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Pseudohypoparathyroidism: report of case with systemic and oral manifestations

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Abstract

Pseudohypoparathyroidism is a rare sex-linked dominant disease. The clinical symptoms are associated with an end-organ defect manifested by a lack of response in bone or kidney target cells to parathyroid hormone. Clinical signs are described with emphasis on pertinent oral findings which may be the first signs of the disease.

Pseudohypoparathyroidism (PHP) is a rare disease of hypocalcemia first described in 1942 as Albright's hereditary osteodystrophy.[1,2] He reported 3 patients who presented with clinical symptoms of idiopathic hypoparathyroidism, but whose level of parathyroid hormone was normal.[3] Further studies concluded that the clinical symptoms were not associated directly with parathyroid hormone release, as determined by an unresponsiveness to parathyroid hormone extract (Ellsworth-Howard test), but were associated with an end-organ defect.[2-5] The disease was renamed pseudohypoparathyroidism. The most common presenting symptom is tetany or convulsions, which may be misdiagnosed as epilepsy, especially in infants.[2] A dentist may diagnose this disease from changes that affect the dentition — enamel hypoplasia, short blunted roots, and delayed eruption. This case report presents the systemic and oral manifestations of the disease in an adolescent male and reviews the literature.

Case Report

A 13-year-old black male with confirmed pseudohypoparathyroidism was admitted as an outpatient to Children's Hospital of Michigan for evaluation. His initial diagnosis was made following an ophthalmological examination of his cataracts at age 10 years, 10 months.

Physical findings demonstrated a healthy-appearing, cooperative child. He weighed 34.7 kg (10th percentile) and his height was 133.7 cm (<3rd percentile, Fig 1). His facies were coarse, with patchy areas of hair loss (Fig 2). He manifested bilateral lens opacities due to the presence of cataracts, which were scheduled for surgical removal. His skin appeared dry and coarse.

Subcutaneous calcifications were detected just posterior and inferior to the right external ear, the left lower thorax, right axilla and over the lower left quadrant of the abdomen. He had moderate mental retardation and was enrolled in both physical therapy and occupational therapy programs within the school system. The neurological examination revealed a positive Chvostek's sign. An electroencephalogram was performed and revealed mild excessive sharp wave activity dominant on the left side which resulted in recurrent seizures.

The radiologic examination indicated diffuse calcifications in the region of the basal ganglia with a thickened calvarium. Radiographs confirmed the presenting brachydactyly of the first, fourth, and fifth metacarpals and the first and fifth metatarsal (Fig 3).

The dental examination revealed delayed eruption of maxillary first molars and premolars, with impaction of the mandibular second permanent molars. The maxillary permanent right central, left central, and left lateral incisors were avulsed. The texture of the enamel on all premolars was rough and pitted with circumferential grooves. Radiographically, the enamel of the second molars appeared hypoplastic. These hypoplastic defects were soft and carious in many areas, requiring extensive restorations. The roots of

