Inappropriate Antidiuretic Hormone Secretion

TWO CASES PRESENTING WITH PULMONARY TUBERCULOSIS

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SUMMARY

Two cases of pulmonary tuberculosis with an inappropriate antidiuretic hormone (ADH) secretion are presented, and the possible mechanism of the syndrome is discussed.

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The syndrome of hyponatraemia and renal salt loss was originally described in patients with pulmonary tuberculosis.[1] Similar findings have subsequently been described in a number of other patients, but the cause has never been precisely determined. These patients do not have the symptoms or signs of the hyponatraemia as do patients with Addison's disease, diarrhoea or salt-losing nephritis (asymptomatic hyponatraemia).[2] Schwartz *et al.*[3] studied two patients with anaplastic bronchus carcinoma and hyponatraemia in 1957, and they suggested that there was an inappropriate secretion of antidiuretic hormone (ADH). It is now well known that malignant cells can produce a variety of peptides, including ADH.

Possible inappropriate ADH secretion has been described in acute porphyria, myxoedema, intracerebral lesions, various forms of malignancy (including bronchus, thymus, and prostate), various pulmonary diseases, and during the use of drugs (e.g. sulphonylureas, thiazide diuretics, vincristine and polymyxin B).[4,5]

The syndrome consists of (*i*) hyponatraemia with a hypo-osmolar serum; (*ii*) hyperosmolar urine with loss of large quantities of sodium in the urine despite (*i*); (*iii*) normal renal and adrenal function; (*iv*) no dehydration, hypotension or oedema; and (*v*) correction of the hyponatraemia and urinary sodium loss by fluid restrictions.

CASE 1

A 40-year-old Black man was admitted with the symptoms of a lung infection of 2 weeks' duration. He had noticed moderate loss of weight and had had profuse night sweats. His blood pressure was 130/90 mmHg, his pulse rate 140/min and his temperature 40°C. There were the signs of a predominantly left-sided pneumonia. The rest of the clinical examination was normal. His chest X-ray film is shown in Fig. 1.

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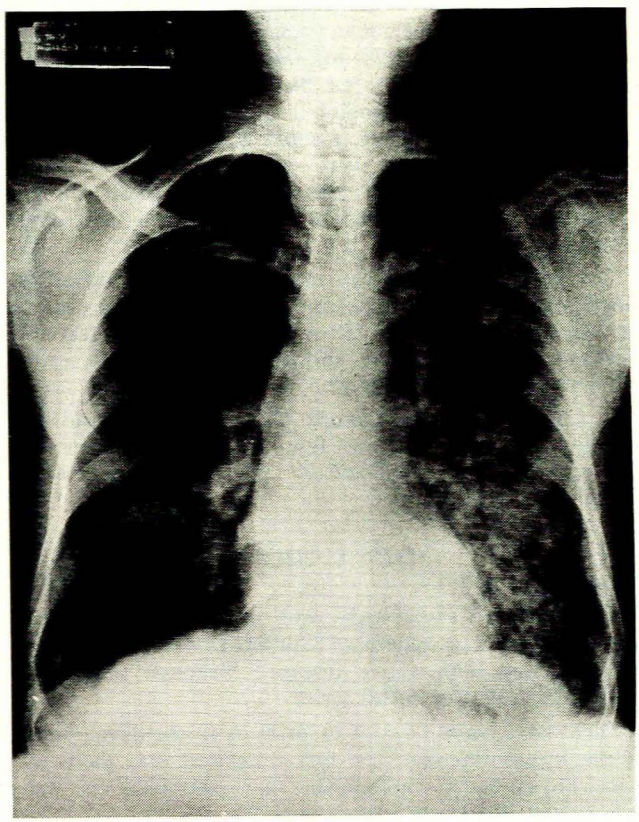

Fig. 1. Chest X-ray film of case 1, showing a diffuse left-sided pneumonic process, with possible hilar glandular enlargement.

The erythrocyte sedimentation rate was 95 mm in the first hour (Westergren) and the Tine test strongly positive. *M. tuberculosis* was repeatedly cultured from his sputum

TABLE I. BIOCHEMICAL DETERMINATION OF CASE 1 SHOWING INITIAL HYPONATRAEMIA

Date	13.11	15.11	20.11
Serum Na^+ (mEq/L)	127	133	139
Serum K^+ (mEq/L)	3,7	4,7	4,5
Blood urea (mg/100 ml)	28	26	28
Serum osmolality (m-osmole/kg)	262	270	280
Urine osmolality (m-osmole/kg)	675	515	306
Plasma cortisol (μg/100 ml)	25		
Creatinine clearance (ml/min)	70		
Urine Na^+ (mEq/L)	17		10

and stomach juices. The essentials of his initial and follow-up biochemical tests are presented in Table I.

