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Case Report

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RARE CAUSE OF REFRACTORY TETANY - PSEUDOHYPOPARATHYROIDISM

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ABSTRACT

End-organ resistance to PTH is the cause of pseudohypoparathyroidism. A 20 year old woman presented with features of tetany and was found to have severe hypocalcemia, hyperphosphatemia and elevated PTH (parathyroid hormone) level, suggestive of pseudohypoparathyroidism. She didn't have features of Albright's hereditary osteodystrophy (AHO) which is seen only in some subtypes of this disease. Pseudohypoparathyroidism should always be considered in the differential diagnosis of refractory hypocalcemia and tetany.

KEYWORDS: pseudohypoparathroidism, end organ resistance to PTH, hypocalcemia, tetany.

INTRODUCTION

Parathyroid hormone (PTH) causes a net increase in serum calcium. Its actions include increased osteoclastic activity in bone, increased stimulation of the synthesis of 1, 25-dihydroxycholecalciferol by the kidney and increased renal tubular reabsorption of calcium. PTH also inhibits the absorption of phosphate and bicarbonate by the renal tubule

Based on its etiopathogenesis, hypoparathyroidism can be classified into:

- Primary or acquired condition: there is impaired synthesis or secretion of parathyroid hormone (PTH) due to lack/loss of parathyroid gland (tissue) or to a defect in the synthesis or release of PTH
- Defect in the calcium sensing receptor (CaSR).
- End-organ resistance to PTH (pseudohypoparathyroidism)

We present a case with refractory hypocalcemia and tetany secondary to pseudohypoparathyroidism.

CASE REPORT

20 year old woman presented with fever and generalized maculopapular rash of 8 days duration. The rash was erythematous and oral mucus membranes were involved (Fig 1). She also had carpopedal spasm (tetany). Chvostek's and Trousseau's signs were positive. She had been admitted 3 weeks earlier with hypocalcemia and seizures and had been started on anti-epileptics (carbamazepine and clobazam) and vitamin D/calcium supplements. She had discontinued the Vitamin D/calcium supplements a few days earlier prior to this admission.

Her maculopapular rash was considered likely secondary to antiepileptic drugs (carbamazepine) and were discontinued. Her ionized calcium was 0.55 (1.15-1.32 mmol/L). Total calcium was 4.5 mg/dl. She had normal leukocyte count, eosinophilia (26%). Renal function, liver function and thyroid function tests were all within normal limits. Potassium was 3.0 (3.6-5.1 mmol/L). Vitamin D level was 17 ng/ml (deficient < 30 ng/ml). Phosphorus was 6.9 mg/dl (adults: 2.5-4.5 mg/dl). Intact PTH was 128.1 pg/ml (12-88 pg/ml). ECG revealed prolongation of QT interval. CT scan brain (Fig2) and MRI brain with contrast (Fig 3 a and b) during her previous admission showed bilateral symmetrical calcification of global pallidi and caudate nucleus. She was given intravenous calcium gluconate with improvement in tetany, which recurred the next day. She received calcium gluconate replacement intravenously for 2 days. She was also started on vitamin D replacement and oral calcium supplements. Her symptoms improved prior to discharge.

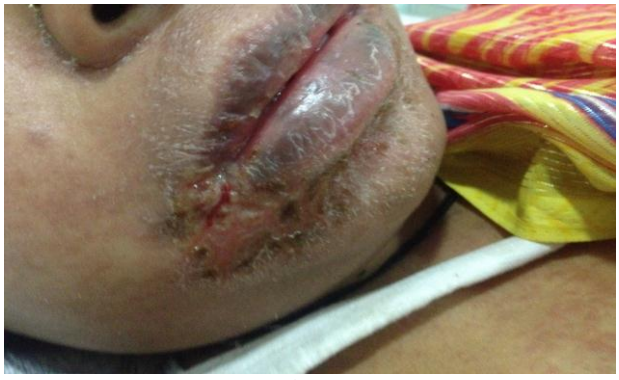

Fig. 1.

