

CASE REPORTS

ORAL MANIFESTATIONS OF ALBRIGHT HEREDITARY OSTEODYSTROPHY: A CASE REPORT

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Albright hereditary osteodystrophy is a hereditary metabolic disorder of dominant autosomal etiology that is commonly characterized by short stature, round face, small metacarpus and metatarsus, mental retardation, osteoporosis, subcutaneous calcification, variable hypocalcemia, and hyperphosphatemia. In this study, we report a clinical case of a 17-year-old woman with Albright hereditary osteodystrophy, and we discuss her clinical, radiographic, and laboratory test characteristics together with the oral manifestations, and we correlate them with the characteristics found in the literature. We also discuss the odontological management of treatment of related periodontal disease and planning for corrections of related malocclusions.

DESCRITORES: Albright's hereditary osteodystrophy. Pseudohypoparathyroidism. Gs protein. Parathormone. Oral manifestations.

INTRODUCTION

Albright hereditary osteodystrophy (AHO), characterized by a metabolic disorder of dominant autosomal heritage, was first described by Fuller Albright in 1942 and is also called pseudohypoparathyroidism (PHP) or acrodysostosis^{8,12,16,18,20,21}.

This anomaly is caused by a mutation in the GNAS1 gene in the q13.11 region of chromosome 20, which results in reduction of quantity and quality of the α subunit of the guanine nucleotide regulatory G protein that is located in cell membranes. The etiopathology of the AHO disease or pseudohypoparathyroidism (PHP) involves the impairing of the functioning of the biochemical pathways responsible for activation of

parathormone receptors^{15,17,19,21}.

Some intrinsic factors, such as genetic mutation, may cause changes in the α subunit, compromising its function and causing the appearance of metabolic disorders. Such disorders may be expressed clinically as the following diseases: PHP, pseudopseudohypoparathyroidism (PPHP), AHO, acromegaly and hyperfunctional thyroid lymph node and McCune-Albright syndrome¹⁶.

Albright hereditary osteodystrophy may be classified as type Ia PHP and

PPHP. The first disorder is characterized by a molecular fault in the α subunit of the Gs protein, interrupting the action of parathormones, thyroid stimulants, and gonadotrophins, consequently promoting the clinical manifestations of this disease. The second disorder is also characterized by deficiency in the α subunit of the Gs protein, but there are no parathormone metabolic changes, although clinical manifestations may occur.^{16,18,19}

The phenotypic characteristics present in AHO are: short stature, obesity, round face, shortening of the metacarpus and metatarsus (most frequently the 4th and 5th ones), calcification in the subcutaneous tissue, short neck, low nasal bridge, mental retardation, cataract, hyperphosphatemia, cone-shaped epiphysis, and osteoporo-

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sis.^{5,8,12,15,20,21} When individuals present these changes plus normocalcemia, the disease can be called PPHP, showing that hypocalcemia can be a variable characteristic of this pathogenesis⁵. The oral manifestations found are primarily a late tooth eruption and/or aplasia or hypoplasia of the dental enamel^{4,5,8}.

Laboratory tests of PHP reveal high serum levels of parathormone—concomitantly with hypocalcemia and hyperphosphatemia—and normal renal function. For treatment of these changes, D vitamin and calcium are administered, with periodic checks of calcium serum levels and urinary excretion. Medication can vary due to different clinical and laboratory characteristics. The prognosis of this metabolic disorder is considered good¹³.

In this study, we report a clinical case of AHO and discuss its clinical, radiographic, and laboratory test characteristics together with its oral manifestations, and we correlate them with the characteristics found in the literature. We also discuss the odontological management of treatment of related periodontal disease and planning for corrections of related malocclusions.

CLINICAL CASE REPORT

A 17-year-old female leucoderma patient was referred to our services, presenting pain and gingival bleeding as the major complaint.

Before the dental clinical procedures, the patient underwent clinical, radiographic, and laboratory tests and genetic evaluation. Tests results showed that the patient had a short stature, obesity, round face, low nasal bridge, short neck, osteoporosis, and motor deficiency due to rheumatoid arthritis in the hand and foot joints (Fig. 1). The presence of subluxations was observed in the joints of the hand with the radius and ulna bones and in the joints of the



Figure 1 - Patient with Albright hereditary osteodystrophy. Round face, low nasal bridge, and short neck.

limbs showed a valgus deformity of the femur bones and joints and imbalance between the femur and tibia and between the tibia and tarsus, resulting in the left leg being shorter than the right one (Figs. 2 and 3). Laboratory tests showed hypocalcemia, hyperphosphatemia, osteopenia, and endocrine dysfunctions, such as early menarche and hypothyroidism. A genetic evaluation revealed a mutation of a gene lo-



