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Transient Pseudohypoparathyroidism Manifested as Recurrent Convulsion in a Neonate

Yenidoğanda Tekrarlayan Nöbet Olarak Presente Olan Geçici Psödohipoparatiroidi

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Abstract

We report case of a neonate who presented with recurrent seizure attacks at the age of 12 days. The baby was managed with anticonvulsant drugs. Eighteen days later, the neonate had repeated episodes of convulsion and was referred to our clinic. During initial work-up, we detected hypocalcaemia and started calcium supplementation along with anticonvulsants. There was another episode of convulsion after 3 days, which prompted us to do a repeat serum calcium assay. It showed hypocalcaemia which was persistent and resistant to calcium supplementation. On further investigation, hyperphosphatemia and raised concentration of parathyroid hormone were detected. Serum magnesium and 25(OH) D level was normal. We suspected pseudohypoparathyroidism-and-hypocalcaemia was managed with calcium and vitamin D therapy. There was no further episode of convulsion and the baby was stable with corrected serum calcium and phosphorus levels during follow-up. *Turk Jem 2015; 19: 65-66*

Key words: Convulsion, hypocalcaemia, pseudohypoparathyroidism

Conflicts of Interest: The authors reported no conflict of interest related to this article.

Özet

Burada 12 günlük iken tekrarlayan nöbet atakları ile başvuran bir yenidoğan sunulmuştur. Bebek anti-konvulzanlar ile tedavi edilmiştir. On sekiz gün sonra benzer şikayetler ile bize refere edilmiştir. İlk değerlendirmede hipokalsemi saptandığı için tedavi kalsiyum desteği ve antikonvulzanlar olarak ayarlandı. Üç gün sonra nöbet tekrarlaması üzerine bakılan kalsiyum düşük saptandı ve dirençli hipokalsemi tanısı kondu. İleri incelemede 25(OH)D düzeyi ve Mg normal ancak fosfor ve PTH yüksek olarak saptandı. Psödohipoparatiroididen kuşkulandık ve tedavi kalsiyum ve D vitamin ile devam etti. İzlemde nöbet tekrarlamadı ve bebek normal düzeltilmiş kalsiyum ve fosfor düzeyleri ile stabil olarak izlendi. *Turk Jem 2015; 19: 65-66*

Anahtar kelimeler: Nöbet, hipokalsemi, pseudohipoparatiroidi

Çıkar Çatışması: Yazarlar bu makale ile ilgili olarak herhangi bir çıkar çatışması bildirmemiştir.

Introduction

Pseudohypoparathyroidism (PHP) is a disorder that presents with hypocalcaemia, hyperphosphatemia, elevated serum level of parathyroid hormone (PTH), and insensitivity to PTH (1). National Institute of Health in the United States has included it within the list of rare diseases (2,3,4). Convulsions due to hypocalcaemia can be misdiagnosed in neonates. This is the case of pseudohypoparathyroidism (PHP) that presented in the neonatal period with convulsions due to hypocalcaemia.

Case Report

A 1-month-old male infant weighing 3.6 kg. was referred to the paediatric medicine unit of our college for evaluation and management of repeated episodes of clonic convulsion. He was a full-term child born by normal vaginal delivery to a consanguineous marriage with a birth weight of 3.2 kg, at hospital with no neonatal problems. The baby had recurrent convulsions at the age of 12 days. There were no other significant complaints. However, the baby had another episode of convulsion 3 days after admission. There was no family history of convulsions, short stature, or other endocrine abnormalities. On physical examination, the child was conscious with normal activities and reflexes. Capillary refill time was 2 seconds, pulse rate-152/min, respiratory rate 44/min, blood pressure 82/54 mmHg, body weight 3.6 kg and head circumference was 36 cm. Anterior fontanel was at level and there was no facial dysmorphism or skeletal malformation. Urine output was adequate. Other systems were normal.

