RARE PRESENTATION OF ADRENAL INSUFFICIENCY IN AN INFANT WITH HOLOCARBOXYLASE SYNTHETASE DEFICIENCY

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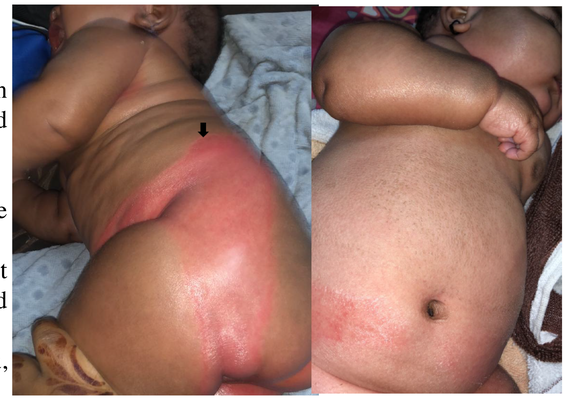
INTRODUCTION

Biotin deficiency is either nutritional or related to synthesis/recycling defects. It is not known to be associated with adrenal insufficiency. However, we are reporting a rare case presented with adrenal insufficiency secondary to excessive steroid use, found later to be having holocarboxylase synthetase deficiency in an infant who also developed protein-S deficiency, thought to be secondary to the underlying pathology (1-2)

CLINICAL CASE

- A term female infant born, to non-consanguineous parents, in a good condition with birth-weight 3.1kg (10th-centile) developed an extensive nappy dermatitis in her first couple of weeks of life, which followed by erythematous scaly patches on her back and excoriation on her abdomen.
- At 2-month, she started gaining weight for which she crossed the centiles rapidly.
- At 3-month, the rash got worse, therefore she was prescribed mometasone 1% cream and clotrimazole-betamethasone which the mother continued to apply in large amounts over large body areas for 2-months.
- At 5-month, she presented to the Emergency Department with an acute history of poor activity and respiratory distress after abrupt stop using of the steroid creams. Examination revealed cushingoid appearance, weight 8.3kg (>99th centile), with dry peeling and depigmented skin indicating signs of steroids side effects. A necrosis of her right toe was also noted.
- She had volume and catecholamine refractory shock associated with severe lactic acidosis, hypoglycemia, hypokalemia, hypernatremia, and normal renin and aldosterone levels.



- Adrenal insufficiency was considered based on the history, hypoglycemia and her shock. Hydrocortisone (20mg/m^2/day) was started. Lactic acidosis continued and peaked to 19mmol/L and started improving a week after.
- After 2-weeks of stabilizing her and establishing the feeds. She acutely became irritable and deteriorated. Acidotic breathing with similar biochemical derangements to her first presentation but with normal glucose and ammonia levels. Refractory lactic acidosis up to 21mmol/L and she needed high ionotropic support and hemodialysis to reduce the acidosis.
- Later metabolic screen indicated biotin deficiency for which she was initiated on Biotin therapy. The baby improved dramatically within 48-hours.
- The thrombophilia workup revealed functional protein-S deficiency.
- Whole exome sequencing revealed compound heterozygous mutations in **HLCS gene**, consistent with the diagnosis of holocarboxylase synthetase deficiency. No mutations were found to explain protein-S-deficiency

Table 1. Investigations and results

Investigations	Results	Reference value
Glucose (mmol/l)	1.4	3.5-7
Lactate (mmol/l)	10	0.7-2.1
Potassium (mmol/l)	2.7	3.5-5
Sodium (mmol/l)	155	135-145
Renin (mIU/l)	13.8	< 36
Aldosterone (pmol/l)	183	117-580
Protien S (u/ml)	0.247	0.54-1.18
Cortisol (nmol/L)	454	>550 in shock

CONCLUSION

- Very rare presentation of the above mentioned three pathologies at one time. Hypernatremia, hypokalemia, obesity and hypertension were not reported previously in Biotin/holocarboxylase synthetase deficiency, two disorders notoriously known to be associated with failure to thrive.
- Steroid use should be restricted in infancy as it caused adrenal insufficiency in this case, that had complicated the picture.

REFERENCES

1. Neary N, Nieman L. Adrenal insufficiency: Etiology, diagnosis and treatment. Current Opinion in Endocrinology, Diabetes and Obesity. 2010.
2. Venkataraman V, Balaji P, Panigrahi D, Jamal R. Biotinidase deficiency in childhood. Neurol India. 2013;61(4):411–3.

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