Case Report with Literature Review

Osteopetrosis Complicated by Osteomyelitis of the Maxilla: A Rare Finding from a Radiologist Point of View

Hajer Alfadeel

Faculty of Medicine, Omer Almukhtar University, Elbeida, Libya.

hajer.alfadeel@omu.edu.ly

Abstract :

Osteopetrosis is a rare inherited skeletal disorder, characterized by osteoclast dysfunction, impaired bone resorption, and poor bone remodeling. This result in the formation of compact and fragile bones, which appear very radiopaque on radiographic examination. The increased brittleness of bones manifests as recurrent pathologic fractures, while the decreased blood supply to bones due to reduction of marrow spaces causes increased vulnerability for infections. When secondary infection occurs in the facial bones, it commonly affects the mandible; this case report discusses the rare occurrence of maxillary osteomyelitis in a patient with osteopetrosis. To the best of my knowledge, this is the first reported adult case in the region.

Key words :Osteopetrosis. Osteomyelitis. Maxilla. Radiological findings.

الملخص:

اوستيوبتروسيس هو اضطراب وراثي نادر يصيب الهيكل العظمي يمتاز باختلال في وظيفة الخلايا المسؤولة عن العملية الفسيولوجية لامتصاص العظام والتي تمنع تراكم العظم المكون من قبل الخلايا العظمية، ينتج عن هذا الخلل في اعادة تشكيل العظام تكوين عظام مضغوطة وهشة، والتي تظهر كثيفه في صور الأشعة. تتجلى هشاشة العظام في شكل كسور مرضية متكررة في المرضى المصابين اما انخفاض إمدادات الدم للعظم بسبب تقليل مساحة النخاع بالعظم المتراكم فيتجلى بزيادة فرصة تعرض العظام للالتهاب. عظمة الفك السفلي هي الاكثر عرضة للالتهاب في هؤلاء المرضى. يناقش هذا التقرير الحدوث النادر لالتهاب عظمة الفك العلوي في مريض يعاني من هذا المرض النادر.

Introduction:

Osteopetrosis is a rare skeletal disease entity that comprises a group of clinically and genetically heterogenous conditions, which share the hallmark of increased bone density on radiographs. Its overall incidence is difficult to estimate, ranging from 1 in 100000 to 500000 depending on its genetic variant (Nilesh, 2020; Stark and Savarirayan, 2009). The general skeletal sclerosis is primarily due to failure of osteoclasts to resorb bone leading to defective bone remodeling and accumulation of immature bone (Nilesh, 2020, van Hove et al., 2014). 'The common clinical findings that usually lead to the detection of the disease are fractures and osteomyelitis of the mandible' (Krithika et al., 2009). Osteomyelitis of the maxilla is rare even in the presence of an underlying predisposing condition like osteopetrosis (Carvalho et al., 2018; Nilesh, 2020). This article reports a case of osteopetrosis complicated by extensive osteomyelitis of the entire maxilla and highlights the radiological manifestations of the disease.

Case Report

A 41-year-old male Libyan patient presented to University Hospital in Elbeida, Libya with left femoral fracture, the patient had previous numerous bone fractures. Radiograph of the pelvis and femurs demonstrated generalized marked increase in bone density of the visible bones with absence of medullary architecture, and loss of differentiation between the cortex and the medulla. Bilateral femoral plate fixations and displaced proximal shaft fracture of left femur at the proximal end of the plate (Figure 1). Past medical history revealed diagnosis of osteopetrosis, which was consistent with the radiographic findings.

Admission hematologic tests were within normal limits. The patient underwent surgical fixation of the fracture with a dynamic compression plate after removing the previously inserted plate-screw fixation of the left femur.

