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Case Report

A Case of Osteopetrosis with Orbital Inflammation Secondary to Maxillary Osteomyelitis

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Keywords
Osteopetrosis · Maxillary osteomyelitis · Orbital Inflammation · Caries · Periostitis

Abstract
Introduction: Osteopetrosis is a rare heritable disorder characterized by increased bone density resulting from osteoclast dysfunction. Major complications include bone fracture, osteomyelitis, anemia, and cranial nerve compression. Optic atrophy can occur due to compression of the optic nerve. Although osteomyelitis of the jaw is a common complication, it rarely occurs in the maxilla. Here, we report a case of a 74-year-old female with osteopetrosis who developed maxillary osteomyelitis, leading to orbital inflammation. ***Case Presentation:*** She was referred to our clinic for 2 months of ptosis and swelling of the left eyelid and temporal region. Previous imaging revealed a left intraorbital occupying lesion, but a biopsy of the temporal subcutaneous tissue did not provide a definitive diagnosis. After 7 months, she presented with severe temporal swelling and purulent discharge. Upon examination, maxillary osteomyelitis resulting from caries of the upper jaw was observed. Treatment with oral antibiotics, drainage of the temporal skin fistula, and regular cleaning of the maxillary drainage improved her symptoms. ***Conclusion:*** This is a rare case of maxillary osteomyelitis associated with osteopetrosis, causing orbital inflammation.

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Introduction

Osteopetrosis is caused by a failure in osteoclast differentiation or function, often associated with specific mutations [1]. It is classified into three categories: infantile autosomal recessive (malignant), intermediate autosomal dominant type I, and adult autosomal dominant type II (ADO). ADO type II typically develops after puberty and generally has a better prognosis but can still lead to complications such as anemia, recurrent fractures, and osteomyelitis [2]. While osteomyelitis can affect the jaw bone, it rarely involves the maxilla [3].

We present the case of a patient with osteopetrosis (ADO type 2) who had upper eyelid swelling and temporal swelling at the time of initial examination. This case had a rare condition in which inflammation caused by maxillary osteomyelitis spread to the orbit and temporal lobe meninges through the weakened cheekbones and temporal bones.

Case Report

A 74-year-old female with a previous diagnosis of osteopetrosis presented with a 2-month history of left upper eyelid swelling, ptosis, and temporal swelling. Previous computed tomographic scans revealed a left intraorbital occupying lesion.

During the initial visit, the patient's decimal best corrected visual acuity was 0.1 in the right eye and 0.15 in the left eye, with −24- and −22-diopter correction, respectively. The axial length was 33 and 32 mm in the right and left eye, respectively, and long axis and axial myopia were observed in both eyes. Intraocular pressure was 15 mm Hg in the right eye and 15.3 mm Hg in the left eye. The protrusion of the eye was 19 mm in the right eye and 22 mm in the left eye. Mild conjunctival injection, adduction disorder, and abduction disorder were observed in the left eye. Chorioretinal atrophy and optic atrophy were observed in both eyes. The patient had no any recent onset of decreased visual acuity. No abnormalities were noted in the anterior segment and eye movements of the right eye.

The orbito-encephalic MRI with gadolinium enhancement revealed hypersignals predominantly in the lateral left orbit, with extension to the eyelids, temporal subcutaneous area, and vicinity of the auricle (Fig. 1). Hypersignals also spread to the ventral temporal lobe, skull base, meninges, and maxillary sinus. The optic nerve and extraocular muscles were compressed by the mass and deviated to the nasal side. Blood tests showed anemia (Hb, 7.4 g/dL), increased CRP (12.35 mg/dL), mildly elevated β2-microglobulin (2.63 mg/L), and soluble IL-2 receptor (671 U/mL). WBC was normal.

The patient underwent a subcutaneous soft tissue biopsy of the temporal swelling due to the high risk associated with an intraorbital biopsy involving a bone incision. The histopathological examination showed inflammatory tissue changes without malignancy, but a definitive diagnosis could not be made at that time. We determined that the anemia was due to osteopetrosis, and because there were no anemia symptoms, the patient was continued to be monitored by her family doctor. During a follow-up visit 5 months later, there was a slight worsening of the temporal swelling without redness or tenderness. However, after 2 months, the patient developed redness, tenderness, and pus discharge from the temporal swelling (Fig. 2).