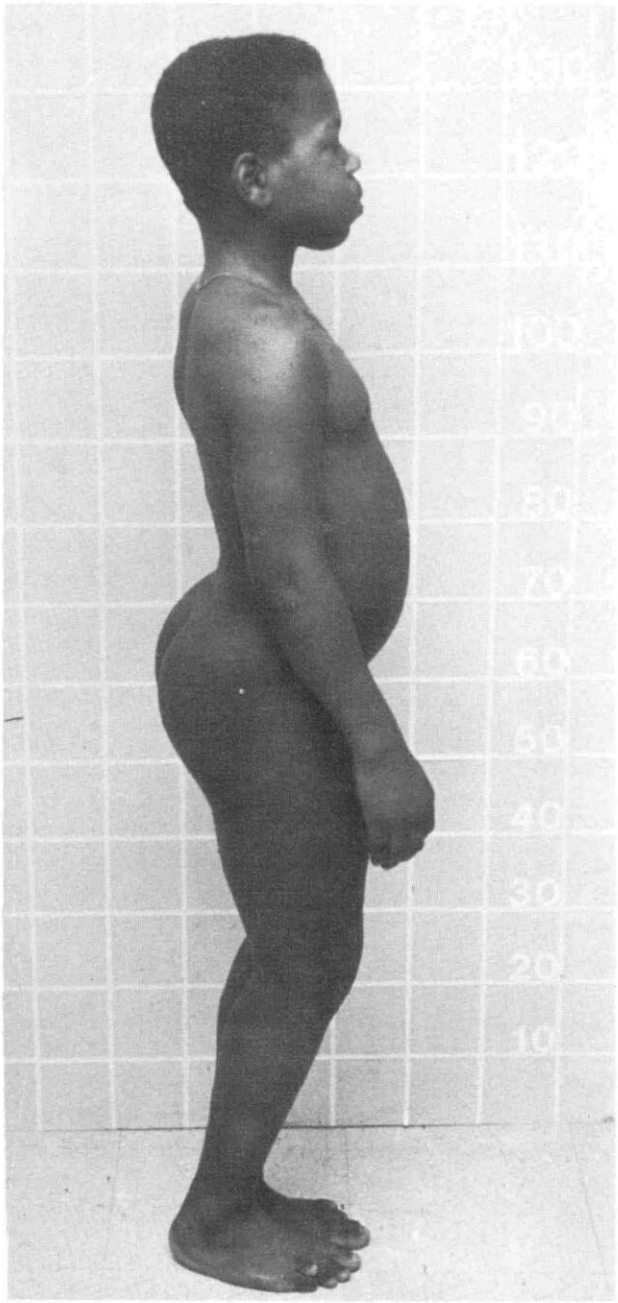


FIG 1. Patient's height falls below the third percentile and weight falls within the tenth percentile.

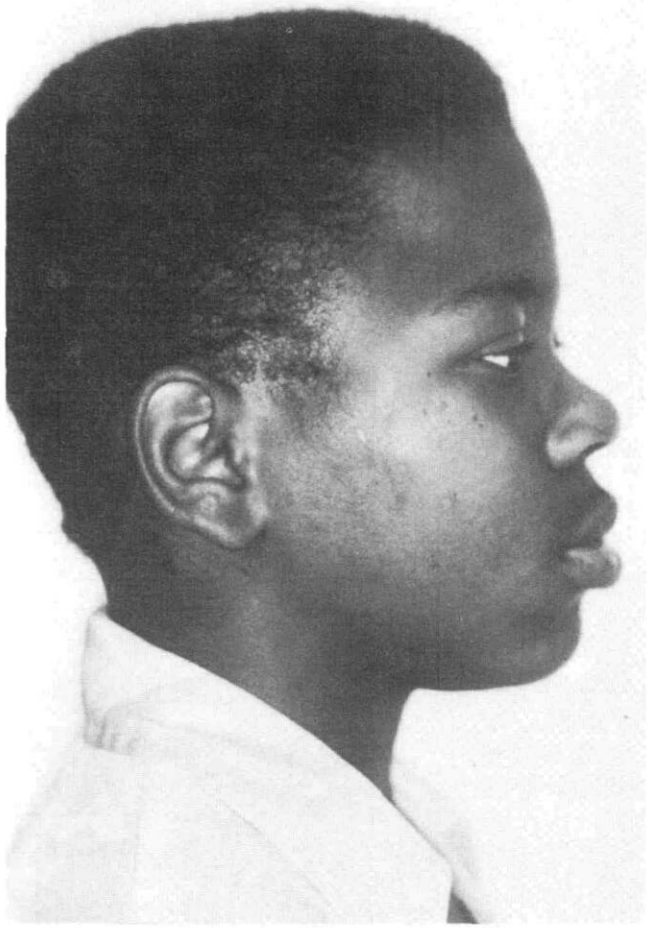


FIG 2. Coarse facies with patchy hair loss are characteristic of the disease. Postauricular subcutaneous calcifications are seen.