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Laboratory investigations revealed; serum glucose: 78 mg/dl, serum calcium: 6.8 mg/dl, total leukocyte count: 13,900/cu mm and negative septic-screen. Serum magnesium level was normal (1.97 mg/dl). CRP and CSF analyses were within normal limits. Skeletal X-ray and computed tomography scan of the brain were normal. Abdominal ultrasound showed no renal abnormality or foci of calcification. To correct hypocalcaemia, the child was put on I-V calcium gluconate (2 ml/kg, 8 hrly). Recurrence of seizure prompted thorough metabolic screening which revealed normal serum ammonia, lactate and arterial blood gas analysis. Blood urea was 17 mg/dl and serum creatinine-0.60 mg/dl. Further investigations revealed; serum calcium: 4.3 mg/dl, serum phosphorus: 7.30 mg/dl (normal 3.8-6.5 mg/dl), serum parathormone level: 154 pg/ml (normal 15.00-68.00 pg/ml), and alkaline phosphatase level: 527 IU/L (normal 42-362 IU/L). Serum alkaline phosphatase level is increased in most of the cases excepting a few conditions like hypophosphatasia. Level of 25(OH) Vitamin D was within normal limit. Serum calcium and phosphorus levels of the mother were normal.

With these findings of persistent hypocalcaemia, hyperphosphatemia and high serum parathormone levels, the diagnosis of PHP was made. Then, the child was treated not only by calcium supplementation, but also with calcitriol (0.25 mcg/day). Serum calcium and phosphorus became normal within 10 days of calcitriol treatment. The anticonvulsants were gradually tapered off and finally withdrawn. The child was discharged with calcium and calcitriol supplementation. On follow-up at two months of age, the infant was asymptomatic with normal serum calcium and phosphorus levels. Urine calcium to creatinine ratio was maintained within normal limits.

Discussion

Fuller Albright coined the term PHP in 1942 for patients having parathormone (PTH)-resistant hypocalcaemia and hyperphosphatemia with certain skeletal defects (2,3,4). PHP is a rare disease and its prevalence is 3.4 per million populations in Japan (5). No other data is found from the rest of the world. The parathyroid glands are normal or hyperplastic in PHP. Either endogenous or administered PTH is not able to raise the serum calcium level or lower the serum phosphorus level. PHP is divided into two main types; type 1 and type 2. Type 1 is further subdivided into two subtypes; Ia and Ib. Type 1 is characterised 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 (6). Type Ia is caused by molecular defect in the gene (GNAS 1) which encodes the alpha subunit of the stimulatory G protein (Gsa) (2). Most of the patients with type Ia PHP have distinctive morphological abnormalities including rounded face, short stature, shortened fourth metacarpal, and dental hypoplasia; which are collectively called as Albright hereditary osteodystrophy (AHO) (1). In this type, hypocalcaemia develops before 3 years on rare occasion (7).

Features of AHO are absent in patients with subtype Ib PHP. They have normal expression of Gsa protein in tissues other than kidney, where they express resistance with low urinary CAMP response to PTH. PTH responsiveness is preserved in bone resulting in hyperparathyroid skeletal lesions. Isolated renal resistance to PTH is caused by defective promoter or enhancer region of the GNAS 1 gene that is not able to support expression of Gsa protein in the kidney but not in other tissues (8). This is an autosomal dominant disorder. The gene is located in band 20q 13.3 near the GNAS locus and is paternally imprinted (4). Patients with type 2 have no skeletal and developmental defects like type Ib, but they show normal urinary CAMP response to PTH. Treatment is directed towards correction of hypocalcaemia using calcium and active forms of vitamin D.

So far, a few cases of neonatal PHP have been reported in the literature and most of them presented with convulsions in the early neonatal period. Our case presented with recurrent episodes of convulsion in the late neonatal period, which is an unusual presentation of PHP. There were no skeletal or developmental defects. There was no lytic skeletal lesion of hyperthyroid bone disease either. We could not measure urinary CAMP because of limitation of facilities. Nevertheless, from other evidences as mentioned above, we can comment that our case belongs to type 2 PHP which is also less common.

Conclusion

Pseudohypoparathyroidism is a rare disease and can present with unusual manifestations in the neonatal period. We assume that high index of suspicion is the key to proper diagnosis and treatment. Hypocalcaemia should be excluded in all infants presenting with seizures. Persistent hypocalcaemia, despite calcium supplementation, can be a clue for the diagnosis of PHP.

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