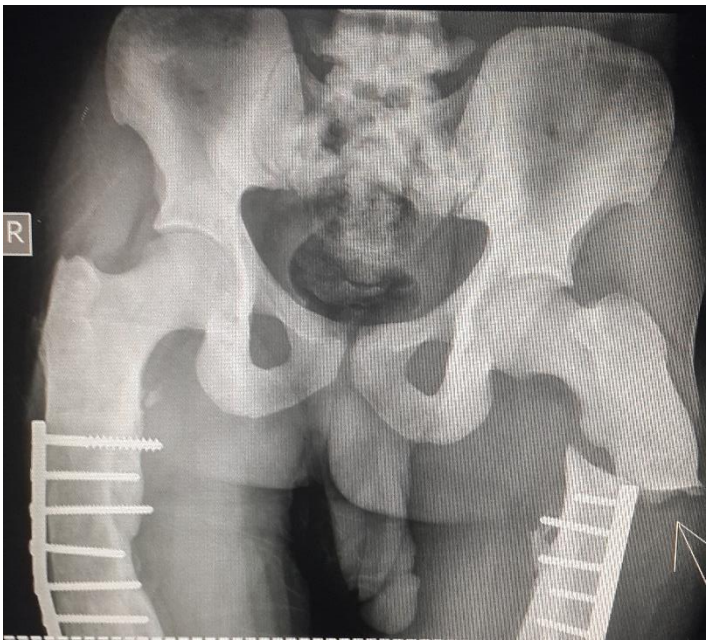

Figure 1. Anteroposterior x-ray pelvis and proximal femur depicting bilateral fixation in both femurs as an evidence of earlier surgical intervention for femoral shaft fractures, re-fracture of left femoral shaft at the proximal end of the plate with sever medial fracture displacement. A uniform increase in bone radiodensity with decreased corticomedullary demarcation, consistent with the patient's known diagnosis of osteopetrosis.

The patient reported intermittent discharge from his right cheek and chronic nasal obstruction, the problem started few years back with dental extraction from his right posterior maxilla followed by infection at the extraction site extending to the region of right maxilla. He was then treated with medications and surgical removal of bone from the maxilla but no documents were available with the patient. Several months later, an intermittent discharge developed from his right cheek at the previous surgical incision site, the patient also reported sporadic intraoral drainage from right posterior maxilla and right nasal regurgitation of fluid. Facial examination revealed a sinus at the right infraorbital region with induration at the opening. Intra-oral inspection revealed near complete absence of teeth in the upper and lower jaws, and absent right posterior maxillary alveolar ridge consistent with previous surgical resection, a deep defect in right posterior maxilla was identified. The patient was refereed to the radiology department for non-contrast computed tomography (CT) of paranasal sinuses (PNS). The study was done using 64-detector CT scanner with axial and coronal image bone

algorithm reconstruction in 1mm slice thickness. The scan revealed typical signs of osteopetrosis as generalized marked sclerosis of facial bones and skull base, obliterated sclerotic paranasal sinuses and mastoid air cells. Evidence of previous partial maxillectomy (Figure 2A). Extensive bony destruction of right maxilla extending to hard palate and nasal cavity, accompanied with sequestration formation (Figure 2B-D), a wide fistulous tract between the maxillary bone and oral cavity (Figure 2C). An anterior maxillary bony defect is seen corresponding with cutaneous sinus formation (Figure 2D). The diagnosis in keeping with osteopetrosis associated with sever chronic osteomyelitis of right maxilla.

As the patient refused any surgical intervention in the current medical institute, he was treated conservatively with intravenous antibiotics (Ceftriaxone, Metronidazole); Pus from the right cutaneous sinus was flushed and drained with daily irrigation with saline. He was discharged on long-term use of amoxicillin.

