Short reports

Congenital nephrogenic diabetes insipidus in a baby girl

Nephrogenic diabetes insipidus (NDI) is generally transmitted as a sex-linked recessive disorder (Bode and Crawford, 1969), but sporadic cases have been reported in both sexes (Anand *et al.*, 1972; Zimmerman and Green, 1975). Recent studies of NDI suggest a defect in the adenylate cyclase enzyme system which is believed to mediate the action of antidiuretic hormone on the renal tubule (Bell *et al.*, 1974; Monn *et al.*, 1976). This report describes a 15-month-old girl with severe NDI in the absence of a family history of the disorder.

Case history

This 15-month-old child was first seen at 6 weeks for fever and possible sepsis. She was the product of a 36-week gestation and normal delivery with a birthweight of 1.9 kg. There was no family history of diabetes insipidus or of similar symptoms. On admission she was lethargic and dehydrated with doughy skin. Urine specific gravity was 1.008 and urine osmolality 247 mmol/kg water. The serum Na concentration was 170 mmol/l, Cl 147 mmol/l, bicarbonate 13 mmol/l, K 4.3 mmol/l, blood urea nitrogen 28 mmol/l (80 mg/100 ml), serum creatinine 97 μ mol/l (1.1 mg/100 ml), and serum osmolality 379 mmol/kg water. Blood, urine, and

spinal fluid cultures were negative. She was given 0.3% sodium chloride IV but her weight decreased by 7% during the next 8 hours and her urine output averaged 20 ml/h despite the severity of dehydration. She was then considered to have diabetes insipidus. After dehydration and anaemia were corrected she was given 0.05 units aqueous vasopressin IV followed by an infusion of 0.05 units over one hour. The urine volume before, during, and after the infusion was 25-28 ml/h and urine osmolality was always less than 75 mmol/kg water. Subsequently, the IM administration of 0.5, 1.0, and 2.0 units Pitressin tannate in oil on successive days did not lead to a change in urine volume or osmolality. A voiding cystourethrogram was normal and although the excretory urogram showed poor visualisation of the kidneys because of a lack of concentration of contrast material, there was no evidence of hydronephrosis.

After informed consent had been obtained from both parents, she was admitted to the clinical research centre at 15 months. Her developmental appraisal was normal. The serum electrolytes, blood urea nitrogen, and creatinine were normal. Urinary screen for amino-acids and sugars was normal. Mild bilateral hydronephrosis, hydroureter, and a large bladder were seen on the excretory urogram. Both parents demonstrated the ability to concentrate urine to greater than 850 mmol/kg water when deprived of water for 12 hours.

Table Effects of vasopressin

15-min intervals	Urine volume ml/min	Osmolality (nmol/kg per water)		Inulin clearance ml/min per 1.73 m ²	Cyclic-AMP	
		Urine	Serum		Concentration	Excretion
					pmol/μl	nmol/min
Control period						
1	2.7	34	278	50	0.06	0.16
2	2.3	35			0.06	0.14
3	2.1	30			0.07	0.15
4	1.9	31			0.14	0.26
Mean	2.3	33			0.08	0.18
Test period (vasopressin 8 mU/kg per hour)						
5	2.5	32	268	55	0.09	0.22
6	2.5	33			0.06	0.15
7	2.0	28			0.06	0.13
8	2.8	34			0.07	0.19
Mean	2.5	32			0.07	0.17
After test						
9	2.7	34	272	60	0.08	0.21
10	2.5	35			0.07	0.17
11	2.3	31			0.15	0.35
12	1.8	36			0.14	0.27
Mean	2.4	34			0.11	0.25

Cyclic-AMP study. The results are summarised in the Table. Neither the urine volume nor osmolality changed appreciably during the study. The inulin clearance increased by 20% from 50 ml/min to 60 ml/min per 1.73 m^2 . The urinary concentration of 3', 5'-adenosine monophosphate (cyclic-AMP) averaged 0.08 pmol/ μl during the control period, 0.07 pmol/ μl during the test period, and 0.11 pmol/ μl the following hour, a 37% increase over the control value. The rate of excretion of cyclic-AMP averaged 0.18 nmol/min for the control period, 0.17 nmol/min during the test period, and 0.25 nmol/min the following hour, a 39% increase over the control value.

Discussion

While investigators have debated the pattern of inheritance of NDI, the 'Hopewell hypothesis' of Bode lends strong evidence that NDI is a sex-linked disorder (Bode and Crawford, 1969). Bode also found that most female carriers suffer a partial defect of concentrating ability with maximum specific gravity reduced to less than 1.018. The partial expression of the defect in carriers has been explained by the Lyon hypothesis of random X chromosome inactivation. This theory may help to explain the fairly large numbers of women with NDI that have been reported. It is probable that many of these were carriers. There are few well documented recent reports of women with the full expression of this disorder (Wiggelinkhuizen *et al.*, 1973; Zimmerman and Green, 1975).

