Hereditary Osteodystrophy with Multiple Hormone Resistance—A Case Report

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Hereditary Osteodystrophy, also called pseudohypoparathyroidism, Type 1A (PHP), is a very rare condition composed of a heterogeneous group of autosomal dominant disorders with the common feature of organ resistance to multiple hormones. These patients produce the right amount of hormones but there is resistance to its effect. PHP is difficult to diagnose and the lack of diagnosis may have serious implications for the patient. We report a case of PHP, diagnosed by the dentist, due to the dental and jaw manifestations.
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INTRODUCTION

Hereditary Osteodystrophy, also called pseudohypoparathyroidism (PHP), and Albright syndrome, is a very rare condition composed of a heterogeneous group of autosomal dominant disorders with the common feature of organ resistance to multiple hormones that use cyclic adenosine-3 5-monophosphate.(cAMP), such as parathyroid hormone, thyroid stimulating hormone, gonadotropins and thyroid hormone.[1] These patients produce the right amount of parathyroid hormone but there is resistance to its effect.

Short stature, round facies, short neck, soft tissue calcifications, skeletal anomalies, such as osteopenia and shortened of III, IV, V metacarpals, absent knuckles, cataracts, tetany and in some cases mental retardation (47% to 75%) are usual findings.[2] Hypocalcemia, hyperphosphatemia, weakness, fatigue, cramps, diffuse osteopenia and abdominal pain are also present. Dental implications are enamel hypoplasia, widened root canals, shortened roots, delayed eruption, impacted teeth with open apices and bone cysts.[3] Laboratory tests show hypocalcemia, hyperphosphatemia and increased serum levels of parathyroid hormone.

PHP is caused by end organ resistance to a variety of hormones. Skeletal resistance to parathyroid hormone results from Vitamin D deficiency caused by inability of the kidney to convert 25 hydroxycholecalciferol to 1-25 dihydroxycholecalciferol, and homeostatic calcium release from bone does not respond to parathyroid hormone. Intestinal calcium absorption is reduced. Defects have been reported as a deletion of chromosome 20q[4] and 15q.[5] The problem results from a mutation in the GNAS1 gene which encodes a guanine nucleotide binding protein.[6]

Radiographically, the bone of these patients may present a picture of osteoporosis. Before starting a therapy, a thorough physical examination, serum calcium, phosphate, magnesium and parathyroid hormone (PTH) levels are mandatory. Genetic testing is also useful.

Patients with PHP may have complications such as seizures, low libido, low sexual development, lack of energy, blurred vision, hypersensitivity to light, cramps, abdominal pain, obesity and moderate mental retardation.

The hypocalcemia when treated with calcitriol (dihydroxyvitamin D) and calcium may achieve normocalcemia. The patients are also sometimes treated with hormonal replacement. If the blood phosphate levels remain high, a low phosphorus diet or phosphate binders (such as calcium carbonate) may be necessary. In order to avoid intoxication

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with vitamin D, serum calcium should be measured regularly and kept between 8 and 9 mg/dl.

CASE REPORT

A 14 year old African American female presented to Nova Southeastern University for dental treatment. Her mother complained about "delayed eruption" Medical history disclosed hypothyroidism and decreased levels of serum calcium levels, treated for three years with synthroid and calcitriol. Her mother stated that the girl was doing very poorly in school.

The patient was pleasant and collaborative. Extra-oral examination revealed a short stature female patient with a moon-shaped face, low nasal bridge, short neck and moderate obesity. (Fig. 1) Her short hands showed lack of knuckles.(Fig. 2) Intraoral examination showed generalized enamel hypoplasia of primary and permanent dentition and clinical absence of some permanent teeth. (Fig. 3) Panoramic radiography exhibited diffuse generalized osteopenia, numerous impacted maxillary and mandibular teeth, generalized short roots with open apices and widened root canals. Other radiographic findings include thickened inferior border of the mandibular lamina dura and loss of the cortical bone in the alveolar ridge and sockets. Left maxillary canine and 3rd molar and both mandibular 3rd molars presented radiolucency around the crown, suggestive of dentigerous cysts. (Fig. 4)

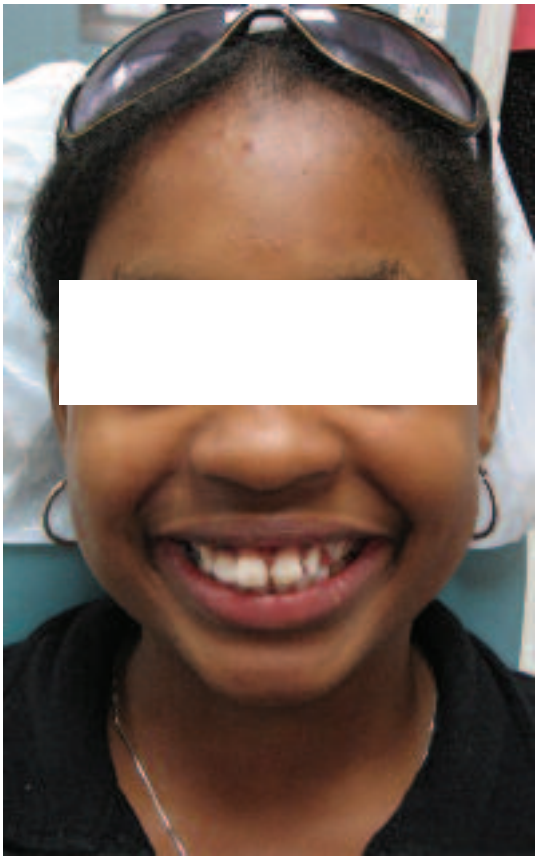

Figure 1: Photograph showing round face and short neck

Our findings were reported to her medical team. The patient was also referred to oral and maxillofacial surgery for a second opinion about treatment of the dentigerous cysts and for orthodontic consultation.

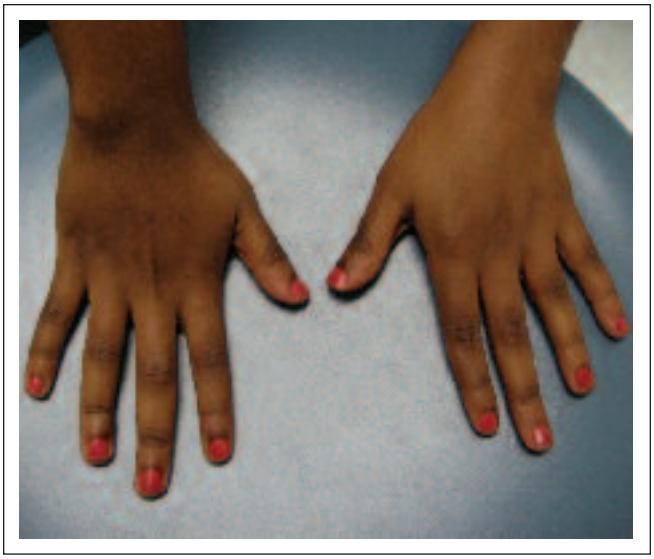

Figure 2: Photograph of patient's hand exhibiting lack of knuckles.

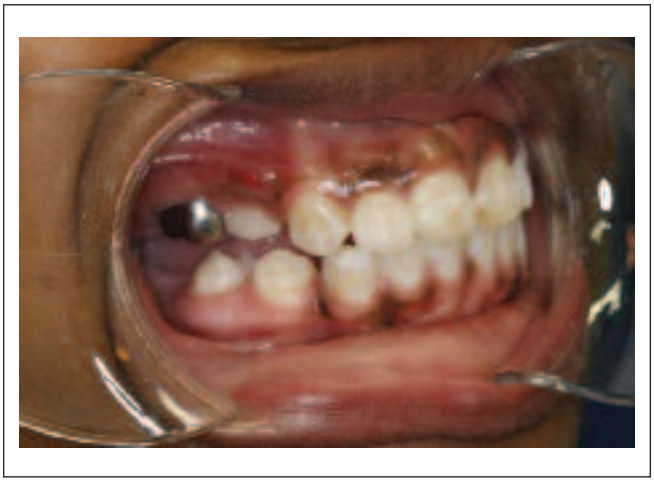

Figure 3: Enamel hypoplasia and clinical absence of teeth.

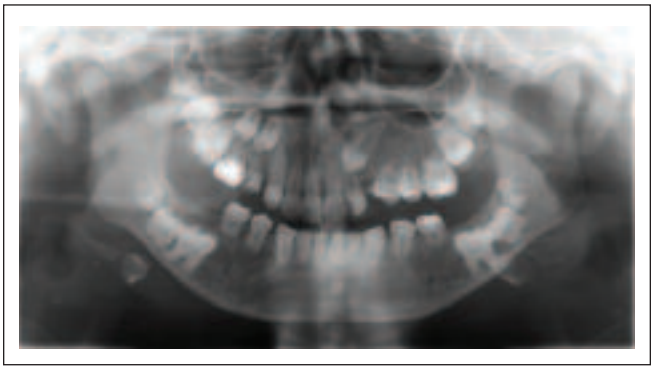

Figure 4: Panoramic radiography. Osteopenia, widened root canals, shortened roots with open apices and impacted teeth can be seen.

CONCLUSION

Pseudohypoparathyroidism refers to a heterogeneous group of disorders caused by lack of organ response to several hormones. This condition was described by Albright in 1942.[7] PHP is difficult to diagnose and the lack of diagnosis may have serious implications for the patient, due to the delay of treatment and because there are other conditions that mimic PHP. Secondary causes of hyperparathyroidism may mimic PHP. This also occurs with true hypoparathyroidism as seen in DiGeorge syndrome. Renal failure should also be ruled out in these patients. If the patient is not treated, tetany and seizures are common presentations of hypocalcemia.

Treatment with calcitriol may produce normocalcemia, and serum phosphate may reach normal levels. However, the most serious risk is overcorrection, which leads to kidney damage. Patients treated with vitamin D should be followed to avoid these complications. These patients may require also hormone replacement for hypothyroidism and hypogonadism. The dental manifestations in this case were the key for diagnosis by the dentist of this very rare condition called pseudohypoparathyroidism type 1a

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