Mandibular osteomyelitis and multiple skeletal complications in Albers-Schönberg disease

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ABSTRACT

Albers-Schönberg disease, or autosomal dominant osteopetrosis type II, is the most common form of the rare disease, osteopetrosis. Mandibular osteomyelitis is a rare complication of the disease. A host of other skeletal complications may also occur. Mandibular osteomyelitis along with bilateral severe coxa vara and pars fracture is very rare in Albers-Schönberg disease. We present the occurrence of these complications in a 24-year-old man with Albers-Schönberg disease. His mandibular osteomyelitis was successfully treated.

Keywords: Albers-Schönberg disease, mandibular osteomyelitis, osteomyelitis, osteopetrosis

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Fig. I Photograph shows the sinus over the jaw exuding creamy yellow pus.

Fig. 2 Pantomographic radiograph of the mandible shows bilateral chronic osteomyelitic changes with dislocated left molar and premolar teeth, and a sequestrum at the left alveolar margin.

INTRODUCTION

Osteopetrosis is a very rare form of inherited bone disorder due to a defective osteoclastic function where bones are rendered fragile and prone to infections in spite of being radiodense. Autosomal dominant osteopetrosis type II (ADO II) or Albers-Schönberg disease is the most common form of osteopetrosis. Classically, it has been termed as milder or benign osteopetrosis. Non-traumatic long bone fractures, hip osteoarthritis and mandibular osteomyelitis are some of the distinguished complications of ADO II. We report such a case of ADO II in a 24-year-old man who unfortunately experienced all the above-mentioned complications. This case, along with other reported cases by different authors in various peer-reviewed journals, casts doubt about the so-called "benignity" of ADO II.

CASE REPORT

A 24-year-old man presented to our outpatient department with a complaint of a discharging sinus from the left side of his chin for the last five months. He had visited several dentists and physicians during this period, and has completed multiple courses of antibiotic therapy without any result. The sinus exuded creamy yellow pus from time to time, the amount of which was scanty throughout. There was neither any history of haematemesis or haemoptysis, jaundice, prolonged fever, loss of weight, any visual or hearing problem, consumption of uncooked milk, any haematological disorder in the family, nor any history of tuberculosis anywhere in the body. There was a history of fractures after trivial trauma of the femoral shaft and neck, tibia bilaterally, and the right arm during the last ten years. The fracture episodes were separated by several years and all of them had delayed union. Tibial fractures united with angulation and shortening. The right-sided fracture of the femoral neck had non-union, and the right arm had malunion. Since then, he could not fully pronate his right hand and walked with a limping gait due to hip pain. He was born of a non-consanguineous marriage. He had two elder sisters and a younger sister in her late teens. His father lived elsewhere. None of the family members had history of fractures or similar type of illness.

