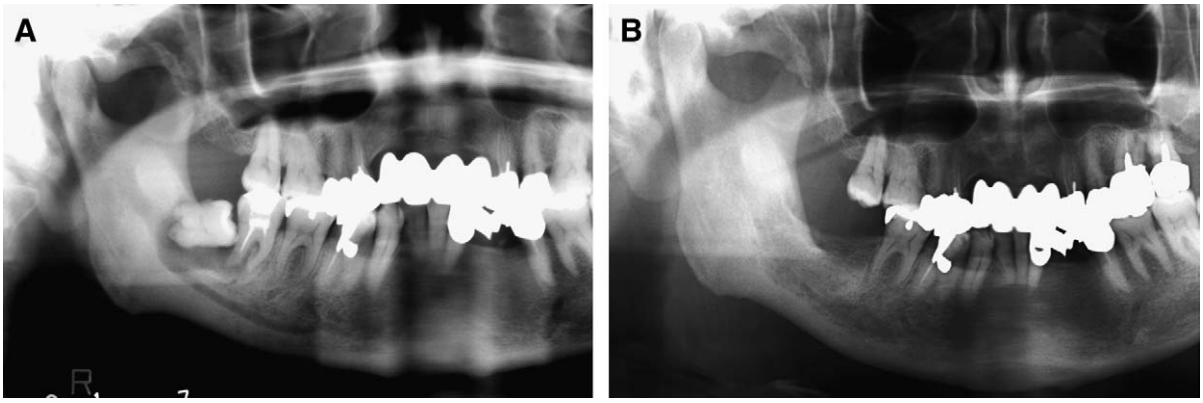


Fig 1. **A,** Focal sclerosing osteomyelitis (condensing osteitis) caused by an infection around the mandibular third molar. Extensive bone sclerosis is observed from the right ramus to the molar region. **B,** Approximately 4 years after the removal of an infected focus and molar teeth. Sclerotic change is largely diminished.

*Comments*

Suppuration is the clinical sign of bacterial infection, so that osteomyelitis with suppuration is usually successfully treated by antibiotic therapy.[11,18] In contrast, in nonsuppurative cases, antibiotic treatment is ineffective and the lesions usually have a protracted course with recurrent exacerbations and remissions.[21,22] It is unlikely that nonsuppurative lesions are caused by bacterial infection.[23,24] Thus, suppurative and nonsuppurative lesions have not only different clinical signs but also different causes and responses to treatment. It may be meaningful to divide osteomyelitis lesions into 2 types, suppurative and nonsuppurative; however, some confusion may arise among clinicians in some cases, because confirmation of the presence of suppuration is difficult in some suppurative lesions and suppuration from a periodontal pocket may be seen in nonsuppurative lesions.

### Garre's osteomyelitis and osteomyelitis with periosteitis (periosteitis ossificans)

These terms are used to identify lesions with a large amount of periosteal reaction, but periosteal reaction can be seen in any type of osteomyelitis lesion; the amount or periosteal reaction depends on the activity of the osteoblastic cells in the periosteum. Thus, several separate diagnostic entities are included in Garre's osteomyelitis and in periosteitis ossificans.[25] Furthermore, Garre's work was done before the invention of radiography and Garre himself never used his name as a diagnostic term.[26]

We conclude that the terms acute and chronic, focal and diffuse, sclerosing, primary and secondary, suppurative, and periosteitis are not appropriate for the diagnosis and classification of mandibular osteomyelitis.

## PROPOSED CLASSIFICATION FOR MANDIBULAR OSTEOMYELITIS

Based on the probable cause, the presence or absence of suppuration, the radiographic and histologic findings, the response to antibiotic therapy, the prognosis, and the complications, mandibular osteomyelitis can be divided into 2 distinct conditions (Table II). Among several diagnostic terms that have been proposed for each condition, we selected "bacterial osteomyelitis" and "osteomyelitis in SAPHO syndrome." The term bacterial osteomyelitis clearly identifies the cause of the disorder. Osteomyelitis in SAPHO syndrome is the only term that represents the nature of this condition, which is a systemic disease characterized by a combination of osteomyelitis, arthritis, and skin diseases (pustulosis, psoriasis, and acne). The characteristics of each condition are described below in detail.