Figure 2 - Femur with valgus deformity.

metacarpus with the phalanges, as well as shortening of the carpal and tarsal bones, primarily on the 4th metatarsus. Computerized tomography of the lower

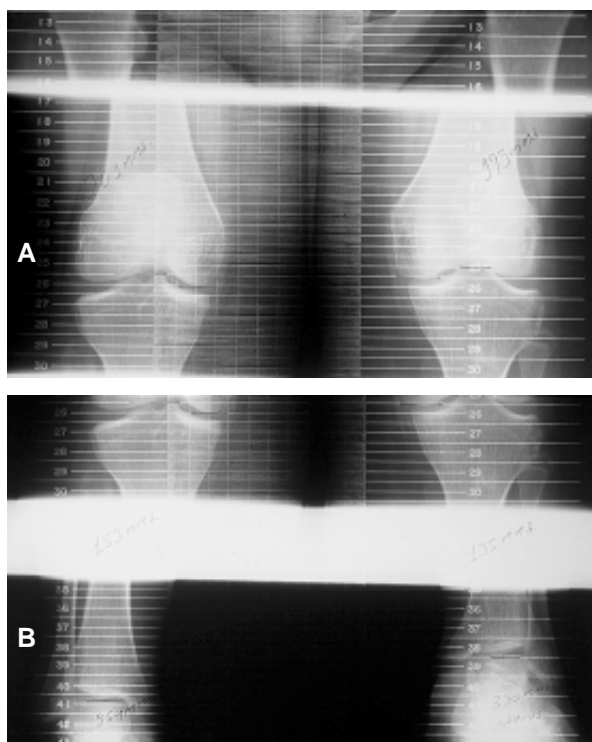


Figure 3 - Imbalanced joints between femur and tibia (A) and between tibia and tarsus (B).

cated on chromosome 20 in the q13.11 region, establishing a diagnosis of AHO. There was no report in the clinical history of the patient of individuals with AHO in the family.

The extrabuccal clinical exam showed the presence of a factitious lesion on the inferior lip, labial hypotonicity, lack of labial sealing, and crepitation on the temporomandibular joint (TMJ) during opening and closing of the mouth. Panoramic radiographs of the maxillomandibular complex and lateral ones of the cranium and face and of the TMJ showed calvaria thickening, severe open bite at the anterior region (Fig. 4), lack of anodontia and micrognathia, normal chronology of tooth eruption, and occlusion disharmony due to crowding of anterior teeth and superior and inferior premolar teeth (Fig. 5); no signs of any TMJ anatomical abnormalities were seen.

The intrabuccal exam showed deep hard palate, lack of enamel hypoplasia, xerostomia, presence of bacterial plaque on all dental elements, gingival hyperplasia and spontaneous bleeding located primarily in the areas of crowded teeth, predisposing the patient to periodontal disease (Fig. 6).

The patient underwent periodontal treatment and motivation to practice buccal hygiene, with the performance of scaling, planing, and coronary and radicular polishing procedures, fluoride application, and orientation on brushing technique during a period of 2 months with 8 sessions of treatment. After this period, a significant improvement in the clinical picture was observed; the patient was then referred to orthognathous and orthodontic treatments for aesthetic and functional correction of the malocclusion.

DISCUSSION

In AHO, genetic mutation in the GNAS1 gene of chromosome 20 causes

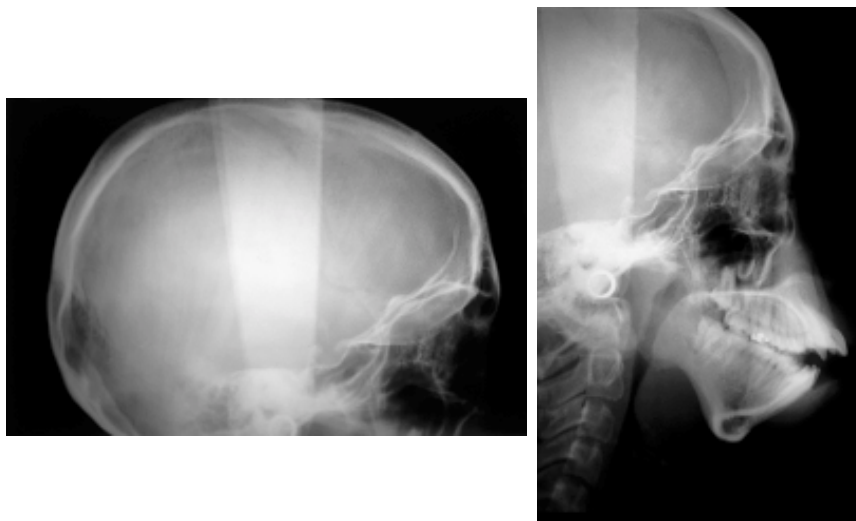


Figure 4 - Lateral radiograph of the cranium and face: (A) calvaria thickening and (B) severe open bite.

