Nephrogenic syndrome of inappropriate antidiuresis (NSIAD) managed with fluid restriction and salt supplementation

Lisa A Amato[1,2], Charles F Verge[1,2], Jan L Walker[1,2] Kristen A Neville[1,2]

[1]Endocrinology, Sydney Children's Hospital, Randwick, Australia; [2]School of Women's and Children's Health, UNSW, Randwick, Australia

BACKGROUND

NSIAD is a rare genetic cause of hyponatremia, due to activating mutations in the AVPR2 gene, encoding the Arginine Vasopressin Receptor Type 2, and located on Xq28[1]. Of the fewer than 30 reported cases, most have been managed with fluid restriction and urea[2,3].

OBJECTIVE:

Illustration of the presentation of a family with NSIAD and approach to management.

METHODS:

The clinical, biochemical and genetic findings of the case are presented.

CASE HISTORY:

- 14 month old boy presented with hyponatraemic seizures, following increased water intake the previous day
- Previously healthy and developmentally normal
- Initial investigations consistent with inappropriate antidiuresis (serum Na 114 mmol/L, serum K 3.7 mmol/L, urine sodium 51 mmol/L and urine osmolality 301 mmol/kg)
- Vasopressin level associated with hyponatraemia (Na 127mmol/l) was low (1.7pmol/l)
- Thyroid and adrenal function and imaging of the head, chest and abdomen were normal
- No evidence of intracerebral, respiratory or renal infection
- Water restriction was ineffective until salt supplementation was given as extra salt sprinkled on food

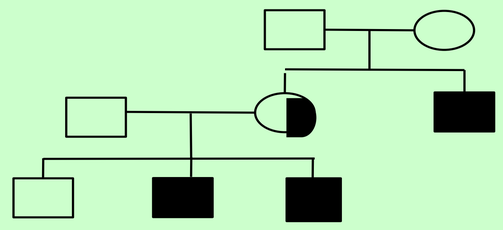
	D1 6am VBG	9pm	D2 9am	6pm	D3 9am	D4 11am	4pm	D5 1am	10am	D6 9am	D7 9am	D8 9am
Na (mmol/L)	126	127	126	131	127	118	121	127	129	135	131	137
K (mmol/L)	4	5.6	5.3	5.5	5	4.5	5.4	5.4	5.2	4.8	5.5	5.8
Ur (mmol/L)		4.6	2.6	3.3	3.1	5.1	7.1	7.7	6.1	4.6	4.2	5
Cr (umol/L)		23	23	19	17	15	29	51	22	21	22	17
Osmolality (mmol/kg)		257	257		258	252	258			278		
Urine Na (mmol/L)			104		210	117			83	107	107	
Urine Osmolality (mmol/kg)			462		791	801			813	864	933	
IV NaCl (0.9%)												
Fluid restriction												
Oral sodium												

Table 1. Biochemistry and management over the first 8 days

- Over the following four months sodium levels remained stable when allowed to drink to thirst and with extra salt sprinkled on food (Na 137-138 mmol/L)
- Sequencing of the AVPR2 gene found that the child was hemizygous for a c.409C>T missense mutation which results in amino acid substitution p.Arg137Cys, previously described as causing NSIAD

FAMILY HISTORY:

- Maternal Uncle (now 38 years old)
  - Hyponatraemic seizures as a child (serum Na 118 mmol/L, urine Na 146 mmol/L, urine osmolality 893 mmol/kg)
  - Misdiagnosed as inappropriate vasopressin secretion secondary to seizure activity
  - No genetic results to date
- 5 week old brother developed RSV bronchiolitis and right upper lobe pneumonia, requiring respiratory support, 5 months after presentation of the index case
  - Associated with hyponatraemia (serum Na 125, serum osmolality 272 mmol/kg, urine osmolality 191 mmol/kg)
  - Urea given for 24 hours whilst acutely unwell but otherwise managed with fluid restriction and oral/iv sodium supplementation
  - No genetic results to date
- Mother found to carry the same genetic mutation



DISCUSSION

- Activating mutations of AVPR2 first described in 2005[1]
  - 4 distinct mutations now identified[1,4,5]
- Phenotypic variability described, with varying severity of symptoms and age at presentation, even in families who carry the same genetic mutation[2,6,7]
  - Phenotypic variability may be explained by:
    - Skewed x inactivation in women
    - Individual variation in vasopressin levels or aquaporin expression
    - Environmental effects
- Most reported cases have been treated with fluid restriction and/or urea[2,3]
  - Fluid restriction alone may be ineffective in patients whose electrolyte free water loss is negative, and osmole replacement may be required[8]
- Prognosis is generally good and symptoms usually improve as children get older and the diet becomes less fluid based[2,3,6]
  - Developmental delay has been described in some children with recurrent seizures

CONCLUSIONS:

- This case illustrates the importance of considering NSIAD in children with hyponatraemia, with unexplained SIAD, low vasopressin levels and/or a positive family history
- Treatment is possible with water restriction but osmole replacement may also be required in some patients and this can be given as oral salt supplementation or urea
- The long term outcome is good

References:

1. Feldman et al, NEJM 2005; 352: 1884-90
2. Gupta et al, Eur J Endo 2009; 151 503-8
3. Huang et al, J Peds 2006; 148: 128-31
4. Carpentier et al, *J Am Soc Nephrol* 2012; 23: 1635-40
5. Erdelyi et al Kidney International 2015; 88: 1070-78
6. Cho et al, Int J Ped Endo 2009; 431527
7. Decaux et al J Am Soc Nephrol 2007; 18: 606-612
8. Furst et al *Am J Med Sci 2000;* 319 (4): 240-44

55ESPE 706--P2

Endocrinology and Multisystemic Diseases

Lisa Amato

DOI: 10.3252/pso.eu.55ESPE.2016

Poster presented at: ESPE 2016 PARIS