

Case Report

Avascular necrosis of the hip: A unique presentation of pseudohypoparathyroidism

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ABSTRACT

Pseudohypoparathyroidism is a rare, heterogeneous disorder characterized by parathyroid hormone resistance. Its association with avascular necrosis of the hip has been reported infrequently in the past. We report the case of a 27-year-old lady with pseudohypoparathyroidism Type 1 whose initial presentation was with avascular necrosis of bilateral hip. Apart from the common clinical features of pseudohypoparathyroidism, clinicians should also be aware of the rarer presentations such as avascular necrosis. A good clinical history and physical examination are warranted for early diagnosis in order to prevent serious morbidity in these patients.

Keywords: *Albright's hereditary osteodystrophy, Avascular necrosis, Hypocalcaemia, Pseudohypoparathyroidism.*

Pseudohypoparathyroidism (PHP) was first described by Fuller Albright et al in 1942 in a patient with parathyroid hormone (PTH) resistant hypocalcemia, hyperphosphatemia and the typical Albright's hereditary osteodystrophy (AHO) phenotype which consists of short stature, round facies, brachydactyly, soft tissue ossifications and mental retardation [1]. It is a sporadic or inherited genetic disorder caused due to mutation in *GNAS1* gene and can be subdivided into specific entities (Ia, Ib, Ic and II) according to the renal cAMP response to PTH, AHO phenotype and G_{α} bioactivity [2]. The prevalence of pseudohypoparathyroidism and AHO phenotype is about 0.79 cases per 100,000 [3]. Although this condition has its typical phenotypic features, it is often missed by physicians. Early diagnosis can prevent morbidity and mortality for the patient in the form of hypocalcemic seizures.

There are only three reports of avascular necrosis of the hip in pseudohypoparathyroidism in the published literature, all of which are in children [4-6]. We herein report for the first time an adult PHP presenting with avascular necrosis of bilateral hip to add to the existing literature.

CASE REPORT

A 27-year-old unmarried lady presented to us with a complaint of bilateral hip pain for two years duration. The pain was insidious in onset, slowly progressive, dull aching in nature and more on the right than the left side. It was aggravated on weight-bearing and

relieved on lying down and intermittently radiated to the knees. She had no history of fracture, trauma, glucocorticoid intake or fever. She was not a smoker and does not consume alcohol. She had visited multiple physicians for the same, however, her symptoms persisted. She was on Tab. Levothyroxine 25mcg once daily for subclinical hypothyroidism.

She had no history of diabetes, hypertension, blood disorders (e.g. sickle cell anemia or coagulopathies), hypocalcemic tetany or seizures or any other chronic systemic illness in the past. She had undergone cataract surgery in the left eye two years back. She had attained menarche at the age of 12 years with persistent oligomenorrhoea thereafter and had a less than average scholastic performance which resulted in her dropping out from the school in 10th standard.



Figure 1: Pseudohypoparathyroidism Type 1 with round face and dental malocclusion.



Figure 2: X-ray anteroposterior view of left hand showing short fourth and fifth metacarpals (solid arrow) and subcutaneous calcifications (dashed arrows).

On examination, her pulse was 80/min (regular in rhythm), blood pressure was 124/80 mm Hg. Height was 143.5cm (<3rd centile) with a height standard deviation score (SDS) of - 3.16. Her weight was 51.2 kg with a Body Mass Index (BMI) of 24.8 kg/m². She had a round face with dental malocclusion (Fig. 1), short 4th and 5th metacarpals and metatarsals. Her sexual maturity rating was that of a normal adult. Chvostek's and Trousseau's signs were negative.

X-ray of the hand showed areas of subcutaneous calcification and short 4th and 5th metacarpals (Fig. 2). There was a gross restriction of internal rotation of both hip joints. X-ray pelvis showed a loss of rounded contour of the bilateral hip joints with patchy sclerosis and lucency. Blood investigations revealed parathyroid hormone resistance as suggested by hypocalcemia,



Figure 3: T1 weighted MRI of hip showing bilateral collapsed femoral heads with irregular non enhancing necrotic areas with a peripheral enhancing rim.

hyperphosphatemia with elevated PTH (Table 1). Magnetic resonance imaging (MRI) of the hips showed bilateral collapsed femoral heads with irregular necrotic non enhancing areas with peripheral enhancing rims confirming avascular necrosis of the hip (Fig. 3). The above clinical and radiological signs were suggestive of Albright's Hereditary Osteodystrophy.

