Avascular Necrosis of the Mandibular Condyle Associated with Intensive Steroid Therapy : Case Report

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Abstract

Avascular necrosis or osteonecrosis has been discussed as a possible cause of condylar degeneration and pain. Avascular necrosis is a degenerative disease originates from diminished blood flow in the bone marrow. Avascular necrosis is seen in relationship with idiopathic, corticosteroids, alcoholism, sickle cell disease, pregnancy, and Caisson's disease. Corticosteroid has been suggested to be an etiologic factor affecting bone organization, fat metabolism, and blood vessel. Indeed, corticosteroid can affect the bilateral joints of the shoulder, hip, and knee. However, the occurrence of the avascular necrosis of in the temporomandibular joint alone has not been reported. The clinical, laboratory, radiographic, and imagings features of a case of the condylar process of the mandible are presented.

Introduction

Avascular necrosis (AVN) or osteonecrosis is a degenerative disease originates from diminished blood flow in the bone marrow. The risk factors for avascularization have been thought to include circulatory obstruction due to hyperplasia of the membrane in a blood vessel, stricture of a branch, and vein abnormality, but the primary causes are not known[1,2]. AVN has been reported to occur secondary to protracted steroid therapy for diseases such as systemic lupus erythematosus (SLE), rheumatoid arthritis, and asthma, and in post-renal transplantation[2,3], and corticosteroid has been suggested to be an etiologic factor affecting bone organization, fat metabolism, and blood vessel[4]. Combination chemotherapy that includes high-dose steroid for malignant lymphoma can affect the bilateral joints of the shoulder, hip, and knee[2,5,6]. However, the occurrence AVN of in the temporomandibular joint (TMJ) alone has not been reported.

We report a case of AVN of the TMJ alone, accompanied by internal derangement and open bite, occurring after use of steroid.

Case Report

In October, 1994, a 37-year-old woman who had no history of trauma or alcoholism visited our clinic with the complaint of trouble in eating and extreme open bite. She had a two-year history of bilateral TMJ reciprocal clicking and slight pain. At the initial examination the interincisal distance during maximal opening (IMO) measured 40 mm without pain or sound, and she showed circular open bite, with occlusion of only bilateral second molar teeth, but attrition was found in all teeth of the maxilla and mandible (Fig. 1). There were no abnormalities in laboratory findings.

She had been surgically treated for thymoma in 1978, and had required the administration of steroid due to its recurrence and the development of non-Hodgkin's lymphoma in 1991. Combination chemotherapy included CABVO-VIP (pirarubicin 30 mg/day, cyclophosphamide 800 mg/day, etoposide 100 mg/day, ifosfamide 1500 mg/day, vincristine sulfate 1.5 mg/day, methotrexate 200 mg/day, and peplomycin sulfate 15 mg/day) two courses of administration together with pred-nisolone (40 mg/day : the first treatment from June 21 to July 12, 1993, and the 2nd treatment from August 19 to September 15, 1993 ; total, 2000 mg). The serum total cholesterol (T-Cho) value was 3.34 mmol/L just before the 2nd treatment (on 16 Aug, 1993) but was 5.38 mmol/L 4 weeks later (on 13 Sep, 1993) (Table 1).

