Obstructive sodium-losing nephropathy – a case report and review

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Summary

The third case in the literature of sodium-losing renal disease due to obstruction is presented. The experimental evidence and limited clinical experience is reviewed which suggests that the sodium loss is due to an inappropriate response in the adaptive processes that are initiated by the loss of functioning nephrons. The immediate treatment is by replacement of sodium but in the long term the condition may be reversed by very cautious reduction in sodium intake. Definitive treatment may be indicated where obstruction is the cause and consequently this should be sought in all cases of salt-losing renal disease.

Introduction

In chronic renal failure the ability of the kidney to regulate sodium balance is usually well preserved, but some patients when depleted of sodium are less able than normal to reduce their urinary sodium output to compensate appropriately (Coleman *et al.*, 1966). In rare cases the sodium depletion becomes clinically obvious as reported by Thorn, Koepf and Clinton (1944) and they coined the term 'salt-losing nephritis'. It was Peters *et al.* (1929), however, who first identified a group of uraemic patients with an excessive urinary chloride and for whom a daily addition of 7-10 g of sodium chloride to the diet was recommended. Since 1944, some 50 cases of salt-losing nephropathy have been reported (Joiner and Thorne, 1952; Enticknap, 1952; Levere and Wesson, 1956; Cove-Smith and Knapp, 1973; Popovtzer *et al.*, 1973) and it is now obvious that many renal conditions can cause it. Only 2 cases have been reported where urinary obstruction was thought to be a contributory cause (Morgan *et al.*, 1978) and in one of these (Patient 1) the obstruction was only putative. A further example of a sodium-losing state in a patient with a single obstructed kidney is now described.

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Case report

A 62-year-old housewife presented as an emergency giving a 4-week history of bruising, nose bleeds, vomiting after meals, and with pain in the chest and arms related to exercise. She had also noticed palpitations, breathlessness, and a tendency to faint. There was no history of dysuria, nocturia or haematuria.

Her past history included a left nephrectomy for nephrolithiasis and haematuria following her second pregnancy at the age of 26 years. At 37 years she had a right salpingo-oophorectomy for cystic endometriosis and a papilloma with features of mucin-secreting adenocarcinoma was removed from the bladder. Annual cystoscopy over 22 years revealed one papillomatous recurrence (treated by diathermy) and at the age of 42 years her BP was found to be 250/150 mmHg and accompanied by proteinuria and a plasma urea of 8.5 mmol/l. The following year she had a hemicolectomy for a polypoid colonic adenocarcinoma which involved local nodes, and treatment for hypertension included reserpine, methyldopa, propranolol and diuretics. Over the next 7 years the plasma urea rose to 13 mmol/l although her BP was adequately controlled. She was then lost to regular follow-up.

On admission she was nauseated, pyrexial and anaemic with patches of purpura and bruising. She was not in heart failure and her BP on methyldopa 250 mg thrice/day and bendrofluazide 5 mg daily was 175/85 mmHg lying and 140/65 mmHg standing.

Biochemical findings included: a plasma urea 20 mmol/l; creatinine 924 μ mol/l; bicarbonate 19 mmol/l; sodium 137 and potassium 3.7 mmol/l; and the creatinine clearance was 8 ml/min. The Hb was 6.7 g/dl, ESR 68 mm/hr, and a platelet count was 86 $\times 10^9$ /l. At a time when urine flow was still maintained, intravenous urography showed a solitary obstructed right kidney. During antegrade pyelography 250 ml

of urine was removed and ureteric occlusion demonstrated at the level of S_{1-2} . Cytoscopy revealed a poorly-differentiated mixed transitional and squamous cell tumour infiltrating all layers of the bladder wall and occluding the right ureteric orifice. As judged by palpation, local structures were also involved. Over the next 11 days the plasma sodium fell further from 126 to 115 mmol/l and her weight from 63.8 to 61.7 kg yet urinary sodium output never fell below 80 mmol/24 hr. Over the same period she became clinically dehydrated with loss of tissue turgor, cool extremities and symptomatic postural hypotension despite discontinuation of hypotensive therapy. After decompression of the kidney and free drainage for 3 days, clinical deterioration and hyperkalaemia (6.9 mEq/l) prompted peritoneal dialysis, following which *in situ* ureterostomy was performed. Five weeks later her creatinine clearance was 7 ml/min. and ureteropyelography suggested con-

tinuing obstruction at the pelvi-ureteric junction although urine flow was maintained. Sodium supplements (Fig. 1) and additional methyldopa 250 mg twice/day were given as required and a course of radiotherapy (5900 rad) was commenced once the bladder diagnosis was established. She was eventually discharged home on sodium supplements, drinking 3 litres of water daily and charting her own fluid balance. On discharge her plasma urea was 9.1 mmol/l, creatinine 472 μ mol/l, sodium 136 mEq/l, potassium 4 mEq/l, bicarbonate 23 mEq/l and Hb 7.6 g/dl. Thirteen weeks later she died of peritonitis following perforation of a sigmoid diverticulum. A post-mortem was not obtained.

Discussion

Salt-losing renal disease was evident in that this patient could not reduce her urinary sodium output

FIG. 1. The effect of sodium supplementation on plasma concentration and urinary sodium output in a patient with a single obstructed kidney.

significantly below 80 mmol/l despite being clinically dehydrated and having a plasma sodium below 120 mmol/l whilst on an oral intake of about 25 mmol/day. Investigations confirmed renal failure due to ureteric obstruction. The normal plasma sodium on admission implied adequate intake until the onset of vomiting which was attributed to deteriorating renal function. As in other examples the patient remained well until the onset of negative sodium balance which is frequently associated with anaemia, nausea, vomiting and a tendency to faint (Polak, 1971). Unlike most other cases, there was a long previous history of renal disease including a total nephrectomy.

