Pseudohypoparathyroidism and Seizure: A Rare Case Report

Psödohipoparatiroidizm ve Nöbet: Nadir bir olgu sunumu

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ÖZET

Psödohipoparatiroidizm; hipokalsemi, hiperfosfatemi, artmış serum parathormon düzeyi ve paratiroid hormonunun biyolojik aktivitesine duyarsızlık ile karakterizedir. Genellikle Albright'ın herediter osteodistrofisi olarak bilinen karakteristik bir fenotip ile ilişkilidir. Psödohipoparatiroidi çoğunlukla erken yaşlarda ortaya çıkar. Biz burada hipokalsemiye bağlı nöbet ile ortaya çıkmış 50 yaşında bir erkek hasta sunuyoruz. Hastada Albright'ın herediter osteodistrofisinin tipik özellikleri olan yuvarlak yüz, boy kısalığı ve kısa boyun saptandı. Çekilen beyin tomografisinde bilateral serebellum, putamen ve dentat nükleusta diffüz kalsifikasyon saptandı. Hasta kalsiyum karbonat ve kalsitriol desteği ile tedavi edildi. Bu vaka hipokalsemiye bağlı nöbeti olan hastalarda psödohipoparatiroidi olabileceğini hatırlatmak amacıyla bildirildi.

Anahtar kelimeler: Psödohipoparatiroidi, nöbet, kalsifikasyon

ABSTRACT

Pseudohypoparathyroidism is characterized by hypocalcemia, hyperphosphatemia, increased serum parathyroid hormone values and insensitivity to the biological activity of parathyroid hormone. Pseudohypoparathyroidism is often associated with a characteristic phenotype known as Albright‘s hereditary osteodystrophy. Pseudohypoparathyroidism usually presents at an early age. We describe a 50-year-old man who presented with seizure due to hypocalcemia. He has typical features of Albright's hereditary osteodystrophy, which include a round face, short neck and stature. Diffuse calsifications were seen on the bilateral cerebellum, putamen and dentate nucleus in computerized tomography. The patient is treated successfully by calcium carbonate and calcitriol supplementation This case was reported in order to remind pseudohypoparathyroidism in patients with hypocalcemic seizures.

Key words: Pseudohypoparathyroidism, seizure, calcification

INTRODUCTION

Pseudohypoparathyroidism (PHP) is a rare sporadic or inherited genetic disorder characterized by hypocalcemia, hyperphosphatemia, increased serum concentration of parathyroid hormone (PTH) due to resistance to action of PTH. PHP was first reported in 1942 by Albright who presented three cases of hypocalcemia and Albright hereditary osteodystrophy (AHO) phenotype of short stature with round facies, obesity, brachydactyly, mental retardation, and subcutaneous calcification (1). PHP is classified as types Ia, Ib, Ic, and type II according to molecular pathogenesis and clinical phenotype. PHP is a complex disorder with extreme individual variability. The diagnosis of this rare condition is often delayed and leading to an initially inappropriate approach and therapy. We reported a case 50-year-old that PHP presenting with AHO and seizure due to hypocalcemia in this article.

CASE REPORT

A 50 year-old male patient was first admitted to our hospital with tonic-clonic generalized seizure and hypocalcemia. The patient’s first episode as a tonic-clonic generalized seizure had occurred. Upon arrival, his consciousness was confused. Kernig’s sign and hypertonia were not detected. The deep tendon reflexes were bilaterally equal, and he had no pathologic

reflexes. Trousseau and Chvostek signs were positive. There was no history of any other neurologic disease, malabsorption and malnutrition. There was no family history of similar illness, or bony abnormality.

The patient's height was 158 cm and her weight was 69 kg, with a body mass index of 27.6 kg/ m^2. Physical examination showed that he had round face, short neck and stature. His general examination was otherwise unremarkable. ECG showed prolonged corrected QT interval.

On laboratory investigation: he had serum calcium was 4,5 mg/dl, (normal 8.4- 10.8 mg/dl), serum phosphorus was 6,4 mg/dl, (normal 2.3-4.7 mg/dl), with alkaline phosphatase of 99 IU/L (normal range 30-120 IU/L). Serum magnesium level was 1.7 mg/dl, (normal 1.5-2.5 mg/dl). Intact parathyroid hormone levels were 96 pg/ml (normal 15-65 pg/ml). Hemogram, 25OH-vitamin D, liver, renal and thyroid function tests were normal. Other endocrine hormone levels were normal (IGF-I, gonadotropins, testosterone, prolactin, cortisol, were all within the reference range). Computerized tomography (CT) of the brain revealed marked, symmetric calcifications on the bilateral putamen and dentate nucleus (figure 1).