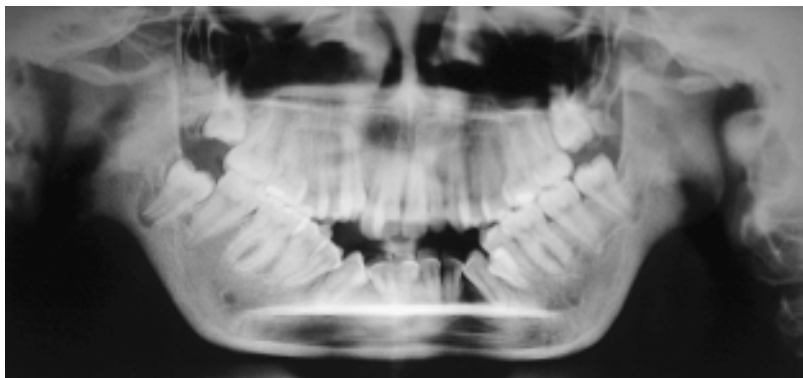


Figure 5 - Panoramic radiograph showing lack of anodontia, unaltered chronology of tooth eruption, and crowded teeth.

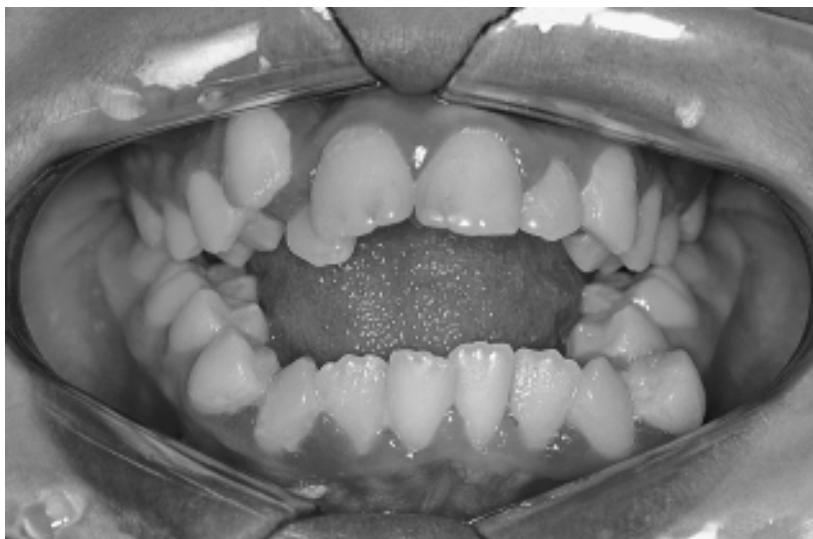


Figure 6 - Clinical intrabuccal exam showing calculus, accumulation of bacterial plaque and areas of spontaneous bleeding at the anterior superior and inferior region.

a defect in the a subunit of the Gs protein of the cell membrane, resulting in several phenotypic manifestations^{1,15,17,19}.

A lack of family history of individuals with AHO in this study is not contrary to the dominant autosomal heritage type of this disease, as indicated by the sporadic cases described in the literature^{15,17}. In our study, we found that the genetic mutation occurred on chromosome 20, which is in accordance with studies reported by Luttikhuis et al.¹⁴, Jones⁸ and Farfel et al.⁶ These authors observed mutations in the 20q13.11 region of the chromosome 20^{2,8,20}. Other investigators have also verified deletion in the region 2q37 of chromosome 2, and brachydactyly was one of the phenotypic characteristics of this genetic mutation¹⁴⁻¹⁷.

The AHO case reported here was classified as subtype Ia pseudohypoparathyroidism, with several mutations in the a subunit of the Gs protein, resulting in loss of function of the Gs protein. This loss of function leads to tissue resistance to multiple hormones whose receptors couple to the Gs protein^{12,16}. This genetic disorder manifested clinical signs including obesity and short stature due to hypothyroidism and early menarche. According to Namnoun et al.¹² menstrual cycle irregularity arises from gonadal hypofunction, promoting a decrease in estrogen secretion.