### Bacterial osteomyelitis

*Etiology.* Bacterial osteomyelitis is caused by intraosseous bacterial spread. While most cases are secondary to odontogenic infections, hematogenous osteomyelitis may also occur. The typical pathogenic organisms are *Staphylococcus* species, *Peptostreptococcus* species, and *Pseudomonas aeruginosa*, among others. Less common causes, including fungal infections, mycobacterial infections, syphilis, and actinomycosis, must also be considered.[5,27,28] The condition may be subclassified, based on the causative organisms.

*Clinical features.* The characteristic findings in bacterial osteomyelitis are pain, swelling, and suppuration (from the fistular tract). The symptoms may be severe or mild, and there may be a mixture of severities in any given case. The lesions may start acutely or insidiously, and acute exacerbations may occur

**Table II.** Proposed classification and clinicopathologic findings of mandibular osteomyelitis

| | *Mandibular osteomyelitis* | |
|---|---|---|
| | *Bacterial osteomyelitis* | *Osteomyelitis in SAPHO syndrome* |
| Synonyms | (acute) suppurative ost.<br>(chronic) suppurative ost.<br>secondary chronic ost. | (chronic) diffuse sclerosing ost.<br>chronic sclerosing ost.<br>primary chronic ost.<br>osteomyelitis sicca<br>chronic sclerosing nonsuppurative ost.<br>chronic recurrent multifocal ost. |
| Cause | bacterial infection | unknown |
| Sex | male predominance | female predominance |
| Pain/swelling | yes | yes |
| Suppuration/abscess formation | yes | no |
| Radiographic findings | osteolytic pattern<br>sequestrum formation<br>lamellated type p.r. | mixed pattern<br>solid type p.r.<br>external bone resorption<br>bone enlargement |
| Histologic finding | inflammation of bone<br>abscess, necrotic tissue<br>sequester formation | inflammation of bone<br>reactive hyperplasia of bone<br>resemblance to fibrous dysplasia |
| Antibiotic therapy | effective | ineffective<br>(antiinflammatory drugs including corticosteroids and pamidronate treatment are recommended) |
| Prognosis | good<br>(cured within 6 months) | Poor<br>(often continues more than 6 months) |
| Complications | none | osteomyelitis/arthritis at the other bones/joints<br>skin diseases (palmoplantar pustulosis, pustular psoriasis, acne) |

*Ost.,* osteomyelitis; *p.r.,* periosteal reaction.

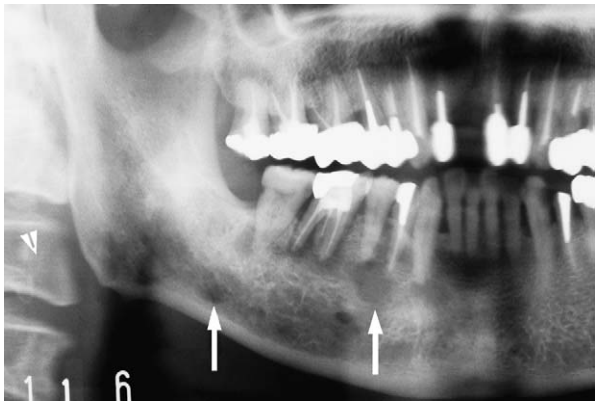

Fig 2. Bacterial osteomyelitis in the right mandible. The margin of the lesion is ill defined, but cortical bone resorption sites are seen with moderately well defined margins (*arrows*).

intermittently in the chronic stage. The degree and duration of the symptoms depend on various factors such as the virulence of the causative organisms, the presence of underlying disease, and the immune status of the host.

*Radiographic features.*[29] Bone resorption is prominent and radiography shows an osteolytic pattern. Sclerotic areas may be seen around the osteolytic area in long-standing lesions or in cases with pre-existing FSO. On plain radiographs, the margin of bone resorption is ill defined, but may be well defined at the site of cortical bone resorption (perforation) (Fig 2). The periosteal reaction is usually lamellated, and appears as a thin, faint, radiopaque line adjacent to, and almost parallel or slightly convex to, the surface of the bone. A radiolucent band separates the new periosteal bone from the bone surface. If the process occurs repeatedly, an "onionskin" appearance is observed, caused by the presence of multiple lamellae. On CT images, the pattern of osteolytic change in the bone is continuous, not scattered, and spreads to the periosteum through sites of perforation of the cortical bone (cloacae) (Fig 3). The margin of the zone of cortical bone resorption is moderately well defined and the remaining cortical bone appears to be of almost normal density. Periosteal reaction may be seen around the site of perforation (Fig 4).