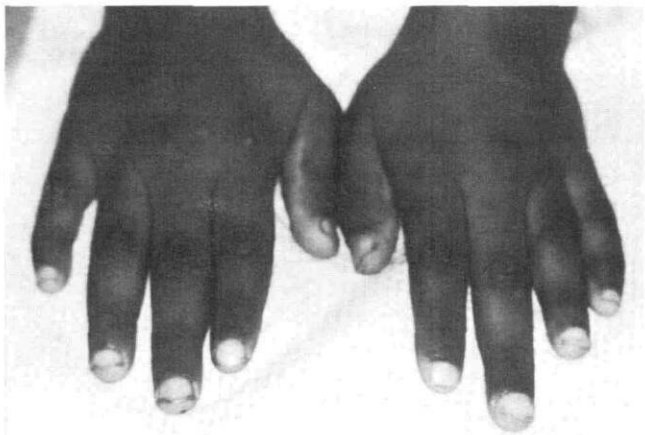
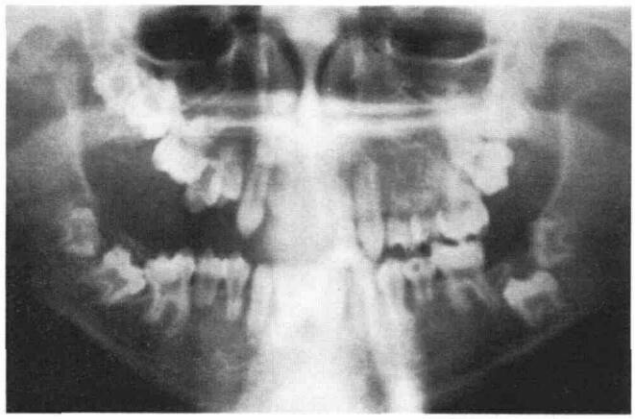


FIG 3. Right and left hands exhibit brachydactyly of the first, fourth, and fifth metacarpals.

the premolars and permanent second molars were shortened and blunted. The lamina dura density was increased (Fig 4).

At age 4, the patient exhibited seizure activity which was documented poorly. He was treated with phenobarbital on an intermittent basis due to poor parental compliance. After the diagnosis of pseudohypoparathyroidism was confirmed, the seizures were considered to be hypocalcemic induced. He was maintained on phenobarbital 75 mg b.i.d., and calcitriol 1.5 mg with calcium carbonate 500 mg b.i.d. to maintain a normal serum calcium level. At



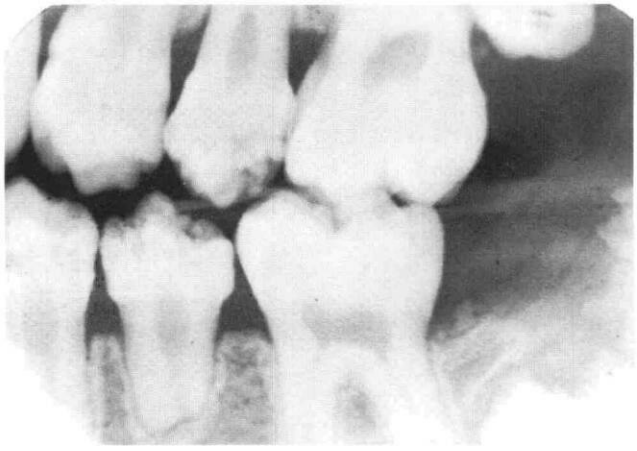


Fig 4a. *(above)* Panoramic radiograph reveals delayed eruption of maxillary and mandibular permanent right first molar and premolars, short roots with open apices, and impaction of the mandibular second molars.
Fig 4b. *(below)* Periapical radiograph reveals areas of enamel hypoplasia, increased density of the lamina dura, and shortened root of the mandibular left second premolar.

age 14 years, 3 months, his parents discontinued administration of the phenobarbital. His physician agreed with the decision since his serum calcium levels were stabilized and he had had no known seizures since discontinuation of the phenobarbital.

Systemic Manifestations

The end-organ defect which occurs is a result of either unresponsiveness in bone or kidney target cells to parathyroid hormone (Type I), or uneffective phosphate diureses in the kidney (Type II).[3,4,6,7] The unresponsiveness causes a decreased mobilization of calcium in the bones, impaired calcium absorption from the intestine, and failure in the renal tubule to excrete phosphate.[8,9] As a result, serum calcium is reduced from a normal of 9 mg/100 ml to 4-8 mg/100 ml and serum phosphate is elevated to 10-12 mg/100 ml, accompanied by a decrease in alkaline phosphatase.[9]

Clinical tests for latent tetany include checking for Chvostek's sign. This twitching of facial muscles near the eye and mouth results from tapping the facial nerve at the point of origin anterior to the parotid gland.[5,10] Another valuable clinical test is detection of Trousseau's phenomenon, the induction of a carpal spasm by inflating a blood pressure cuff above the systolic pressure for at least 1 min.[10,11]