Immediately on admission there were no signs of dehydration but they appeared as the plasma sodium fell. In other cases (Morgan *et al.*, 1978) loss of skin elasticity was not described. However, both these patients and the present one showed signs of diminished plasma volume but not pigmentation as reported by others (Walker *et al.*, 1965). Nephrocalcinosis and hypertension were considered possible causes of her sodium depletion but plasma and urinary calcium were normal, no calcification was seen on abdominal X-ray, regular anti-hypertensive treatment had been prescribed during out-patient follow-up, she was not hypertensive on admission and had no signs of hypertensive disease; in particular, chest radiology and fundoscopy were normal although electrocardiography suggested left ventricular strain. The hyponatraemia was not due to either inappropriate ADH secretion (she was clinically dehydrated with postural hypotension) or post-obstructive natriuresis (marked negative sodium balance was present before ureterostomy).

Up to 180 mmol daily of oral sodium supplements, both chloride and bicarbonate, were required to avoid symptoms of sodium depletion. These doses can cause hypertension and oedema (Levere and Wesson, 1956; Morgan *et al.*, 1978) and, at times, they became a limiting factor in this case. Normal subjects have no difficulty in increasing sodium excretion to match intake but in this condition there is a lowered ceiling, as well as a raised floor, to urinary excretion and the natural history of the condition appears to be in inevitable and progressive reduction of the living space in between (Thorn *et al.*, 1944).

Mechanisms to explain sodium-losing renal disease are not known. It has been reported in glomerulonephritis (Thorn *et al.*, 1944; Sawyer and Solez, 1949; Murphy, Settimi and Kozokoff, 1953), pyelonephritis (Joiner and Thorne, 1952; Enticknap, 1952; Nussbaum, Bernhard and Mattia, 1952), polycystic kidney disease (Borst, 1949), nephrocalcinosis, analgesic nephropathy (Cove-Smith and Knapp, 1973) and renal tract obstruction (Morgan *et al.*, 1978). Although this is apparently a non-

specific pathological change, it seems to occur more commonly in tubular than in glomerular disorders (Kleeman, Okun and Heller, 1966).

In chronic renal failure, sodium excretion by each nephron can progressively increase and preserve sodium balance even in severe cases (Danovitch, Bourgoignie and Bricker, 1977). In certain and unpredictable instances, this adaptation appears to become excessive and not rapidly reversible so that an excess of sodium can be lost daily (Thorn *et al.*, 1944). When this is not matched by increased intake, reduction of extracellular fluid volume and of glomerular filtration occurs, which further worsens the renal failure. A recent study of 5 patients with chronic renal failure (including one with polycystic renal disease losing up to 340 mmol sodium/day) showed that careful stepwise reduction in sodium intake over 3-4 months can lead to decreases in sodium excretion and therefore sodium requirements (Danovitch *et al.*, 1977). The salt-losing tendency seems to be a consequence of an adaptive but reversible increase of sodium excretion as filtration falls, and not necessarily of irreversible anatomical change.

The site within the kidney where critical changes may occur is also not known. The distal tubule is implicated since hydronephrosis naturally in patients can lead to diminished acidification of urine, concentrating power and ammonia excretion (Bertram, 1961) and experimentally in dogs can increase urinary sodium concentration and total sodium excretion (Suki *et al.*, 1966). There is a presumed loss of functioning renal tissue, and an increase in filtration with diminished fractional sodium reabsorption in the proximal tubule, the reason for which is not known. In dogs (Olsen, 1976) decreased sodium reabsorption has been shown to be proportional to the degree of renal pelvic dilatation. Medullary damage itself, more marked in chronic hydronephrosis than in other forms of renal disease, might contribute to increased distal tubular flow by causing a reduction in overall medullary osmolarity. In non-obstructive salt-losing renal disease the evidence for a tubular lesion is partly based on the frequency of acidosis and hyperkalaemia and defects in the acidification of urine (Petersen, 1956). Incidentally aldosterone production is usually increased and rises further during salt depletion (Walker *et al.*, 1965), which explains why corticosteroids have little effect in treating this condition.

Other suggestions (Coleman *et al.*, 1966) have included the argument that the failing kidney is unable to generate a normal sodium concentration gradient between distal tubular fluid and the plasma and that the sodium concentration in the fluid cannot fall below a certain value depending on urine flow. During the osmotic diuresis of chronic renal failure, total

sodium excretion might be expected to rise and lead to depletion. However, patients with sodium-wasting renal disease have not yet been shown to have specifically higher urine flow rates or to be filtering especially increased osmotic loads. The changes seen during careful sodium restriction (Danovitch *et al.*, 1977) were not accompanied by obvious alteration of these parameters.

In conclusion, evidence to date suggests that the condition is related to defects of tubular function that are probably independent of permanent anatomical damage. Adaptive processes in the nephron which normally help to preserve sodium balance in the presence of chronic renal failure seem to become inappropriate for immediate needs and lead to excessive sodium loss. Clinically, the difficulty lies in the recognition of salt depletion. Any dehydrated uraemic patient complaining of anorexia, nausea and vomiting must be suspected of being deficient in sodium, and supplements should be given by mouth or parenterally as necessary. With the latter route the clinical response can be more accurately and quickly assessed but precautions must be taken to guard against fluid overload. One or 2 litres of normal saline are safe and will often give rise to marked clinical improvement. Considerably more may eventually be needed. The urinary concentration or preferably the daily excretion of sodium should be monitored carefully.

The clinical presentation is similar to an Addisonian crisis, but failure of response to adrenal steroids and persisting signs of renal failure should prompt the diagnosis. In either case, sodium replacement is an integral part of the treatment and is frequently rewarded with prolonged survival.

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