Drainage from maxillary molars was observed, and she was diagnosed with maxillary osteomyelitis. Bacterial culture identified *Streptococcus gordonii* and *Gemella haemolysans* in the pus from caries. CT revealed bone destruction in the left frontal, zygomatic, ethmoid, and sphenoid bones, along with swelling of the temporal soft tissue and thickening of the maxillary sinus mucosa (Fig. 3). Otorhinolaryngology examination ruled out spread of inflammation from maxillary sinusitis to the orbital region due to the absence of bone destruction at the border between the maxillary sinus and orbit. It was speculated that the

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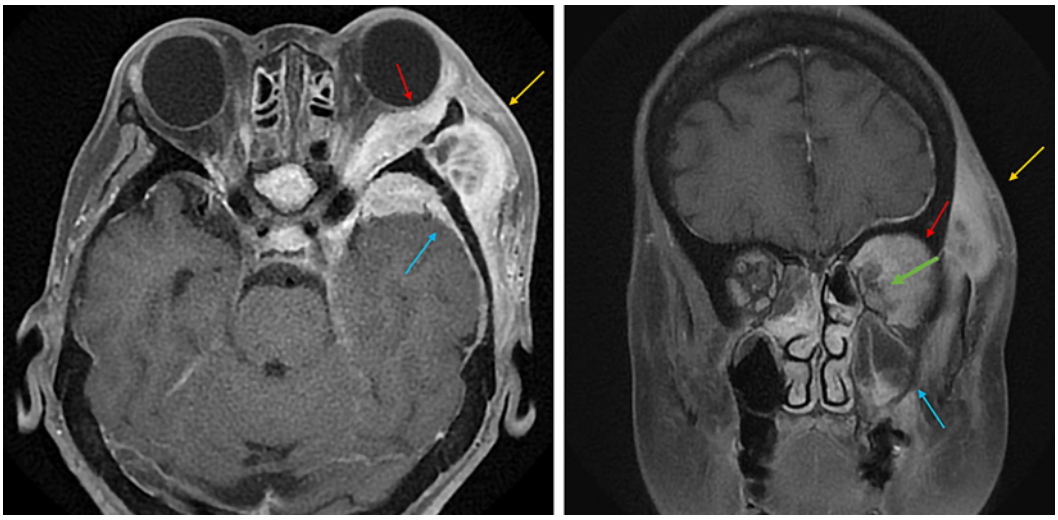

Fig. 1. Gadolinium-enhanced MRI of the orbital region revealed hypersignals predominantly in the lateral side of the left orbit (red arrow). The optic nerve and extraocular muscle were compressed by the orbital lesion (green arrow). Abnormal signals spread to the eyelid, subcutaneous temporal region, vicinity of the auricle (yellow arrow), scull base on the ventral temporal lobe, meninges, and maxillary sinus (blue arrow). Inflammation of the maxilla spreads to the inside of the orbit and the meninges via the zygoma and temporal bone on the side wall of the orbit.

inflammation from maxillary osteomyelitis spread to the temporal soft tissue and orbit via the cheekbone. The patient was treated with oral levofloxacin at 500 mg/day for 7 weeks. She also underwent temporal abscess incision, placement of drains, and cleansing of the maxillary drainage site. Oral minocycline (200 mg/day) was continued for 1 month. The swelling of the upper eyelids and orbital space-occupying lesions improved, and the conjunctival hyperemia of the left eye and eye movement disorder also improved. During the course of treatment, the corrected visual acuity of the left eye decreased to 0.08; however, after treatment, the best corrected visual acuity improved to 0.2. Currently, she only undergoes regular oral cleaning. No recurrence of infection was observed during the 15-month follow-up period (Fig. 4).

Discussion

Osteopetrosis is a hereditary disease characterized by increased bone density due to osteoclast differentiation and dysfunction. Its prevalence is estimated to be about 1 in 100,000 to 500,000 [1, 4]. Osteopetrosis is broadly divided into three types: autosomal recessive osteopetrosis, intermediate autosomal dominant osteopetrosis (ADO type 1), and adult autosomal dominant osteopetrosis (ADO type 2) [2]. Autosomal recessive osteopetrosis typically develops in the first few months of life and causes blindness and hearing loss due to narrowing of the neural foramen. Abnormal expansion of bone interferes with medullary hematopoiesis, resulting in pancytopenia, and secondary expansion of extramedullary hematopoiesis sites [1]. ADO type 1 develops in the second and third decades of life, and ADO type 2 develops after puberty. ADO type 2 patients often have a full life expectancy; however, they might develop several bone complications, including recurrent fractures, osteoarthritis, and infections [2]. This case was presumed to be ADO type 2 based on the medical history, but it was unclear whether the visual acuity was due to optic nerve atrophy associated with osteopetrosis or chorioretinal atrophy due to axial myopia.

