

Oral Findings in Patients with Mucopolipidosis Type III

Weber Céio CAVALCANTE¹
Luciano Cincurá Silva SANTOS¹
Josiane Nascimento dos SANTOS¹
Sara Juliana de Abreu de VASCONCELLOS¹
Roberto Almeida de AZEVEDO¹
Jean Nunes dos SANTOS²

¹Department of Oral and Maxillofacial Surgery, Santo Antônio/Irmã Dulce Hospital, Salvador, BA, Brazil

²Department of Prosthodontics and Integrated Clinics, Dental School,
UFBA - Federal University of Bahia, Salvador, BA, Brazil

Mucopolipidosis type III is a rare, autosomal recessive disorder, which is part of a group of storage diseases as a result of inborn error of lysosomal enzyme metabolism. It is characterized by the gradual onset of signs and symptoms affecting the physical and mental development as well as visual changes, heart, skeletal and joint. Although oral findings associated with mucopolipidosis type II have been extensively reported, there is a shortage of information on mucopolipidosis type III. This paper presents radiological and histological findings of multiple radiolucent lesions associated with impacted teeth in the jaw of a 16 year-old youngster with mucopolipidosis type III.

Key Words: mucopolipidosis, pseudo-Hurler's syndrome, lysosomal metabolic diseases, storage disease.

INTRODUCTION

The extracellular matrix and the cell surface are composed by various molecular components, in which are found the proteoglycans. These substances are linked covalently to the glycosaminoglycans, which are catabolized, gradually, by the lysosomal enzymes. Because of the genetic alterations, the post-translational modification of these lysosomal enzymes promotes the appearance of these clinical conditions characterized as mucopolipidosis (1).

The lysosomal enzymes are addressed to the lysosomes by post-translational addition of the mannose-6-phosphate, reaction, which is characterized by the phosphotransferase enzyme. Phosphotransferase deficiency results in the incapacity to catabolize all of glycosaminoglycans. Thus, the enzymes responsible for catabolizing the glycosaminoglycans fail to be transported to the interior of the lysosomes and accumulate at high concentrations in the plasma, serving

as a diagnostic evidence for mucopolipidosis (2).

Mucopolipidosis can be classified into 4 categories: type I, characterized by the deficiency of the lysosomal enzyme sialidase; types II (inclusion-cell disease) and III (pseudo Hurler polydystrophy), which are caused by deficiency of the enzyme N-acetylglucosaminy-1-phosphotransferase (NAGFT), and type IV, caused by the deficiency of the mucopolipin enzyme (3).

Deficiency of the enzyme N-acetylglucosaminy-1-phosphotransferase is the fundamental cause of the mucopolipidosis types II and III, and the differential diagnosis is based on the age of occurrence, clinical symptoms and severity (4,5). Also known as pseudo-Hurler polydystrophy, mucopolipidosis type III (ML III) appears to be milder than the mucopolipidosis type II (ML II), in which patients exhibit coarse facial features, early restricted joint movements and a more severe psychomotor delay (6). In ML III, the symptoms appear later on, with reports of survival rate until adulthood and no reports of oral findings (3).

This paper reports a case of ML III with oral involvement in a young patient.

CASE REPORT

A 16-year-old Caucasian female patient was referred to the Department of Oral Maxillofacial Surgery and Traumatology of the Federal University of Bahia, Brazil, by a general dentist due to the presence of impacted teeth in the maxilla and mandible.

The adolescent was the only daughter of a non-consanguineous couple, father and mother with 48 years of age. The child was born at term through a cesarean section, with weight of 3.750 kg and height of 44 cm. Around 5 years of age, skeletal alterations were detected, manifested by joint stiffness, low weight and height development and difficulty to run and go up stairs. The patient had normal neurological development for her age, attending the ninth grade of high school.

In the extraoral physical exam, it was noted that the patient showed good general condition, long biotype, short necked, protruded thorax, anicteric, eupneic, decreased flexibility at the hands, elbows, shoulders,

knees and cervical region, short neck, slightly coarse face, and good lip seal (Figs. 1 and 2A).

