Inappropriate secretion of antidiuretic hormone in Guillain-Barré syndrome

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Summary

Hyponatraemia occurred in five cases with severe Guillain-Barré syndrome who required assisted respiration.

In one, the syndrome of inappropriate secretion of ADH was demonstrated and probably accounted for the hyponatraemia in the other four. The water overload thus produced may have contributed to the neurological deterioration and the peripheral and pulmonary oedema seen in some of these cases.

Introduction

Although the syndrome of inappropriate secretion of antidiuretic hormone (ADH) has been described in acute polyradiculitis of the Guillain-Barré type, this association appears to be rare; seven cases only have been recorded in the literature (Fourman & Leeson, 1958; Poyart & Pocard, 1964; Cooper, Green & Wang, 1965; Posner *et al.*, 1967). The object of this communication is to report and discuss the findings in five cases with this syndrome.

Case report

Case 1. A 63-year-old housewife was admitted to hospital with an 11-day history of an illness beginning with influenza-like symptoms followed later by paraesthesiae and weakness of all limbs. Examination revealed a flaccid quadriplegia and an impairment of all modalities of sensation in a stocking-glove distribution. Two days later, lung function tests fell (vital capacity from 3 to 1.6 l) and she developed bilateral facial nerve palsy, dysphagia and severe respiratory paralysis necessitating tracheostomy. Intermittent positive pressure ventilation (IPPV) was instituted using an East-Radcliffe ventilator with a hot water humidifier in circuit. Fluids were given via a nasogastric tube and intravenous infusion. Blood pressure ranged from 200/140 to 80/30 mmHg and skin turgor was normal.

Investigations and results

Cerebrospinal fluid protein: 65 mg/100 ml, no cells seen. Urinary porphyrins absent. Urinary 17-hydroxycorticosteroids: 16.3 mg/day. Creatinine clearance: 114 ml/min. Blood urea: 34 mg/100 ml. Results of the balance study performed over a period of 12 days are shown in Fig. 1. Sodium concentrations were measured by flame photometry and osmolalities with a Fiske Osmometer. Despite an intake of 100-200 mEq of sodium, plasma sodium concentration showed a progressive fall on a fluid intake of 3-4 l/day, urinary excretion of sodium continued and there was a positive fluid balance except on Days 2 and 7. Also, plasma osmolality fell but urinary osmolality remained higher than that of the plasma. When fluid intake was restricted to approximately 850 ml/day (Day 8), plasma sodium concentration and osmolality rose despite the marked reduction in sodium intake. A negative fluid balance resulted and urinary excretion of sodium diminished. X-ray of chest revealed pulmonary oedema on Day 6 when the partial pressure of oxygen was only 84 mmHg but this cleared when the pressure rose to 108 mmHg on Day 11. The minute volume and oxygen supplement were the same on these two occasions.

Clinically, the paralysis progressed, the patient became apathetic and developed peripheral oedema during the period of positive water balance. Restriction of fluid intake was associated with neurological recovery and weaning off the ventilator was achieved on Day 14.

Retrospective survey of four other cases

Hyponatraemia (plasma sodium concentration 130 mEq/l or less) in all four cases developed with deterioration in the neurological condition. Each developed respiratory failure and dysphagia necessitating tracheostomy and IPPV. Nutrition was maintained via the nasogastric route and on occasions parenterally. One patient's clinical course was complicated by a subarachnoid haemorrhage. Urinary 17-hydroxycorticosteroid and creatinine clearance estimations ruled out the presence of Addison's

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FIG. 1. Case 1. Changes in plasma sodium, plasma and urine osmolalities and urinary sodium and fluid output in relationship to fluid and sodium intake. *Urinary sodium excretion not measured; solid columns, balance of fluid allowing for 500 ml insensible loss. ● — ●, Plasma sodium.

disease and impaired renal function respectively. In all cases the specific gravity of urine did not fall below 1.010 during the period of hyponatraemia, and peripheral oedema was recorded. Pulmonary oedema occurred in three of four patients. All cases made a good recovery and none received steroids.