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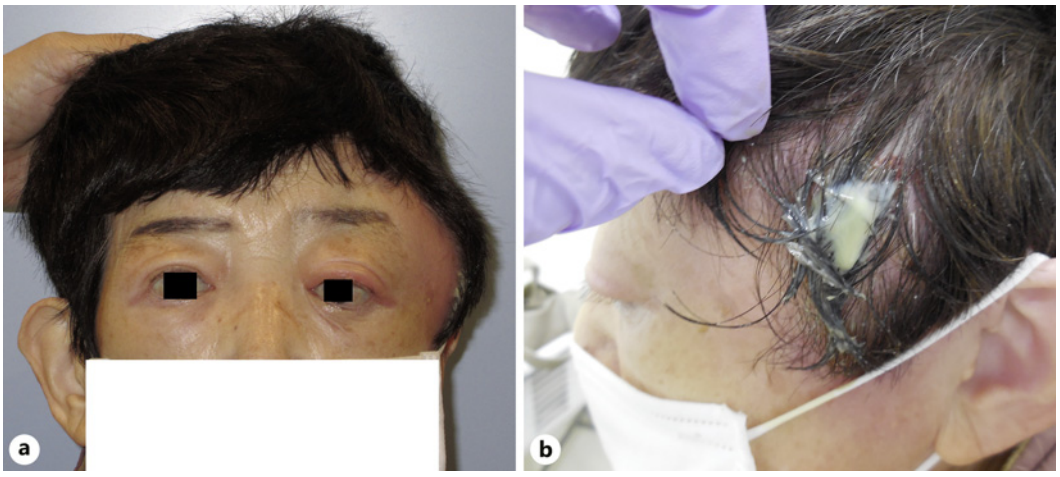

Fig. 2. Facial photos. **a** Redness and tenderness in the temporal region. **b** Purulent discharge from the left temporal region.

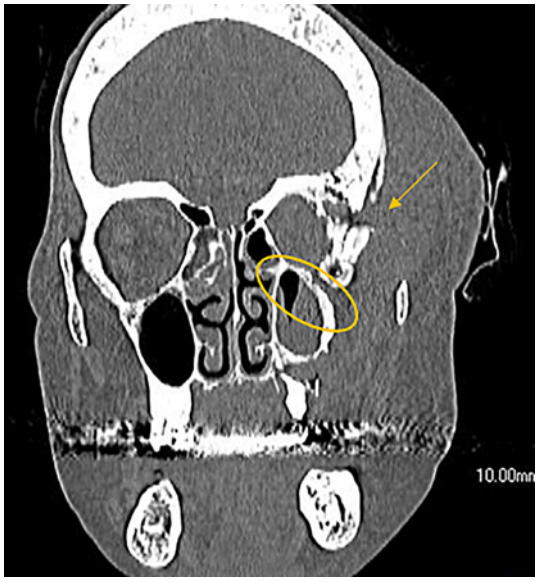

Fig. 3. Plain CT image of the orbital region of the head showed bone destruction in the left frontal bone, zygomatic bone, ethmoid bone, and sphenoid bone (arrows). No bone destruction at the border between the maxillary sinus and the orbit (oval) was observed.

It increases the susceptibility of bones to osteomyelitis due to decreased vascularity. Local infections, such as odontogenic infections, have a higher likelihood of leading to osteomyelitis, which occurs in 10% of reported cases of osteopetrosis [5]. Osteomyelitis primarily affects the mandible and rarely affects the maxilla because the maxilla has a thinner cortical bone and contains numerous collateral blood vessels [5]. In total, 24 cases of maxillary osteomyelitis complicated by osteopetrosis have been reported from 1971 to 2020 [6], but there were no reports from journals in the ophthalmology field. The age ranged from 8 to 66, and this case was the oldest at 76 years old compared to previous reports. Among these cases, 5 cases presented with purulent discharge from the periorbita, and 4 of 5 cases were in their 10s (Table 1) [3, 7–9]. There were 4 cases of visual impairment and optic nerve atrophy due to optic nerve compression. Multiple fractures and drainage from the infraorbital region were observed in all cases. Total 5 of 24 cases of maxillary osteomyelitis caused by osteopetrosis reported in the past were in the 10s, and four of them

