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Case Report

Pseudohypoparathyroidism leading to bilateral hip fracture: A case report ☆,☆☆

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ABSTRACT

Pseudohypoparathyroidism (PHP) is a group of disorders characterized by end-organ resistance to parathyroid hormone (PTH), resulting in high serum PTH, low calcium, and high phosphate levels. Among its 5 subtypes, PHP type 1a is the most common and leads to hereditary osteodystrophy, marked by short stature, short metacarpals, and electrolyte abnormalities such as hyperphosphatemia and hypocalcemia, which can cause tetany and seizures. Rarely, PHP patients can experience pathological fractures of long bones. This report discusses a 22-year-old female with PHP who presented with myoclonic seizures and bilateral hip fractures. Initial symptoms included fits, flank pain, and later, leg weakness. Diagnosis was based on clinical history, elevated serum PTH, low calcium, high phosphate, bilateral cataracts, hypothyroidism, basal ganglia calcification, and family history. Treatment began with IV calcium, followed by alfacalcidol, oral calcium, and antibiotics, leading to symptom remission. Hip fractures were managed with a POP cast and later closed reduction. The patient was discharged with calcium and 1,25 dihydroxy Vitamin D supplementation and scheduled for regular follow-up.

Introduction

Pseudohypoparathyroidism (PHP) and its related syndromes are a group of heterogeneous disorders categorized by end-organ resistance to parathyroid hormone (PTH) leading to high serum PTH levels. Resistance to PTH causes hyperphosphatemia and hypocalcemia [1]. These patients do not respond to the administration of PTH because they have impaired signaling of PTH at the receptor level [2], having a mutation in the GNAS gene [3].

Pseudohypoparathyroidism is divided into 5 major subtypes, namely, type 1a (PHP-1a), PHP type 1b (PHP-1b), PHP type 1c (PHP-1c), PHP type 2 (PHP-2), and pseudopseudohy-

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poparathyroidism (PPHP) [4,5]. PHP type 1a is the most common and leads to a group of symptoms called heredity Osteodystrophy. This is characterized by short stature, short metacarpals, round face, and electrolyte abnormalities like hyperphosphatemia and hypocalcemia leading to tetany and seizures in some cases [6]. Very rarely, these patients can present with pathologically fracture-prone long bones [7]. PHP type 1c has the same presentation as type 1a but differs as type 1c does not have abnormal activity of Gs alpha protein. PHP type 1b has a normal phenotype which differentiates it from type 1a and type 1c.

In this case report, we present a very rare case of PHP presenting with myoclonic seizures and bilateral hip fracture in a 22-year-old female. The patient has a family history of similar incidences and a past history of hypoparathyroidism and bilateral cataracts.

Case presentation

A 22-year-old, short-statured female presented to the emergency department with a 6-day history of myoclonic fits, 10 to 12 episodes per day, each lasting for 15 to 20 seconds. She did not have any history of up rolling of eyes, tongue biting, urinary and fecal incontinence, postictal state, fever, headache, neck pain, nausea, or vomiting. She provided a history of sudden fall during one of these episodes of fits and developed bruises on the lateral side of her left thigh. She also lost hold of both of her legs. She was taking nonsteroidal anti-inflammatory drugs for flank pain. Flank pain was associated with decreased frequency of urination but without any association with burning micturition, oral ulcers, or photosensitivity. She was diagnosed with hypothyroidism at the age of 14 and was taking 100 μg of levothyroxine. She developed bilateral cataracts at the age of 18 and was treated surgically.

Before her presentation to the emergency department, she gradually developed an altered state of consciousness without any limb or body weakness. She had half and half nails and a short fifth metacarpal in both of her hands with a 12/15 score on the Glasgow-Coma Scale (GCS).

Radiographs of the short fifth metacarpal (Fig. 1) and bilateral femur neck fracture (Fig. 2) are shown below.

Laboratory investigations were carried out on 3 different occasions during initial treatment. A complete blood count showed high levels of total leukocyte count and creatine kinase, suggestive of her recent seizure activity. Her laboratory results are presented in Table 1.

Serum electrolyte investigations were conducted and showed hypocalcemia and hyperphosphatemia as shown in Table 2.

Serum parathyroid hormone levels were extremely raised with the value of 201212.6 pg/mL. ECG revealed a normal sinus rhythm but with an elevated QT interval, likely caused by hypocalcemia. EEG was performed and bilateral frontal dysfunction was discovered. Other than that, it was unremarkable. A plain CT of the head showed extensive calcification of the basal ganglia with a subsequent MRI confirming the finding.

Diagnosis of pseudohypoparathyroidism was made based on the history of fits, short stature, and short fifth metacarpal supported by laboratory values of low calcium, high phosphate, and high PTH. The patient's mother also had similar symptoms as described by the family. The mother had passed away in a road accident when the patient was 3 years old. Due to the cost involved and no immediate effect on the management of the patient, genetic analysis was deferred to a later time. In the meantime, the patient was counseled about the diagnosis and its implications for any future children.