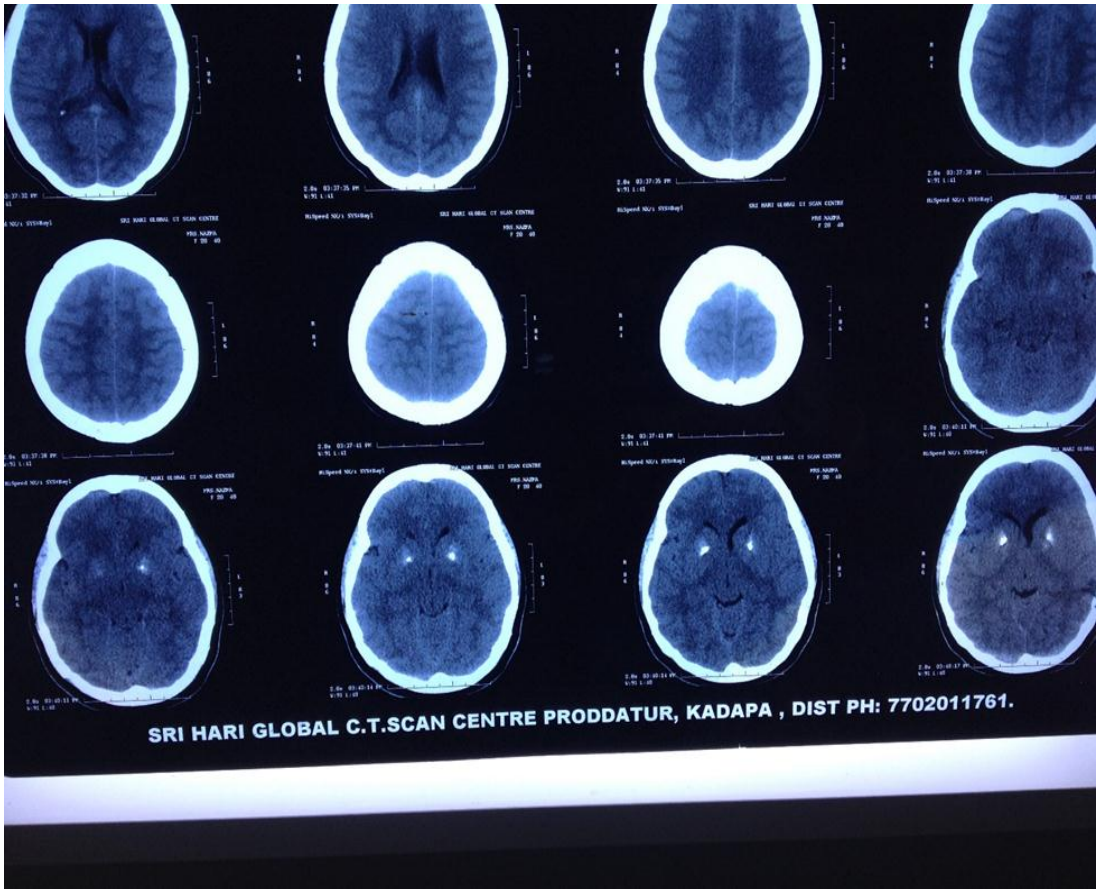

Fig. 2.

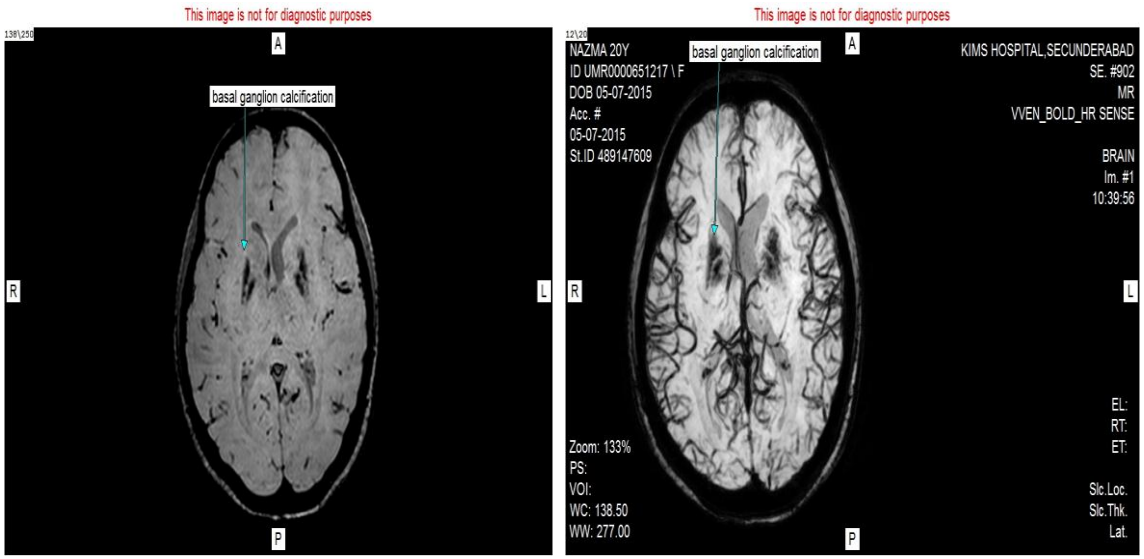

Fig. 3. a and b

DISCUSSION

Pseudohypoparathyroidism (PHP) refers to a group of heterogeneous disorders defined by target organ (kidney and bone) unresponsiveness to PTH. Renal tubular resistance to PTH causes hypercalciuria with resultant hypocalcemia.