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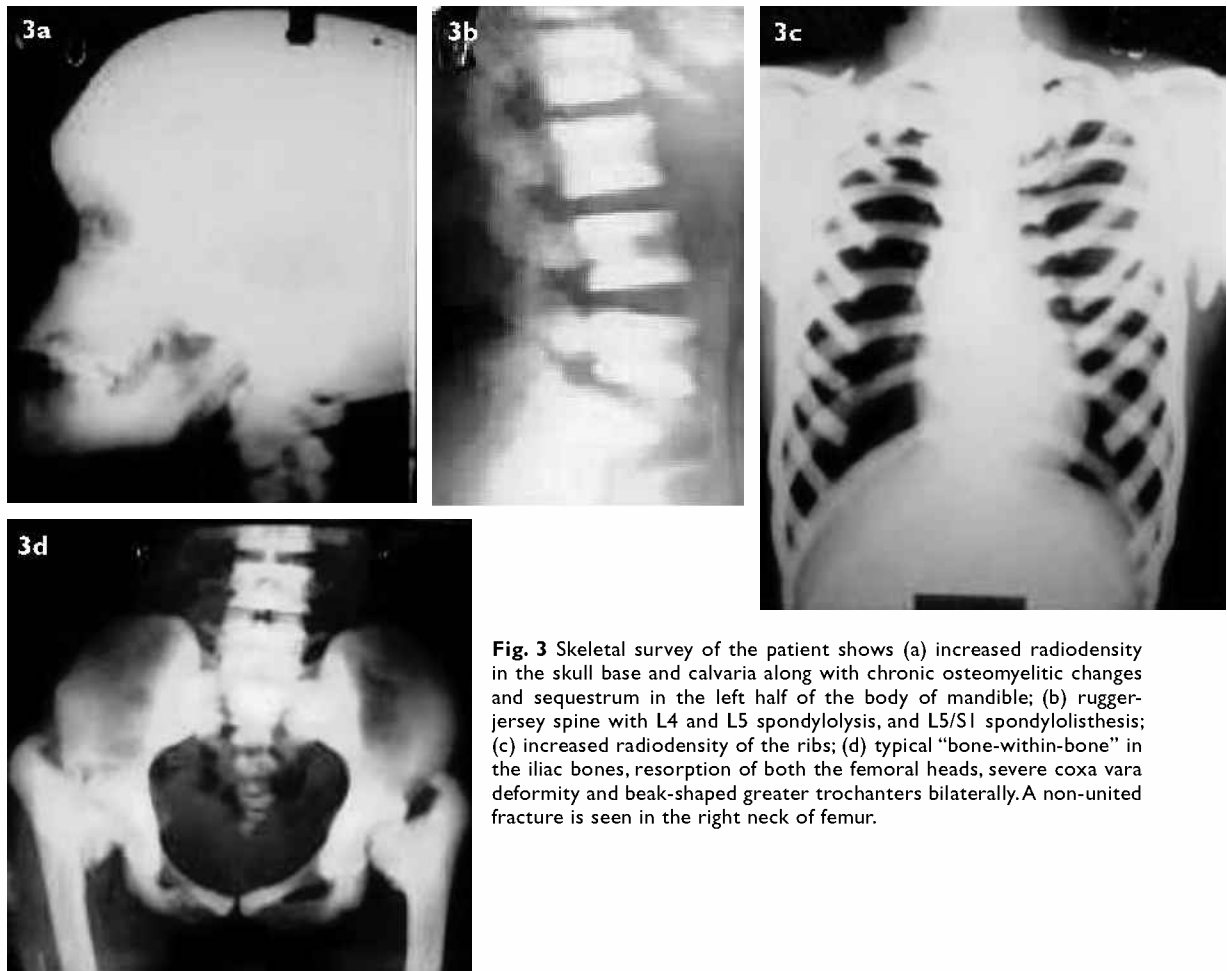Fax: (91) 33 2358 7282
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Fig. 3 Skeletal survey of the patient shows (a) increased radiodensity in the skull base and calvaria along with chronic osteomyelitic changes and sequestrum in the left half of the body of mandible; (b) rugger-jersey spine with L4 and L5 spondylolysis, and L5/S1 spondylolisthesis; (c) increased radiodensity of the ribs; (d) typical "bone-within-bone" in the iliac bones, resorption of both the femoral heads, severe coxa vara deformity and beak-shaped greater trochanters bilaterally. A non-united fracture is seen in the right neck of femur.

On examination, the patient was of normal intelligence. The conspicuous finding during the general survey was a discharging sinus with creamy yellow pus, below the midpoint of the left half of the chin (Fig. 1). He had scoliosis at the dorsolumbar region, with convexity towards the left and a disproportionate short stature which was mainly due to bilateral lower limb shortening both above and below the knee joints. The patient had a waddling gait, with a bilateral limp due to pain at the hip joints. A fixed varus deformity of 20° at the right elbow restricted full pronation. Mild anaemia was noted. Examination of the cranial nerves, including the optic fundi and auditory nerves, was normal. There were no focal neurological deficits. Apart from mild hepatosplenomegaly, examination of other systems was essentially normal. Biochemical and haematological investigations revealed the following: Hb 9.6 g/dL, haematocrit 31.9%, reticulocyte 1.4%, total leucocyte count of $7.7 \times 10^3/\mu L$ with polymorphs 48%, lymphocytes 51%, eosinophil 1%, MCV 96.1 fl, MCH 31.2 pg, MCHC 33.2 g/dL, erythrocyte sedimentation rate 32 mm (first hour), normal platelet count and coagulation profile, and without apparent evidence of extramedullary haematopoesis. Serum albumin was 4.1 g/dL, calcium 9.49 mg/dL, phosphorus 5.0 mg/dL, alkaline phosphatase 173 IU/L, and arterial blood gas report was normal.

