A Case of X-Linked Adrenal Hypoplasia Congenita; Adrenal Hypoplasia Congenita, Glycerol Kinase Deficiency and Duchenne Muscular Dystrophy

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Introduction:

X-linked adrenal hypoplasia congenita (AHC) is caused by mutations of the NR0B1 gene encoding DAX1 on chromosome Xp21. It is estimated that more than 50% of boys with idiopathic adrenal insufficiency have mutations in the NR0B1 gene product, DAX1. AHC also occurs as part of a contiguous gene deletion syndrome together with Duchenne muscular dystrophy, glycerol kinase deficiency (GKD), mental retardation, or a combination of these conditions. Glycerol kinase plays a critical role in metabolism by converting glycerol to glycerol 3-phosphate in an ATP dependent reaction. In humans, glycerol kinase deficiency results in a wide range of phenotypic variability; patients can have severe central nervous system and metabolic abnormalities, while others possess hyperglycerolemia and glyceroluria with no other apparent phenotype. Here, we report a male 5 years old with AHC who presented with adrenal insufficiency, GKD, and duchene muscular dystrophy due to a mutation in the DAX-1 gene.

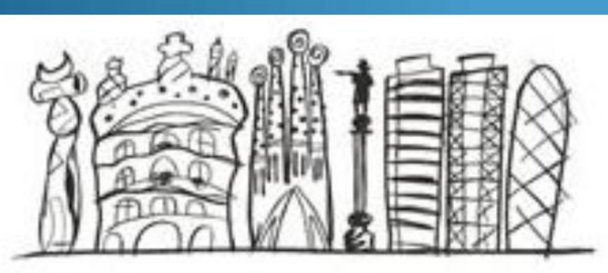
Case:

A 5 years old male patient who presented with vomiting, bruising, fainting, growth and failure to thrive was hospitalized. The patients physical examination revealed that weight was 13.6 kg (< %3 p), length 106 cm (< %3 p). He was dehydrated, lethargic. His external genitalia was well developed with intrascrotal testes of 2 ml in volume. There was skin hyperpigmentation. The patient underwent a detailed clinical investigation including genetic testing. The initial laboratory tests showed sodium: 126 meq/L, potassium: 7,3 meq/L, glucose: 64 mg/dl, blood urea nitrogen: 32 mg/dl, basal cortisol level: 1,2 µg/dl, adrenocorticotropic hormone (ACTH) level: >1250 pg/ml, 17 hydroxyprogesteron(17-OHP): 0,1 ng/ml, dehydroepiandrosterone-sulphate: 0,1 µg/dl, total testosterone: 0,1 ng/ml. There was no evidence of unusual organic acid profile in urine organic acid screening. Hydrocortisone, fludrocortisone and sodium chloride supplement were initiated. This treatment corrected electrolyte abnormalities and the patient improved. Adrenal glands were not visualized on abdominal ultrasound.

The diagnosis was AHC. Further, we investigated for contiguous deletion syndrome. His creatinine phosphokinase (CK) (7592 U/L, normal: 35-195) and triglyceride (TG) (1045 mg/dl normal: 0-200) levels were elevated. Our patient had pseudotriglyceridemia because the large amount of glycerol in their serum is falsely identified as triglyceride. Molecular analysis of the NR0B1 (DAX1) gene revealed a complete deletion. With these findings, we made a diagnosis of Xp21 contiguous gen deletion syndrome.

Discussion

DAX-1 deficiency should be kept in mind in male patients with primary adrenal insufficiency without congenital adrenal hyperplasia. Furthermore, CK and TG levels should be measured in all male patients with adrenal hypoplasia. These simple tests may help to make early diagnosis and appropriate genetic counseling for next pregnancy.



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