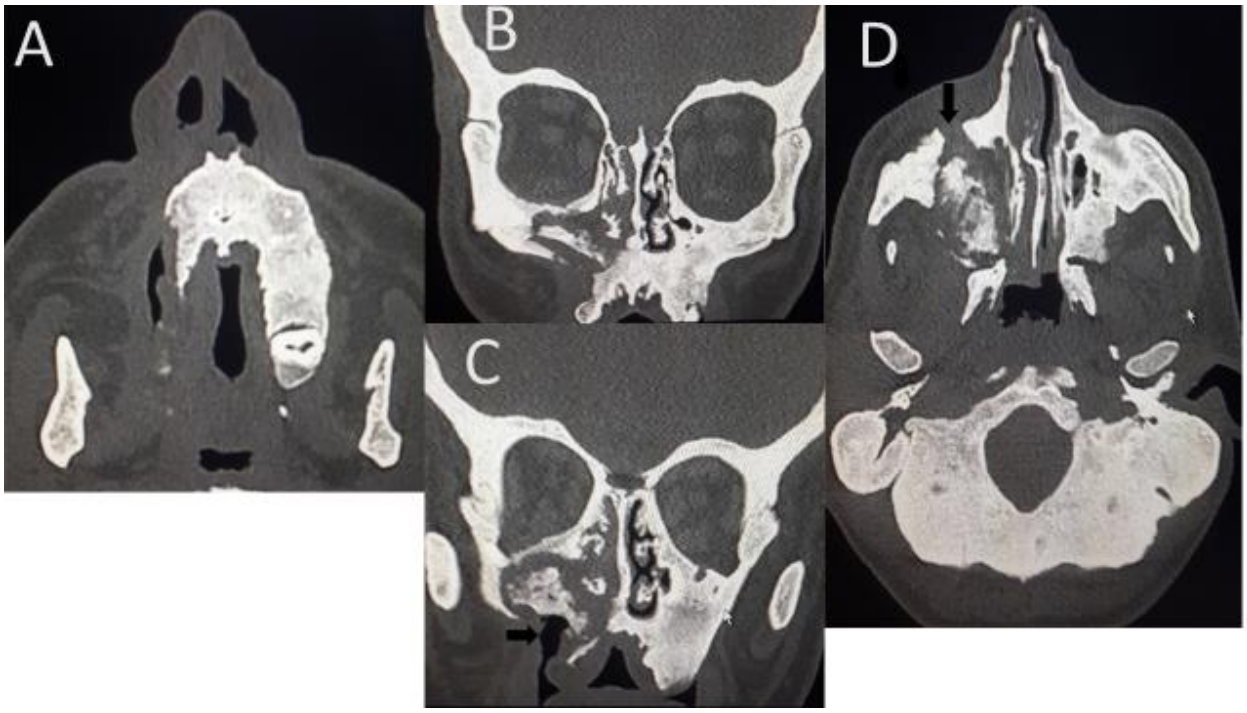

Figure 2. (A) Large Bone defect of right alveolar ridge consistent with previous surgical intervention. (B-D) Extensive bony destruction of the entire right maxilla accompanied with sequestration formation, destruction of right nasal cavity with soft tissue density opacification contiguous with the maxilla. (C) Wide fistulous tract (arrow) extending from right maxilla into oral cavity. (D) Bony defect of anterior maxilla (arrow) corresponding to the cutaneous sinus opening.

Discussion

Osteopetrosis, a rare bone disorder first reported in 1904, is caused by failure of osteoclast development or function related to a variety of genetic mutations, These conditions can be inherited as autosomal recessive, dominant or X-linked (Liu et al, 2016; Stark & Savarirayan, 2009). The abnormal function of osteoclasts along with normal osteoblastic activity result in incremental bone deposition caused by lack of bone resorption required for normal bone remodeling. This leads to the formation of hard and structurally weak bone, which can readily fracture. Poor blood supply to the bone due to bone marrow obliteration reduces bone healing and increases the risk of infections (Krithika et al., 2009; Nilesh, 2020; Tohidi and Bagherpour, 2012).

Osteopetrosis is generally divided into three types: severe infantile malignant autosomal recessive, intermediate autosomal recessive and adult autosomal dominant osteopetrosis. The most severe form is the infantile type, which is fatal within few years of life as a result of anemia with congestive heart failure or sepsis caused by bone overgrowing in the bone marrow space. Whereas onset of primarily skeletal manifestations such as fractures and osteomyelitis in late childhood or adolescence is typical of the adult autosomal dominant type (Liu et al, 2016; Stark and Savarirayan, 2009).

The mainstay of the diagnosis of osteopetrosis is clinical and largely based on the radiographic appearance of the skeleton. There are diffuse sclerosis, affecting the skull, spine, pelvis and appendicular bones, cortical thickening with medullary encroachment, poorly pneumatized or undeveloped paranasal sinuses and mastoid air cells. There is no demarcation of cortex and medulla in the long bones. Other radiological findings seen in osteopetrosis are sharply demarcated sclerotic bands involving both endplates giving sandwich vertebra appearance, and bone within a bone appearance (sclerotic bone foci in the bones) particularly in the vertebrae and phalanges (Garcia et al., 2011; Stark and Savarirayan, 2009; Yadav et al., 2016).

