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Diagnosis of Albright Hereditary Osteodystrophy (AHO) in a 20 Years Female: A case Report

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ABSTRACT

Albright hereditary osteodystrophy (AHO) is a rare metabolic, autosomal dominant syndrome that may or may not be associated with parathormone deficiency (pseudohypoparathyroidism). It is a rare genetic autosomal dominant maternally transmitted disorder in which there is resistance in the target organ to parathyroid hormone. The syndrome manifests as hypoparathyroidism, causing patients to experience hypocalcemia and hyperphosphatemia. But contrary to low PTH levels, raised levels of PTH are present in serum. Characteristic presentations in a patient are short stature, round face, shortened fourth/fifth digits, mental retardation, developmental delay, subcutaneous calcification, and loss of smell and hearing.

We report a case of Albright hereditary osteodystrophy (AHO) in a 20-year-old female who presented to us in OPD of a tertiary care hospital.

Keywords: Albright Hereditary Osteodystrophy(AHO), Pseudohypoparathyroidism.

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INTRODUCTION

In the emergency department, hypocalcemia with the symptoms is frequently encountered that needs admission. It has different causes, with vitamin D deficiency being the most common.[1] Pseudohypoparathyroidism is a rare congenital disease in which there is end-organ resistance to parathyroid hormone. This disorder presents similarly to hypoparathyroidism, with patients having low calcium and high phosphate levels. Instead of a low PTH level, a raised level of PTH is present in the serum.[2] PHP is classified as either Type 1 or Type 2. Type 1 is further subdivided into 1A, 1B, and 1C. Type 1A PHP is also associated with specific features such as short stature, round face, and small hand bones, which is collectively known as Albright hereditary osteodystrophy (AHO).

Albright hereditary osteodystrophy (AHO) was initially diagnosed by Fuller Albright in 1942.[3] Albright osteodystrophy is a form of osteodystrophy[4] and is described as the phenotype of pseudohypoparathyroidism; this is a disorder in which there is no response to parathyroid hormone in the body.[5] AHO has a group of signs, including a round face, short stature, brachydactyly, subcutaneous ossification, and dental abnormalities.[6] Developmental delay, weight gain, and relative macrocephaly may be the other characteristics of AHO.[7] Although some previous literature had also mentioned hypogonadism and menstrual irregularities in females with AHO, the cause of female reproductive dysfunction in AHO remains unclear.[8]

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In AHO, common presentations in individuals were short stature, obesity, and shortened fourth and fifth digits. AHO, when seen in relation with end-organ resistance to parathormone, is termed pseudohypoparathyroidism.[9] The disease is caused by alteration in the gene (GNAS1 gene), which results in complete or partial deficiency of Gs–alpha activity and inactivation of adenylate cyclase when PTH binds to its receptor; hence, it leads to resistance to parathormone action.[10] Here is a case report of a 20-year-old female with characteristic physical and menstrual characteristics of Albright hereditary osteodystrophy (AHO).

Case Presentation

A young female housewife, 20 years of age, married for the last year, a resident of District Swat, presented to us in the Medical Outpatient department (OPD) of Saidu Group of teaching hospitals with complaints of generalized body weakness, tingling sensation in the finger and around the mouth, fever, palpitations, epigastric pain, and burning micturition on and off for the last seven years. She was treated by different health care professionals for seven years, but she has not improved completely. She also had a history of recurrent tingling in her limbs, which was managed conservatively by a general practitioner. In addition, the patient menarche started at 14 years of age with fully developed secondary sexual characteristics and had oligomenorrhea for which she had visited a gynecologist multiple times. Regarding her socioeconomic status, she belongs to a poor background. No history of cousin marriage in her parents, normal birth history, and normal neonatal period. On further inquiry regarding her growth history, she turned out to be developmentally delayed. Her history was not significant for radiation exposure, blood transfusion, or any surgery, including thyroid and head and neck surgery. She is not allergic to any drug used till now.