Ophthalmological, neurological, cardiac and urological exams were done at the Clinics Hospital of the Federal University of Bahia (HUPES) and did not reveal any alterations in the patterns of normalcy. The orthopedic examination, also conducted at HUPES, found that the patient had skeletal dysmorphism, decreased joint movement, bent knees and shortening of the 5th toe.

The patient underwent laboratory tests accompanied by the genetic service of HUPES, such as urine and plasma. The presence of arylsulfatase A, lysosomal enzyme serum, which summed to the non-aggressive phenotypic aspect of the disease favored to the final diagnosis of the ML III.

Intraoral examination revealed malocclusion, dental rotation, absence of the second and third molars, as well as the first inferior molars. No anterior open bite was observed (Fig. 2B-D).

Analysis of the panoramic radiograph showed well delimited radiolucent images, involving impacted teeth in the mandible and maxilla, compatible with cystic

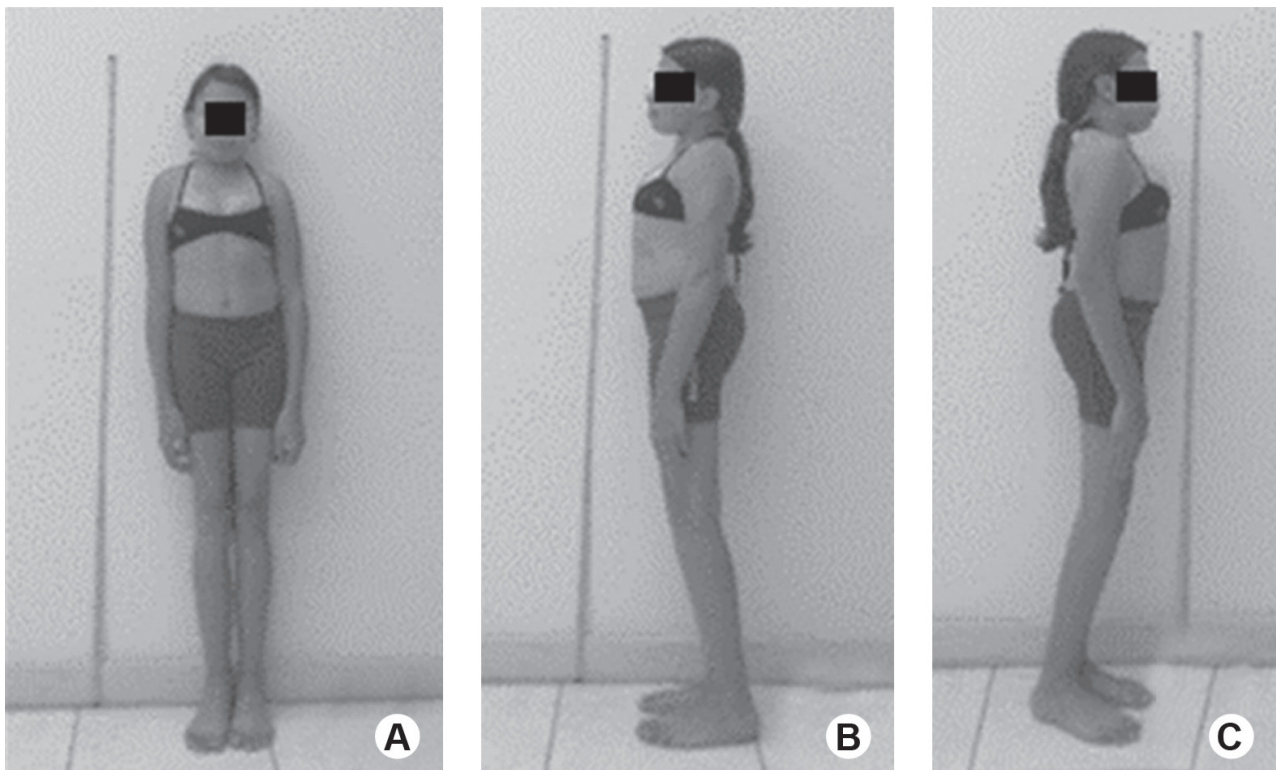


Figure 1. A 16 year-old youngster with ML III, exhibiting long biotype, short stature (1.5 m), protruded thorax and joint stiffness (A-B).

images (Fig. 3).