Discussion

The syndrome of inappropriate secretion of ADH may be diagnosed if the following criteria are satisfied (Bartter & Schwartz, 1967):

- (1) Hyponatraemia with continued renal excretion of sodium.
- (2) Urine osmolality greater than that appropriate for the tonicity of the plasma except during an acute isotonic expansion of the extracellular fluid volume.
- (3) Normal renal and adrenal function.
- (4) Absence of clinical evidence of fluid volume depletion.
- (5) Fluid restriction leads to a rise in plasma sodium concentration and diminished urinary sodium excretion.

Case 1 satisfied these criteria. There was, however, not a good correlation between fluid balance and the degree of fall and rise in plasma sodium concentration, particularly when plasma sodium was less than 115 mEq/l. Bartter & Schwartz (1967) encountered similar findings and proposed an osmotic 'inactivation' of intracellular solute to account for this. A retrospective survey of four other patients with hyponatraemia revealed that the specific gravity of their urine did not fall below 1.010 (330 mOsm/kg H₂O approximately) when their plasma sodium was less than 130 mEq/l (<260 mOsm/kg H₂O approximately) indicating the inappropriate presence of ADH.

Inappropriate secretion of ADH may be provoked by surgery or anaesthesia (Wynn & Rob, 1954) and by subarachnoid haemorrhage (Joynt, Afifi & Harbison, 1965) but not by IPPV (Baratz, Philbin & Patterson, 1970). In the present series the hyponatraemia developed with and was related to the activity of the polyradiculitis and this has been noted previously (Fourman & Leeson, 1958; Poyart & Pocidalo, 1964; Cooper *et al.*, 1965). Case 1 had a plasma sodium concentration of 127 mEq/l before tracheostomy but the possible potentiating effect of subarachnoid haemorrhage in one of the other cases could not be excluded. The site of the lesion responsible for the inappropriate release of ADH is not known. Posner *et al.* (1967) considered either a central lesion in the limbic-supraoptic-hypophyseal system, or a peripheral one affecting the glossopharyngeal and vagus nerves which convey impulses from stretch receptors in the left atrium, carotid sinus and aortic arch known to influence ADH secretion. The peripheral lesion was favoured because of lack of histological confirmation of hypothalamic pathology (Haymaker & Kernohan, 1949). In the present series vagus nerve involvement was a feature common to all cases as evidenced by dysphagia and loss of palatal reflex.

The progressive fall in sodium concentration due to retention of fluid in Case 1 was accompanied by

mental apathy and an increase in paralysis which improved on restricting fluid. A vicious circle seems to develop in acute polyradiculitis. When the paralysis is most severe, disturbance of salt and water balance is most marked and an excess intake of water causes further neurological deterioration and may perpetuate the paralysis. The occurrence of pulmonary oedema in Guillain-Barré syndrome has not been commented on previously except at necropsy (Haymaker & Kernohan, 1949) and in one case by Sladen, Laver & Pontoppidan (1968) which they attributed to IPPV. However, inappropriate secretion of ADH has not been shown to occur as a result of IPPV (Baratz *et al.*, 1970). Pulmonary oedema was witnessed in four of the five cases reported here. It is suggested that inappropriate secretion of ADH with its resultant fluid overload probably contributed to the development of pulmonary oedema in these cases. This would also explain the peripheral oedema seen in all the five cases and in others previously reported (Spalding & Crampton Smith, 1963; Bendixen *et al.*, 1965; Poyart & Pocidallo, 1964) although circulatory stasis due to immobility and sympathetic paralysis may have played a part.

Hyponatraemia in association with acute polyradiculitis has been commented on by other investigators (Schaltenbrand & Steger, 1951; Hewer *et al.*, 1968); inappropriate secretion of ADH may thus complicate this disease more frequently than is realized. Posner *et al.* (1967) considered that water overload contributed to the death of two patients in their series. Patients with acute polyradiculitis should, therefore, have their plasma-sodium concentrations carefully monitored, and the significance of hyponatraemia appreciated. It is easy to give too much water to patients fed via a nasogastric tube or intravenously. In the Guillain-Barré syndrome a 'normal' intake of water may prove fatal.

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