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# *Medical Memoranda*

## Associated Autonomic Dysfunction and Carcinoma of the Pancreas

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Autonomic dysfunction and a disturbance in water and electrolyte balance attributable to "inappropriate" secretion of antidiuretic hormone have been reported in a patient with carcinoma of the bronchus (Ivy, 1961). In the case described here autonomic dysfunction was accompanied by excessive urinary sodium excretion and by hypovolaemia due to failure to secrete aldosterone. A carcinoma of the pancreas was present.

### Case History

The patient, a man of 68, was first seen in December 1966 with vague lower abdominal pain. His appetite was poor and he had lost weight. Examination was negative apart from a blood pressure of 220/120. Haemoglobin was 15·3 g./100 ml. and E.S.R. 33 mm. in the first hour (Westergren). Serum sodium was 136 mEq/l., potassium 4·1 mEq/l., and blood urea 27 mg./100 ml. Chest *x*-ray and barium-meal appearances were normal. A barium-enema examination showed a constriction in the descending colon, but laparotomy in January 1967 did not reveal any disease of the large intestine. Gall stones were present but the common bile duct was not dilated. Cholecystectomy was performed.

In May 1967 he was readmitted to hospital because of several episodes of giddiness and near-syncope over a period of six weeks. He was pigmented and had postural hypotension; the blood pressure fell from 170/90 to 105/65 on standing. There was no overshoot in arterial pressure after the Valsalva manoeuvre, indicating the absence of baroreceptor reflexes. He had been impotent for several years but had noted dryness of the skin for a few months only. Inability to sweat was confirmed when quinazarin powder distributed on the skin remained drv and did not change colour on exposure of the patient to artificial heat for one hour (Guttman, 1940). Full neurological examination showed nothing abnormal.

Serum sodium was 125 mEq/l., potassium 4·4 mEq/l., blood urea 44 mg./100 ml., the creatinine clearance 60 ml./min., and a 24-hour urine specimen contained 70 mEq of sodium. Osmolality measured by an osmometer (Advanced Instruments Inc., U.S.A.) was 260 mOsm. in the serum and 620 mOsm. in the urine. There was no glycosuria or amino-aciduria and the *p*H of an early morning specimen of urine was 5·6. The haematocrit was 48% and the plasma volume, measured by isotope dilution of $^{131}$I-labelled human serum albumin, was 33·8 ml./kg. (normal 41 ± 5·6 ml./kg.). The urinary 17-hydroxycorticosteroids, measured by the method of Appleby *et al.* (1955), were 8·1 mg./day at rest and rose to a maximum of 89·2 mg. after repeated intramuscular injections of 40 units of corticotrophin gel given eight-hourly for three days. Urinary aldosterone excretion, measured by the method of Thomas and Oake (1969), was 5μg./day (normal 2-13·8 μg.) on a constant daily intake of 100 mEq of sodium and only 3 μg./day after six days on 10 mEq of sodium daily (normal 14·4-40·2 μg.). The urinary sodium on this last day of salt restriction was 24·6 mEq, but it fell to 2·2 mEq when fludrocortisone acetate was given in doses of 0·2 mg. every six hours, indicating normal renal tubular function. On a daily maintenance dose of 0·1 mg. of fludrocortisone acetate the haematocrit fell from 48 to 38%, the serum sodium rose to 138 mEq/l., and the blood urea fell to 24 mg./100 ml. Blood pressure was well maintained, but a small postural change was still present, due presumably to a loss in sympathetic venous tone (Page *et al.*, 1955).

The patient then developed obstructive jaundice and further abdominal pain. A second laparotomy in June 1967 revealed a small primary growth in the pancreas with malignant deposits in the liver. The adrenal glands were intact. No attempt was made to perform a palliative bypass and he died 10 days later. Permission for necropsy was refused, but sections of a deposit in the liver showed a well-differentiated adenocarcinoma with no mucus-secreting cells, compatible with a primary carcinoma of the pancreas.

### Comment

Schwartz *et al.* (1957) first recognized that some patients with carcinoma had excessive secretion of antidiuretic hormone and that this was "inappropriate" in the presence of reduced tonicity of the plasma. The low serum sodium was attributed to haemodilution and sodium depletion, renal loss of sodium being related to overexpansion of the extracellular fluid volume and corrected by restriction of water intake.

The case we have described had evidence of sodium depletion only, due to an increase in urinary sodium excretion. The serum sodium was low but the blood volume was decreased. Postural hypotension, which is not a feature of the syndrome of "inappropriate" secretion of antidiuretic hormone, was a prominent symptom and improved on treatment with a salt-retaining steroid. It is suggested that in the present case the defect of aldosterone secretion was due to some impairment of the renin–angiotensin mechanism induced by degeneration of the sympathetic supply of the kidney. Whether the autonomic denervation was related to the carcinoma is conjectural, but postural hypotension developed abruptly in a previously hypertensive man who had a carcinoma of the pancreas.

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