She was conscious of severe pain differing from the usual pain at the bilateral TMJ and trismus
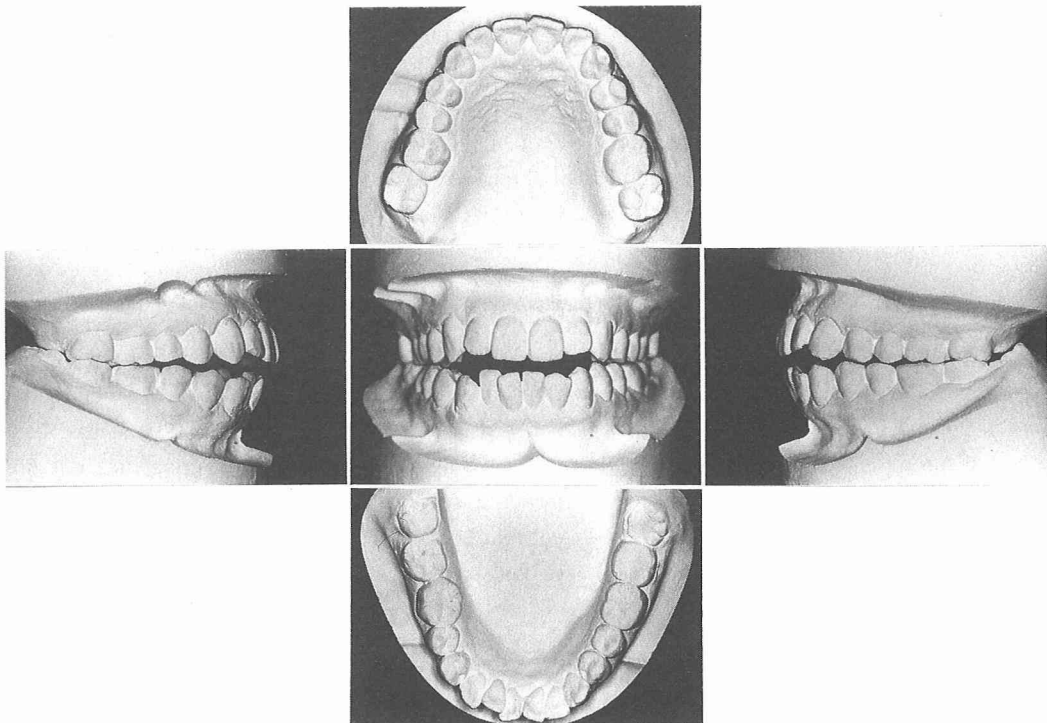
Fig. 1. On the plaster model occlusion was seen of the bilateral second molars alone, but attrition was seen in all incisors, canines, premolars and molars.

Table 1. Serum enzyme activities

Serum	1993							1994		1995		
(normal range)	14June	14July	16Aug	13Sept	18Oct	29Nov	27Dec	10Jan	24Oct	21Nov	23Jan	20Mar
T-Cho (3.36-5.95 mmol/L)	4.01	4.63	3.34	5.38	4.47	4.32	4.42	4.97	4.37	4.47	4.60	4.91
ALP (1.6-4.7 μkat/L)	2.9	2.2	2.9	2.6	2.9	4.2	4.9	4.4	3.4	2.9	6.3	4.6

T-Cho=total-cholesterole ; ALP=alkaline phosphataze.

in October, 1993. The serum alkaline phosphatase (ALP) was 4.2 μkat/L on November 29, 1993. The pain of the bilateral TMJ persisted for two months and resolved spontaneously in January, 1994. However, she had the sensation of abnormal occlusion, and the circular open bite was confirmed. Other data in the examinations of liver and kidney function were normal.

Radiography disclosed flattening and sclerosis of bilateral heads of the condylar processes (Fig. 2, A and B), but the TMJ showed normal movement upon mouth opening and closing. On the sagittal and coronal T1-weighted magnetic resonance (MR) images, the head of the right condylar process showed low signal intensity extending to the mandibular notch, and that on the left showed an high signal intensity surrounded by alow intensity area. The T1-weighted image sagittal MR image revealed anterior disc displacement without reduction (ADWR) on opening and closing of the mouth and flattening of the head of the condylar process on both sides (Fig. 3 and 4). The bone scintigraphic image showed uptake at bilateral TMJ (Figs. 5, 6, A and B), but not at other joints of bones. Axial, sagittal and coronal computed tomographic scans disclosed sclerotic change of the right condylar head (Figs. 7, A, 8, A and B), and osteolytic cortical bone was seen at the left condylar head. Coronal computed tomography (CT) revealed extreme flattening of bilateral condylar heads.

Stabilizing splint and exercise of the TMJ were applied. Six months later, the sagittal and coronal T1-weighted MR image still showed low signal intensity of the right condylar head (Figs. 9, A and 10, A), whereas it showed improvement of the signal intensity of the bilateral condylar heads (Figs. 9 B and 10 B). The morphological change of ADWR on occlusion was no longer seen. The serum ALP isozyme level was 274 IU/L five months after the first MR imaging examination. Progression of occlusion was not seen.