*Histologic features.* On histology, infected bone is replaced by inflammatory components including polymorphonuclear leukocytes, lymphocytes, plasma cells, and pus (abscess). The osteoblasts are destroyed or absent, and the bone trabeculae are resorbed by osteoclasts. The area of suppuration is composed of disintegrating polymorphonuclear leukocytes and necrotic tissues.[5]

*Treatment and prognosis.* Antibiotic treatment in combination with surgical procedures is effective. In most cases, the symptoms subside and disappear

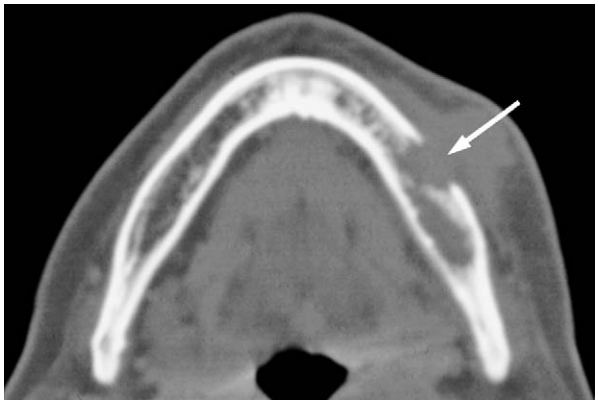

Fig 3. An axial CT image of a bacterial osteomyelitis case shows cortical bone perforation (*arrow*). The remaining cortical bone has almost normal density.

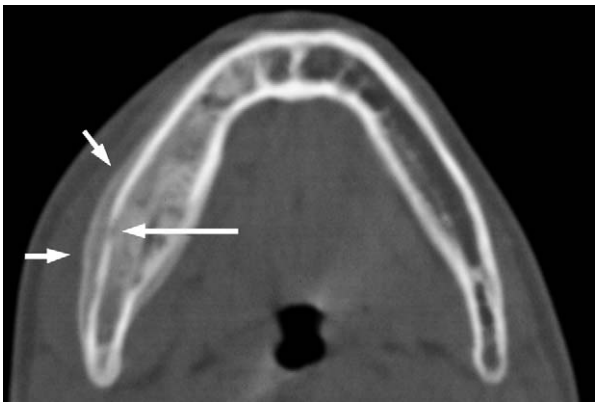

Fig 4. An axial CT image of bacterial osteomyelitis reveals lamellated periosteal reaction (*short arrows*) on the almost normal cortical bone around the perforated site (*long arrow*).