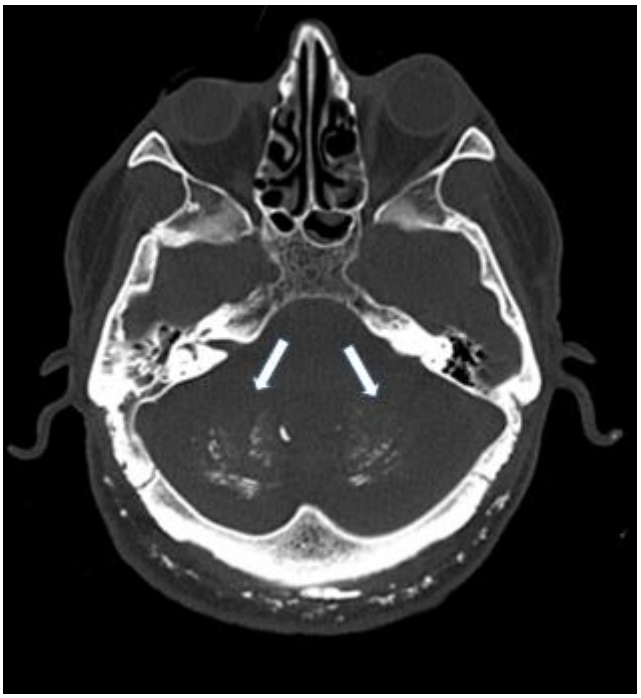

Figure 1. Calcification of bilateral caudate nucleus, putamens and cerebellum is documented in brain CT scan.

The EEG confirmed the non specific dysfunction pathway. In this case the hypocalcemia, hyperphosphatemia, high serum PTH level, normal renal function, vitamin D and alkaline phosphatase with the presence of AHO, the diagnosis of PHP type 1a was made.

During hospitalization the calcium gluconate infusion was continued and then converted to oral calcium carbonate (2 g/day) together with oral calcitriol (1 mcg/day). The patient's seizures were considered to be associated with PHP. He never developed any seizure after treatment. The laboratory values two week after treatment; he had serum calcium was 8,9 mg/dl, (normal 8,4- 10.8 mg/dl), serum phosphorus was 4,6 mg/dl, (normal 2.3-4.7 mg/dl), with alkaline phosphatase of 84 IU/L (normal range 30-120 IU/L) and parathyroid hormone levels were 87 pg/ml (normal 15-65 pg/ml). He was discharged to continue the same treatment and to follow up after 3 months.

DISCUSSION

PHP is a group of rare endocrine diseases characterized by hypocalcemia, hyperphosphatemia and an elevation of PTH values due to a variable resistance to this hormone in its target organs, mainly the proximal renal tubule (1). Its exact prevalence in diverse populations is currently unknown, although it has been estimated to be 3.4 per million people in Japan (2). PHP usually presents at an early age but in literature late onset PHP was published at 4. and 5. decade such as our case (3).

PHP is often associated with a characteristic phenotype known as Albright's hereditary osteodystrophy. Typical features of Albright's hereditary osteodystrophy include learning difficulties, central obesity, round facies, brachydactyly, cataracts, band keratopathy and metastatic calcification. Brachydactyly, especially of the fourth and fifth digits, is a common (4). In a series reported by Papaionnou, the incidence of diagnostic features is as follows: short metacarpals or tarsals (92%), short stature (76%), round face (71%), mental retardation (64%), obesity(61%), ectopic calcinosis (35%) (5). In our case, he has typical features of

Albright's hereditary osteodystrophy, which include a round face, short neck and stature and brachydactyly.

PHP is classified as types Ia, Ib, Ic, and type II according to molecular pathogenesis and clinical phenotype. Type 1 is characterized by low or absent renal cyclic adenosine monophosphate (cAMP) production in response to PTH. Type 2 shows increase in urinary cAMP in response to PTH but absent or subnormal phosphaturic response. In PHP-Ia patients, the Gsα protein itself is inactivated. In contrast, in PHP-Ib patients, the Gsα protein is lacking. PHP-Ic patients exhibit significant decreases in the manganese-stimulated adenylate cyclase activity (6). Patients with PHP-Ia may develop resistance to other hormones which act via Gs-coupled receptors such as thyrotrophin-secreting hormone, gonadotrophins, and growth hormone releasing hormone (7). Patients with PHP-Ia present a characteristic phenotype called Albright's hereditary osteodystrophy. PHP-Ib or PHP II has normal phenotype without the AHO syndrome (8). Molecular characterization is currently a reliable method to differentiate the various subtypes of PHP (9).

The main differential diagnoses of hypocalcaemia with secondary hyperparathyroidism were vitamin D deficiency and PHP. Vitamin D deficiency mimicking PTH resistance has been described but alone rarely causes significant hypocalcaemia without a rise in alkaline phosphatase (10). Further investigation of urinary cAMP response to exogenous PTH infusion test was needed to measure in this patient to differentiate the type of PHP, but in our case PTH preparation is not available at present time and we cannot do this test. However, the patient who has hypocalcemia, hyperphosphatemia, high serum PTH level, normal renal function, vitamin D and alkaline phosphatase with the presence of AHO, the diagnosis of PHP type 1a was made.

The goals of therapy are to maintain the appropriate serum calcium concentration and urinary calcium excretion. Treatment includes the use of vitamin D active metabolites (alfacalcidol and calcitriol) and calcium supplementation. Patients with symptomatic hypocalcaemia should be treated with intravenous calcium to bring the calcium levels to within the lower range of normality. It is recommended that all patients undergo a biochemical examination every three months (9). A strict follow up is essential to adjust the therapeutic dosage and to

preserve a difficult biochemical balance (9). In our patient, two weeks after calcitriol and calcium supplement, the serum calcium and phosphorus level returned to normal limit.

CONCLUSION

In conclusion; Pseudohypoparathyroidism can present with unusual manifestations in the adulthood such as hypocalcemia related seizures.

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