The differential diagnosis that can be considered for osteopetrosis radiographically are conditions that can produce diffuse osteosclerosis, which can include other sclerosing bone dysplasias, such as pyknodysostosis, craniometaphyseal dysplasia, diaphyseal dysplasia,

melorheostosis, osteopoikilosis, and osteopathia striata (Pavan et al., 2018; Sallies, 2020; Tohidi and Bagherpour, 2012).

In osteopetrosis, the defective remodeling of bone with thickening of cortex and narrowing or obliteration of the medullary cavities results in bone fragility, hematopiotic insufficiency, osteomyelitis, and cranial nerve entrapment (Nilesh, 2020). Waguespack et al. (2007) who studied the largest group of patients with autosomal dominant osteopetrosis identified four main clinical manifestations of the disease: fractures (the most prevalent manifestation), osteomyelitis of the jaws typically manifested in older adult patients, visual loss and bone marrow failure which typically had their onset in childhood.

Intermediate autosomal recessive osteopetrosis is usually diagnosed toward the end of the first decade of life. Patients often present with pathological fracture. Clinical characteristics include delayed motor and cognitive development, mild disproportional short stature and dysmorphic features. Cranial nerve compression and mandibular osteomyelitis are common features. This is a rarer form of osteopetrosis. Most patients survive into adulthood but with significant disability (Barry et al., 2007).

The patient in the current report had two of the main clinical manifestations of osteopetrosis at time of presentation to the radiology department, multiple old and new femoral fractures, and osteomyelitis of the jawbone, as well as the typical radiologic findings for the disease.

Common dental findings in osteopetropsis are unerupted, malformed, or delayed teeth and many dental caries due to vulnerable enamel and dentin (Celakil et al., 2016). In osteopetrosis, bones are susceptible to infection due to poor vascularity causing poor bone healing and less favorable outcomes. The most common site of involvement is the mandible most commonly associated with dental extraction as the trauma to the periosteum facilitates the spread of infection to the bone. Maxillary involvement is extremely rare due to its cortical bone morphology and rich collateral blood supply (Celakil et al, 2016, Nilesh, 2020; Sallies et al., 2020). According to Barry et al. (2007) and Krithika et al. (2009), osteomyelitis of the maxilla is such a rare occurrence that when presented, the possibility of an underlying osteopetrosis should be considered. A literature review via pubmed research using terms osteopetrosis, osteomyelitis of maxilla revealed 20 reported cases of osteomyelitis of the maxilla associated with osteopetrosis confirming that it is a very rare entity.

The hallmark characteristics of osteomyelitis are destruction of bone and periosteal new bone formation. The distinguishing feature of chronic osteomyelitis is necrotic bone formation (sequestrum) (Singh et al., 2010; Pineda et al., 2009). Some studies have reported that CT is more useful to diagnose osteomyelitis and evaluate maxillofacial infections than conventional radiography (Celakil et al., 2016). Table 1 summarizes the case reports that have demonstrated the use of CT for the assessment of maxillary osteomyelitis in osteopetrosis. In the present case, CT have demonstrated the increased bone radio-density of the skull and face, obliteration of medullary cavity and maxillary sinuses, extensive sequestration of maxilla, and the complication of oro-maxillary fistula formation, which are indicative of the protracted nature of the infection process.

Table 1. Reported cases of osteopetrosis-associated-maxillary osteomyelitis where CT was done.

