

# Chronic Recurrent Multifocal Osteomyelitis Involving The Skull

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## Abstract

We report a rare case of chronic recurrent multifocal osteomyelitis of the skull. A 21-year-old man presented with headache and fever. Skull radiography revealed hypertransradiancy with multiple round marginal irregular osteoclasia. Computed tomography (CT) scan showed a thick skull, heterogeneous diploe, and a lot of hardened macular shadow; however, the underlying brain tissue was normal. <sup>99m</sup>Tc-methylene diphosphonate (MDP) bone scintigraphy showed high activity in the skull and tibia. During surgery for this bone lesion, inflammatory changes were noted; however, they were not neoplastic. Chronic recurrent multifocal osteomyelitis of the skull bone is extremely rare and we could find only 1 reported case in the literature.

## INTRODUCTION

Chronic recurrent multifocal osteomyelitis (CRMO) is a type of osteomyelitis and mainly occurs in children or young adults. It affects the metaphyses of long bones such as tibia, femur, fibula, and collar bone, and radiography shows multiple synchronous or metachronous lesions. The prognosis of this condition is excellent, but its cause is unknown [1]. Herein, we report a rare case of CRMO in which the skull was involved.

## CASE REPORT

**History and Examination:** A 21-year-old man visited The neighboring hospital for throbbing headache and fever. Because a blood test showed high levels of inflammatory markers, he visited the hospital for receiving a detailed physical examination. His intracranial pressure increased, causing abducens nerve paralysis, and he was admitted to the Department of Neurology of the Kitasato University Hospital. The findings on admission were mild papilledema, abducens nerve paralysis, and a stiff neck.

Lumbar puncture showed increased monocyte count and cerebrospinal fluid pressure. Culture of the spinal fluid revealed no abnormal findings. The patient was hospitalized in our department, and biopsy of the skull was performed in order to obtain a definite diagnosis.

**Laboratory and Radiographic Findings:** The white blood cell count was 14800/mL, with 82% neutrophils and 11% lymphocytes. The erythrocyte sedimentation rate was 44

mm/h and C-reactive protein level was 1.9 mg/dL. The antinuclear antibody test was positive, and blood cultures were negative.

Radiography of the skull showed hypertransradiancy with multiple round marginal irregular osteoclasia (Fig. 1). Head computed tomography (CT) scan revealed a thick skull, heterogeneous diploe, and a lot of hardened macular shadow. No intracranial lesions were found. Magnetic resonance imaging (MRI) scans revealed diploe and thick skull with outer table erosion appearing as “worm-eaten” spots (Fig. 2). <sup>99m</sup>Tc-methylene diphosphonate (MDP) bone scintigraphy showed heterogeneous radioisotope (RI) accumulation in the skull and abnormal accumulation of RIs in the diaphysis and the proximal metaphysis of the tibia (Fig. 3). Gallium scintigraphy showed no RI accumulation.

**Surgery:** The patient underwent right frontal skull biopsy. Surgical findings showed no abnormalities, except bone hypertrophy of around 1.5 cm. No abnormal findings were noted in the dura mater.

**Pathological Findings:** Hematoxylin and eosin-stained sections revealed bone tissue with marrow fibrosis and inflammatory cell invasion (Fig. 4). This was thought to be caused by chronic inflammation. No tumor components were found.

**Outcome:** On the basis of the clinical presentation and pathological findings, the patient was believed to have CRMO. Spontaneous remission was observed

postoperatively, and the patient was discharged from the hospital. No recurrence has been observed.

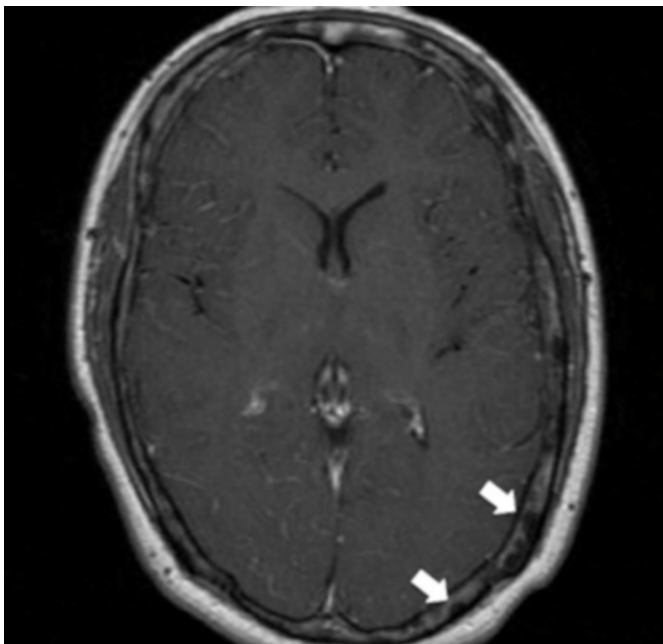
**Figure 1**

Fig.1 Skull X-ray showed the hypertransradiancy which reveals multiple circle, marginal irregular bone destruction.



