

Premature Pubarche, Hyperinsulinemia, Hypothyroxinemia and Hyperintensities in Basal Ganglia: All Caused by a Single Congenital Defect

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Objective: Premature pubarche is the occurrence of pubic hair <8 years of age in girls and is mostly idiopathic but can be due to various virilising conditions such as congenital adrenal hyperplasia and androgen secreting tumours. To present two cases with premature pubarche and associated endocrine problems which have not been described previously.

Case: Two girls, presented 10 years apart with the same complaint of early pubarche at age 7 years, with inappropriately low dehydroepiandrosterone sulfate levels. In addition to hyperandrogenemia (elevated testosterone and androstenedione) and advanced bone age, both had hyperinsulinemia, hypothyroxinemia, and hyperintensities in basal ganglia. The 2nd case also had symptomatic hypoglycemia. Investigations revealed a common congenital defect explaining all these manifestations.

Conclusion: Pathogenetic mechanisms leading to all these manifestations will be discussed.

A Case Report of Xp21 Contiguous Gene Syndrome: Adrenal Hypoplasia Congenita, Glycerol Kinase Deficiency, and Duchenne Muscular Dystrophy

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Objective: X-linked adrenal hypoplasia congenita (AHC) is characterized by primary adrenal insufficiency caused by deletion or mutation of the DAX-1 gene and is frequently associated with hypogonadotropic hypogonadism. It can occur as a part of Xp21 contiguous gene syndrome together with glycerol kinase deficiency and Duchenne muscular dystrophy. We report a new subject with this rare disease.

Case: Twin male sibs at the ages of 30 days were hospitalized because of feeding difficulties, vomiting, and weight loss. Parents had no consanguinity and there was no family history of endocrine or renal diseases. One of the twins died in a few hours. Other patient's physical examination revealed that weight was 2100 g (his twin's was 1800 g) and body length 49 cm; blood pressure: 70/40 mm-Hg, heart rate: 140 beats/minute, respiratory rate: 50 breaths/minute, body temperature: 36 °C. He was dehydrated and lethargic. External genitalia were well developed with intrascrotal testes of 2 mL in volume. There was no skin hyperpigmentation. Laboratory findings were as follows: Na 97 mEq/L, K 5.1 mEq/L, adrenocorticotropic hormone (ACTH) >1250 pg/mL, cortisol 6 µg/dL (3-23), plasma renin activity: 50 ng/mL/hr (3-35), 17(OH)P 18 ng/mL (0.3-1.1), dehydroepiandrosterone sulfate: 24 µg/dL (5-111), luteinizing hormone: 0.71 mU/L (0.02-7), follicle stimulating hormone: 0.43 mU/L (0.16-4.1), total testosterone 0.76 ng/mL (0.7-4). After initial therapy for adrenal crisis, hydrocortisone and fludrocortisone were given at replacement doses. Ten days later, steroid hormone treatment was halted and ACTH stimulation test (250 µg) was performed. Peak levels of cortisol, 17(OH)P, and 11-deoxycortisol were 1.02 µg/dL, 3.11 ng/mL, and 3.2 ng/mL, respectively. This test excluded defects in steroid biosynthesis associated with salt-losing congenital adrenal hyperplasia. On ultrasound examination, adrenal gland could not be visualized. Therefore, a diagnosis of AHC was established. Furthermore, we investigated for contiguous gene syndrome. Serum creatinine phosphokinase [CPK, 9974 U/L, (N:35-195)] and triglyceride [TG, 439 mg/dL, (N:0-200)] levels were markedly elevated. On follow-up period of

9 months, his motor and mental development were noted to be delayed. Array comparative genomic hybridization analysis was planned to show Xp21 deletion syndrome.

Conclusion: Serum CPK and TG levels should be measured in all male patients who present with an adrenal hypoplasia. These simple tests may help early diagnosis and appropriate genetic counseling for next pregnancy.

Pseudohypoparathyroidism Type 1a: A Case Report

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Objective: Pseudohypoparathyroidism (PHP) is a group of disorders characterized by end-organ resistance to the parathyroid hormone (PTH). PHP type 1a includes multi-hormone resistance syndrome, Albright's hereditary osteodystrophy, and obesity and is caused by mutations in GNAS exon 1 through 13. Characteristic features of disease are hypocalcemia, hyperphosphatemia, elevated PTH, obesity, round facies, and subcutaneous calcification. The disease is inherited from affected mother. On the other hand, pseudopseudohypoparathyroidism (PPHP) occurs if the mutation is paternally inherited. In PPHP, calcium and phosphorus levels are generally normal. In this report, we want to present a boy with PHP type 1a who has normal calcium and elevated thyroid stimulating hormone (TSH) levels, which is a rare event.

Case: The 12-10/12-year-old boy was admitted with the complaint of short stature. On physical examination, brachydactyly, round facies, and short neck were observed as well, indicating PHP 1a. However, serum calcium, phosphorus, alkaline phosphatase, vitamin D, and PTH levels were normal. These results were compatible with PPHP. On the other hand, TSH levels were found to be high (8 µIU/mL, normal range 0.5-4.8 µIU/mL), free thyroxine levels slightly low (0.7 ng/dL, normal range 0.8-2.3 ng/dL), urine iodine level normal, and thyroid antibodies to be negative. These features were compatible with PHP type 1a. Therefore, genetic analyses were performed and p.D826H (C2476G>C) heterozygous mutation was found in GNAS. The genetic analyses of parents revealed maternal inheritance. As far as we know, this mutation was not reported before and was found to be high risky for being a cause of the disease according to mutation taster and human splicing finder.

Conclusion: In this report, we want to emphasize that normocalcemia can be a finding of PHP type 1a.