Malignant infantile osteopetrosis: dental effects in paediatric patients. Case reports

V. LUZZI, G. CONSOLI, V. DARYANANI, G. SANTORO*, G.L. SFASCIOTTI, A. POLIMENI

Abstract

Malignant Infantile Osteopetrosis is a hereditary pathology caused due to osteoclastic cells which are incapable of carrying out their functions and hence do not resorb osseous tissue where required. Thus the consequence is that during growth phase, the medullary cavities and nervous tissue cavities do not undergo sufficient growth and the corresponding organs do not develop adequately. The aim of this study is to outline the role of the pediatric dentist who has to carry out protocols of primary, secondary, tertiary prevention intervening at many levels. Clinical features and dental effects are described. Two case reports are presented in this study.

Conclusion

Oral problems of osteopetrosis are delayed tooth eruption, absence of some teeth, malformed teeth, enamel hypoplasia, disturbed dentinogenesis, hypomineralisation of enamel and dentin, propensity for tooth decay, defects of the periodontal membrane, thickened lamina dura, mandibular protrusion, and the presence of odontomas. Tooth removal should be limited as it may induce bone fractures and osteomyelitis. The role of the pediatric dentist is defined.

Keywords: Malignant infantile osteopetrosis, Osteoclastic cells, Pedodontic prevention.

Introduction

Malignant Infantile Osteopetrosis (MIOP) is a hereditary disease which is part of a heterogenous group of thickening primitive or congenital osteopathies (Table 1), secondary to a primitive disturbance in ossification or to a congenital alteration of metabolism [Flanagan et al., 2002].

Osteopetrosis is divided into four types: malignant infantile osteopetrosis, intermediate osteopetrosis, and two types of autosomal osteopetrosis. Malignant infantile osteopetrosis is usually diagnosed within the first year of birth by bone sclerosis and bone marrow obliteration. This type is very severe and usually results in death within a few years. The intermediate type usually appears before the age of ten and leads to recurrent pathologic fractures and cranial nerve compression. Autosomal dominant osteopetrosis is usually mild and consists of two subtypes. Type I involves marked thickening of the cranial vault. Type II patients have predominantly sclerosis of the pelvis, the vertebrae and the base of the skull. Type I and II patients may often be long-lasting asymptomatic, but will eventually present with pathologic fractures, bone pain, and the effects of cranial nerve compression [De Baat et al., 2005].

Etiology shows osteoclastic cells to be incapable of carrying out their functions and hence not able to resorb osseous tissue where required. Thus the consequence is that during growth, the medullary cavities and nervous tissue cavities do not grow enough and the corresponding organs do not develop adequately. Many genes have been identified as responsible, but the Genes Atp6i and CLCN7 (which codifies for the protein membrane of the osteoclasts) are frequently involved [Blinda et al., 2003; Sobacchi et al., 2001]. Genetic mutation provokes an alteration in the function of the osteoclastic cells and render them incapable of the required resorption of the osseous tissue. As consequence, during growth the medullary cavities and the nervous tissue cavities do not grow sufficiently and the organs do not develop adequately, thus creating an imbalance incompatible with life.

Therapeutic orientation provides the integral correction of the primary disease through medullary implant, and treats the complications [Eapen et al., 1998; Shapiro, 1993; Jalevic et al., 2002; Dini et al., 2000]. The aim of this study is to outline the role of the pediatric dentist who has to carry out protocols of
Primary, secondary, and tertiary prevention intervening at many levels [Peretz and Ram, 2002]: frequent check ups of dental eruption is very important, maintenance of oral hygiene, and interception of dental problems [Björvåt et al, 1979].

**Epidemiology**

MIOP HAS an autosomal recessive type transmission which is different from the two other forms of osteopetrosis, which are more favourable and more frequent not only due to the modality of transmission but also for their clinical manifestations. They are: benign delayed osteopetrosis (with autosomal dominant transmission) and intermediate osteopetrosis (with autosomal recessive transmission) [Senel et al., 2002; Yang et al., 1999]. There is a certain discordance about the number of cases in literature due to confusion with other rare forms of thickening osteopathies.

Presently, with the most accurate means of investigations the incidence has been estimated at 1:20,000-500,000 for the dominant form, and at 1:200,000 for the two clinical forms with autosomal recessive transmission [Michigami et al., 2002; Long et al., 2001].

**Clinical aspects of MIOP**

The clinical aspects consist of primary and secondary pathologies (Table 2). The primary pathologies are a result of medullary insufficiency while the secondary are due to the primary deficit: hepatosplenomegaly due to hyperfunction as a result of medullary deficit; mental retardation due to absence of expansion of cranium; nervous compression due to increase in osseous volume; spontaneous fracture due to the high fragility of bone even though it has a high density due to an arrest in the resorption of calcium; constant presence of osteomyelitic foci (maximum presence in the mandible, followed by maxilla) due to the reduced perfusional capacity of osteopetrotic bone (at high density) [Kornak et al., 2001]; and finally frequent dental alterations (of number, form, volume, development and structure) [Toraldo et al., 2002; Dini et al., 2000].