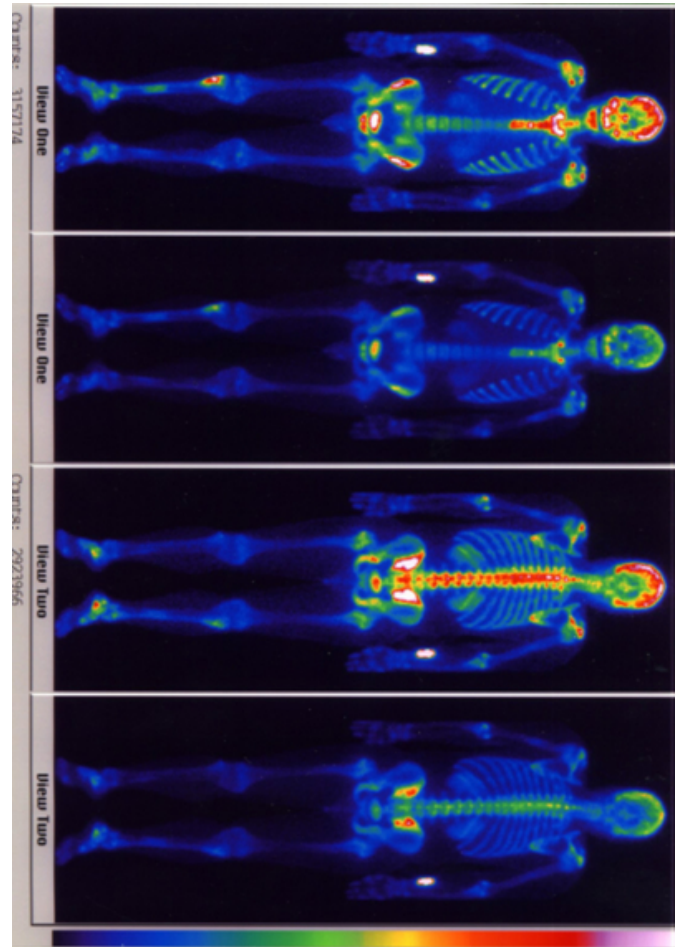
**Figure 2**

Fig.2 Head MRI showed diploe and an outer table of a hypertrophic skull suffered a loss in the shape of a worm-eaten spot.



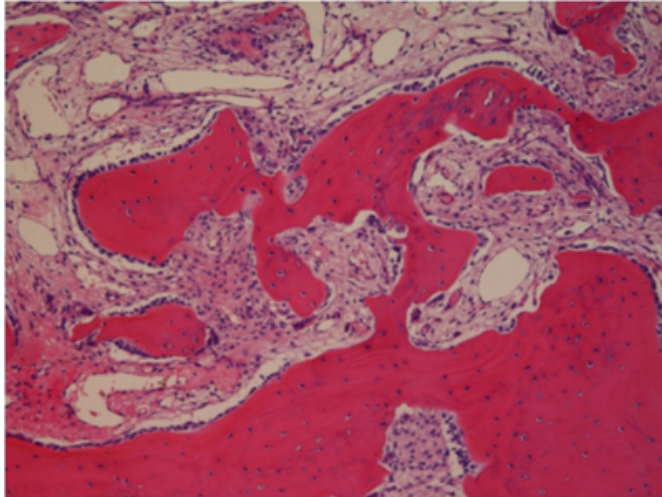
**Figure 3**

Fig.3 Tc MDP bone scintigraphy showed abnormal accumulation of a radioisotope in a skull, tibia proximal side and portion diaphysis.