Discussion

MR and bone scintigraphic imaging are useful for the diagnosis of AVN[6~10]. Signal hypointensity appears to reflect restorative organization following responsiveness around the ischemic region[7]. Bone scintigraphy demonstrates osteonecrosis and is useful for the assessment of bone metabolism in the early stage[11]. When uptake is seen on the bone scintigraphic image in the region of MR signal hypointensity, granulation or fibrous tissues formed between the areas of osteonecrosis and of normal tissues develop to the extent that bone sclerosis and necrotic debris are present in some cases, and granulation or fibrous tissues have probably been replaced by normal fat marrow in other cases[8].

In our patient, the T1-weighted MR image disclosed a low-signal area in the region extending from the right condylar head to the mandiblar notch, but a high-signal area surrounded by low-signal area was seen on the left side. The abnormal accumulation in bilateral heads of the condylar processes observed in bone scintigraphy suggested active AVN. The CT scans showed necrosis with extreme flattening of the bilateral condyles and also sclerosis in the right condyle.

Fig. 2. Plain radiograph revealed flattening and bone sclerosis of the bilateral mandibular condyles (black arrow).

Typically, idiopathic AVN develops gradually from osteonecrosis to osteoarthrosis. On the other hand, AVN derived from steroid use is confirmed by MRI within the first 12 months of the withdrawal of steroid, and the improvement is seen on MRI after more than 12 months[12,13]. In our patient the delay of the severe pain and the open bite, as well as the improvement of the signal seen at the second MR imaging study, occurred 20 months after the discontinuation of steroid therapy, suggesting that it is likely that use of steroid was responsible for these signs and symptoms, which fulfilled the criteria noted by Fisher[12] for AVN associated with steroid use.

Following combination chemotherapy for lymphoma, AVN has been reported in 0.12—10% of the patients[5~7,14], and corticosteroids in combination chemotherapy have been implicated as a major aetiological factor in the pathogenesis of AVN[6]. Bilateral AVN has been reported to occur in 50 —80% of patients, although the symptoms at onset are usully bilaterally asymmetrical[8,14]. It is commonly believed that a predilection for AVN of the femoral head, the distal femoral condyles, humeral head, and talus in patients under treatment with steroid treatment may be the effect of metabolic factors involving lipid metabolism[11,15,16], local characteristic factors affecting the blood supply to the affected head, and mechanical stress the weight-bearing condyle[17].