The patient's appearance includes a round head and face, reduced height and stocky build.[3,12] The skin appears dry and coarse and the nails are hypoplastic and ridged.[8] The hair ranges from thin and prematurely gray to partial or complete alopecia.[5] Seventy-five per cent of patients exhibit brachydactyly of the first, fourth, and fifth metacarpals and the first and fifth metatarsals.[8,12] Photophobia with lenticular cataracts is a result of prolonged hypocalcemia.[5,8-10,13] The electrocardiogram may be normal with the presence of a prolonged Q-T wave. Pernicious anemia is a rare finding.[2,14]

Calcium deposits cause bilateral, but asymmetrical, metaplastic bone formation in the subcutaneous tissue, particularly in the facial planes.[4,5,15] However, there is generalized bone demineralization.[8] Cephalometric radiographic indications of the disease are the presence of discrete, symmetrical calcifications in the basal ganglia area, the dentate nuclei of the cerebellum and the falx cerebri, with an increased density of the facial bones.[5,8,12] Mental retardation and emotional lability are common.[3,16,17] The electroencephalogram is usually abnormal, but improves following successful anti-tetanic treatment.[5]

The disease is considered to be sex-linked dominant, but the exact genetic basis is unknown.[2,3,7,9-11] There is a predilection for females, however males are affected to a greater degree than females.[2,5,7] When the disease is accompanied by candidiasis and adrenal deficiency, the syndrome is considered autosomal recessive and referred to as Addison's disease.[9,10]

Oral Manifestations

Changes affecting the dentition are considered of diagnostic value in 37-50% of patients with PHP.[3,7,9,10,12,15] Teeth exhibit a calciotraumatic response coinciding with the age of onset and reflecting the periods of hypocalcemia during tooth development.[5]

The wedge-shaped teeth are hypocalcified and exhibit random pits and grooves in the enamel. Teeth in females are not as thin as in males due to the Lyonization effect of sex-linked disorders.[7] Because the average age of onset is 8½ years, primary teeth rarely are affected, while premolars and second and third molars are affected most severely.[5,18] Often there is an overall delay in eruption of permanent teeth

with short, incomplete root formation.[5,14] Periapical radiographs may reveal increased density of the lamina dura.[3,5] The dentin exhibits interglobular calcifications, with incremental lines being highlighted in all areas, especially at the root apex.[8]

Discussion

The patient exhibited the classic clinical picture found in PHP. He presented with hypocalcemia, a positive Trousseau's phenomenon, Chvostek's sign, shortened height, hair loss, dry skin, brachydactyly, and subcutaneous calcifications. On the cephalometric radiograph, calcifications in the region of the basal ganglia were present with a thickened calvarium. The level of mental retardation was moderate. The presence of cataracts led to the medical evaluation and diagnosis.

The most striking dental finding in the patient was enamel hypoplasia as indicated by the dull white color; randomly oriented pits and circumferential grooves; and extensive caries. The hypoplasia was most evident in the canines, premolars, and radiographically in the second molars. The premolars and second molars displayed shortened roots and open apices with widened pulp chambers. The lamina dura was thickened in this case. The mandibular second molars were impacted with delayed eruption of the maxillary right molars and premolars.

Seizures due to tetany from below-normal levels of serum calcium are often the initial clinical symptom. This patient began seizure activity at age 4 and was treated with phenobarbital intermittently. An electroencephalogram is usually abnormal, as in this patient. Subsequent to establishing normal serum calcium levels, these hypocalcemic-induced seizures were eliminated. These seizures frequently are treated with diphenylhydantoin; this may be inadequate since the seizures are due to reduced serum calcium levels. In addition, the diphenylhydantoin will aggravate further the serum calcium levels due to its rachitic-producing effects. In order to help maintain normal serum levels, patients are requested to reduce dietary intake of food high in phosphorus such as milk, eggs, and cheese. However, complete control may be difficult due to rapid calcium absorption changes in adolescents, and frequent reassessment is necessary.

Recent studies have shown that short stature, delayed dental eruption, smaller tooth size and shortened roots, as well as decreased serum calcium levels may be caused by the administration of some anticonvulsant drugs.[19-21] Therefore, a dentist may conclude erroneously that a patient who presents with a history of diphenylhydantoin therapy and dental aberrations may have misdiagnosed PHP.

Summary

The clinical manifestations of PHP have been presented. Systemically, the patient presented with decreased serum calcium, increased serum phosphorus, shortened height, dry skin, brachydactyly, cataracts, subcutaneous calcifications, and cephalometric evidence of basal ganglia calcification. The dental findings included enamel hypoplasia, shortened roots with open apices, thickened lamina dura, delayed eruption, and impaction of second molars.

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