### Figure 4

Fig.4] Photomicrograph of the biopsy specimen revealed a bone tissue having inflammatory cells invasion and a marrow ingredient with fiberization. The tumor component was not found. (hematoxylin and eosin staining, original magnification [40)



### DISCUSSION

Approximately 200 cases of CRMO have been reported; however, a general description of CRMO was reported for the first time by Giedion in 1972 [1], and this report was about CRMO involving the facial bones [2, 3, 4]. Skull involvement in CRMO is very rare, and to our knowledge, only 1 case of CRMO involving the skull but not the facial bones has been reported [5]. Wedman reported a case in which osteomyelitis was localized in the frontal and sphenoid bones; our report is the first one on osteomyelitis involving the whole skull [5].

CRMO accounts for 2% to 5% of all cases of osteomyelitis and is a rare disorder. Symmetry is multiple and occurs in the bone that two places of CRMO is more than it. In addition, chronic osteomyelitis is characterized by repeated cycles of symptomatic remission and aggravation; systemic symptoms are mild. CRMO occurs mainly in childhood and predominantly in women (sex ratio, 1:5) [2]. The commonly affected sites are metaphyses of the femur, tibia, and clavicle and the spine [6, 7]. Histopathological examination shows atypical chronic inflammatory infiltration or chronic granulomatous lesions; the bacterial culture is negative and the patient does not respond to antibiotic treatment [7]. Radiographic images (eg, bone fusion images) show parts of metaphyses with bone consolidation, periosteal reaction, or multilayer shadow. MRI is useful to assess the range of focus and activity. During the active phases, bone marrow involvement presents with decreased signal intensity on T1-

weighted images and scattered, increased signal intensity on T2-weighted images. The reason for this is the presence of an edema in the marrow due to an inflammatory reaction. Because of the slightly decreased signal intensity on T1-weighted images and slightly increased signal intensity on T2-weighted images in our case, we thought that the disease was in an active phase. In addition, very specific findings were recognized by MRI, ie diploe and outer table erosion appearing as “worm-eaten” spots. Because MRI is superior to detect diploe, we think that MRI findings are important after a differential diagnosis has been made or when the status of the disease (active or passive) has been evaluated.

Histological features include presence of an acute inflammation; ie, mainly neutrophils at the initial stage and lymphocytes at the end stage of the disease, and another characteristic finding is osteosclerosis and reproduction [8]. Because the bone tissue image showed inflammatory cells, lymphocytes, and bone marrow fibrosis, we were able to diagnose our case as being at a stage of chronic inflammation. When making such a diagnosis, a histopathological image of the biopsy specimen is necessary. However, a diagnosis cannot be made on the basis of pathological findings only. General clinical symptoms and neuroradiological findings are also important.

Viral and bacterial infections are suggested as causes of CRMO [5], but the causal viruses and bacteria have not been identified. Because the inflammatory reaction improves after treatment with steroids, immunological abnormalities, eg, expression of antinuclear antibody and rheumatoid factors, are suggested to be responsible for the development of this condition [2, 3, 4]; however, there are no evidences o support this theory. In our case, meningitis was diagnosed, which improved by medication with an antibiotic. Thus, the possibility that a bacterial infection contributed to disease development is considered. In addition, an immunological abnormality was also considered, because the antinuclear antibody test was positive; however, these findings are not believed to be conclusive evidences of the cause.

Bone fusion images of systemic bones suggest that the clinical condition of idiopathic massive osteolysis is similar to that of CRMO. The following characteristics suggest that idiopathic massive osteolysis is similar to CRMO: (1) the cause is unknown, (2) progressive bone fusion is noted, (3) the commonly affected sites are the femur, ileum, rib, scapula, and humerus, (3) it is multifocal and involves the skull, and (4) it mainly affects children and young adults [9]. The neuroradiological findings of idiopathic massive

osteolysis closely resemble those of CRMO, but it is different from CRMO at points showing a bone fusion image with blood vessel and lymph duct hyperplasia pathologically and not to admit bone neogenesis and inflammatory change [9, 10].

As for treatment, nonsteroidal anti-inflammatory drugs (NSAIDs) are in general used to relieve the pain. We used steroids and immunosuppressive drugs for another intractable case; however, at present, there is no established therapy. The symptoms in our patient improved naturally, but they may recur; therefore, careful follow-up is required in the future.

In addition, in recent years, a long-term sighting of CRMO was reported, that a severe dysfunction which a difference of length of lower extremity by an early epiphyseal choke and valgus deformity of a knee are found in and which left mastication disorder is left is reported [11, 12]. Therefore, studies to identify the cause of CRMO and establish a therapy are expected in the future.

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