The patient was referred to the surgical Center of the Santo Antônio Hospital, Salvador, BA, Brazil, and submitted to surgical procedure under general anesthesia for the removal of multiple retained dental units.

During the surgical procedure, it was found thick fibrous material adhered to teeth 17, 18, 27, 28, 36, 37, 38, 46, 47 and 48 (Fig. 4A). All the material collected in the surgery was sent for histopathological analysis at the Department of Surgical Pathology of the Dental School, Federal University of Bahia. The patient recovered well postoperatively, without complications.

The histopathological analysis revealed a fibrous tissue rich in collagen fibers, with the presence of odontogenic epithelial remains, spots of mineralization

and discreet lymphocyte infiltrate compatible with normal dental follicle, though thick (Fig. 4B-D).

DISCUSSION

The literature demonstrates oral repercussions of ML II, however, it does not mention such findings in type III. Among the oral manifestations found in ML II are gingival and alveolar thickness evolving to open bite. Other findings are delayed tooth eruption, dental impaction, dental hypocalcification, lack of lip seal and accumulation of mucopolipidic material at the dental follicle (7-9). As to the case presented, delay in the dental eruption and the presence of impacted teeth were also present, however, open bite and lack of lip

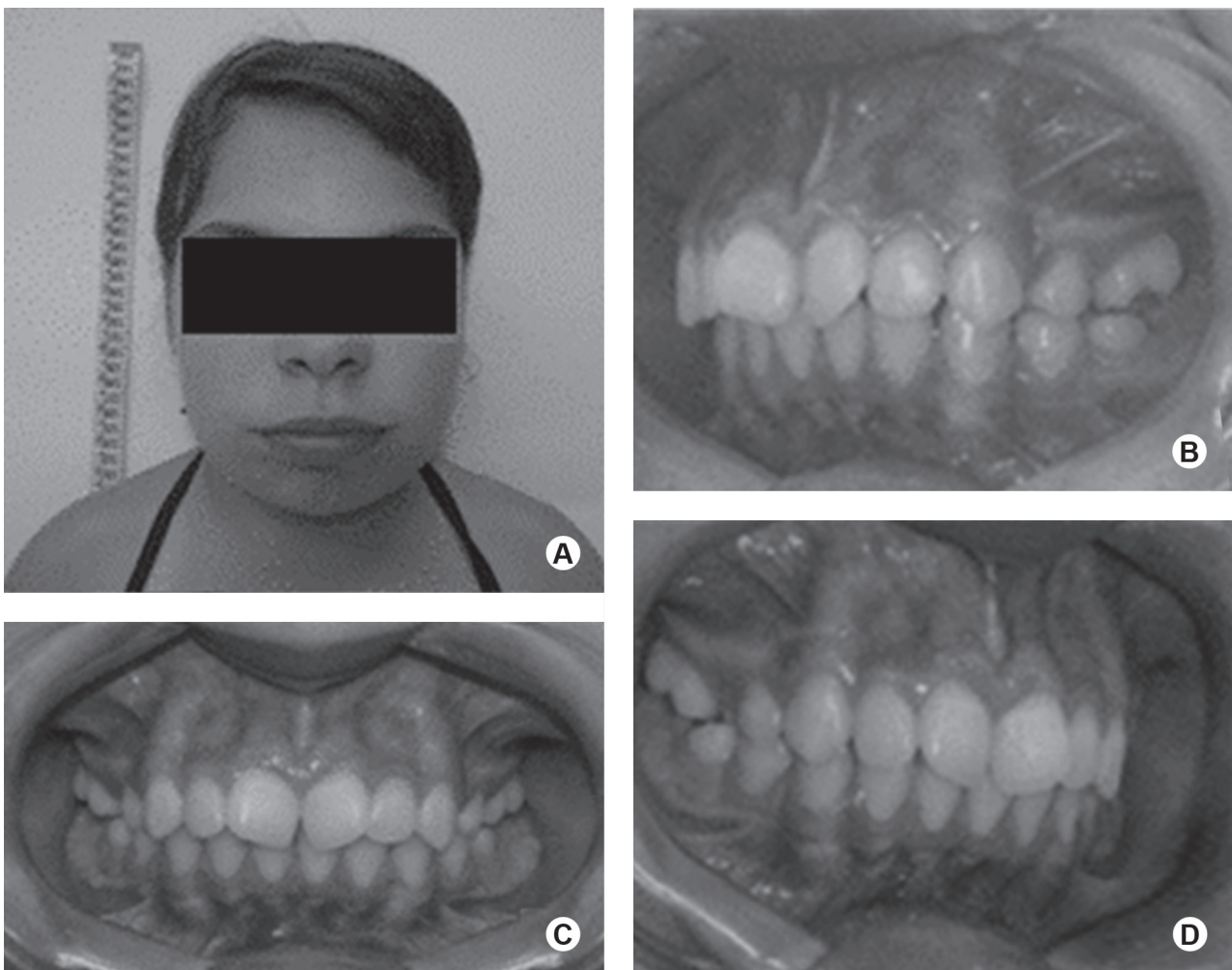


Figure 2. Extraoral examination demonstrating short neck, slightly coarse face, and good lip seal (A). Intraoral examination showing malocclusion, dental rotation, absence of teeth 18, 17, 27, 28, 36, 37, 38, 46, 47 and 48 (B, C and D).

seal were not observed.

Clinical manifestations of ML III include partial dystrophy like Hurler's syndrome or mucopolysaccharide type I, characterized by short stature. Another clinical

manifestation is mental deficiency, in a lesser degree when compared with ML II. Valvular cardiac diseases and corneal opacities are also reported. Among the ML III manifestations, the skeletal alterations are the



Figure 3. Panoramic radiograph showing radiolucent images associated with impacted teeth.