Abeles[4] found 17 patients with AVN (4.7%) among 365 SLE patients who had steroid therapy ; the affected patients had been taking prednisolone at more than 40 mg/day. Sakamoto et al.[18] noted that the 40 patients with AVN among 65 patients with collagen disease who had been taking steroid therapy at 30—50 mg/day showed serum T-Cho activity of more than 2.59 mmol/L 4 weeks after the
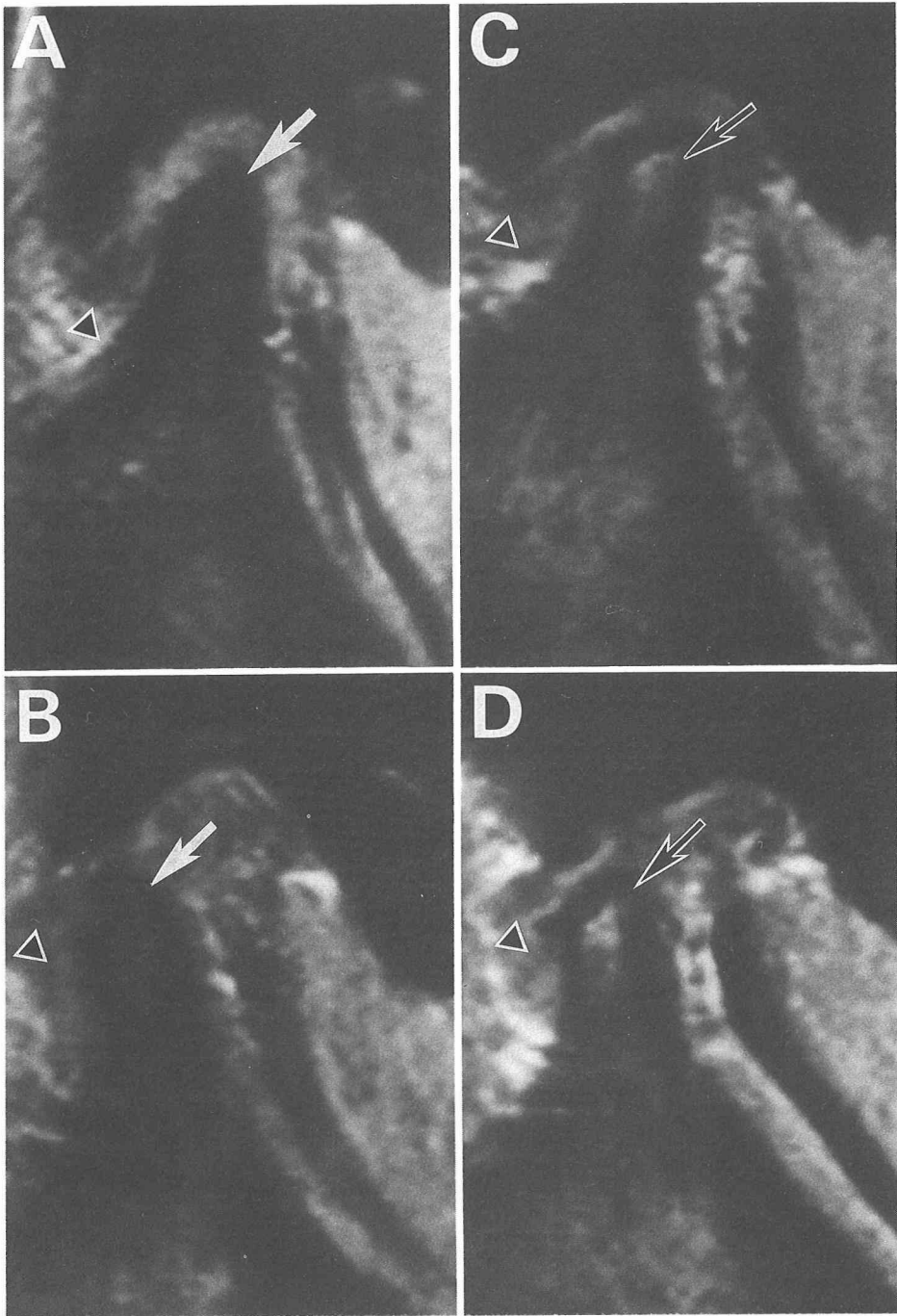
Fig. 3. Sagittal T1-weighted images (FE 30/13, $\theta = 30°$). Bilateral anterior disc displacement was seen in opening and closing mouth (black triangle), and flattening of the condyle (white arrow and black arrow) was also seen. A, Right TMJ on mouth closing. B, Right TMJ on mouth opening. A and B, Low signal intensity was observed in the area between the condylar head (white arrow) and mandibular notch. C, Left TMJ on mouth closing. D, Left TMJ on mouth opening. C and D, The left mandibular condyle showed an area of high signal intensity surrounded by a low signal intensity area (black arrow).
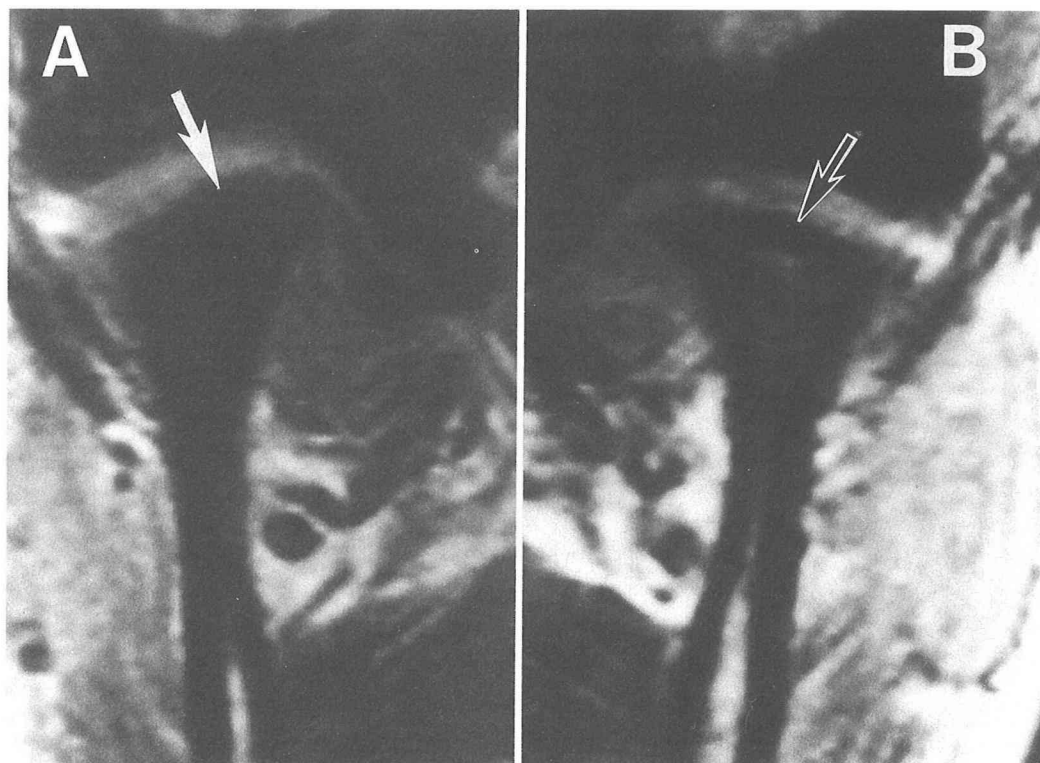
Fig. 4. Coronal T1-weighted images (FE 30/13, $\theta = 30°$). A, Right TMJ on mouth closing. Low signal intensity was seen in the condylar head (white arrow). B, Left TMJ on mouth closing. A high-signal area surrounded by a low-signal area was observed (black arrow).

