Pseudohypoparathyroidism Type 1B with Hypothyroidism

RAJESH JOSHI AND MUZNAH KAPDI
From the Department of Pediatrics, BJ Wadia Hospital for Children, Parel, Mumbai.

Correspondence to:
Dr RR Joshi,
Department of Pediatrics,
BJ Wadia Hospital for children,
Parel, Mumbai. rrj23@rediffmail.com
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Pseudohypoparathyroidism due to deficient end organ response to parathyroid hormone (PTH) is characterized by hypocalcemia, hyperphosphatemia and increased serum PTH. We report a case of an 8-year-old girl with pseudohypoparathyroidism without features of Albright's hereditary osteodystrophy. The case is of interest as the child on serial follow-up over a period of 2 years developed hypothyroidism. This is a rare feature seen in pseudohypoparathyroidism type1b.

Key words: *Albright's hereditary osteodystrophy, Hypothyroidism, Parathyroid hormone, Pseudohypoparathyroidism.*

Pseudohypoparathyroidism (PHP) is a group of disorders characterized by resistance to parathyroid hormone, resulting in hypocalcemia. Several types of PHP have been identified: Type 1a- presents with features of Albright hereditary osteodystrophy (AHO - short stature, obesity, round facies, subcutaneous ossifications, brachydactyly and mental retardation in some patients) and types 1b and 2 (without features of AHO) [1] . We report a patient with PHP without features of AHO who developed hypothyroidism on follow up.

CASE REPORT

An 8-years-old girl presented with involuntary inward turning of thumb and tingling in hands for 3 months.She had similar complaints one year back, which were diagnosed as hypocalcemia (serum calcium-7.9 mg/dL). She was treated with calcium supplements for 2 months following which she had temporary relief. She weighed 25 kg and measured 125 cm in height (within normal centiles). Examination did not reveal skeletal abnormalities or dysmorphism. Chvostek's and Trousseau's sign were positive. Laboratory investigation revealed serum calcium 6.6 mg/dL, iCa^{++}–0.83 mmol/dL (low), serum phosphorous 7.4 mg/dL(high) and alkaline phosphatase 187 IU/mL (normal levels). Levels of parathyroid hormone were very high (iPTH-560pg/mL; normal value: 8.9-59.8 pg/mL). Complete blood count, 25OH-vitamin D, and liver and renal function tests were normal. Thyroid functions (TFT) were normal [free(f)T^3–3.2 pg/mL; fT^4–1.3 ng/dL; TSH-5 IU/mL]. She was treated with calcium supplements and calcitriol. On follow up, serum calcium levels and urinary calcium/creatinine were monitored to achieve good calcemic control and to prevent calciuria . TFT were monitored six monthly. She developed hypothyroidism (TSH: 15.5 IU/mL; fT^3: 3.68 pg/mL; fT^4:1.19 ng/dL) two years after diagnosis, for which she was treated with thyroxine 50 mcg daily and subsequently increased to 75 mcg. She is now 11½-year old, having normal growth and pubertal changes (thelarche).

The underlying pathophysiology in PHP is a defect at the PTH-receptor (genetic mutation in the alpha subunit of the receptor G-protein causing altered messenger action), leading to end organ resistance to the action of PTH. Resistance to other hormones (which function via the alpha subunit of G protein), most commonly thyroid-stimulating hormone and rarely gonadotrophins and growth hormone releasing hormone may be seen in type 1a [2,3]. PHP Ib typically shows no other endocrine abnormalities, although resistance to thyroid-stimulating hormone (leading to primary hypothyroidism) has been reported rarely [4,5] PHP type 2 does not present with any other hormone resistance . Our patient probably had PHP type1b.

PHP Ib is caused by deletions in the differentially methylated region (DMR) of the GNAS locus, located on chromosome 20q13.11. It is mostly a sporadic disorder, but sex-influenced autosomal dominant inheritance has been reported [1]. Parents of our patient did not have any phenotypic or biochemical evidence of PHP. PHP type Ib is characterized by renal PTH resistance whereas PTH responsiveness is preserved in the bone and other tissues resulting in lack of AHO features.Measurement of cAMP excretion after PTH infusion is a differentiating feature between type 1b and 2 (decreased in type 1b and normal in type 2) [2]. However, this test was not affordable.

Administration of oral calcium and calcitriol remains the mainstay of treatment. The goals of therapy are to maintain serum calcium levels within the reference range so as to avoid hypercalciuria. Thyroid function tests should be evaluated periodically even in absence of features of AHO, as hypothyroidism develops rarely, as seen in our patient.

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Chronic Myeloid Leukemia in a Child with IgA Nephropathy

AMISH UDANI, VIJAYAKUMAR MAHALINGAM, PRAHLAD NAGESWARAN AND *SUDHA EKAMBARAM
*From the Department of Pediatric Nephrology and *Pediatrics, Mehta Children's Hospitals, Chennai, India.*

Correspondence to:
Dr M Vijayakumar, Consultant Pediatric Nephrologist, Mehta Children's Hospitals, No.2(e) Mc Nichols Road, 3rd Lane, Chetput, Chennai 600 031, Tamilnadu, India.
doctormvk@gmail.com,
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We report an 11 year old boy with IgA nephropathy developing chronic myeloid leukemia on follow-up. This association suggests that a B cell defect might be involved in the pathogenesis of these two conditions.

Key words: *Chronic myeloid leukemia, IgA nephropathy.*

There is increasing evidence of abnormal glycosylation of immunoglobulin A1 (IgA1) subclass due to B-cell defect in the pathogenesis of immune-complex mediated IgA nephropathy [1]. The occurrence of IgA nephropathy and leukemia has been reported rarely in children [2]. Here we report a child with IgA nephropathy developing chronic myeloid leukemia (CML) on follow-up.

CASE REPORT

An 11-yr-old boy was diagnosed acute nephritic syndrome at 3 year back in view of hypertension, hematuria, proteinuria (spot urine protein to creatinine ratio 0.75), mild renal insufficiency (serum creatinine 1.1 mg/dL), and normal serum albumin and cholesterol. He had no anemia, leukocytosis or electrolyte disturbances. He was treated with salt and fluid restriction and oral nifedepine for hypertension. Serum complement C3 level was normal, anti nuclear antibody and anti double standard DNA was negative. In view of persistent hypertension, renal insufficiency, microscopic hematuria and proteinuria he was referred for evaluation. On examination, the patient was well nourished (weight 46 kg, and height 157 cm) with periorbital edema and blood pressure140/84 mm Hg. Systemic examination was normal. Urinalysis showed 2+ albumin, red blood cells and Up/Uc ratio of 0.33. Blood investigations showed a creatinine of 1.0 mg/dL, albumin 4.2 g/dL and potassium 5.1 mEq/L. Ultrasonogram of the kidneys showed normal size kidneys. Renal biopsy showed seven glomeruli of which two were completely sclerosed and one showed segmental sclerosis and proliferation. Remaining