Inappropriate secretion of Anti-Diuretic Hormone in chronic obstructive airways disease with chest infection and respiratory failure

Dr. S.G. Dhanwant A.M. M.B.B.S. F.R.A.C.P.

Dr. J. Tjia A.M. M.B.B.S. F.R.C.P.E. D.T.C.D. Senior Consultant Chest Physician and Head, Unit III

Dr. S.C. Poh M.B.B.S., Medical Officer

Tan Tock Seng Hospital, Singapore.

INTRODUCTION

The syndrome of inappropriate secretion of anti-diuretic hormone (SIADH) has been described due to neoplasia. neurological disorders, drugs, endocrine and pulmonary diseases. Sometimes the aetiology is unknown and the condition is labelled as idiopathic.

This syndrome first recognised in bronchogenic carcinoma (Schwartz et al 1957, Schwartz et al 1960) has now been observed in a variety of chest illnesses. Hyponatraemia in far advanced pulmonary tuberculosis is not uncommon (Chung and Hubbard 1969, Bryant 1972). There is evidence that in some of these cases it is due to inappropriate secretion of ADH (Weiss and Katz 1965, Vorherr et al 1970). It has also been reported in staphyloccal pueumonia (Stormont and Waterhouse 1962), cavitating aspergilloma (Otz et al 1959) and other pulmonary infections (Bryant 1972, Rosenow et al 1972, Spanos and Spry 1974). Except in two cases, one reported by Rosenow et al (1972) and the other by Spanos and Spry (1974) where ADH estimations were done, the diagnosis in most of these cases is based on the clinical picture. In fact the hyponatraemic state in the two cases reported by Otz et al (1959) appears to be due to the iodide therapy rather than the cavitating aspergilloma.

We describe one case of chronic obstructive airways disease with chest infection and respiratory failure in which the syndrome of inappropriate secretion of ADH developed.

CASE REPORT

A 70 year old male Chinese was admitted with a history of two days of severe dysnoea associated with a cough productive of purulent sputum. He first developed exertional dysnoea when he was 50 years old. This gradually became worse and was occasionally associated with chest infection which responded satisfactorily to treatment. At the age of 61 he developed (L) hemiparesis from which he recovered partially. He had smoked 50 cigarettes a day since the age of 18. In 1971 when he was 67 he was admitted and diagnosed as having chronic obstructive airways disease, chest infection and respiratory failure. The relevant biochemical findings then were: blood gases: pH 7.26. pCO_2 59 mm. Hg, $Hb0_2$ saturation 94% (on 0_2 via ventimask), Serum electorlytes: K 4.6 mEq/L, Na. 128 mEq/L, CI. 92 mEq/L and blood urea 42 mgm%. He was given broncho-dilators, antibiotics, steroids and 0_2 via ventimask. He made good progress and on discharge was taught how to administer the 0_2 via the ventimask at home. He stayed reasonably well till the present admission in October 1974 when he was found to be febrile, dysnoeic, cyanosed and clubbed. There was no ankle oedema or signs of dehydration. The B.P. was 170/110 and the pulse rate 84/minute with occasional extrasystole. In the chest the air entry was poor with bilateral rhonichi and creps. There was minimal (L) hemiparesis. Investigations showed Hb. 17 gm%, total white

14,000/c.mm with 98% polymorphs. Direct sputum smearfor a.f b. (x3): –ve. Urine microscopy: nad. X-ray chest showed emphesematous lungs and the E.C.G. showed a 'p' pulmonale with atrial ectopics.

He was managed with ampicillin, cephaloradine, ventolin, aminophylline, bisolvon prednisolone and 24% 0_2 via ventimask. His condition improved and remained static till about the 10th hospital day when he again became dysnoeic, cyanosed and had rhonchi and creps in both the lungs. He developed tremors of the hands and weakness of all the four limbs. The upper limbs were mildly rigid. The jerks were equal and the planter response was down going. Gradually he lapsed into Coma II.

(The clinical progress, blood gases, serum electrolytes and other relevant studies are shown in figure I.).

Despite adequate ventilation his neurological condition remained unchanged. In view of the hyponatraemia the diagnosis of inappropriate secretion of ADH was considered and the relevant investigations were done. Meanwhile he was put on oral NaCl without any improvement. Because of his chronic obstructive airways disease he was put on only very minimal fluid restriction. Gradually his hyponatraemia and the neurological state began to improve. He became conscious and could speak a few words clearly and rationally. The tremors and rigidity disappeared and apart from the minimal (L) hemiparesis the power in the limbs improved. But as the neurological state improved his respiratory condition deteriorated. His sputum became thick and yellowish and the dysnoea worsened. At this stage the family decided to take him home.