start of steroid therapy. Furthermore, they found that the incidence of AVN in multiple joints increased with the T-Cho activity. The T-Cho level of 2.04 mmol/L 4 weeks after the start of the second steroid therapy regimen in the present patient might have been a reason that the TMJ alone, and not multiple joints, was affected.

The mandibular condyle is supplied by very active posterior blood vessles[19], whereas that of the femoral and humeral heads consists of two end arteries to the superior and inferior retinaculum that arise from the circumflex vessels[2,20]. An ADWR of the TMJ is unlikely to compromise the vascularity sufficiently to cause necrosis because of the rich posterior blood supply[21]. This may be a reason that the mandibular condyle is rarely affected. The use of steroid might have induced the disruption of the arteries in our patient. Chuong[15], Arlet[17], and Warner et al.[22] noted that interference with the venous outflow from the marrow space may be the primary factor in cases of nontraumatic AVN due to decreased venous outflow and gradually increased intraosseous pressure. Schellhas[23] found that ADWR was demonstrated on T1-weighted images as a low signal intensity area in 31 (91.2%) of 34 patients diagnosed with AVN of the mandibular condyle examined using MR imaging. He speculated that the AVN had occurred due to disk pressure on the blood vessel supplying the mandibular condyle.

ADWR was seen, using arthrography or MR imagings, in 0—4% of healthy volunteers with asymptomatic and clinically normal TMJ[24~26], and in 32—38% of indviduals with TMJ signs and symptoms[26,27]. Therefore, if ADWR is an etiologic factor in AVN of the mandibular condyle,
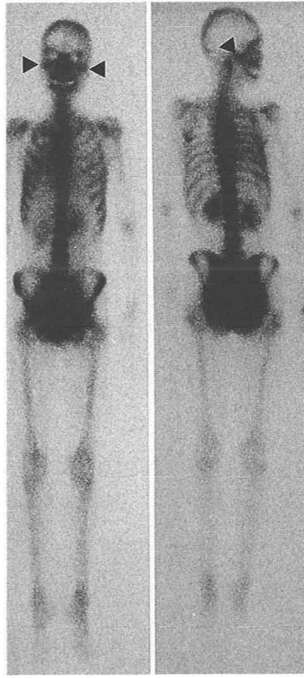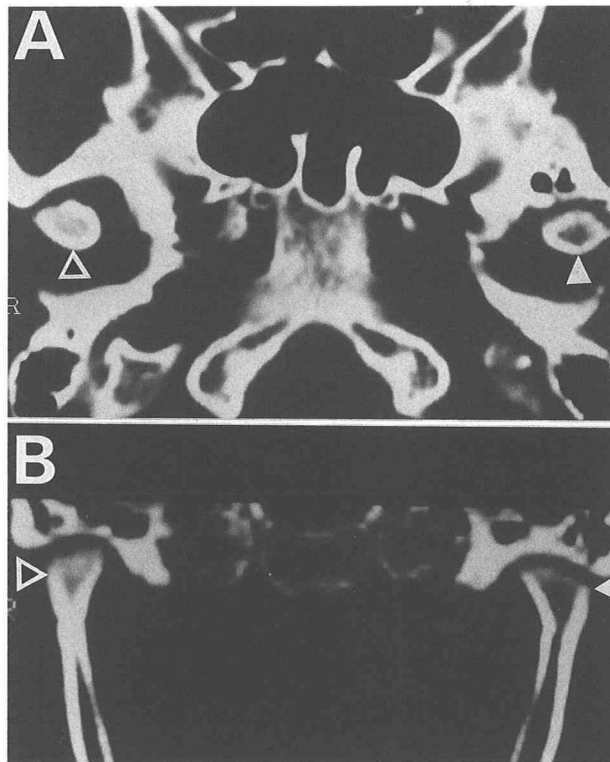
Fig. 5. Bone scintigraphy showed uptake in the bilateral TMJ alone (black triangle).
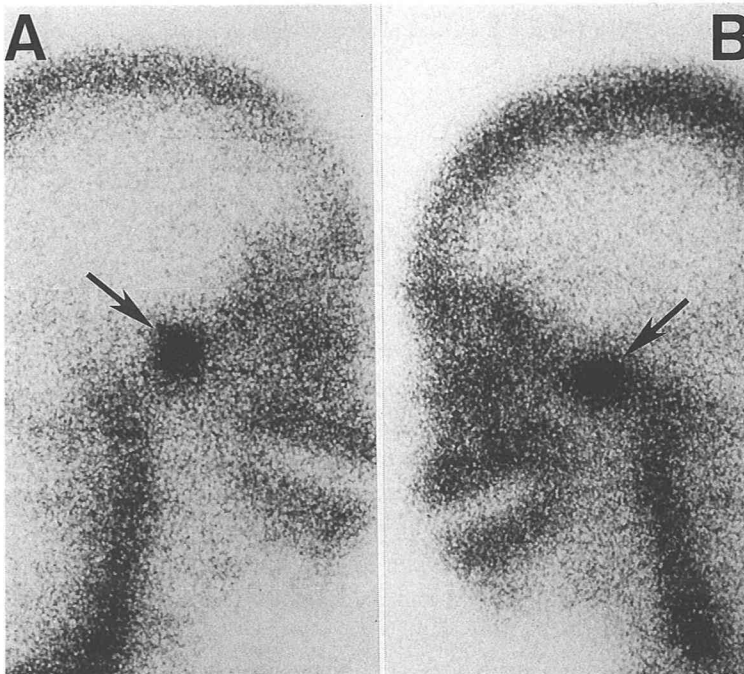
Fig. 6. Bone scintigraphy demonstrates uptake in bilateral TMJ (black arrows).
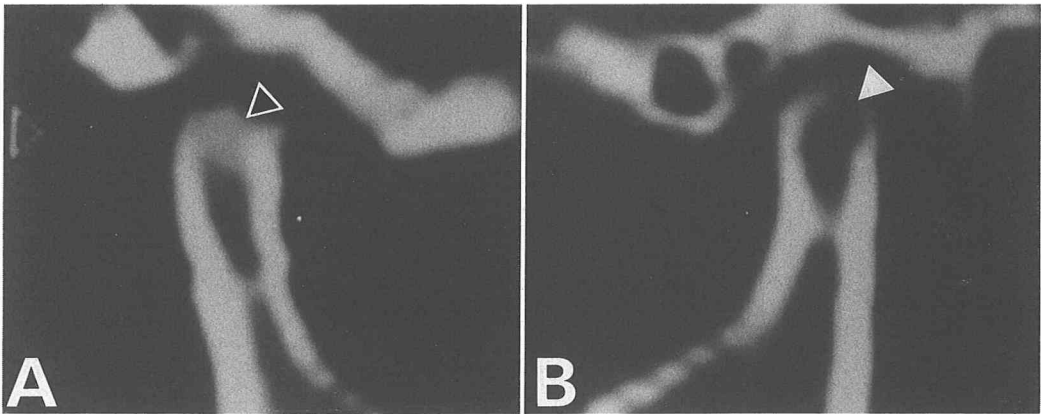
Fig. 7. Sagittal CT scans. A, The right mandibular condyle shows sclerotic change of the bone (black triangle). B, The left mandibular condyle shows cortical osteolysis (white triangle).