**Clinical dental aspects of MIOP.** The clinical features are found in all of the subjects affected by infantile malignant osteopetrosis. The objective examination of the face shows a bone alteration in the face bulk, which undergoes hypertrophic growth and thus there is a facial asymmetry with frontal prominence, bilateral exophthalmus with signs of petechiae and ecchymoses [Van Hul et al., 2002; Scimeca et al., 2003; Helfrich and Gerritsen, 2001]. The physiologic processes related to the mechanism of osteogenesis are altered and with eruption anomalies (often congenital agenesis or dental inclusions). Some anomalies result in alterations in form and volume of both crown and root often associated with complete lack of root or an anomalous pulp chamber [Jalevik et al., 2002].

Also common is the structural anomaly resulting in enamel hypoplasia which is a predisposing factor for progressive and destructive caries and consequent gingival inflammation [Conor et al., 2003]. Radiographic examination reveals alterations in the periodontal ligament, in the resorption of primary teeth with early exfoliation and osteomyelitic foci in the maxilla [Björvåt et al., 1979].

In Table 3 all the dental aspects of MIOP are reported.

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<td>Cranial hyperstosis</td>
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**Table 1**

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<td>Anemia</td>
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<td>Low platelet count</td>
<td>Mental Retardation</td>
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<td>Granulocytopenia</td>
<td>Osteomyelitis of jaw bones Pathological fractures Dental anomalies</td>
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**Table 2 - Clinical manifestation of MIOP**
Case reports

A 9 year old patient was referred to the Dental Clinic of “La Sapienza” diagnosed with MIOP at the age of 1 year; at 1 year and a half she was treated with a haploidentical medullary bone implant (her mother was donor). The patient showed left mandibular swelling, which failed to respond to antibiotic therapy, and a fistula on the left as a consequence of an osteomyelitic process.

At the extraoral examination the patient showed facial asymmetry, left swelling, bilateral exophthalmos, frontal prominence, diffuse petechiae and ecchymoses (Fig. 1).

At the oral examination, in the lower arch the following were detected: dysmorphic and hypoplastic teeth with gingival flogosis and osteitic processes in the premolar region, and mandibular swelling, whereas in the upper arch the following were observed: structural anomalies and a marked gingival flogosis (Fig. 2-4).
The orthopantomograph (Fig. 5) showed diffuse caries in both jaws while the periodontal ligament could not be evaluated and the radiographic aspect of bone appeared normal. The lateral cranial teleradiograph (Fig. 6) shows bone rarefaction at the mandibular ramus, high density of the upper arch, maxillary sinus not visible, cortical thickening of the frontal and sphenoid bones. Diffuse caries in both arches.

The surgical treatment consisted of surgical clean up of the mandible and a pharmacological therapy.

A 2 year old patient (Fig. 7-9) diagnosed with MIOP was referred to our unit. The case history also recorded an accidental extraction of upper left central incisor while breastfeeding.

The patient had to undergo allogenic medullary osseous implant, but extraction of inferior central incisors and upper right central incisor was necessary in order to intubate the child during the surgery.

At the clinical examination the residual teeth are very mobile and marginal gingiva is edematous.
Discussion
The role of the paediatric dentist in MIOP is to follow the protocol of primary, secondary or tertiary prevention depending on the gravity and stage of clinical symptoms [Pomarico et al., 2005; Skeie et al., 2004]. Primary prevention permits to monitor the dental eruption in the phase of transition in order to prevent the development of both odontogenic diseases and non odontogenic ones, such as inflammation or cysts and dento-scheletrical anchilosis. This requires the planning of closely spaced appointments to analyse and record any possible clinical signs related to dental and skeletal growth with the help of radiographs if required. The pediatric dentist in this phase should also remove any source of infections and prevent their development [Kotsanos et al., 2005].

Pretreatment prophylaxis with antibiotics must be considered. In the case of low platelet count any bloody procedure is contraindicated. Even oral hygiene carried out at home could produce prolonged bleeding with a high risk of septicemia [Rajab, 2002]. In these cases it is advised to use gauze and soft toothbrushes along with proxa brush. In order to improve oral hygiene in such patients the efficacy of chlorhexidine spray at 0.2% concentration has been proved, it has to be used daily especially in the inflamed and ulcerated areas [Mentes, 2001].

Conclusion
MIOP is a hereditary bone disease caused by a transmission of autosomal recessive gene and the prognosis for survival is 30% at 6 years. It is often associated with anaemia and thrombocytopenia. Hepatosplenomegaly, mental retardation, fragility of bones, high susceptibility to fractures are some of the clinical features of this pathology [Iacobini et al., 2001; Chalhoub et al., 2003; Album et al., 1999]. With regards to the face, asymmetry with frontal prominence, bilateral exophthalmus with signs of petechiae and ecchymoses are observed [Kornak et al., 2001].

Frequent dental alterations of number, form, volume, development and structure are noted. The role of the paediatric dentist is to carry out primary, secondary and tertiary prevention depending on the stage of disease.

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