An Unusual case of Hereditary Nephrogenic Diabetes Insipidus (HNDI) affecting mother and daughter

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Introduction

HNDI is an uncommon disorder due to a resistance to Anti Diuretic Hormone (ADH) leading to a reduced urinary concentrating ability. The X-linked form is fully expressed in hemizygous male patients, but nephrogenic diabetes insipidus may also present in heterozygous females where it must be distinguished from autosomal and other secondary causes. We report a mother and daughter with symptomatic HNDI due to a heterozygous deletion in exon 1 of the AVPR2 gene which has not been previously described.

Case

A 5 year old girl was referred for investigation of polyuria and polydipsia from infancy. The patient had a water deprivation test elsewhere at age 3 that was inconclusive. A degree of water restriction was imposed which resulted in headaches. The thyroid, cortisol, renal and calcium profiles were normal. Her mother showed similar symptoms that had not been previously investigated. Hypertonic saline test was performed.

Hypertonic Saline Test

Plasma Osmolality(mosm/kg)	Plasma Sodium(mmol/l)	Urine Osmolality(mosm/kg)	Arginine Vaso - Pressin(AVP)(pmol/l)
301	146		
307	149		
313	152	212	>64.
POST DESMOPRESSIN			
316	153	243	
313	149	190	
319	153	210 (2.5 hours post DDAVP) 231 (3.5 hours post DDAVP) 153 (4.5 hours post DDAVP) 149 (6 hours post DDAVP)	

AQP2 (Aquaporin) and initial AVPR2 gene sequencing did not reveal a mutation, but subsequent quantitative PCR analysis revealed a heterozygous large exon 1 deletion of the AVPR2 gene .The same deletion was also found in the child's mother. The patient's symptoms have significantly improved on appropriate treatment. Results of skewed X inactivation studies on mother and daughter are awaited.

Conclusion

Clinical phenotype of HNDI in a symptomatic female is due to skewed X chromosome inactivation of the normal X chromosome allowing the mutant X chromosome expression in the kidneys[1,2]. Deletions in AVPR2 gene with skewed X inactivation, although very rare should be considered in symptomatic females with HNDI.

Acknowledgement

We thank Dr Sharon Whatley, Biochemical genetic service, Cardiff &Vale University Health Board, Cardiff for helping us to analyse blood samples for AVPR2 gene analysis.

References

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