CASE REPORT

Infantile osteopetrosis associated with osteomyelitis

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SUMMARY

Osteopetrosis is a rare inherited disorder characterised by the inability to reabsorb and remodel bone due to an osteoclast dysfunction. An increase in bone mass and density results in severe skeletal malformation and bone marrow failure, which may be fatal. The aim of this study was to report a case of infantile osteopetrosis in a 6-year-old boy, who primarily complained of dental problems. The patient developed an osteomyelitis after a primary tooth extraction. We also reviewed the literature about this genetic bone disease, since the management of dental problems of these patients can be a challenge to the dentist. The diagnosis, clinical and radiographic features and treatment of the case were discussed in this work.

BACKGROUND

Osteopetrosis comprises a group of rare hereditary bone disorders characterised by a marked increase in bone density due to defective bone resorption, caused by the failure of normal osteoclast function. This disease is classified into three different clinical forms: an infantile malignant autosomal recessive form, a less severe intermediate autosomal recessive form and adult autosomal dominant osteopetrosis.^{1 2}

The lack of bone resorption and the encroachment by bone of the medullary spaces leads to

compensatory extramedullary haematopoiesis, which causes hepatosplenomegaly and anaemia. The occlusion of intracranial foramina may result in blindness, deafness, as well as oculomotor and facial nerve palsies. Defective bone resorption also leads to macrocephaly, frontal bossing, hypertelorism, exophthalmos, increased intracranial pressure, retarded linear growth and psychomotor delay.^{1 3–6} Dental findings include delayed tooth eruption, absence of some teeth, enamel hypoplasia, abnormal pulp chambers, a tendency to early decay, defects of periodontal membrane and thickened lamina dura. Osteomyelitis of the jaws often occurs after odontogenic infection or oral surgical procedures.^{2 7–9}

The severe infantile forms of osteopetrosis are associated with diminished life expectancy, with most children dying in the first decade as a complication of bone marrow failure and overwhelming infection.^{4–6} The only curative therapy is allogeneic bone marrow transplantation. However, in some patients, because of the severity of their disease, aggressive treatment is not warranted and palliative care is indicated.⁵

CASE PRESENTATION

A 6-year-old boy was brought to the Department of Social and Pediatric Dentistry of Federal University of Bahia with the symptom of pain and

Figure 1 Extraoral aspect of the patient showing increased mandible volume, hypotelorism (A) and evident frontal bossing (B).

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Figure 2 Increased abdominal volume.

swelling on the right side of the mandible ([figure 1](#)). The patient was short in stature and had locomotor difficulties. During the general examination, some abnormalities such as hypertelorism, frontal bossing and increased abdominal volume were detected ([figures 1 and 2](#)).

The patient was partially edentulous in both jaws. Almost all the teeth present were decayed and poor hygiene was noticed. Considerable bone bulging was detected on the right side of the mandible, which was associated with pus discharge, being compatible with osteomyelitis ([figure 3](#)). The patient's mother reported that the boy had undergone an extraction of a decayed primary tooth in that jaw area a few weeks before the visit to our department.

INVESTIGATIONS

A panoramic radiograph ([figure 4](#)) revealed areas of bone sequestration in the mandible and some retained primary teeth. The absence of some permanent tooth germs could also be seen, as well as some impacted and/or malformed permanent teeth. The radiograph of the mandible showed extremely dense bone, with loss of usual trabecular pattern.

Radiographs of the skull, thorax and long bones ([figures 5 and 6](#)) revealed diffuse increased density of the mineralised tissues. The radiograph of the long bones evidenced the

Figure 3 Intraoral examination showing the precarious condition of the present teeth and a considerable bulging in the right side of the mandible.

Figure 4 Panoramic radiograph of mandible bone, showing areas of bone sequestration, retained primary and permanent teeth, the absence of some permanent tooth germs, as well as bone density.

obliteration of marrow spaces by continuous bone deposition and lack of resorption.

An abdomen ultrasound showed an increase in the spleen and liver volume, suggesting hepatosplenomegaly. On laboratory evaluation, high levels of total acid phosphatase (22.4 U/L) were seen, which is a characteristic of severe osteopetrosis. The patient also presented moderate anaemia (9 g/dL). Other biochemical parameters such as calcium, phosphorus and serum alkaline phosphatase showed regular ranges.

DIFFERENTIAL DIAGNOSIS

Based on clinical, radiographic and laboratory findings, a diagnosis of infantile osteopetrosis associated with mandible osteomyelitis was made.

TREATMENT

After discussion with the medical service, it was decided to perform a sequestrectomy and extraction of all primary teeth, retained or not, as well as all the retained permanent teeth. Under general anaesthesia and antibiotic cover (clindamycin), multiple extractions were performed in both jaws, as well as debridement of necrotic bone tissue in the mandible ([figure 7](#)). Antibiotic therapy was maintained postoperatively for 30 days (20 mg/kg/day every 8 h).

OUTCOME AND FOLLOW-UP

Postoperative monitoring revealed a good healing process except for the recurrence of the fistula on the right side of the mandible after 3-month follow-up ([figure 8](#)), which was controlled with antibiotics.