Study	Patient's age	Patient's gender	CT findings
Long et al. (2001)	54	Male	Decreased marrow spaces and necrotic bone in left anterior maxilla
Junquera et al. (2005)	60	Female	Bone lysis of left maxilla
Barry et al. (2007)	28	Female	Bony destruction of left nasal cavity, left maxillary sinus and hard palate
Krithika et al. (2009)	8	Male	A defect on the left side of the maxilla as a result earlier surgical intervention. Soft tissue density lesion in the right maxillary antrum and both nasal cavities. Bilateral maxillary and ethmoidal sinusitis
Trivellato et al. (2009)	25	Male	Periosteal bone formation
Khademi et al. (2011)	15	Male	Destruction of both nasal antrum accompanied with sequestration formation and sclerosis of maxilla, zygomatic and ptyregoid plates. A fistulous tract between the maxillary bone and oral cavity
Kulyapina et al. (2016)	66	Male	generalized sclerosis of facial bones, sinus obliteration, large area of bone destruction in the right maxilla and sequestrum formation
Jayachandran & Kumar (2016)	20	Male	Abnormal increase in density of all bones and complete obliteration of both maxillary sinuses. Osteomyelitic changes in right maxilla

Carvalho et al. (2018)	40	Male	Left temporoparietal and maxillary swelling
Pavan et al. (2018)	13	Male	irregular margins and permeative destruction of right maxilla, surrounding thick sheath of periosteal reaction, A wide sinus tract passing through the right maxillary sinus extending superiorly into the floor of the orbit, where the medial part of infra-orbital ridge is destructed
Sallies et al. (2020)	26	Male	increased bone opacity with poor differentiation between medullary and cortical bone. Right sided maxillary osteomyelitis
Nilesh (2020)	45	Female	Erosive changes involving medial and lateral walls of left maxillary sinus, maxilla and alveolar bone

Common CT findings of facial and cranial skeleton in the reviewed patients in Table 1 were generalised sclerosis of jawbones, calvarium and skull base, poorly aerated mastoids and underdeveloped or absent maxillary sinuses, bone destruction with sequestrum involving maxilla. Fistula/sinus tracts were demonstrated in two cases (Khademi et al, 2011; Pavan et al. 2018).

Because of compromised bone healing ability in osteopetrosis. Minor events, such as surgical trauma from tooth extraction, are known to be associated with osteomyelitis in such cases (Nilesh, 2020). Out of the 11 patients reviewed in Table1, a history of tooth extraction was present in nine (81.8%) cases (Barry et al., 2007; Jayachandran & Kumar, 2016; Junquera et al., 2005; Khademi et al., 2011; Kulyapina et al., 2016; Krithika et al., 2009; Nilesh, 2020; Sallies et al., 2020; Trivellato et al., 2009).

Osteomyelitis in patients with osteopetrosis can be intractable because of poor healing ability caused by poor bone vascularity, and can be refractory to various treatment modalities (Celakil et al, 2016; Pavan et al., 2018). This was evident in the present case as the patient was dealing with the disease for years before, reported multiple courses of antibiotic treatment, and had undergone earlier surgical approach, as judged by the CT scan. Therefore, good dental care and oral hygiene are extremely important in patients with osteopetrosis. Decayed teeth should be endodontically treated and tooth extraction should be avoided, if possible, and minimal trauma with extreme caution against infections should be followed

when extraction deemed necessary to avoid the development of potentially intractable osteomyelitis (Nilesh, 2020; Liu et al., 2016).

There is no consensus regarding the treatment for osteomyelitis in the maxilla associated with osteopetrosis as the condition is very rare; no evidence from clinical prospective studies is available in the literature (Carvalho et al., 2018, Junquera et al., 2005). According to Carvalho et al. (2018), complete healing was achieved in only 44.4% of the reported cases of maxillary osteomyelitis in patients with osteopetrosis while most cases remained with incomplete healing and still dealing with the disease. All successfully healing cases were treated by prolonged use of at least two different antibiotic treatments combined with surgical procedures (sequstrectomy or partial resection). Prolonged hyperbaric oxygen therapy was reported as a successful treatment method by some authors (Carvalho et al., 2018; Junquera et al., 2005). Surgical closure of oro-antral communication after removal of necrotic bone is accomplished by local flap (Nilesh, 2020). Obturators are ideally used to close the maxillary defects (Sallies et al., 2020)

In conclusion, although rarely encountered, osteopetrosis characteristics of dense bones on radiographs and CT are easily recognized by radiologists. Maxillary osteomyelitis is considered rare but may develop in a patient with osteopetrosis following tooth extraction, a chronic course or recurrence of the disease is expected. This report documents the CT findings of chronic maxillary osteomyelitis secondary to osteopetrosis.

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