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Research Paper

Pseudohypoparathyroidism:-A Rare Disorder

Medical Science

KEYWORDS :

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ABSTRACT

Pseudohypoparathyroidism refers to a group of distinct inherited disorders. Patients are characterized by symptoms and signs of hypocalcaemia in association with distinctive skeletal and developmental defects. The hypocalcaemia is due to a deficient response to PTH, which is probably restricted to the proximal renal tubules. Hyperplasia of the parathyroid, a response to hormone-resistant hypocalcaemia, causes elevation of PTH level. Neuromuscular and neurologic manifestations of hypocalcaemia include muscle spasms, carpopedal spasm, facial grimacing, and, in extreme cases, laryngeal spasm and convulsions. Increased intracranial pressure occurs in some patients with long-standing hypocalcaemia, often in association with papilledema. Mental changes include irritability, depression, and psychosis. The QT interval on the electrocardiogram is prolonged. Arrhythmias occur. Intestinal cramps and chronic malabsorption may occur. Chvostek's or Trousseau's sign can be used to confirm latent tetany.

BACKGROUND:-

A 15 year old male patient came to our causality on 1st October 11:54am in altered Sensorium. There is history of convulsions 4 days back which involved both upper and lower limb with frothing from mouth and up rolling of eyeball followed by fall from bed followed by postictal confusion for 45 min ..

Pt is having past history of convulsions 2 years back, was taking treatment from some private hospital and had stopped taking medication since 6 months. There was no other significant past history, personal history and family history.

On physical examination pt had normal temperature on touch with pulse rate of 78/min/regular and blood pressure of 118/74mmhg in supine position. Pt had normal respiration with bilateral air entry present with clear lung field and respiratory rate of 20/min. Pt had normal cardiovascular activity with no murmur and normal abdomen. On CNS examination pt was semiconscious, not fully oriented, deep tendon reflexes were absent on both sides, plantars were downwards and both eye pupils were normal and reacting to light...

Pt's blood count was within normal limits with LOW serum total calcium level [4.90] and an LOW ionized calcium level of [2.05]. Alkaline phosphatase was persistently raised. 25 OH cholecalciferol was low (9.6). Intact PTH was high (552.4). Inorganic phosphorus was high (6.07). Magnesium was normal (1.95) ... X RAY CHEST PA was normal and sinus tachycardia was present on ecg. X RAY wrist showed short right 4th metacarpal. On NCCT scan of brain there was no definite focal lesion so we went for MRI BRAIN WITH CONTRAST. MRI BRAIN WITH CONTRAST showed normal MR study of brain and no evidence of recent infarct/ischemic area found.

Endocrine reference was done for history and lab findings were suggestive of pseudohypoparathyroidism.

Initially pt was managed on higher antibiotics, eptoin and calcium tablets with supportive treatment. Then patient was shifted to inj. Calcium gluconate TDS and Tab.calcitriol (0.25mg) BD . Then pt. was discharged on oral calcium with active vit D3 suplliment.

DISCUSSION:-

PHP refers to a group of distinct inherited disorders. Patients are characterized by symptoms and signs of hypocalcemia in association with distinctive skeletal and developmental defects. The hypocalcemia is due to a deficient response to PTH, which is probably restricted to the proximal renal tubules. Hyperplasia of the parathyroids, a response to hormone-resistant hypocalcemia, causes elevation of PTH levels

The classification scheme is based on the signs of ineffective PTH action (low calcium and high phosphate), urinary cyclic AMP response to exogenous PTH, the presence or absence of *Albright's hereditary osteodystrophy (AHO), and assays to measure the concentration of the* $G_{s\alpha}$ subunit of the adenylate cyclase enzyme. Using these criteria, there are four types:Pseudo hypoparathyroidism(PHP) types Ia and Ib; pseudopseudohypoparathyroidism (PPHP), and the related disorder progressive osseous heteroplasia(POH), and PHP-II

Table 353-6 Classification of Pseudohypoparathyroidism (Php) and Pseudopseudohypoparathyroidism (Pphp)

Type	Hypocalcemia, Hyperphosphatemia	Response of Urinary cAMP to PTH	Serum PTH	$G_{s\alpha}$ Subunit Deficiency	AHO	Resistance to Hormones in Addition to PTH
PHP-Ia	Yes	↓	↑	Yes	Yes	Yes
PHP-Ib	Yes	↓	↑	No	No	Yes (in some patients)
PHP-II	Yes	Normal	↑	No	No	No
PPHP	No	Normal	Normal	Yes	Yes	No

Abbreviations: ↓, decreased; ↑, increased; AHO, Albright's hereditary osteodystrophy; PTH, parathyroid hormone.