The patient was given IV Calcium Gluconate. She was started on alfacalcidol 0.5 mg/day, calcium tablets 170 mg/day, and broad-spectrum antibiotics 500 mg twice a day. The patient also underwent 3 sessions of hemodialysis during her stay at the hospital. Significant improvement was seen in her electrolyte panel after hemodialysis. These parameters are presented in Table 2.

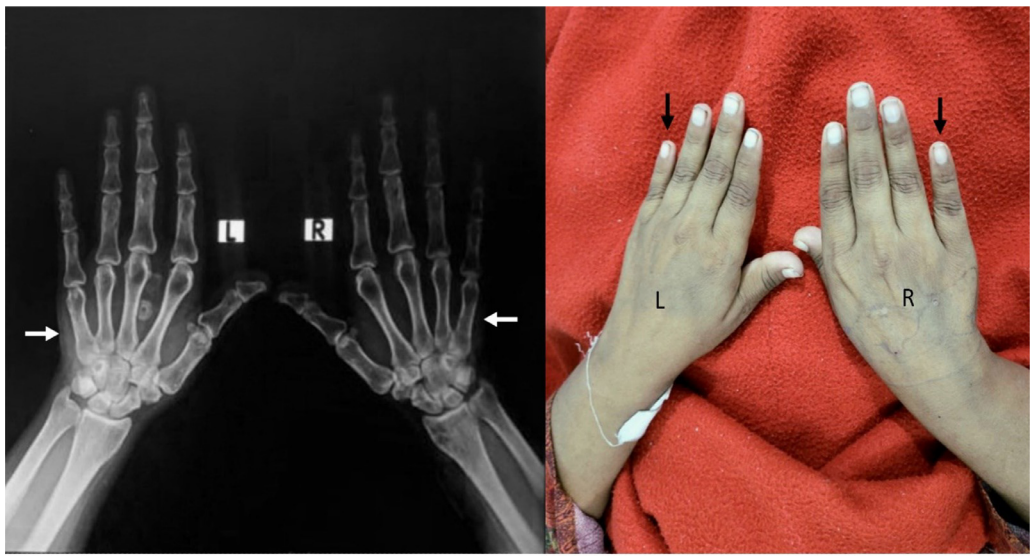

Fig. 1 – Radiograph and picture showing short fifth metacarpal bones.

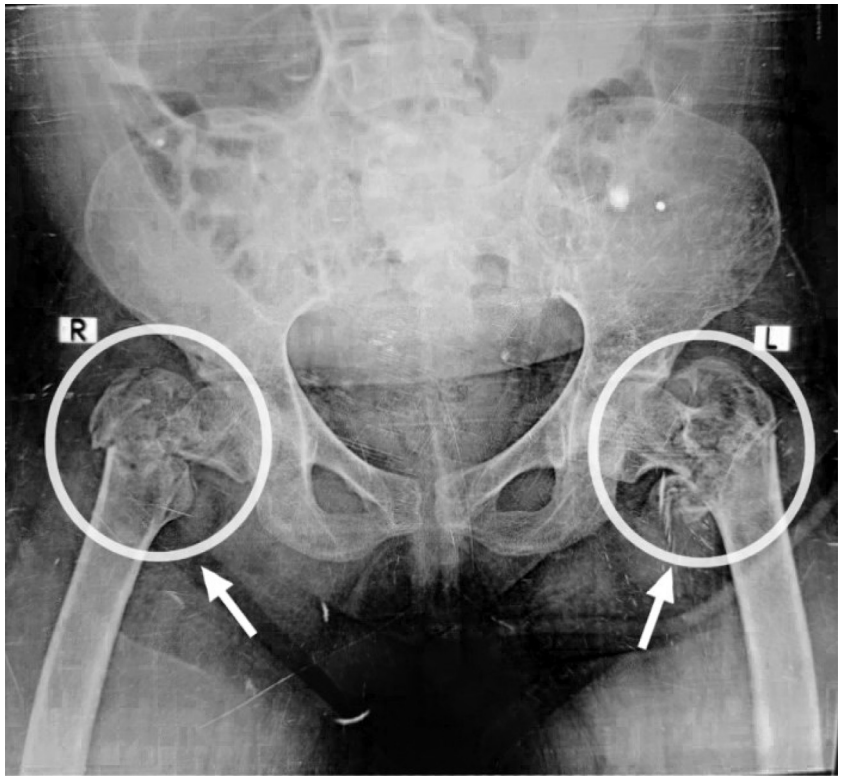

Fig. 2 – Radiograph showing bilateral fracture of neck of femur.

Table 1 – Laboratory reports showing before and after treatment fluctations in blood cell counts.

	On the day of admission	One day post admission	Three days post admission
Complete Blood Count (CBC)			
Hb (g/dl)	5.2	4.8	6.8
Hct (%)	15.76	17.87	19.89
MCV (fL)	73	74	75
TLC (cells/mm^3)	17.30	15.56	11.66
PLT (x10^3/mL)	415	373	303

Table 2 – Laboratory reports showing before and after treatment fluctations in serum calcium and serum phosphate levels.

