Inappropriate anti-diuretic hormone (ADH) secretion in association with carcinoma of the bladder

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Summary
A case of carcinoma of the bladder complicated by the syndrome of inappropriate anti-diuretic hormone secretion is reported. Management of the syndrome is discussed.

Introduction
Ectopic production of anti-diuretic hormone (ADH; vasopressin) is a well recognized phenomenon in patients with malignant disease, and was first described with carcinoma of the bronchus (Schwartz et al., 1957). Confirmation has come from radioimmunoassay studies using tumour extracts of bronchogenic carcinoma in vitro (George, Capen and Phillips, 1972).

The syndrome has also been described in cases of carcinoma of the duodenum (Lebacq and Delaerc, 1965); pancreas (De Sousa and Jenny, 1964); adrenal cortex (Falchuk, 1973); prostate (Sacks et al., 1975); thymus (Haas, Rosey and Choubrac, 1975) and in Hodgkin’s disease (Cassileth and Trotman, 1973).

The purpose of this paper is to report a patient with squamous cell carcinoma of the bladder and inappropriate ADH secretion in whom no other cause for the syndrome was found. Treatment of the tumour, together with fluid restriction and fludrocortisone in large doses, resulted in a temporary clinical and biochemical recovery. This association appears not to have been previously reported.

Case report
A 77-year-old retired school teacher presented to the surgical clinic with a 3-month history of constipation and frequency of micturition. Apart from a partial thyroidectomy for Graves’ disease when aged 30 years, her general health had been good and she was taking no regular medication.

No abnormality was found on clinical examination; initial investigation showed a plasma sodium of 130 mmol/l (130 mEq/l), but was otherwise normal. Barium enema was also normal, but an intravenous pyelogram demonstrated a filling defect suggestive of tumour in the bladder.

She was admitted to hospital for cystoscopy, at which a large tumour mass was seen on the right lateral bladder wall. Biopsy showed a well differentiated squamous carcinoma, and treatment was started with radiotherapy.

Two days later the patient deteriorated, becoming drowsy without focal neurological signs, hypothermic and oliguric. Clinically she was not dehydrated and her blood pressure was 100/60 mmHg.

Investigations at that stage showed a haemoglobin of 10.4 g/dl; white cell count 12·1 × 10⁹/l; plasma urea 4·15 mmol/l; plasma sodium 104 mmol/l; plasma chloride 75 mmol/l; plasma potassium 4·2 mmol/l; plasma bicarbonate 22 mmol/l; plasma osmolality 219 mosmol/kg of water; urine osmolality 560 mosmol/kg of water; plasma cortisol 718 mmol/l. During the first 24 hr the total urine output was 100 ml.

A diagnosis of inappropriate ADH secretion was made and treatment was started with fluid restriction to a maximum of 1 litre daily, fludrocortisone 8 mg daily, and triiodothyronine 20 μg daily, because of the possibility of hypothyroidism as an added factor.

Over the course of 10 days her condition improved—urine output rose to 800 ml daily, plasma sodium rose to 123 mmol/l and plasma osmolality to 256 mosmol/kg of water. Fluid restriction was therefore lifted, and 1 week later the dose of fludrocortisone was reduced progressively. She continued to improve, and 3 weeks after her initial acute deterioration she was able to resume radiotherapy, which was completed with no ill effects. At that stage plasma sodium concentration was normal, but 2 weeks later fell again to 124 mmol/l requiring a further course of fludrocortisone. Fluid restriction was not reimposed.

The patient remained clinically well for a further 6 weeks, but then deteriorated with abdominal pain and signs of peritonitis. Plasma sodium fell to 122 mmol/l (on fludrocortisone 0·4 mg daily), the patient became severely oliguric and died 4 months after commencement of radiotherapy.

At post-mortem a vesico-peritoneal fistula related to the ulcerating bladder carcinoma was found. A metastasis was seen in one lumbar vertebra, but there was no evidence of spread elsewhere; in particular the pituitary gland was normal. One normal sized lobe of thyroid was identified.

Thyroid function tests subsequently available
These include known also elevated and value (normal levels of individuals).

In the absence of hypopituitarism these results are interpreted as illustrating the well recognized effect of severe chronic illness on thyroid function in euthyroid patients (Carter et al., 1974); they would not substantiate a diagnosis of primary hypothyroidism.

Urinary ADH secretion is thought to correlate well with plasma concentration. Radioimmunoassay on an initial urine sample was therefore performed by using preheated porous silica beads for extraction of the hormone (Khokhar, Ramage and Slater, 1975). This gave a value of 341 pg/ml, markedly elevated and undoubtedly inappropriate for the levels of plasma and urine osmolality at that stage (normal value up to 156 pg/ml in normally hydrated individuals).

Discussion

Though inappropriate ADH secretion is perhaps best known in the context of malignant disease, it is also known to occur in other clinical situations. These include recent trauma and surgery, nonmalignant pulmonary and neurological disease, hypopituitarism, hypothyroidism and acute porphyria (Bartter, 1970). The evidence in this case, however, points strongly to ectopic production of ADH by the bladder tumour. Carcinoma of the bladder has previously been reported as responsible for ectopic secretion of parathyroid hormone (Svane, 1964), and the production of another polypeptide hormone such as ADH is therefore not unexpected.

Since the syndrome of inappropriate ADH secretion was first described, fluid restriction and hypertonic saline infusion have been accepted forms of treatment. The former, however, is tedious and the latter is largely ineffective.

A more recent proposal for rapid correction of hyponatraemia has been the use of intravenous frusemide with replacement of urinary electrolyte losses (Hantman et al., 1973). For management of chronic hyponatraemia due to inappropriate ADH secretion, long term treatment with oral lithium (White and Fetner, 1975) or oral demethylchlortetracycline (De Troyez and Demanet, 1975) has been suggested. An attack on the tumour responsible remains, however, the basis of management whenever possible, and was at least partly effective in this case.

Fludrocortisone in high dosage was advocated for correction of hyponatraemia in 1963 (Ross, 1963). Its mode of action is unknown. The administration of large amounts of the potent mineralocorticoid
aldosterone is ineffective in this context (Ross, 1963). The need for high dosage is illustrated in this case during the patient's terminal illness, when 0.4 mg daily proved inadequate in preventing continued hyponatraemia.

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References


Non-African Burkitt lymphoma presenting as dysphagia

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Summary
Cases of non-African Burkitt lymphoma are rare, but the clinical manifestations of this and the African type are similar. The authors believe that this patient is the first described presenting with dysphagia without intrinsic gastrointestinal disease.

Case report
A 38-year-old Caucasian male was referred to the Department of Medical Oncology, Hackney Hospital, London, with a large retroperitoneal mass. He presented with a 1-month history of progressive dysphagia and vomiting, associated with weight-loss of 5 kg. A barium meal showed hold-up at the cardia of the stomach. Oesophagoscopy showed dilatation with debris within; no evidence of malignant disease was seen. At laparotomy, a large lobulated retroperitoneal mass was found, displacing the stomach anteriorly and laterally and compressing the cardia. A biopsy and a gastrostomy were performed and the patient transferred to the authors’ unit.

On examination he was thin, not clinically anaemic and there was no lymphadenopathy. There was mild bilateral ankle oedema. Examination of the
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