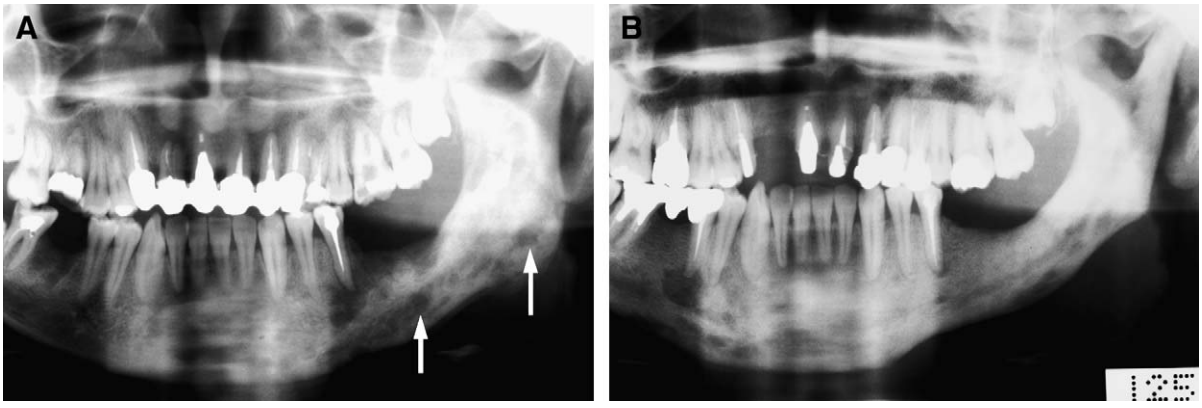


Fig 5. **A,** Panoramic radiograph of left mandible with osteomyelitis in SAPHO syndrome. Osteolytic areas (*arrows*) are observed in areas with severe sclerotic changes (mixed pattern). **B,** More than 5 years after the radiographs in *A* were taken, the left mandibular bone volume has been reduced by bone resorption on external bone surfaces and osteosclerotic changes are prominent.

completely within 3 months; recurrence is rare.[11,18] After effective treatment, the radiographic abnormalities gradually return to a normal appearance.[30]

*Diagnosis.* Pain, swelling, suppuration, and osteolytic changes on radiography are the diagnostic criteria for bacterial osteomyelitis. Histopathologic examination is not always done because these characteristic findings are readily recognizable and the response to antibiotic treatments is confirmatory.[11,27] In some cases, the limited amount of abscess formation makes it difficult to differentiate this condition from nonsuppurative lesions (osteomyelitis in SAPHO syndrome), but a rapid response to antibiotic treatment will indicate the appropriate diagnosis.

## Osteomyelitis in SAPHO syndrome

*Etiology.* Some authors have suggested that a bacterial infection causes osteomyelitis in SAPHO syndrome because of the positive results on bacterial cultures. *Propionibacterium acnes*, *Peptostreptococcus intermedius*, *Actinomyces* species, and *Eikenella corrodens* have been reported to be cultured from cases of osteomyelitis in SAPHO syndrome.[19,22] However, the possibility of contamination of the sample cannot be denied, and the poor results obtained with antibiotic treatment, and the effectiveness of corticosteroids for palliation without simultaneous administration of antibiotics, indicate the possibility of a noninfectious origin.[7,22] One study has suggested that a chronic tendoperiostitis is the cause.[23]

*Clinical features.* Pain and swelling are seen, but suppuration is never found in this condition. The symptoms may start gradually or suddenly and persist for a long time, with repeated exacerbations and remissions. The lesions are often extensive: Condylar process involvement is not rare and the entire mandible may be involved.[23,31]

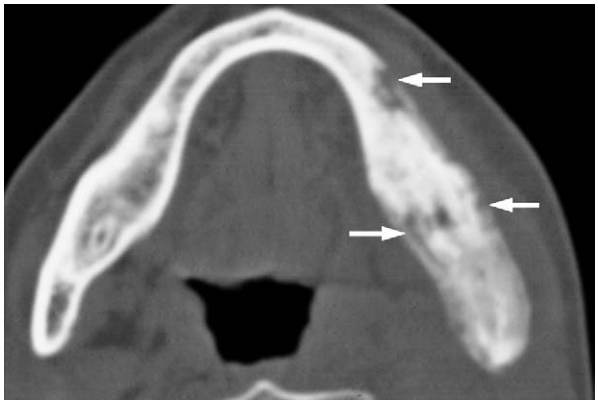

Fig 6. An axial CT image of mandibular osteomyelitis in SAPHO syndrome. Osteolytic areas (*arrows*) are scattered in the lesion. Solid periosteal reaction is seen.

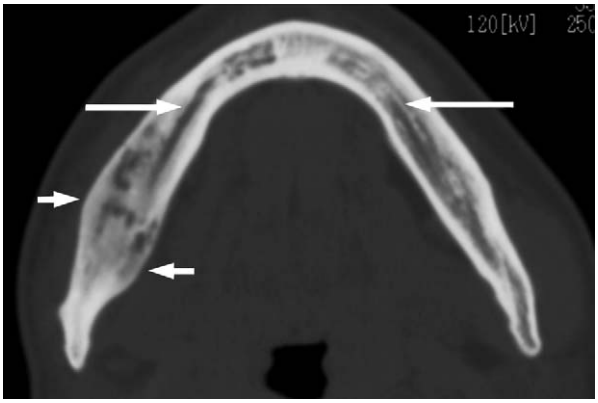


Fig 7. An axial CT image of mandibular osteomyelitis in SAPHO syndrome at the level of mandibular canals (*long arrows*) shows the enlargement of the left mandible (*short arrows*).