Figure 5 Skull radiograph showing diffuse increased bone density.

Figure 6 Thorax (A) and long bone radiographs (B) showing dense sclerotic bones.

Dental rehabilitation was planned, with the construction of complete removable dentures for both jaw bones.

DISCUSSION

Osteopetrosis is a rare disorder of bone metabolism, characterised by deficient osteoclast function, leading to impaired bone resorption.^{10–15} The diagnosis is essentially radiological, where a generalised bone sclerosis can be seen, as well as thickening of the base of the skull, loss of diploe and reduction or absence of the medullary spaces. The foci of sclerosis found in the vertebrae, pelvis and long bones are considered pathognomonic findings.¹⁶ In this case report, the sclerosis of long bones and vertebrae, as well as the thickening of the skull, could be clearly visualised on radiographic examination.

Haematopoietic stem cell transplantation (HSCT) is the only treatment that has been proven to significantly alter the course of disease.⁵ In these patients, the orthopaedic, neural and dental problems that are already present rarely improve, but their haematopoietic potential is restored and long-term prognosis is favourable. Since osteoclasts are of haematopoietic origin, and in most forms of malignant osteopetrosis the defect is intrinsic to osteoclasts, HSCT can restore osteoclast function and promote bone resorption in these patients.^{16–17} Other treatment alternatives such as the use of corticosteroids, colony-stimulating factor 1, vitamin D and interferon γ have been reported to be inefficient.^{18–22}

Strategies based on gene therapy are considered a promising alternative of treatment for patients with osteopetrosis. Encouraging results were obtained in mice submitted to neonatal transplantation of genetically modified haematopoietic stem cells, using an oncoretroviral vector expressing murine *Tcigr1* gene, which is mutated in the majority of patients with osteopetrosis, and is essential for bone resorption. The authors observed an improvement in bone resorption after the treatment.^{17–23} Although genetic testing is important to confirm the diagnosis and to make the differentiation between the subtypes of osteopetrosis, it could not be performed in our case, due to the difficulty in accessing such services.

Children who survive infancy may present challenging dental and oral conditions.⁷ Sclerosis and the consequent avascularity of the jaw bones make them extremely susceptible to infections, osteomyelitis and fractures. Extractions are usually difficult and the healing of bony sockets is poor, resulting in irregular alveolar ridges.^{2–3}

The poor development of dental structures, resulting from increased bone density, is probably caused by progressive inadequacy of the supply nutrients to the developing tooth germs.^{8–24} Likewise, osteoclasts are needed for alveolar bone resorption, which removes the area of jaw overlying the tooth crown, and for resorption of the roots of deciduous teeth. They are also involved in the development of the permanent tooth roots, allowing the tooth crown to move into the oral cavity.²⁵ Thus, failure of tooth eruption and formation are common

Figure 7 Appearance of the affected mandible during the surgical approach (A) and the retained primary and permanent teeth surgically removed (B).

Figure 8 Postoperative follow-up showing the recurrence of a mandible fistula.

findings in patients with osteopetrosis.²⁶ Dental findings concerning osteopetrosis also include enamel hypoplasia, abnormal pulp chambers, a tendency to early tooth decay and early loss due to caries.^{8 9}

The histological examination of an unerupted extracted tooth from an osteopetrotic child revealed that the cementum interface had areas of ankylosis and absence of alveolar ligament.² These findings could explain the common observation of impacted primary and permanent tooth germs in patients with this disease. In the present case, the patient presented a mandible osteomyelitis. In addition, only a few primary teeth, which were almost all decayed, were present in the oral cavity. Several unerupted and/or malformed primary and permanent tooth germs could be visualised on radiographic examination. Even over antibiotic cover and after the surgical approach of the mandible osteomyelitis, as well the removal of any infectious focus in both jaws, the patient exhibited the recurrence of mandible fistula, confirming the difficulty of dental management of patients with osteopetrosis. Since impacted and ankylosing teeth, as well as extensive caries in the teeth that have erupted, can lead to severe osteomyelitis,^{27 28} it was decided, in the present case, to extract all primary and permanent teeth, based on their precarious condition, as well as the condition of malformation that could be observed in the radiographic examination with respect to the unerupted teeth. Furthermore, the patient resided in a rural area with little access to health services, which could represent a hazard to the child's health, due to the high risk of developing severe infections such as sepsis.²⁸

Learning points

- Adequate surgical treatment and preventive oral healthcare, as well as dental/periodontal management in patients with osteopetrosis are critical, especially when mandibular tooth extraction is under consideration, in order to avoid worsening of the patient's clinical condition.
- The dentist may be the first professional to examine children with osteopetrosis, due to the evident dental problems it is associated with, so it is extremely important for the dentist to be aware of the general and dental conditions of a patient with osteopetrosis.
- Despite the severe systemic problems and limitations present in these patients, it is important that dental care is not neglected, providing them with a better quality of life.

Competing interests None.

Patient consent Obtained.

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