**Fig. 8.** CT scans showing extremely flattened bilateral mandibular condyles. A, Axial CT scan disclosed sclerotic change of the right mandibular condyle (black triangle), and cortical osteolysis of the left condyle (white triangle). B, Coronal CT scan revealed sclerotic change of the right mandibular condyle (black triangle), and on the left side cortical osteolysis (white triangle) is seen.
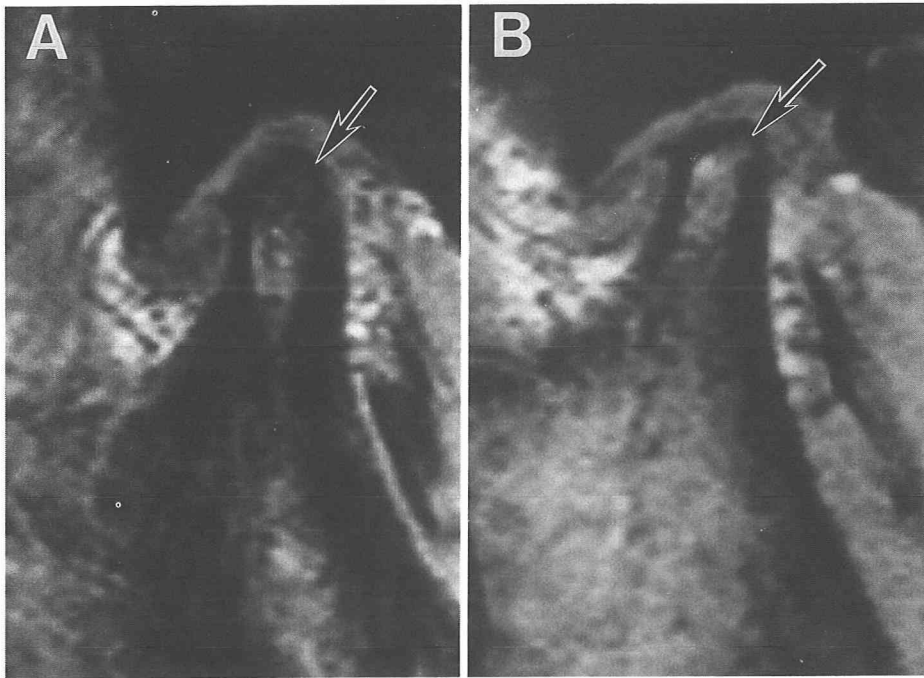
Fig. 9. A, Right TMJ on mouth closing. B, Left TMJ on mouth closing. Six months after the first examination, sagittal T1-weighted MR images (FE 30/13, $\theta = 30°$) revealed improvement of the low signal intensity in the bilateral mandibular condyles (black arrow). Anterior disc displacement on mouth closing and morphological change were not seen.
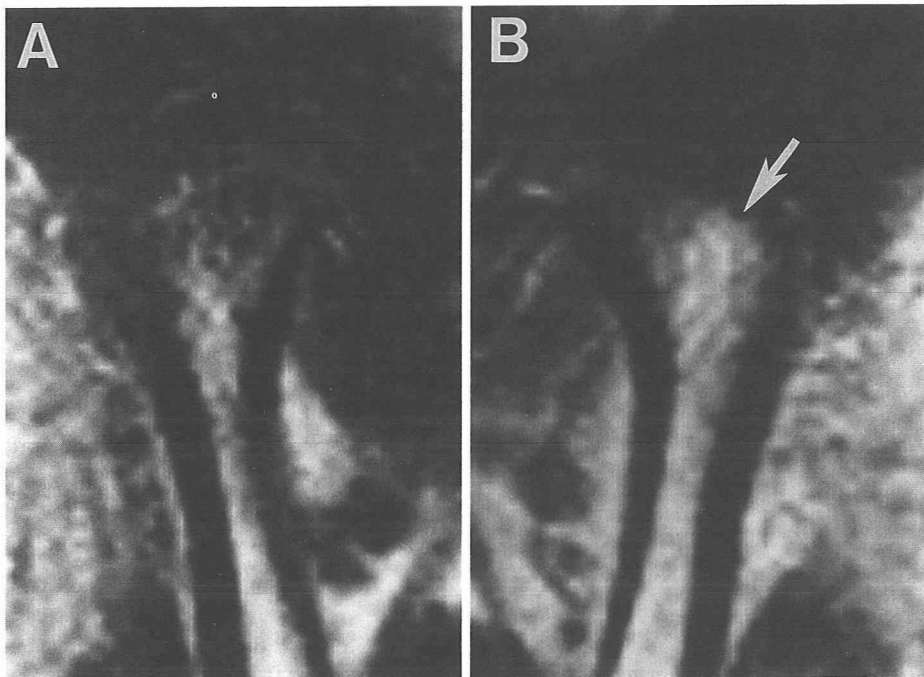
Fig. 10. A, Right TMJ on mouth closing, B, Left TMJ on mouth closing. Six months after the first examination, coronal T1-weighted MR images (FE 30/13, $\theta = 30°$) disclosed improvement of the low signal intensity in the bilateral mandibular condyles (white arrow).

