Central European Annals of Clinical Research

Endoped Abstract

Primary Adrenal Insufficiency—Diagnosis and Management Challenges

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Submitted: 26 October 2020, accepted: 14 November 2020, published: 20 November 2020

Abstract: We present the case of a child with mild axial hypotonia and episodes of persistent hyponatremia and hyperkalemia early in life, followed by an asymptomatic long period. During the present hospital admission, dysregulation of the adrenal gland function and detection of two missense variants in NR0B1 (nuclear receptor subfamily 0 group B member 1) gene state with high probability the diagnosis of congenital adrenal insufficiency. Management include substitution therapy and food supplementation with salt with good outcome.

Keywords: Addison disease; adrenal insufficiency; rare disease; autoimmune syndrome

How to cite: Țaranu, I.; Creț, V. Primary Adrenal Insufficiency—Diagnosis and Management Challenges. *Cent. Eur. Ann. Clin. Res.* **2020**, *2*(1), 20; doi:10.35995/ceacr2010020.

Background and Aims

Primary adrenal insufficiency is a rare disease with a prevalence of 1 to 5 per 10.000 in adults from western countries where autoimmune adrenalitis is the most common cause [1]. Diagnostic delay until the third or fourth decade of life might be due to the nonspecific onset symptoms. In children, adrenal insufficiency has both genetic and acquired causes: congenital adrenal hyperplasia, autoimmunity and steroid withdrawal after chronic exposure [2,3]. Important challenges in treatment are the risk of over- and under-replacement dosing and early recognition of association with autoimmune polyendocrine syndrome (APS) [2,3].

We present the case of a child diagnosed with primary adrenal insufficiency with a history of nonspecific symptoms followed by a long asymptomatic period before hospital admission.

Clinical Case

A 3-year and 10-month year old boy was admitted to our hospital with persistent fatigue, loss of appetite and a recent history of multiple episodes of nausea, vomiting and persistent Na^+ low levels which required multiple hospital visits.

The onset of symptoms had begun at the age of 2 months with a mild loss of axial muscle tonus when investigations had revealed persistent hyponatremia and hyperkalemia. Further analysis excluded a kidney disease (i.e., normal diuresis and acid-base equilibrium), but hormonal investigations had revealed a concentration of mineralocorticoids at the normal lower border with a normal level of blood glucocorticoids. Suspicion of congenital hypoaldosteronism was raised, but a first substitution therapy attempt with 0.05 mg fludrocortisone caused severe hypotonia with obnubilation and hypokalemia. Salt supplementation of milk (2.8 g/day) was initiated with parental infusion of 12–14 mEq NaCl 5.85 %/kg/24 h in every infectious episode with acute dehydration. A 2-year asymptomatic period without acid-base disequilibrium followed.

At present hospital admission, repeated measurements of blood gas values revealed persistent metabolic acidosis with hyponatremia. Associated hypoglycemia and ketonemia without ketonuria occurred. Hormonal measures highlighted profound dysregulation of the adrenal gland: high ACTH (adrenocorticotropic hormone) and renin levels associated with low levels of blood aldosterone and cortisol. Genetic testing revealed the presence of two missense variants in NR0B1 gene: NR0B1:uc004dcf.4:exon1:c.T127G:p.C43G and NR0B1:uc004dcf.4:exon1:c.C70T:p.R24C and the congenital adrenal insufficiency was considered. The replacement therapy of oral hydrocortisone acetate 15.15 mg/m^2/day and fludrocortisone 0.1 mg/day with stress dosing was initiated together with salt supplementation of 2 g/day with favorable outcome: normalized natremia and kalemia and aldosterone, cortisol and ACTH levels within normal ranges.

Conclusion

The present clinical case highlights the difficulty of making the diagnosis of congenital adrenal insufficiency in very young children when nonspecific onset of symptoms is followed by an asymptomatic period. Genetic testing should be envisaged. Follow-up management should include monitoring signs of under- and over-replacement therapy.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.

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