CLINICAL VIGNETTE

Pseudohypoparathyroidism: A Case Report and Review

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Case Report

A 54-year-old homeless man made an appointment to establish care. Baseline labs prior to his appointment included a calcium of 6.5. Despite multiple efforts to contact him, he was not available until his scheduled appointment, several days later. The patient was in his usual state of health. PMH was remarkable for a prior history of hypocalcemia 5 years earlier at an outside hospital and seizure disorder diagnosed 10 earlier, currently inactive off his usual therapy of valproic acid for months. He was also prescribed calcium supplements, which he had not taken for 2 weeks.

Other relevant history included spasms in his right forearm lasting 20-30 seconds 1-2 times daily for the last 10 years. He had no history of abdominal pain or other gastrointestinal symptoms, no renal disease, no neck surgery or radiation, no malignancies, no fractures or other bone disease and no palpitations or arrhythmias. Family history was not known. Physical exam was notable for tetany with a positive Chvostek sign bilaterally. EKG showed normal sinus rhythm with a rate of 91 bpm, a normal axis and a QTc of 430. Laboratory studies included a calcium level of 6.5 (albumin 4.3), ionized calcium 0.73, phosphorus 4.3, iPTH 471.2 and vitamin D of 26.2.

PET/CT NaF Bone Scan was notable for 1. Diffusely increased tracer uptake in the axial and appendicular skeleton with focal increased uptake in the left acromial bone as well as bilateral femoral heads which correlated to hypodense cystic lesions on the CT scan compatible with resorptive metabolic bone disease. No evidence for Paget's disease or an osteoblastic process and 2. Marked symmetrical calcification of the basal ganglia, cerebellum, and the brain white matter consistent with the history of hyperparathyroidism and recalcitrant seizure disorder.

He was admitted to the hospital and received a total of 11 grams of calcium gluconate over a 2-day hospitalization. His divalproex sodium was held as he had not been taking it for two weeks prior to admission. With normalization of his serum calcium, his tetany and muscle spasms abated and he remained seizure free. He was discharged on calcitriol 0.25 mg bid and calcium carbonate 500 mg tid.

In the two years since his initial presentation he has remained largely adherent to his medical regimen with surveillance calcium levels in the normal or near normal range. His iPTH nearly normalized to a level of 80.20. He has remained seizure free off antiepileptic medications.

Discussion

Pseudohypoparathyroidism (PHP) was the first described hormone resistance syndrome. It was originally described in 1942 by Albright, along with Albright Hereditary Osteodystrophy (AHO). These are rare genetic disorders with an incidence of less than 1 per 100,000. They are characterized by resistance to parathyroid hormone with subsequent hypocalcemia and hyperphosphatemia.

Pseudohypoparathyroidism includes a heterogeneous group of disorders. Classifications include Pseudohypoparathyroidism Type I (A-C) and Type II. Physical manifestations of these disorders are related to the electrolyte disturbance and include cataracts, tetany, paresthesias, seizures and muscle spasms.

The pathophysiology of PHP Type I is related to a blunted response of the intracellular messenger cAMP to PTH stimulation. In contrast, the exceedingly rare PHP Type II shows a normal cAMP response to PTH, but a notable decrease in phosphaturic response to PTH stimulation, suggesting a downstream defect in the PTH-mediated transduction pathway in target cells. Of note, there is speculation that PHP II is related to vitamin D deficiency, as it has been noted that calcium and vitamin D supplementation ameliorate the phosphaturic response to PTH in PHP II patients.

PHP I is further subclassified into Types Ia-Ic. These subclassifications are based on the presence or absence of various factors, including AHO (with its phenotypic manifestations of brachydactyly, rounded face, short stature, central obesity and mental retardation), heterotopic ossification, various biochemical responses to a PTH infusion and genetic determinants.[1]

Most forms of PHP are caused by mutations and/or epigenetic influences on gene expression at the complex GNAS locus on chromosome 20q13.3. While many genetic defects responsible for the different forms of PHP are present within the GNAS locus, the mechanism for PTH resistance remains incompletely understood.[2]

Standard treatment of PHP involves the use of calcium supplements and calcitriol to normalize calcium levels. In severe cases with associated skeletal changes, cinacalcet may be useful in normalizing PTH levels and reversing skeletal changes.[3]

REFERENCES

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