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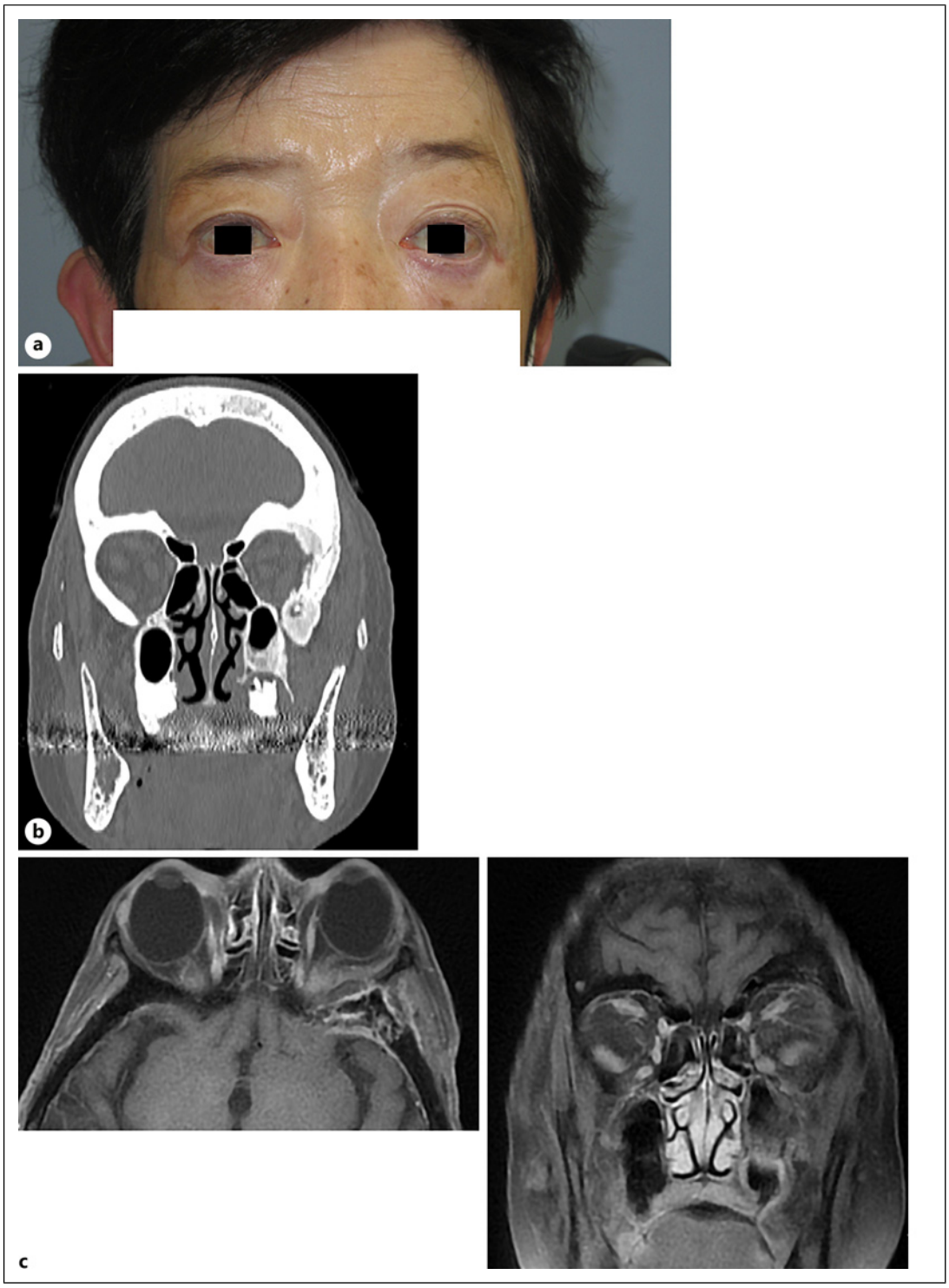

Fig. 4. Latest facial photo, simple CT image, and contrast-enhanced MRI image. **a** Swelling of the left eyelid and temporal region improved. **b** No progression in bone destruction was observed. **c** Intraorbital lesion shrank, and abnormal signals in the temporal region improved.