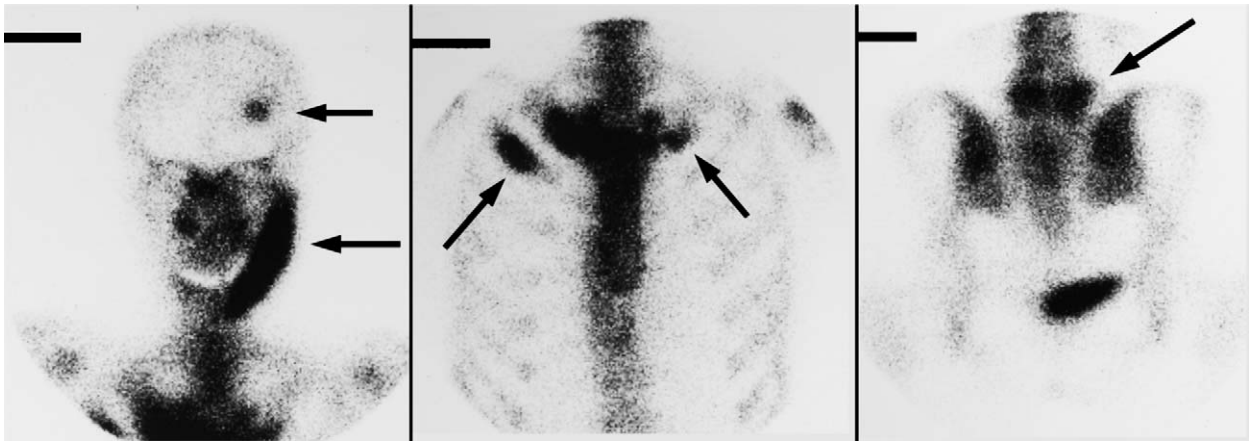

Fig 8. A technetium-99m bone scan of a patient with SAPHO demonstrates the abnormal accumulation in the frontal bone of the skull, left mandible, 1st and 2nd right ribs, 1st left rib, and 5th lumbar vertebra. There were no overt symptoms in the region of the frontal bone or the 5th lumbar vertebra.

*Radiographic features.*[32] The radiographic findings are complex and variable, and no consistent relationship has been confirmed among osteolysis, osteosclerosis, and periosteal reaction. Because of active bone remodeling, deformation of the condylar process or displacement of the mandibular canal may be seen.[23,33] On plain radiographs, progressive bone sclerosis with scattered osteolyses (mixed type) is a common finding (Fig 5, *A*). However, bone resorption may be prominent at the early stage or when symptoms flare up, whereas only the sclerotic changes may be observed during the more quiescent chronic stage. The lesions are associated with solid periosteal reaction. Cortical bone resorption is diffuse and extensive, and may occur externally. Bone resorption on the external bone surface is a pathognomonic finding and is usually confirmed on panoramic radiographs from the inferior border of the mandibular body to the posterior border of the mandibular ramus. In advanced cases, a remarkable reduction of mandibular bone volume is observed (Fig 5, *B*). On CT images, the density of the partially resorbed cortical bone may be identical to that of the sclerotic cancellous bone and the periosteal reaction. Low-density areas (osteolytic lesions) may be scattered within these otherwise uniformly dense regions (Fig 6). In some cases, the original cortex is almost or entirely disrupted and a cortex-like radiopaque zone, newly formed by periosteal bone deposition, is observed external to the site of the original cortex and the mandible appears enlarged (bone enlargement) (Fig 7).