Individuals with PHP-I, the most common of the disorders, show a deficient urinary cyclic AMP response to administration

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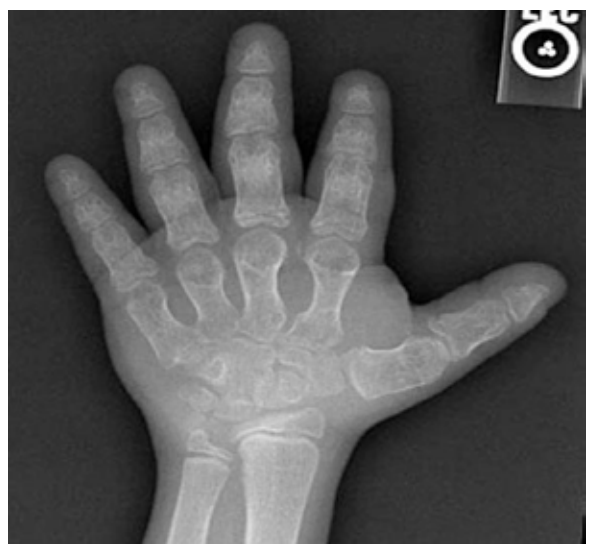
of exogenous PTH. Patients with PHP-I are divided into type Ia and type Ib. Patients with PHP-Ia show evidence for AHO and reduced amounts of Gsα protein/activity in readily accessible tissues, such as erythrocytes, lymphocytes, and fibroblasts. Patients with PHP-Ib typically lack evidence for AHO and they have normal Gsα activity. PHP-Ic, sometimes listed as a third form of PHP, is really a variant of PHP-Ia, since the mutant Gsα shows normal activity in certain in vitro assays.

Most patients who have PHP-Ia reveal characteristic features of AHO, consisting of short stature, round face, skeletal anomalies (brachydactyly), and/or heterotopic calcification. Patients have low calcium and high phosphate levels, as with true hypoparathyroidism. PTH levels, however, are elevated, reflecting resistance to hormone action.

Amorphous deposits of calcium and phosphate are found in the basal ganglia in about one-half of patients. The defects in metacarpal and metatarsal bones are sometimes accompanied by short phalanges as well, possibly reflecting premature closing of the epiphyses. The typical findings are short fourth and fifth metacarpals and metatarsals. The defects are usually bilateral. Exostoses and radius curvus are frequent. Impairments in olfaction and taste and unusual dermatoglyphic abnormalities have been reported. PHP-II refers to patients with hypocalcemia and hyperphosphatemia who have a normal urinary cyclic AMP, but an impaired urinary phosphaturic response to PTH. These patients are assumed to have a defect in the response to PTH at a locus distal to cyclic AMP production. It remains unclear why the PTH resistance in some patients, labeled as PHP-II, can be treated with vitamin D supplements.

The diagnosis of these hormone-resistant states can usually be made without difficulty when there is a positive family history for features of AHO, in association with the signs and symptoms of hypocalcemia. In both categories—PHP-Ia and PHP-Ib—serum PTH levels are elevated, particularly when patients are hypocalcemic. However, patients with PHP-Ib or PHP-II usually do not have phenotypic abnormalities, only hypocalcemia with high PTH levels, as evidence for hormone resistance. In PHP-Ib, the response of urinary cyclic AMP to the administration of exogenous PTH is blunted. The diagnosis of PHP-II is more complex, in that cyclic AMP responses in urine are, by definition, normal. Vitamin D deficiency must be excluded before the diagnosis of PHP-II can be entertained.

Treatment of PHP is similar to that of hypoparathyroidism, except that calcium and vitamin D doses are usually lower. Patients with PHP show no PTH resistance in the distal tubules—hence, urinary calcium clearance is not affected and they are at less risk of developing nephrocalcinosis than in patients with true hypoparathyroidism. Variability in response makes it necessary to establish the optimal regimen for each patient, based on maintaining the appropriate blood calcium level and urinary calcium excretion.



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