There was no initial response to broad-spectrum antibiotics, but the patient improved dramatically on antituberculosis therapy (streptomycin, para-aminosalicylic acid (PAS) and isoniazid (INH), and the chest X-ray film showed a marked improvement after 10 days.

CASE 2

A 35-year-old Black man was admitted because of haemoptysis of 1 month's duration. He had coughed up a great amount of bright red blood during the few days before admission (haemoglobin 5,5 g/100 ml), and loss of weight had been severe. He was acutely sick, dyspnoeic and very feverish, but there was no oedema or dehydration, and his blood pressure was 110/80 mmHg. There were clinical and radiological signs of a right upper lobe consolidation.

The serum Na^+ was 126 mEq/litre, K^+ 3,9 mEq/litre, blood urea 28 mg/100 ml, serum osmolality 264 m-osmole/kg and urine osmolality 755 m-osmole/kg. The creatinine clearance was 80 ml/min, and plasma cortisol 41 µg/100 ml. Urinary sodium excretion was 5,0 mEq/litre.

In spite of intensive therapy his condition deteriorated rapidly, and he died a few days after admission. Tuberculosis was histologically proved at postmortem examination.

DISCUSSION

Hyponatraemia associated with tuberculosis is more common than it is generally realised. It may be found in 10% of cases with active disease.[6] Negroids were more affected than Whites in this series.

There have been 3 major theories as to the development of the hyponatraemia. The first suggested that there was some physiological mechanism that combined the lung and kidney in sodium metabolism.[1]

Simms *et al.*[2] thought that there was a lowered intracellular osmolality because of the chronic disease, and that the osmoreceptors had adjusted to this condition. They observed that the hyponatraemia was usually not markedly changed by intravenous administration of sodium. There was a very rapid natriuresis.

In 1957 Schwartz *et al.*[3] postulated the inappropriate ADH secretion theory after extensive balance studies on 2 patients with bronchus carcinoma. The secretion is inappropriate because the continued ADH secretion is not appropriate to the hyponatraemic plasma that would normally inhibit ADH secretion. The presence of a hyperosmolar urine, with a hypo-osmolar serum, can best be explained by the action of ADH, on condition that the glomerular function is normal.[7] There is thus an osmoregulatory imbalance with inefficient inhibition of ADH by a hypotonic state.

It is now known that tubercular tissue may contain ADH or a similar biologically active peptide.[8] However, there are still two possibilities, firstly, that the peptides may be synthesised in the tubercular tissue, or secondly, that they may be secreted by the posterior hypophysis and adsorbed by the lung tissue. There may be metabolic changes in the cells of tubercular tissue that enable them to synthesise ADH or absorb it from the circulation. The hyponatraemia improves when antituberculosis therapy is begun,[6,7] as happened in case 1.

We may now postulate that in the presence of normal kidney and adrenal function, the hyponatraemia of pulmonary tuberculosis is due to an inappropriate ADH secretion.

REFERENCES

1. Winkler, A. W. and Crankshaw, O. F. (1938): J. Clin. Invest., **17**, 1.
2. Simms, E. A. H., Welt, L. G., Orloff, J. and Needham, J. W. (1950): *Ibid.*, **29**, 1545.
3. Schwartz, W. B., Bennett, W., Curelop, S. and Bartter, F. C. (1957): Amer. J. Med., **23**, 529.
4. Rapoport, S., West, C. D. and Brodsky, W. A. (1951): J. Lab. Clin. Med., **37**, 550.
5. Taclob, L. T. and Needle, M. A. (1973): Med. Clin. N. Amer., **57**, 1425.
6. Chung, D-K, and Hubbard, W. W. (1968): Amer. Rev. Resp. Dis., **99**, 595.
7. Goldberg, M. (1963): Amer. J. Med., **35**, 293.
8. Vorherr, H., Massry, S. G., Fallet, R., Kaplan, L. and Kleeman, C. R. (1970): Ann. Intern. Med., **72**, 383.