On general physical examination, the patient was alert and cooperative. Blood pressure was 120/80 mmHg, temperature was 98°F, and the pulse rate was 86 beats/min. She had short stature with a round face, scoliotic posture, brittle nails, and hair, and had no web neck with normal ears. On physical examination of the hands there was brachydactyly of the 4th and 5th metacarpals (Figure 02). Chovstek and Trousseau signs are positive about hypocalcemia.

After initial assessment, the patient was admitted to the medical ward for further evaluation to reach a proper diagnosis. First, whole venous blood samples were taken for baseline investigations, including full blood count (FBC), liver function tests (LFTs), renal function tests (RFTs), and midstream urine samples for urine routine examination (urine R/E). On complete blood count (CBC), hemoglobin (HB) was 6 g/dl, total leucocyte count was 33,000/mm, and mean corpuscular volume (MCV) was 55 fl; both LFTs and RFTs tests were in the normal range, while urine R/E showed numerous pus cells. Serum calcium and 25-OH vitamin D levels were also determined from the blood sample. In laboratory reports, serum calcium (Ca) = 7.8 mg/dl and 25OH vitamin D levels = 8 ng/ml (normal = 20-50 ng/ml); both of them were below the normal limit (Table 01). To confirm the etiology of hypocalcemia, blood samples were taken to determine the serum parathyroid level (serum PTH) in the laboratory. In lab reports, serum PTH levels were too high, i.e., 283.5 pg/ml (normal 10-55 pg/ml), which shows resistance to parathyroid hormone. The corrected calcium calculated was 7.6 mg/dl.

Radiologically, an X-ray of her hands showed shortening of the 4th and 5th metacarpals (Figure 01). An ultrasonography of the thyroid and parathyroid gland did not show any abnormalities. CT Scan of the Spine shows scoliotic posture and collapse of vertebral bodies (Figure 03).

Management

The patient was managed symptomatically with intravenous calcium initially and encouraged to follow up twice a year with measurement of serum calcium, phosphorous, parathyroid hormone, and TSH levels along with a 24-hour' urinary calcium-to-creatinine ratio for titration of therapy.



Figure 01. X-ray of hand shows bilateral short fourth(4th) and fifth(5th) metcarpals



Figure 02. Short bilateral Fourth and Fifth Metacarpal Bones of Hand

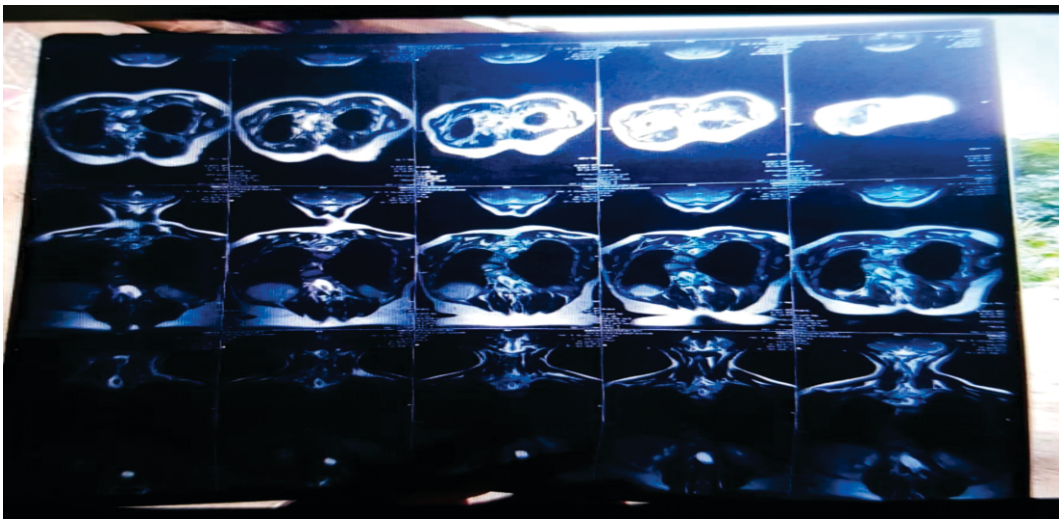


Figure 03. Scoliotic posture with collapsed vertebral bodies evident on CT-Scan.