FIG. I

DATE	CLINICAL PROGRESS	THERAPY	BLOOD GASES				SERUM ELECTROLYTES (mEq/L)			OTHER INVESTIGATIONS
			pH	HCO_3	pCO_2	$Hb.0_2$%	K	Na.	Cl.	
11.10.74			7.44	26.7	41	90	3.8	130	80	Blood urea 34 mgm%; Hb. 17 gm %.
21.10.74	DYSNOEIC. CYANOSED. TREMORS. WEAKNESS. RIGIDITY		7.37	29	62	87.5	4.8	114	72	Blood urea 26 mgm%.
	COMA I – II.		7.38	30	57	93				
22.10.74	C.N.S. : NO CHANGE	ORAL NaCl	7.37	27.8	52	93	4.2	111	70	
24.10.74	C.N.S. : NO CHANGE		7.33	24.5	51	95	4.2	110	65	Blood urea 27 mgm %.
26.10.74	C.N.S. : NO CHANGE	FLUID RESTRICT	7.38	30.9	65	91.5				
28.10.74	C.N.S. : NO SIGNIFICANT CHANGE		7.4	32.3	57	91	3.8	114	74	Urine electrolytes: K 10; Na. 21; Cl. 24. Plasma osmolality: 254 mOsm/L. Urine osmolality: 305 " /L. S.G. of urine: 1.018
30.10.74	CONSCOIUS. NO TREMOR OR RIGIDITY. ABLE TO COMPREHEND AND SPEAK FEW WORDS. OLD (L) HEMIPARESES.		7.4	31	63	94	4.0	124	73	
1.11.74	C.N.S : STABLE MORE DYSNOEIC FEBRILE WITH THICK, YELLOW SPUTUM		7.37	34	74	93	4.2	122	85	Hb: 12.4 gm%.
3.11.74	C.N.S. : STABLE FURTHER DETERIORATION OF RESPIRATORY STATE		7.38	28	61	–	43	134	75	Blood urea 52 mgm %.

NORMAL VALUES IN OUR LABORATORY

BLOOD GASES :

pH: 7.40
HCO_3 : 24mM/L
pCO_2: 40mmHg
HbO_2 97%

Serum Electrolytes : (mEq/L)
K : 3.4–4.8;
Na: 137 149;
Cl : 95 106;

Urine electrolytes : (mEq/day)
K : 4–42
Na : 10–220
Cl : 200

Plasma osmolality : 280–290 mOsm/L.

DISCUSSION

The cardinal features of this syndrome are 1) hyponatraemia with corresponding hypoosmalality of the serum and extracellular fluid 2) continued renal excretion of Na 3) absence of clinical evidence of fluid depletion, that is normal skin turgur and B.P. 4) osmolality of the urine greater than that appropriate for the concomitant tonicity of the plasma 5) normal renal and adrenal function (Bartter and Schwartz 1967, Bryant 1972). A low blood urea in the presence of hyponatraemia in an adult strongly suggests the diagnosis of SIADH (Bartter and Schwartz 1967). An undisputable diagnosis can be made upon finding high plasma levels of ADH and the detection of ADH in the urine when the plasma osmolality is below 283 mOsm/Kg. (Miller and Moses 1972).

We were unable to measure ADH levels but our patient had most of the features listed above to meet the diagnosis of inappropriate secretion of ADH. Other causes of hyponatraemia were considered and excluded. Clinically there was no evidence of Addison's disease. He was non-oedematous and there was no evidence of renal, cardiac or hepatic disorder. The skin turger, B.P. and urea was normal thus excluding volume depletion. He had not received any diuretics. Drugs have been known to cause the SIADH (Moses & Miller 1974). But none of the drugs that our patient was on have as yet been implicated in the production of this syndrome.

The clinical features are due to water intoxication and depend upon the severity of the hyponatraemia. The patient is usually asymptomatic when the serum Na is above 120 mEq/L Anorexia, nausea, vomiting and apathy is common when the Na. level is between 110–120 mEq/L. Neurological symptoms and signs such as irritability, confusion, personality changes drowsiness weakness, loss of reflexes, bulbar and pseudo-bulbar palsy, convulsions and coma develop when the Na. levels fall below 110 mEq/L (Bartter and Schwartz 1967, Bryant 1972). Our patient developed tremors of the hands, weakness and rigidity of the upper limbs, confusion, stupor and finally lapsed into coma when the Na. levels were about 111 mEq/L. Hypoxia and CO_2 retention could have been partly responsible for some of the neurological signs but it is unlikely, since appropriate correction of the blood gases did not alter the neurological state where as fluid restriction resulted in fairly rapid improvement of the hyponatraemia and the clinical picture.