indviduals with TMJ signs and symptoms may be at increased risk of developing AVN of the mandibular condyle associated with steroid treatment.

Smith et al.[28] reported that the TMJ is aload-bearing joint over the normal functional range of bite force positions and angles. The posterior band of the meniscus, which is the relaxation region, and the anterior part of the mandibular condylar head bear the load of the bite force[28]. In the patient with ADWR, the relaxation region has failed and the superior lamina of bilaminar zone which could not adapt to relaxation sustain the load, resulting in increase of the mechanical stress on the anterior portions of the mandibular condylar heads[26,28].

AVN causes extreme pain, which occurs approximately 1 month after combination chemotherapy with steroid, and the pain is known to be originated from microfracture following the treatment[11,15,20]. Microfracture and depression of the condylar head may shorten the ramus of the mandible followed by open bite. In our patient the serum ALP isoenzyme level was 4.2 μkat/L when severe pain was present (in November, 1993) and 6.3 μkat/L during the interval between the first and the second MR imaging examinations (in January, 1995), suggesting that there might have been change of the bone formation activity.

The clinical event of AVN of the condylar process of the mandible may be important because the condylar head is a load-bearing joint subject to mechanical stress over the normal functional range of the bite force, and because AVN is associated with progressive ischemia with ADWR.

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抄録：ステロイド使用による下顎頭骨壊死の1例

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特発性骨壊死は骨髄への血流低下に起因する退行性病変であり，一般的に関節部の変形と疼痛を自覚した時点において発症と見なされ，特発性のほかステロイド・アルコール・鎌形細胞性貧血・妊娠・潜水病とも関係があるとされている．

　阻血状態を招きやすい局所要因としては，栄養動脈の血管内膜の肥厚，閉塞あるいは血栓の形成などの変化や分枝の狭窄，また静脈血流異常による末梢循環障害などの関与が考えられているが，一次的原因であるかは不明である．一方，副腎皮質ホルモンは骨組織自体への直接作用や全身の脂質代謝異常，また血管系にも変化を生じさせることから病因の一つとして考えられており，副腎皮質ホルモン使用後の骨壊死はステロイド性として狭義の特発性骨壊死とは区別されている．実際，ステロイド使用による骨壊死は，肩・股・膝などの多関節部に両側性に好発するとされているが，顎関節部のみに発症した症例は報告されていない．顎関節部のみに発症した理由としては，MRI所見により復位しない関節円板の著明な前方転位が両側性にみられたことより末梢循環障害などの関与と副腎皮質ホルモン投与との関係によるものと考えられた．われわれは，開咬を主訴として来院し，現病歴，画像所見および臨床検査所見から顎関節内障を伴ったステロイド性下顎頭骨壊死と思われた1例を経験したので報告した．