Pantomographic view of the mandible revealed ill-defined osteolytic lesions involving the left half of the body of mandible up to the angle. Gross osteolysis with marginal irregularity was noted at the alveolar margin in the region of dislocated left molar and premolar teeth. There were also some osteolytic areas in the right half of body of mandible at the lower margin. Features were consistent with chronic osteomyelitis (Fig. 2).

The apparent increased radiodensity of the mandible was striking. A skeletal survey of the whole body was done (Fig. 3). Lateral view of the skull revealed generalised increased density of both the calvaria and base of the skull. Evidence of chronic osteomyelitis with sequestrum was seen in the left side of the body of mandible (Fig. 3a). Generalised increased radiodensity of all bones was evident in the

4a

4b

4c

Fig. 4 Characteristic radiological changes of Albers-Schönberg disease in one of the elder sisters, consisting of (a) rugger-jersey spine; (b) increased radiodensity of the skull base and calvaria; and (c) resorption of the left femoral head and severe coxa vara deformity.

postero-anterior view of the chest (Fig. 3b). In the lateral radiograph of the spine, a band of increased radiodensity was seen at the vertebral margins (rugger-jersey spine / sandwich vertebra), along with fracture of the pars interarticularis (spondylolysis) at the lumber fourth and fifth vertebrae, and spondylolisthesis at L5/S1 level (Fig. 3c). Anteroposterior radiograph of the hips and pelvis revealed a "bone-within-bone" appearance, which is typical of osteopetrosis seen in iliac bones. There were also resorptions of both the femoral heads associated with severe coxa vara deformity and beak-shaped greater trochanters bilaterally. A non-united fracture was seen in the right neck of femur (Fig. 3d). A provisional diagnosis of osteopetrosis was made. During a radiological skeletal survey of the family members (the mother, two elder sisters and one younger sister), one of the elder sisters and the younger sister were found to be affected with characteristic rugger-jersey spine, increased radiodensity of the skull, resorption of the left femoral head with coxa vara deformity (Fig. 4a–c, elder sister)

and rugger-jersey spine with increased radiodensity of bones of thorax (Fig. 5, younger sister).

The final diagnosis of ADOII with mandibular osteomyelitis and multiple skeletal complications was made. As hyperbaric oxygen (HBO) therapy was not available in our centre, he was referred to our dental colleagues. Hemimandibulectomy with reconstruction of the jaw was contemplated, but both the patient and his mother refused this option. The patient was put on systemic antibiotic therapy based on culture sensitivity report of the pus from the sinus, along with successful sequestrectomy and saucerisation of the osteomyelitic foci of the jaw. The sinus tract was also excised and the jaw remodelled. Recovery was uneventful and there was no recurrence of the sinus two months postoperatively.

DISCUSSION

Though one case of biphosphonate (pamidronate)-induced osteopetrosis has been reported recently,[1] osteopetrosis is a group of inherited bone disorder where there is severe impairment of osteoclast-mediated bone resorption,[2] thus producing solid dense radiographical appearance of bones which are fragile and susceptible to pathological fractures. Mode of inheritance may be autosomal dominant or recessive. Dominant forms are more common.[3] Two subtypes of ADO are reported based on radiographical features.[4] In type I (ADO I), there are generalised, diffuse osteosclerosis affecting mainly the cranial vault,[4] due to mutation in the gene located in chromosome 11q12-13, precisely in the region where a high-bone-mass syndrome has been localised.[5] Type II (ADO II), the form originally described in 1904 by Albers-Schönberg,[6] is the most common form with an estimated prevalence of up to 5.5/100 000.[7] Clinical manifestations occur in as many as 78% and include

Fig. 5 Radiograph of the younger sister shows a rugger-jersey spine and increased radiodensity of the ribs.

non-traumatic fractures, especially of long bones, cranial nerve palsies, osteoarthritis of the hip and mandibular osteomyelitis.[7] Femoral shaft fractures, either with transverse or short oblique pattern, are the most common. Other common locations are inferior neck of femur and posterior tibia. Upper extremity fractures have also been reported. The fractures may have delayed healing.[7] The radiological penetrance is as high as 90% in some series and is increased after the age of 20 years.[7] There have only been seven reported cases of spondylolysis associated with osteopetrosis.[8] ADO II manifests radiographically with a segmentary osteosclerosis, predominantly at the vertebral endplates (rugger-jersey spine), iliac wings (bone-within-bone sign) and skull base.[3] A gene residing in chromosome 16p13.3 encoding the ClCN7 chloride channel,[9] essential for the acidification of the extracellular resorption lacuna of osteoclast,[10] is mainly defective in ADO II.

