Mysterious diagnosis in a child with failure to thrive

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Introduction

Mutations of several genes encoding the transporters involved in salt reabsorption in the thick ascending limb cause different types of Bartter syndrome (BS), with variable phenotypic expression and severity. Type I and II are the most severe presenting with polyhydramnios, prematurity and characteristically hypokalemia, metabolic alkalosis, polyuria and hypercalciuria.

Case

We report the case of a 9 month old girl referred because of fever, vomiting, dehydration and electrolyte abnormalities despite fluid administration.

Medical history revealed unexplained maternal polyhydramnios, prematurity (34weeks) and dysmaturity (birth weight 1,75kg). She was admitted in a neonatal unit and after a smooth course, was discharged after 36 days (weight 2,2kg). At 4months she presented with feeding difficulties and failure to thrive with no biochemical abnormalities or polyuria were .

At admission, laboratory examination revealed plasma potassium (K) level <3.0 mmol/L, combined with inappropriately high excretion (44%), metabolic alkalosis and hypernatremia (154 mmol/l). Despite IV fluids the biochemical abnormalities persisted but polyuria became prominent Blood pressure (BP) was 115/64mmHg with normal vital parameters. She had pronounced frontal bossing, small hands and a wide nose bridge. Neurological examination was normal.

Additional findings of hyperreninemia hyperaldosteronism, hypercalciuria and nephrocalcinosis were suggestive of a tubulopathy, namely BS. However hypernatremia and high BP are no typical features of BS. The introduction of indomethacin treatment, in addition to K supplementation, compensation of fluid losses and hypercaloric nutrition lead to a stable condition with gradual weight gain.

Mutational screening revealed a homozygous variant of unknown clinical significance of SLC12A1, a gene involved in BS type I. Interestingly there is also a heterozygous gain of function mutation of SCNN1 gene, usually associated with Liddle syndrome (LS). Further genetic testing, including of the parents, is pending.

Conclusion

This is the first report of a girl with a phenotypic overlap between BS and LS. Although genetic analysis revealed homozygosity for a SLC12A1 variant of unknown significance, clinical picture of BS indicates that this is associated with the girl's disease. The heterozygosity for SCNN1B, with subsequently enhanced renal sodium reabsorption, leads us to hypothesize that this variant may balance the renal salt wasting caused by BS.