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Table 1. Reported cases of maxillary osteomyelitis in osteopetrosis with periorbital purulent discharge

Authors	Age, gender	Symptoms and clinical findings	Treatment	Outcome
Infante-Cossio et al. [7] 2014	40M	Cutaneous fistulation in the right infraorbital region and bilateral submandibular area, purulent nasal discharge, blindness caused by optic nerve compression, multiple fractures, dental caries	Amoxicillin-clavulanic acid 1M IV and 3Ms OP, sequestrectomy, curettage	Oral amoxcillin-clavulanic acid on and off for 3 years for cutaneous sinuses
Khademi et al. [8] 2011	15M	Facial swelling and pain, sinus tract drainage in infraorbital regions, severe dental caries multiple fractures, hearing loss, bilateral optic atrophy	Intravenous clindamycin for 2 weeks curettage, sequestrectomy, sinus tract excision	Drainage decreased but did not completely subside in 9-week follow-up
Oğütcen-Toller et al. [9] 2010	18F	Purulent discharge at the medial canthus of her left eye discharge of pus in the infraorbital and upper left molar region, multiple fractures, multiple malformed and partially impacted teeth, blindness	Amoxicilin for 1 w, tooth removal, sultamicilin and ornidozole for 5 w, sequestrectomy, clindamycin for 1 w, sultamicillin and ornidazole for 3 w, cefuroxime axetil for 4 w	No recurrent infection in 2-year follow-up
Krithika et al. [3] 2009	18M	Pus discharge from both cheek carious upper molars on both sides of maxilla, bilateral extraoral sinuses in infraorbital region with purulent discharge, anemia, impaired vision and hearing, multiple fractures	Blood transfusions, intravenous amoxicillin and clavulanic acid, corticotomy	Lost to further follow-up
Krithika et al. [3] 2009	16M	Pus discharge from right cheek following extraction of right upper molar, extraoral sinus in the right infraorbital region with a purulent discharge, enamel hypoplasia, multiple remained deciduous teeth, multiple fractures anemia	Blood transfusion, intravenous levofloxacin for 1 w, sequestrectomy	No recurrent infection in 6M follow-up

had periorbital drainage. Maxillary osteomyelitis that develops in ADO type 1 patients in their 10s might have severe and widespread inflammation. None of these cases exhibited purulent discharge from the temporal region. It was believed that intraorbital inflammation, lower temporal skin abscess, and meningitis at the base of the skull occurred due to the spread of maxillary osteomyelitis to the temporal side of the orbital wall. This resulted in progressive bone destruction in the orbital wall and frontal bone. The drainage from the temporal skin was attributed to the weakened skin barrier function during the temporal

biopsy. Symptoms of ADO type 2 are often mild; however, this case seems to be related to the decline in hematopoietic ability associated with osteopetrosis and the decline in immune function due to aging.

While there is no consensus on the treatment of maxillary osteomyelitis associated with osteopetrosis, it is crucial to eliminate the source of infection [2]. Previous reports have shown that antibiotics alone did not provide sufficient therapeutic effect, and successful cases required multiple treatments such as sequestrectomy, local debridement, curettage, and dental extraction [2]. All previous cases of periorbital drainage were treated with a combination of systemic antibiotics and surgical treatment. In this patient's case, the lesion area was reduced by systemic administration of antibiotics, drainage, and regular cleaning of the oral drainage area without surgical treatment. Currently, there is no recurrence of osteomyelitis observed with regular oral cleansing. This might be because the bone destruction of the maxilla was relatively mild, and the inflammation spread into the orbit through the cheekbones, temporal bones, and their subcutaneous tissue.

The initial symptoms of maxillary sinus osteomyelitis in this patient were eyelid swelling and ptosis. Detailed imaging studies and collaboration with physicians from other departments were crucial in reaching this diagnosis. It took us a considerable time to identify the cause of the inflammatory lesions within the orbit. Although there is no abnormality in the inferior orbital wall, the possibility of inflammation spreading from maxillary osteomyelitis should not be excluded. Osteomyelitis associated with osteopetrosis is intractable and has a risk of recurrence, so a long-term follow-up is required. The CARE Checklist has been completed by the authors for this case report, attached as in online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000536140).

Statement of Ethics

This case report was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. Ethical approval is not required for this study in accordance with local guidelines. Written informed consent was obtained from the patient for publication of the details of their medical case and accompanying images. The manuscript does not include any information that might reveal the patient's identity.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Takafumi Misaki, Fumiko Murao, Kayo Shinomiya, Akihiro Tani, Masayuki Yamada, and Yoshinori Mitamura participated in the analysis of this case. All authors reviewed and approved the manuscript.

Data Availability Statement

The data that support the findings of this study are not publicly available due to their containing information that could compromise the privacy of research participants but are available from the corresponding author T.M. upon reasonable request.

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