Table 01. Laboratory and biochemical investigations

S.No	Laboratory Results	Patient Valve	Normal Valve
1	Serum Calcium	7.6 mg/dl	8.6-10.3 mg/dl
2	Serum PTH	283.5 pg/ml	10-55 pg/ml
3	25-OH Vitamin D	8 ng/ml	20-50 ng/ml
4	Total Leukocyte Count	33,000	4,000-11,000
5	Hemoglobin Count	6 g/dl	12-15g/dl
6	Mean Corpuscular Volume (MCV)	55	80-100
7	Platelet Count	272,000	150,000-350,000
8	Urine R/E Pus Cells	Numerous	
9	LFTs and RFTs	Normal Range	
10	Corrected Calcium =S.CALCIUM+0.8(4 –ALBUMIN)	7.6 mg/dl	
11	Serum Albumin	4gm/dl	3.5-5.5 gm/dl

DISCUSSION

Albright hereditary osteodystrophy (AHO) was reported by Dr. Fuller Albright in 1942.[3] PTH resistance is the main abnormality of PHP, and in untreated patients, there is a striking elevation of PTH in serum.[11] We report an AHO patient with hypocalcemia and a high PTH level. Initially, a clinical diagnosis of pseudohypoparathyroidism was made based on hypocalcemic tetany and hypocalcemia with markedly elevated PTH levels, which showed parathormone resistance. Type 1A (PHP1A), the most common variant, also includes developmental and skeletal defects along with high PTH levels, hypocalcemia, and hyperphosphatemia, called Albright hereditary osteodystrophy (AHO).[12] In general, Albright hereditary osteodystrophy (AHO) specifically appears in Pseudohypothyroidism type 1A patients, and PHP-1B patients have no characteristics of AHO.[13] The main abnormality in PHP type 1a is PTH resistance, which presents as an elevated PTH level in serum, hypocalcemia, and hyperphosphatemia.[14]

Symptomatic hypocalcemia has many causes, with hypoparathyroidism and vitamin D deficiency being the most common. However, rare causes such as pseudohypoparathyroidism, as were present in the current case, should not be neglected. Reported here is a 20-year-old female presenting to us with elevated PTH levels, decreased 25-OH vitamin D levels, and signs and symptoms of hypocalcemia, i.e., muscle spasm, tetany, generalized muscle ache, epigastric pain, and palpitation. Pseudohypoparathyroidism (PHP) is a group of disorders in which the patients have low calcium, high phosphate, and high parathormone (PTH) levels as a result of resistance to PTH in target organs.[15] According to previous literature, PTH elevation follows low calcium, and PHP type Ia is diagnosed clinically based on severe hypocalcemic symptoms such as tetany, paresthesia, and seizures.[16] Low calcium level, decreased calcium movement from bone in response to parathormone, and decreased serum 1,25-(OH)2 vitamin D are the main characteristics of PTH resistance.[11]

Also in our patient, we noted musculoskeletal changes such as brachydactylic metacarpals, both on general examination as well as on radiographs (X-rays attached in fig 01). Spinal changes were also noted on CT scan; these changes include scoliotic posture with collapsed vertebral bodies (figure 03). Brachydactyly is one of the most specific phenotypes of AHO and PHP.[17] Its presence may help in the correct diagnosis. Also, vertebral body compressions in pseudo-hypothyroidism were noted in a study conducted by Y. Yamamoto.[17] In their study, magnetic resonance imaging and myelography computed tomographic scans showed tumor-like ossifications of the paravertebral ligaments that lead to severe compression of the spinal cord at T9/10.

CONCLUSION

Albright hereditary osteodystrophy is a longstanding disease that needs careful clinical examination, and it needs to be treated symptomatically. The main clinical features in our case are tingling sensation in the fingers and around the mouth, low calcium, shortened fourth and fifth metacarpal bones, raised PTH levels, and radiological findings typical of AHO. Only pseudohypoparathyroidism has both the features of hypocalcemia and short metacarpal bones, therefore supporting our diagnosis of pseudohypoparathyroidism in this 20-year-old female.

This case report has been prepared by following CARE guidelines.

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