There are three clinically distinct forms of autosomal recessive osteopetrosis (ARO).[11] The most common ARO (also called the malignant type),[12] has severe manifestations, and presents in the infantile age group, presumably due to mutations either in the TCIRG1 gene which encode for the α3 subunit of the vacuolar H(+)-ATPase[13] or in the ClCN7 gene encoding an osteoclast-specific chloride channel.[10] These patients have bone marrow compromise as a result of bone overgrowth in the marrow space. They usually die from anaemia with congestive heart failure, or sepsis in their infancy or childhood.

The increased susceptibility to severe infection is presumably related to pancytopenia secondary to marrow space obliteration. The second ARO type with carbonic anhydrase II deficiency is associated with renal tubular acidosis and cerebral calcification, extramedullary haematopoiesis, hepatosplenomegaly and pancytopenia.[14] The third recessive type is milder, presenting in childhood with variable orthopaedic and dental symptoms. They tend to have radiographical evidence of the disease, short stature, macrocephaly, increased upper segment/lower segment ratio, decreased arm span, mandibular prognathism, nerve compression, and a tendency for developing fractures and osteomyelitis. Of the 18 affected family members in 11 families with this form reported so far, many children were asymptomatic with only radiographical disease. In many of these cases, there was parental consanguinity.[11]

Patients with osteopetrosis frequently visit the dentists for several complications like dental caries, delayed eruption and early loss of teeth, enamel hypoplasia, malformed roots and crowns, and thickening of the lamina dura; with the most common problem being caries. Constriction of the canals housing neurovascular bundles supplying the teeth and jaws as well as obliteration of the marrow cavities and dental pulp chambers, lead to bone necrosis and dental caries,[15] and ultimately develop osteomyelitis in 10% of cases. Osteomyelitis may be potentially severe with a protracted course due to the accompanying anaemia and neutropenia.

Management of osteopetrosis has to be individualised because of the wide spectrum of clinical symptoms and complications. Medical management of osteopetrosis revolves around modulation of the osteoclasts, either to stimulate the remaining host osteoclasts or to provide an alternative source of the same. Restriction of calcium intake, high-dose calcitriol therapy, steroids, parathyroid hormone and recombinant human interferon gamma-1b, have all been attempted to stimulate the host osteoclasts with variable success rate. HBO therapy has documented a beneficial role in the treatment of mandibular osteomyelitis. Mechanisms of HBO action in osteomyelitis include enhanced leucocytic killing, osteoclastic resorption of the dead osteomyelitic tissue, fibroblastic division, collagen production, neovascularisation, and enhanced permeation of certain antibiotics (aminoglycosides) across bacterial cell walls within the necrotic tissue. As osteoclasts are 100 times more metabolically active than osteocytes, its function is highly oxygen dependant. Bone marrow transplantation has been curative in a significant percentage of patients but an

acceptable donor can be found in only about 40%.

Our case fits with the description of ADO II (Albers-Schönberg disease). Important differential diagnoses considered are pyknodysostosis, metaphyseal dysplasia, diaphyseal sclerosis, melorheostosis, osteopetrosis striata, osteopoikilosis, Engelmann's disease and infantile cortical sclerosis. All these entities have characteristic clinical, biochemical and/ or radiological findings which were not present in this case. The classic manifestations of ADO II such as increased bone density mainly in the spine, cranium, iliac and long bones, non-traumatic long bone fractures, hip osteoarthritis and mandibular osteomyelitis, were all present in this case. Affection of the younger sister and one of the elder sisters found during radiological screening strongly supported our diagnosis. We were not able to perform a genetic study due to lack of logistic support. A case of mandibular osteomyelitis in a nine-year-old girl was also documented recently in the Indian literature.[16] This case merits special mention to reemphasise an important but uncommon manifestation (mandibular osteomyelitis) of a rare disease (ADO II). Severe bilateral hip deformity and spondylolysis at multiple levels as reported in this case were also very rare. Also noteworthy was the constellation of skeletal complications present in a single case, forcing one to seriously think about the so-called "benignity" of the disease.

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