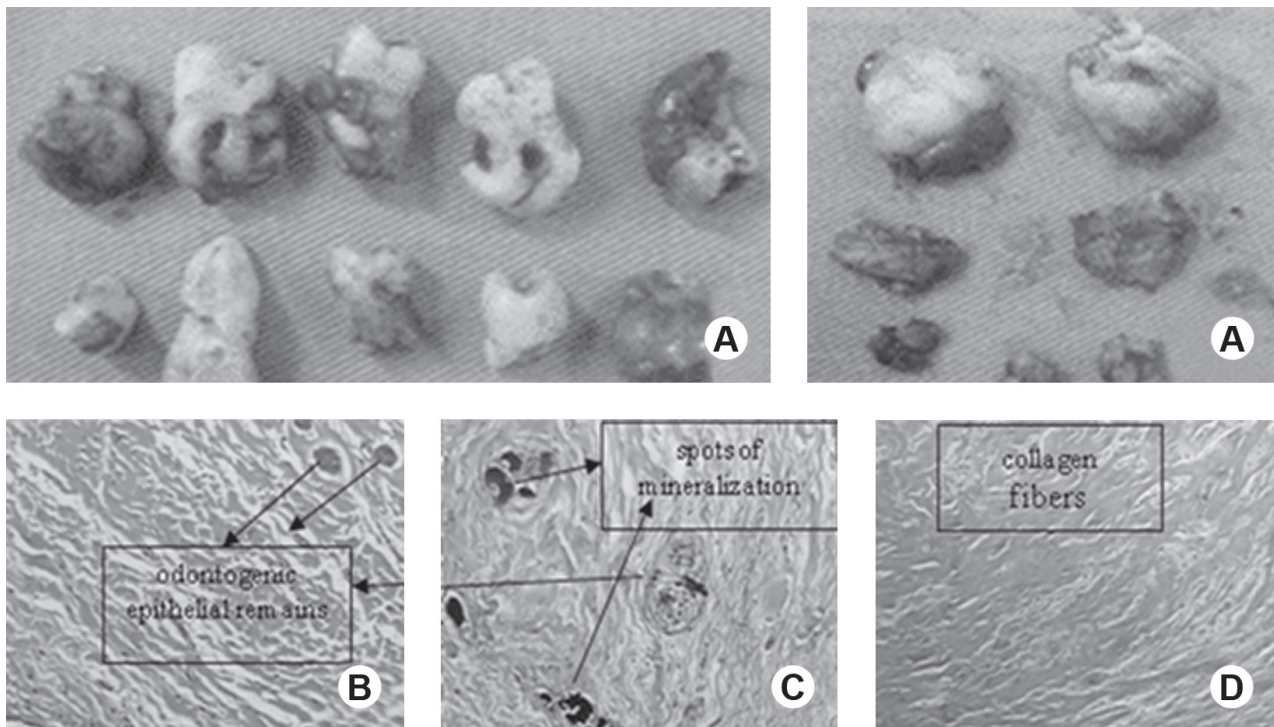


Figure 4. Impacted teeth surrounded with fibrous consistent tissue (A). Histological images with hematoxylin and eosin staining at magnifications $\times 100$, $\times 100$ and $\times 40$, respectively (B, C and D), demonstrating the predominance of collagen fibers, some odontogenic epithelial remains with spots of mineralization.

most discussed in the literature, which suggest the characterization of these diseases by the high turnover rate of bone metabolism in a disordered manner (10). Skeletal and orthopedic complications of ML III include hand and shoulders stiffness, claw-hand deformities, scoliosis, short iliac wings, erosion of the femoral heads, underdevelopment of the posterior elements of the dorsal spine and multiple dysostosis of the skull, vertebral bodies, long bones, clavicles and phalanges, which were observed in the present case (11). As to the intraoral manifestations, the only finding recorded in the literature, until the moment, refers to the abnormal dental spacing (10), which was observed in this case.

There is only one reported case in the literature relating ML III to a severe destruction of the temporomandibular joint, leading to dysphagia and dysphonia, and requiring gastronomy tube placement, but without mentioning intraoral findings (12). No temporomandibular joint alterations were observed in our patient.

It is believed that the clinical skeletal manifestations of this disease are due to the fact that mannose-6-phosphate (M-6-P) also acts in the osteoclastic activity. The osteoclastic lysosomal enzymes, destined for excretion are produced with the aid of this molecule. As a compensatory effect of the lack of these enzymes which are dependent of the mannose-6-phosphate this acid phosphatase seems to be produced in abundance, causing the clinical signs and symptoms observed in mucopolipidosis (10).

The diagnosis of ML III is based on clinical and laboratory findings. Short stature, joint alterations in hips, knees, elbows and spine, are referred clinical reports, also observed in the patient studied. The hematologic laboratory findings of patients with ML III involve the presence of some lysosomal enzymes including arylsulfatase, an enzyme found in the case reported herein (3).