Electrolytes (mEq/L)	On the day of admission	One day post admission	Three days post admission
Sodium	135	136	138
Potassium	3.6	3.3	2.9
Chloride	95	101	100
Calcium	4.8	4.8	8.1
Phosphorus	11.8	11.8	6.6
Magnesium	2.1	2.1	3.3

Initially, fractured bones were stabilized by the application of plaster of Paris. After the improvement of symptoms and correction of the biochemical profile, fractured bones were managed with closed reduction under fluoroscopic guidance. The patient was discharged with Calcium and 1,25 dihydroxy Vitamin D supplementation with a plan to conduct genetic analysis at a later date when financially feasible for the patient. She was provided written advice for the care of fractures and weekly follow-up was arranged.

Discussion

Parathyroid hormone plays an important role in maintaining calcium homeostasis. Pseudohypoparathyroidism (PHP) is a heterogeneous group of disorders in which this homeostasis is disturbed. PHP is characterized by increased concentrations of PTH, hypocalcemia, and hyperphosphatemia. It is an autosomal dominant disorder that occurs as a result of defective

PTH receptors. Therefore, the levels of PTH are elevated but the symptoms mimic those of hypoparathyroidism, hence the name 'pseudohypoparathyroidism'. On a molecular level, there is a deficiency in the Gs alpha component leading to decreased coupling of the PTH receptor to adenylate cyclase such that activation of the PTH receptor does not activate the target cell [8]. Hence, target cells do not respond to PTH in the blood. Decreased PTH response at the level of distal convoluted tubules and intestines results in loss of calcium from the body. This hypocalcemia manifests as neuromuscular irritability like tetany, prolonged QT interval, and risk of arrhythmias. Reduced Vitamin D production at the level of proximal convoluted tubules, and subsequently reduced bone mineralization leading to weak, fragile, fracture-prone bones [9].

Pseudohypoparathyroidism is classified into type I and type II, differentiated based on cAMP response. In PHP type I, the cAMP response is blunted while in PHP type II, the response is conserved [10]. Very few cases of cases of PHP type II have been reported and the molecular defect is unknown. PHP type I is the more common subtype. It is further sub-classified as type 1a, type 1b, and type 1c. Both type 1a and type 1c have similar phenotypic presentations leading to a group of symptoms called hereditary Osteodystrophy. Heredity osteodystrophy is characterized by short stature, short metacarpals, round face, and electrolyte abnormalities like hyperphosphatemia and hypocalcemia leading to tetany and occasionally seizures. PHP type 1a differs from other subtypes in that it has a normal phenotype and doesn't lead to hereditary osteodystrophy. PHP type 1a and type 1c have similar phenotypes but differ in the Gs activity in various membranes. In type 1a, there is partial deficiency in the Gs activity while this is absent in type 1c with the defect hypothesized to be further downstream. Both type 1a and type 1c are also associated with multi-hormone resistance including TSH, GHRH, and Gn hormone resistance, something that is absent in type 1b [11].

Our Patient presented with myoclonic fits and tripping during one of those episodes which resulted in bilateral femur neck fractures, a sign of hypocalcemia-caused bone disease [12]. She has a short stature and a radiograph of her hands demonstrated a shortened fifth metacarpal, a characteristic finding seen in Albright hereditary osteodystrophy, typically present in patients of pseudo-hypoparathyroidism (PHP) [13]. Upon investigation, the lab report demonstrated elevated concentrations of parathyroid hormone (PTH) and phosphate with reduced calcium levels. Neuromuscular irritability, radiographic findings, lab findings, and short stature paint a classic picture of PHP [14,15]. Her family history also supports the diagnosis. In the absence of genetic testing, deferred due to the financial cost involved, it is difficult to determine the subtype of pseudohypoparathyroidism in the patient. The presence of typical hereditary osteodystrophy symptoms rules out PHP type 1b. Both PHP type 1a and type 1c are a possibility in the patient. The higher prevalence of type 1a makes it more likely.

This is a unique case in which the levels of PTH are so profoundly high and levels of calcium so low that the patient developed myoclonic seizures first and subsequently a bilateral hip fracture. Such serious levels of bone loss in PHP have been reported only twice before as per our knowledge, which makes this case extremely rare [7,16].

Conclusion

Our article reports a rare case of pseudohypoparathyroidism in a 22-year-old female that led to seizures and bilateral hip fracture in the patient. Treatment with IV calcium followed by alfacalcidol, oral calcium, and broad-spectrum antibiotics led to remission of symptoms. Hip fractures were managed initially with a POP cast and later with closed reduction. Resistance to parathyroid hormone leading to elevated PTH, hypocalcemia, and elevated phosphate, characterizes pseudohypoparathyroidism. The presence of severe bone disease leading to bilateral hip fractures has been reported only twice before in the literature. This makes our case report extremely rare.

Author contribution

All authors contributed towards data analysis, drafting and revising the paper, gave final approval of the version to be published and agree to be accountable for all aspects of the work.

Ethical approval

Not required as we have acquired consent from the patient.

Patient consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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