NDI is generally associated with otherwise normal renal function. Although our patient has developed hydronephrosis, this is a known complication of NDI (Wiggelinkhuizen *et al.*, 1973). The hydronephrosis is thought to arise from a functional obstruction due to a large flow of urine relative to the size of the collecting system, and may be severe enough to produce renal damage necessitating urinary diversion procedures. The glomerular filtration rate (GFR) in our patient has been below normal, presumably as a result of hydronephrosis.

In recent years, the role of the adenylate cyclase enzyme system in the pathophysiology of NDI has been studied (Dousa, 1974). However, clinical studies on the urinary excretion of cyclic-AMP in response to vasopressin administration have yielded disparate results. Some groups have reported that normal subjects and patients with vasopressin sensitive diabetes insipidus increased their urinary excretion of cyclic-AMP when infused with vasopressin, while this response was not observed in patients with NDI (Bell *et al.*, 1974). Bell *et al.* (1974) reported at least a 10-fold increase in the urinary cyclic-AMP

concentration in normal subjects and patients with diabetes insipidus while no increase occurred in those with NDI. Others have been unable to verify these results (Raij *et al.*, 1974).

Monn *et al.* (1976) evaluated the response of 5 men with congenital NDI to ADH infusion. Three showed a 31–55% increase, one a 12% increase, and one patient a 9% decrease in urinary cyclic-AMP. They thought that NDI might be a heterogeneous disorder, like pseudohypoparathyroidism. Obviously, data on more patients are needed before drawing conclusions.

Zimmerman and Green (1975) reported a sporadic case of severe NDI in a young girl in whom the urinary cyclic-AMP excretion increased by 89% in response to vasopressin. They have proposed two types of NDI. Type I is the classical sex-linked disorder without urinary cyclic-AMP response to vasopressin. In type II NDI urinary cyclic-AMP does increase, suggesting that the defect is distal to the formation of cyclic-AMP. They also suggested that the inheritance of type II is not in accordance with the sex-linked recessive mode.

In our patient there was a 39% increase in the rate of cyclic-AMP excretion after the vasopressin infusion. Because of the increased GFR, it is possible that the increased cyclic-AMP excretion was derived in part from the plasma and not from the kidney itself. It is not clear why the GFR increased during the study, but it may indicate that her renal function improved as a result of relief of the functional urinary obstruction by the indwelling bladder catheter.

We do not know whether our patient's hydronephrosis might have affected the cyclic-AMP response to vasopressin. Monn *et al.* (1976) reported decreased urinary cyclic-AMP excretion in patients with structural renal disorders. It is possible that increased intraluminal tubular pressure may alter the response of the adenylate cyclase system of the renal tubule to vasopressin.

In light of the conflicting clinical studies, it appears premature to classify NDI on the basis of urinary cyclic-AMP response to vasopressin until further studies yield consistent results.

Summary

A 6-week-old girl with fever, hypernatraemia, dehydration, and polyuria failed to concentrate urine in response to exogenous vasopressin administration. There was no family history of nephrogenic diabetes insipidus. When she was 15 months old, the infusion of vasopressin did not produce an increase in urinary cyclic-AMP.

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Heart failure apparently due to overfeeding in a neonate

Congestive cardiac failure in the newborn period is usually due to congenital heart disease, endocardial fibroelastosis, storage diseases, and occasionally, to infections. Heart failure also occurs iatrogenically due to fluid overload during intravenous therapy. We report what we believe to be the first recorded case of heart failure in infancy due to overfeeding by the mother.

Case report

The baby, a girl, was born by normal delivery at 38 weeks' gestation after an uncomplicated pregnancy to a healthy 25-year-old woman and was her first

child. Birthweight was 2670 g which was between the 10th and 25th centiles for gestational age. There were no problems and she was breast fed, being discharged home on the 5th day weighing 2620 g. The mother took the baby to her local infant welfare clinic and was told by the doctor that as the baby was small she should be fed as much as possible. The mother then supplemented breast feeding by giving the baby 200 ml/kg per day of a mixture of two-thirds cows' milk and one-third water and, during the next 2 weeks, the baby gained some 500 g (Fig. 1). As the mother felt that breast feeding was inadequate, she changed over completely to bottle feeding with feeds every 3 hours, each lasting one hour, and a total intake of some 300 ml/kg per day. By the 4th week of life the infant had risen from the region of the 10th to the 50th centile (Fig. 1) but she was by now feeding poorly, breathless, and vomiting. She was seen at hospital and immediately transferred to our newborn intensive care unit as she was in severe congestive heart failure.

Fig. 1 Centile chart for weight for the first 2 months of life.

On admission she had a generalised greyish mottled appearance with gasping respiration at a rate of 120/min. There were diffuse crepitations over the lungs, pitting oedema of the extremities, and the liver was enlarged 5 cm below the costal margin. The heart sounds and pulses were normal and blood pressure was 70/40 mmHg in both arms and legs.

Chest x-ray showed cardiomegaly and probable pulmonary oedema (Fig. 2a) but the ECG was