The treatment of ML III is essentially symptomatic and palliative. The use of intravenous pamidronate has been combined with drug treatment with the aim of reducing bone repercussions of such disease. Pamidronate is a highly potent bisphosphonate widely used in the treatment of patients with bone metastasis from prostate and breast cancer. Bisphosphonates are known for their high affinity for the hydroxyapatite, and are synthetic analogs of the pyrophosphate, which is a physiological regulator of calcification and bone resorption, naturally present in urine and serum. The

action of bisphosphonates is due to the structural similarity with this compound group. Bisphosphonates act indirectly in bone resorption by attaching to the hydroxyapatite crystals, and directly by either inactivating or decreasing the activity of osteoclasts, depending on the type and/or concentration of the drug used (10,13). However, the association of osteonecrosis of the maxilla and mandible with the use of this type of bisphosphonate has been reported (14-17). The patient of the present case did not use this drug.

Based on the oral findings of the present case, it can be stated that the ML III, in the same way ML II, also has specific oral manifestations, which shall be diagnosed and treated as early as possible in order to improve the health conditions of their carriers.

RESUMO

A mucopolipidose tipo III é uma doença rara, autossômica recessiva, que faz parte de um grupo de doenças de depósito, decorrentes do erro inato do metabolismo das enzimas lisossômicas. Caracteriza-se pelo aparecimento progressivo de sinais e sintomas com repercussão no desenvolvimento físico e mental, bem como alterações visuais, cardíacas, esqueléticas e articulares. Apesar de achados bucais estarem bem relatados em associação à mucopolipidose tipo II, esse artigo descreve achados radiográficos e histológicos de múltiplas lesões radiolúcidas, associadas a dentes inclusos nos maxilares, em uma jovem de 16 anos de idade com mucopolipidose tipo III.

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