*Histologic features.* Bone specimens show reactive bone lesions characterized by remodeling of the cortical and subcortical bone and the formation of subperiosteal bone. A striking resemblance to fibrous dysplasia has

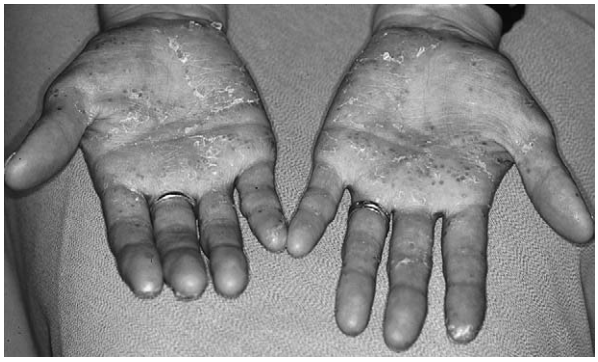

Fig 9. Palmoplantar pustulosis in a patient with SAPHO syndrome. Many pustules and hyperkeratotic changes are seen on both palms.

been reported owing to the absence of signs of inflammatory change. Inflammatory cells, if present, are found in the larger cortical resorption defects and the immediate subcortical area. Microabscess formation may be confirmed, but areas of necrosis have rarely been reported.[21,34]

*Treatment and prognosis.* Well established therapeutic procedures for treatment of infection, such as antibiotic administration, hyperbaric oxygen, curettage, saucerization, decortication, and partial resection of the affected bones, have very limited efficacy and cannot cure the disease.[31] Long-term administration of macrolides[35] and muscle relaxation treatment[23] have been reported to be effective by some authors. Conservative treatment and long-term treatment with analgesics and antiinflammatory drugs have been recommended, and recently treatment with pamidronate has been reported to be effective.[7,22,36,37]

*Complications.* In SAPHO syndrome patients, multifocal osteomyelitis, arthritis, and chronic skin disease (palmoplantar pustulosis, pustular psoriasis, or acne) occur (Figs 8 and 9).[7] However, not all of these manifestations necessarily occur and each may be seen at a different time. Only a single bone (mandible) may be affected, and some bone and joint lesions may show no overt symptoms. Previous studies have reported the occurrence of long intervals between the development of skin and bone lesions and the presence of asymptomatic bone lesions detected only by bone scintigraphy.[38,39] Careful history taking is essential and bone scintigraphy is useful for finding silent bone and joint lesions.

*Diagnosis.* The diagnostic criteria for SAPHO syndrome are (1) chronic recurrent multifocal osteomyelitis, (2) acute, subacute, or chronic arthritis with palmoplantar pustulosis, pustular psoriasis, or severe acne or (3) severe osteitis with palmoplantar pustulosis, pustular psoriasis, or severe acne.[7] Therefore, nonsuppurative osteomyelitis of the mandible with osteomyelitis in other bones, palmoplantar pustulosis, pustular psoriasis, or severe acne can be easily diagnosed as SAPHO syndrome. However, in patients with mandibular lesions only, the differential diagnosis is difficult. Careful clinical observation is required because histologic examination and laboratory tests indicate nonspecific inflammation. Confirmation of the lack of suppuration is essential, and radiographic examination is considered to be the most useful procedure for obtaining an early diagnosis. Bone resorption on external bone surfaces and bone enlargement are pathognomonic, and a mixed radiographic pattern and solid periosteal reaction suggest SAPHO syndrome. In patients with long-standing lesions, a history of cyclic episodes of pain and swelling, long-term antibiotic medication, or repeated surgery indicate the possibility of SAPHO syndrome. If the symptoms continue for several months in spite of antibiotic treatment, osteomyelitis in SAPHO syndrome is highly suspected.

## CONCLUSION

We recommend that mandibular osteomyelitis lesions should be classified into bacterial osteomyelitis and osteomyelitis in synovitis, acne, pustulosis, hyperostosis, and osteitis syndrome (SAPHO syndrome). Diagnostic features of bacterial osteomyelitis are suppuration and osteolytic radiographic change with lamellar type periosteal reaction. The lesions are easily cured by antibiotic treatments. 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. The presence of osteomyelitis in other bones, arthritis, or skin diseases (palmoplantar pustulosis, pustular psoriasis, and acne) strongly suggests this syndrome. Antibiotic therapy is usually ineffective and the symptoms of SAPHO syndrome are often persistent. Our new classification system was decided by the critical assessment of various diagnostic terms and careful review of the clinicopathologic findings of the lesions. We consider that this classification should be used for planning treatment strategies, student education, and clinical research of mandibular osteomyelitis.

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