Our patient had respiratory and neurological abnormalities to begin with and any of these could have been responsible for the inappropriate secretion. His mild stroke was of 9 years duration and on the present admission there was no clinical evidence of progression of the stroke. So it is unlikely to be the causative factor. Similarly chronic obstructive airways disease is unlikely to be responsible since over the years that he had had this no symptoms or signs of inappropriate secretion of ADH had developed. Whether chest infection or respiratory failure or a combination of both was responsible is hard to say.

The mechanism and the site of ADH productive is in nuclear.

The management of these patients is to treat the underlying abnormality and correct the hyponatraemia. Sometimes spontaneous resolution of the primary disorder or effective treatment of the infection will be followed by the disappearance of the SIADH (Bartter and Schwartz 1967, Bryant 1972, Spanos and Spry 1974). Ordinarily fluid restriction will result in improvement in practically all the cases (Bartter and Schwartz 1967). In patients with obstructive airways disease fluid restriction can be dangerous (Bryant 1972) since this can lead to the formation of thick, tenacious sputum with resultant further deterioration of the respiratory state as probably happened in the case of our patient even though the fluid restriction was very minimal. Hypertonic saline solution may be used on a short term basis when there are severe signs of water intoxication (Bartter and Schwartz 1967). Oral salt is ineffective. Large doses of Na. retaining steroids will usually induce a positive balance of Na. but they perse do not represent a treatment of SIADH because they do not affect the underlying problem of over-hydration and because of the potentially harmful complications of the prolonged use of these agents (Bartter and Schwartz 1967).

SUMMARY

A case of inappropriate secretion of antidiuretic hormone in chronic obstructive airways disease with chest infection and respiratory failure is described. The syndrome of inappropriate secretion of antidiuretic hormone (SIADH) in pulmonary diseases is briefly reviewed.

ACKNOWLEDGEMENT

We wish to thank Dr. J. Supramaniam, M.S., Tan Tock Seng Hospital for allowing us to publish this case.

REFERENCES

1. Bartter F.C. and Schwartz, W.B. (1967). The syndrome of antidiuretic hormone. Am. J. Med., 42 790–806.
2. Bryant, D.H. (1972). The syndrome of inappropriate secretion of antidiuretic hormone in infectious pulmonary disease. Med. J. Aust., 1: 1285–1288.
3. Chung, E. and Hubbard, W.W. (1969). Hyponatraema in untreated active pulmonary tuberculosis. Am. Rev. Resp. Dis., 99: 595.
4. Miller M. and Moses, A.M. (1972). Annals, Int. Med., 77: 715.
5. Moses, A.M. and Miller, M. (1974). Drug–induced dilutional hyponatraemia. New Engl. J. Med., 291: 1234–1239.
6. Utz, J.P., German, J.J., Louria, D.B., et al (1959). Pulmonary Aspergillosis with cavitation: iodide therapy associated with an unusual electrolyte disturbance. New Engl. J. Med., 260: 264–268.
7. Rosenow, E.C., Segar, W.E. and Zehr, J.E. (1972). Inappropriate antidiuretic hormone secretion in pneumonia. Mayo Clinic Proceedings, 47: 169.
8. Schwartz, W.B., Bennet, W., Curelop, S. and Bartter, F.C. (1957). A syndrome of renal sodium loss and hyponatramia probably resulting from inappropriate secretion of antidiuretic hormone. Am. J. Med., 23: 529.
9. Schwartz, W.B., Tassel, D. and Bartter F.C. (1960). Further observations on hyponatraemia renal sodium loss probably resulting from inappropriate secretion of antidiuretic hormone. New Engl. J. Med., 262: 743.
10. Spanos, A. and Spry C.J. (1974). Inappropriate secretion of antidiuretic hormone with chronic chest infection. B.M.J., 3: 785–786.
11. Stormont, J.M. and Waterhouse, C. (1962). Severe hyponatraemia associated with pneumonia. Metabolism, 11: 1181–1185.
12. Weiss, H. & Katz, S. (1965). Hyponatraemia resulting from apparently inappropriate secretion of antidiuretic hormone in patients with pulmonary tuberculosis. Am. Rev. Resp. Dis., 92: 609.
13. Vorherr, H., Massey, F.C., Fallet, R. et al (1970) Antidiuretic principle in tuberculous lung tissue of a patient with pulmonary tuberculosis and hyponatraemia. Annals Int. Med., 72. 383.