PTH resistance is characterized by.[1,2]

- Hypocalcemia
- Hyperphosphatemia
- Elevated PTH concentrations

PHP has been divided into two types.

Type 1

In patients with pseudohypoparathyroidism (PHP) type 1, there is a diminished urinary cyclic AMP response to exogenous PTH administration.[3]

Type 1a

PHP type 1a is an autosomal dominant disease with a loss-of-function mutation of the GNAS1 gene, leading to an inability to activate adenyl cyclase when PTH binds to its receptor function. Activation of adenyl cyclase is required for producing the end-organ response to PTH. Patients with PHP type 1a have a constellation of findings known as **Albright's hereditary osteodystrophy (AHO)** that includes round facies, short stature, short fourth metacarpal bones, obesity, subcutaneous calcifications, and developmental delay.[1,4] In addition, the PTH resistance of the renal tubule leads to hyperphosphatemia and hypocalcemia, and secondary hyperparathyroidism and hyperparathyroid bone disease (osteitis fibrosa).

Type 1b

Patients with the type 1b disease have hypocalcemia but do not have the phenotypic abnormalities of AHO. It has been suggested that PTH resistance is confined to the kidney in this disorder, leading to only hypocalcemia, hyperphosphatemia and secondary hyperparathyroidism.[7] This rare autosomal dominant disorder appears to be caused by mutations that affect the regulatory elements of GNAS1, rather than mutations in GNAS1 itself. Type 1b is maternally transmitted.

Type 1c

Patients with PHP type 1c are phenotypically the same as type 1a.

Type 2

Patients with PHP type 2 do not have the features of AHO. They have normal or even elevated urinary cyclic AMP concentrations in response to exogenous PTH administration but without a concomitant increase in phosphate excretion. The molecular defect in this disorder has not been identified.[8]

Pseudo-pseudohypoparathyroidism — these patients with paternally transmitted mutations have the phenotype of Albright's hereditary osteodystrophy (AHO) but with normal serum calcium concentrations and without renal tubular resistance to PTH.[5,6]

Patient in our case report had hypocalcemia and hyperphosphatemia. Het intact PTH level was increased, suggestive of pseudohypoparathyroidism (PTH resistance). She didn’t have short fourth metacarpals or other features of Albright's hereditary osteodystrophy (AHO), which are seen in subtype 1a. Therefore she has subtype 1b or 2. Urinary cyclic AMP concentrations in response to exogenous PTH administration should be performed if available – this is reduced in 1 (both 1a and 1b) and normal or elevated type 2.

CONCLUSION

Pseudohypoparathyroidism should always be considered in the differential diagnosis of refractory hypocalcemia and tetany.

REFERENCES

1. Albright, F, Burnett, CH, Smith, PH, Parson, W. Pseudo-hypoparathyroidism--an example of 'Seabright-Bantam syndrome': report of three cases. Endocrinology., 1942; 30: 922.
2. Chase LR, Melson GL, Aurbach GD. Pseudohypoparathyroidism: defective excretion of 3',5'-AMP in response to parathyroid hormone. J Clin Invest., 1969; 48: 1832.
3. Ahmed SF, Dixon PH, Bonthron DT, et al. GNAS1 mutational analysis in pseudohypoparathyroidism. Clin Endocrinol (Oxf)., 1998; 49: 525.
4. Farfel Z, Brickman AS, Kaslow HR, et al. Defect of receptor-cyclase coupling protein in psudohypoparathyroidism. N Engl J Med., 1980; 303: 237.
5. ALBRIGHT F, FORBES AP, HENNEMAN PH. Pseudo-pseudohypoparathyroidism. Trans Assoc Am Physicians., 1952; 65: 337.
6. Fitch N. Albright's hereditary osteodystrophy: a review. Am J Med Genet, 1982; 11: 11.
7. Murray TM, Rao LG, Wong MM, et al. Pseudohypoparathyroidism with osteitis fibrosa cystica: direct demonstration of skeletal responsiveness to parathyroid hormone in cells cultured from bone. J Bone Miner Res., 1993; 8: 83.
8. Drezner M, Neelon FA, Lebovitz HE. Pseudohypoparathyroidism type II: a possible defect in the reception of the cyclic AMP signal. N Engl J Med., 1973; 289: 1056.