A novel mutation causing Pseudohypoaldosteronism

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Introduction
We present a case of a neonate with a rare cause of life threatening hyperkalaemia, hypotension and metabolic acidosis.

Differential Diagnosis
- Characteristic hypotension, hyperkalaemia, metabolic acidosis
- Aldosterone synthase deficiency
- Renal or Multi Target Organ Disease
- Secondary pseudohypoaldosteronism (Uti, urinary obstruction)

Case History
8 day old girl presented to Emergency dept with 12 hour history of poor feeding and vomitting

Past medical history:
- Term, NVD, birth weight 3.5kg
- First born child, parents consanguineous
- Breastfed, previously well

Initial management
- O2, bag & mask ventilation → HR>100
- 3 x 10mls/kg Saline boluses
- Cardiac monitoring – periods of VT
- IV Cefotaxime & Amoxicillin
- IV Hydrocortisone given empirically
- Venous gas: Ph 7.16, CO2 8.6, O2 3.6, HCO3 23.1, BE - 5.5,
- Na 121 mmol/L, K 10.5 mmol/L
- Blood sugar 3.8mmol/L
- Urgent echo, renal US: normal

Examination
- Mottled, cool peripheries, drowsy & floppy
- HR 66
- Sodium Chloride 12.3
- IV hydrocortisone given
- Urine electrolytes Na 165, K 8
- Trans tubular K gradient 0.6
- Fractional excretion Na 3.9%
- Urine steroid profile
- Aldosterone 45, 200 pmol/L
- Renin >34 ng/ml/h

Pseudohypoaldosteronism
- Rare syndrome of resistance to Aldosterone
- 2 clinically distinct forms
- Systemic form: mutation ENaC, a highly Na selective channel, expressed in the distal nephron, colon, lung and exocrine glands
- Renal form: mutation mineralocorticoid receptor, mild salt losing, improves by early childhood
- Sweat test useful to differentiate 2 forms

Management of hyperkalaemia
- Nebulised Salbutamol continuously
- Cardiac monitoring in PICU
- IV Calcium gluconate 10% 0.2mls/kg
- Insulin infusion 0.5units/kg/hr
- IV fluids 10% dextrose with NaCli @ 2/3 maintenance
- Sodium bicarbonate IVI 1ml/kg/hr
- Sodium resocin 1.5G NG stat

Differential Investigations
<table>
<thead>
<tr>
<th>Investigations</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>U&amp;E, CRP</td>
<td>Na 116, K&gt;10, U13, Cr 53, CRP 5</td>
</tr>
<tr>
<td>FBC</td>
<td>Hb 20.7 WBC 15.3 PLT 369</td>
</tr>
<tr>
<td>Cortisol</td>
<td>793nmol/L</td>
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<tr>
<td>Insulin</td>
<td>16.7ml U/L</td>
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<tr>
<td>ACTH</td>
<td>10ng/L</td>
</tr>
<tr>
<td>17 OHP</td>
<td>4.7mmol/L</td>
</tr>
<tr>
<td>Urine electrolytes</td>
<td>Na 165, K 8</td>
</tr>
<tr>
<td>Trans tubular K gradient</td>
<td>0.6 ↓ ↓</td>
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Pseudohypoaldosteronism

Generalised PHA 1

<table>
<thead>
<tr>
<th>Generalised PHA 1</th>
<th>Renal PHA 1</th>
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<tbody>
<tr>
<td>Genes</td>
<td>SNCN, SNCN, SNCN</td>
</tr>
<tr>
<td>Encoding</td>
<td>ENaC (important for regulatory action, colon, salivary glands, sweat ducts)</td>
</tr>
<tr>
<td>Inheritance</td>
<td>AB, sporadic</td>
</tr>
</tbody>
</table>
| Clinical characteristics | Severe hyperkalaemia, hypotension, 
Resistant to digoxin, digitalis, 
Renal failure, hypothermia, 
Skeletal muscle weakness, hypokalaemia |
| Treatment | IV water and electrolytes |
| Prognosis | Life-long, improves by early childhood |

Epithelial sodium channel, ENaC
- Constitutively open channel
- Number of active channels at the apical cell surface of distal nephron have a profound affect on Na absorption, amount Na excreted in urine
"Also expressed in":
- Lung: maintains composition of airway surface liquid
- Exocrine glands: ionic composition of secretions
- Colon: mediates Na absorption from intestine

Clinical progress
Our case is now 17 months old and well, with no further acute episodes of salt wasting to date.
Na, K normal on medication:
- Sodium Chloride 12.3 mmols/kg/day
- Sodium bicarbonate 3.3 mmols/kg/day
- Low K diet: 0.6mmols/kg/day

Growth:
- weight 91% height 25% & 50% height
- 2 LRTIs, 1 hospital admission
- Café au Lait macules
- Aldosterone 18,000pmol/L, Renin 148.5pmol/ml

References
1. Schild L: The epithelial sodium channel and the control of sodium balance, Biochimica et Biophysica Acta Volume 1802, Issue 12, 2010, 1159 – 1169
6. Edelheit O, Hanukoglu I, Shriki Y, Tfilin M, Dascal N, Gillis D, Hanukoglu A. A novel mutation in SCN1A was found, this is the first case in Northern Ireland
7. Hanukoglu A, Edelheit O, Shriki Y, Gizewska M, Dascal N, Hanukoglu I. Multiple Target Organ Disease (loss ROMK), 8. Edelheit O, Hanukoglu I, Shriki Y, Tfilin M, Dascal N, Gillis D, Hanukoglu A. A novel mutation in SCN1A was found, this is the first case in Northern Ireland