Rare etiology for primary adrenal failure: ACTH resistance?

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Introduction: ACTH resistance syndromes are rare, autosomal and genetically heterogeneous diseases that include familial glucocorticoid deficiency and triple A syndrome. These are characterized by early onset of primary adrenocortical insufficiency associated with hypoglycemia, convulsions and skin pigmentation.

Clinical Case

Case history: 4 years old boy presented with - hyponatremic convulsive episode.
- hypoglycaemia

Diagnosis : **primary adrenal failure**

- low cortisol
- suboptimal ACTH response → Cortisol T60=17,6 ng/dl
- ACTH>1500 pg/ml

Glucocorticoid and mineralocorticoid substitution: Hydrocortisone 15 mg/m2
Improved the clinical and biologic status (normal natremia and glycaemia).

Etiology

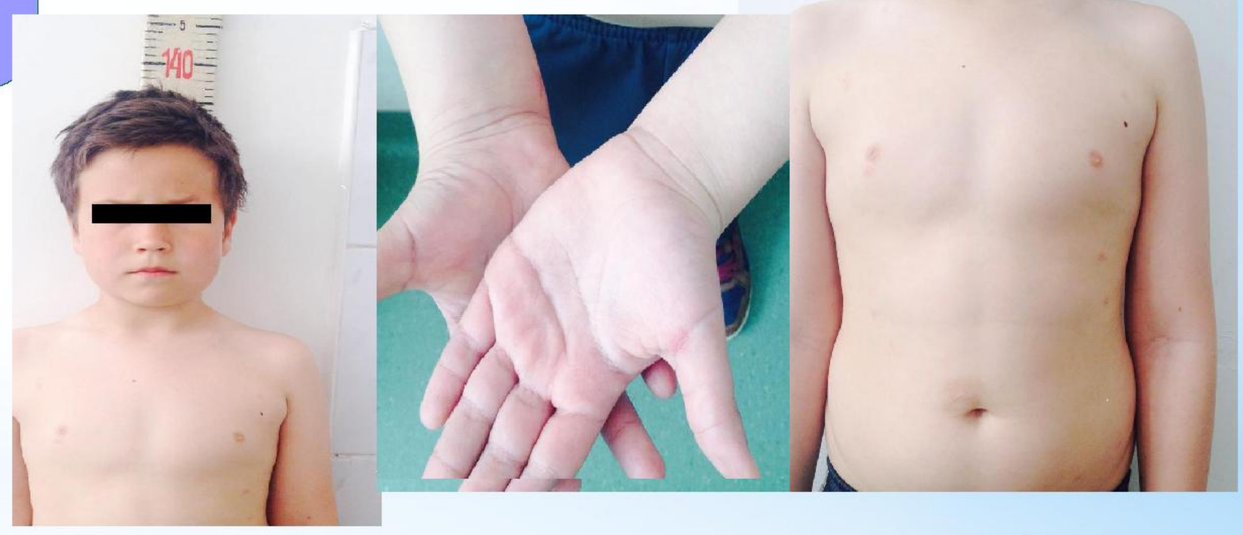
Anti-adrenal antibodies: negative
Anti-microsomal antibodies: negative
Long chain fatty acids: normal
Tuberculosis testing: negative
17-OH progesterone: Normal
Pituitary MRI: Normal
Abdominal CT: Normal Adrenals
No family history of adrenal failure

? **ACTH resistance syndrome**

Clinical examination:

Height=+0,1 DS
BMI (children)=19 kg/m2
BP=100/60 mmHg
Slight facial erytrosis

No skin hyperpigmentation
Hypo lacrimation- dry eyes syndrome
Normal genital area



Paraclinic evaluation after 4 years of hydrocortisone substitution 15 mg/m2:

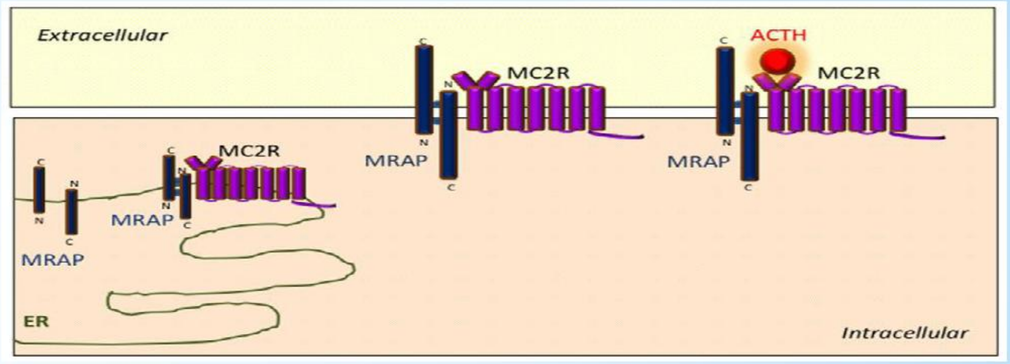
Na=144 mmol/l(135-145); **Cortisol 9 a.m=1,41 ug/dl** (5-25)
K=3,7 mmol/l (3,5-5); **ACTH=1002 pg/ml** (0-46)

Ophthalmologic evaluation:Shirmer test-significant reduction of the lacrimal secretion
No symptoms for achalasia cardia (no dysphagia for solids or liquids)

ACTH resistance syndrome: Molecular analysis for the ACTH receptor gene(MC2R) and MC1R is needed for confirming this diagnosis, but this is not available in our center.

The ACTH receptor (ACTH-R) is a member of the superfamily of G protein coupled receptors.
MSH-R= MC1- R; MC3-R ; MC5-R
ACTH-R= MC2-R ; MC4-R

Coexistent MC2R and MC1R mutations in the same individual, causing an unusual presentation of ACTH resistance without hyperpigmentation have been reported. All such cases have been recorded in Europeans with fair skin, which suggests that MC1R variants could be implicated.



Case particularities

- Usual etiologies for primary adrenal failure were excluded
- low lacrimal secretion → triple A syndrome as possible etiology (AAS gene needs testing)
- no skin hyperpigmentation (high ACTH>1500)-suggesting a possible melanocyte receptor deficiency (MC1-R)
- high levels of ACTH persistent after 4 years of hydrocortison adequate substitution

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