In this study, other changes were observed, such as round face, shortening of the metacarpus and metatarsus, hypocalcemia, hyperphosphatemia, and mental deficiency, which were also described by Eyre and Reed⁵, Phelan et al.¹⁵, Williamson et al.²¹, Jones⁸, Namnoun et al.¹² and Walden et al.²⁰ The 4th and 5th metacarpus and metatarsus frequently are the most compromised structures^{4,5,12,15,20,21}; however, in

our case, only the 4th metacarpus was found compromised.

The subcutaneous calcification at the periarticular regions, mainly located in the hands and feet, are abnormalities found in 50% of the patients with AHO, as described by Eronocodelu et al.⁴, Eyre and Reed⁵, Jones⁸, Namnoun et al.¹², Ringel et al.¹⁶, Miller et al.¹¹ and Walden et al.²⁰. However, such calcifications were not noted in our study, which is in agreement with findings such as those of Shapira et al.¹⁸ We agree with Eyre and Reed⁵ that these calcifications arise from metabolic changes concerning calcium and/or phosphorus.

The clinical and radiographic manifestations found in this case, characterized by short stature, round face, moderate obesity, osteoporosis, mental deficiency, and shortening of the carpal and tarsal bones, can be directly and/or indirectly associated with hypoparathyroidism and hypothyroidism, according to studies conducted by Phelan et al.¹⁵, Shapira et al.¹⁸ and Walden et al.²⁰ In addition, the presence of juvenile generalized rheumatoid arthritis was noted, which could be indirectly related to AHO.

Goldberg et al.⁷ observed the presence of ankylosis at the temporomandibular joint, but this condition was not present in our case. Since we believe that juvenile rheumatoid arthritis together with an occlusal disharmony could cause TMJ disease, we conducted a more thorough investigation of this region.

The oral manifestations of AHO found in the literature include aplasia and/or enamel hypoplasia, late tooth eruption, and enlarged radicular channels susceptible to caries. Such manifestations were not observed in our study. However, we observed the presence of severe periodontal disease with gingivitis and severe chronic peri-

odontitis. An intense inflammatory process was also observed located in the region of the superior and inferior anterior teeth, clinically characterized by spontaneous bleeding, pain, and gingival hyperplasia. In addition, there was also the presence of crowded superior and inferior anterior teeth, impairing proper buccal hygiene and favoring the accumulation of bacterial plaque and calculus.

The labial hypotonicity, deep hard palate, and xerostomia found in this case were changes probably resulting from the fact that the patient was a buccal respirator. In no work from the literature was any correlation between that respiratory dysfunction and AHO reported. Also, we believe that the motor deficiency resulted from rheumatoid arthritis, impairing buccal hygiene and favoring the accumulation of bacterial plaque and the persistence of periodontal disease.

The findings of general and oral manifestations of AHO described in our report contribute to the clinical picture of AHO that is developing in the literature. Extrabuccal and intrabuccal changes in patients with AHO continue to be the object of many studies, since there is little information on the oral manifestations of this disease, which hinders a better understanding of possible correlations between metabolic dysfunctions and oral manifestations. The findings of this study could also facilitate the development of a multidisciplinary approach among medical and dental professionals to promote a more precise diagnosis and knowledge of AHO behavior in the region of the face and the maxillo-mandibular complex. This more precise diagnosis and knowledge of AHO behavior could facilitate better planning of dental treatment of these patients, with a positive effect on their general health.

RESUMO

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GOMES MF e col. - Osteodistrofia Hereditária de Albright: relato das manifestações bucais de um caso. **Rev. Hosp. Clín. Fac. Med. S. Paulo** 57(4):161-166, 2002.

A Osteodistrofia Hereditária de Albright é uma desordem metabólica de caráter hereditário, de etiologia autossômica dominante, caracterizada geralmente por baixa estatura, face ar-

redondada, metacarpos e metatarsos pequenos, retardo mental, osteoporose, calcificações subcutâneas, hipocalcemia e hiperfosfatemia variáveis. Neste estudo, relatamos um caso clínico de uma jovem de 17 anos com Osteodistrofia Hereditária de Albright e discutimos as suas características clínicas, radiográficas, laboratoriais e manifestações bucais, relacionando-as com as encontradas na literatura, bem

como a conduta odontológica pertinente ao tratamento de doenças periodontais e ao planejamento da correção das más oclusões existentes.

DESCRITORES: Osteodistrofia Hereditária de Albright. Pseudohipoparatiroidismo. Proteína Gs. Paratormônio. Manifestações bucais.

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