The patient was prescribed tab calcium carbonate 1500mg/day and tab calcitriol 0.5mcg/day. Her blood investigations a month later showed calcium 9.3mg/dl and phosphate 4.9mg/dl following which the dose of calcium carbonate was reduced to 1000mg/day. Her last follow-up 4 months back showed serum calcium of 8.7mg/dl.

DISCUSSION

Osteonecrosis or Avascular Necrosis (AVN) of the femoral head results due to interruption of arterial blood flow to the proximal femoral epiphysis which leads to a typical pattern of cell death resulting in loss of structural integrity and subchondral fracture. AVN occurs through three mechanisms: vascular interruption, intravascular occlusion from thrombi or embolic fat, or intraosseous extravascular compression from lipocyte hypertrophy or Gaucher cells [7].

The most common risk factors for AVN are corticosteroid and alcohol intake [8]. Traumatic AVN can be due to fracture or dislocation of the femoral head leading to vascular interruption. Apart from this, the intravascular obstruction can occur due to sickle cell disease, thrombophilia or coagulation defects. Decompression sickness is another rare cause of AVN [7]. AVN is often asymptomatic in early stages, although some patients may develop groin pain that can radiate to the knee or buttocks. On physical examination, patients usually present with a limited range of motion at the hip and complain of pain particularly with forced internal rotation [9].

Avascular necrosis in association with pseudohypoparathyroidism has been reported infrequently earlier. Gertner *et al* (1978) reported a four-year-boy with sensorineural hearing loss

Table 1: Blood Investigations of the patient.

Investigation	Report	Reference range
Hemoglobin	12.1 g/dL	12-15
Total Leucocyte Count	8,120/cumm	4000-10000
Platelet count	2,54,000 /µL	150000-410000
Creatinine	0.78 mg/dl	0.51-0.95
Total Bilirubin	0.5 mg/dl	0.3-1.2
Aspartate aminotransferase	33 U/L	<50
Alanine transaminase	22 U/L	<50
Total Protein	7.6 gm/dl	6.6-8.3
Albumin	4.3 gm/dl	3.5-5.2
Alkaline phosphatase	196 U/L	30-120
Uric Acid	3.0 mg/dl	2.6-6.0
Anti-cyclic citrullinated peptide	<7 U/ml	≤ 17
Human leukocyte antigen B27	Negative	
Calcium	5.4 mg/dl	8.6-10.3
Phosphate	6.1 mg/dl	2.5-4.5
Parathyroid hormone (PTH)	190.8 pg/ml	15-65
25(OH)Vit D	34 ng/ml	30-60

with unusual round face and proptosis. He was normocalcaemic with elevated PTH suggesting PTH resistance but did not have AHO phenotype. Imaging showed osteosclerosis and AVN of femoral heads [4]. The second case was reported by Lewington *et al* (2010) in a four-year-old obese girl with dysmorphic features and AHO phenotype who presented with a history of delayed developmental milestones and inability to weight bear and walk without support. Hip imaging showed sclerosis and flattening of the left femoral head suggesting AVN of left hip joint [5]. Salman A (2019) also reported a similar case of a four and half-year-old girl with pseudohypoparathyroidism 1a with presenting with AVN of the right hip; however, she had a history of corticosteroid intake [6]. Our present report is the first instance of an adult individual with pseudohypoparathyroidism presenting with AVN.

The exact cause of AVN in patients with PHP is not known due to the limited amount of the literature. It could be a serious complication of slipped capital femoral epiphysis (SCFE) which is the most common hip disorder in adolescents. Although the exact etiology of SCFE is not known, it is associated with obesity, adolescent growth spurt, mechanical abnormalities and trauma and endocrine disorders. Endocrinopathies account for one-third of SCFE resulting from diseases like hyperparathyroidism, hypothyroidism, growth hormone deficiency and hypogonadism. The frequency of bilateral hip involvement is found to be higher in endocrine-associated SCFE [10].

On searching the literature, we found five reports of SCFE associated with pseudohypoparathyroidism 1b [11-15]. PTH impairs the normal endochondral ossification and diminishes the collagen content of the growth plates. Similarly in PHP, upper femoral metaphyseal resorption due to elevated PTH may lead to the causation of SCFE [11]. However, SCFE has not been reported in a patient of PHP1a or PHP1c, previously.

CONCLUSION

Apart from the common clinical features of pseudohypoparathyroidism, clinicians should also be aware of the rarer presentations such as avascular necrosis and slipped capital femoral epiphysis of the hips. A good clinical history and physical examination are warranted for early diagnosis in order to prevent serious morbidity in these patients.

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