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THE SYNDROME OF INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION

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Summary. Two cases of inappropriate antidiuretic hormone secretion are described occurring in previously fit patients undergoing fairly major maxillofacial surgery. In one case the diagnosis was confirmed by direct measurement of plasma antidiuretic hormone.

The syndrome of inappropriate antidiuretic hormone secretion (S.I.A.D.H.) is a not uncommon syndrome which is most often due to carcinoma of the bronchus where the tumour itself secretes a peptide hormone with antidiuretic activity (Detroyer & Demanet, 1976). There are a wide variety of other causes which include cerebral trauma, anaesthesia, drugs and there have been two reports recently of S.I.A.D.H. associated with severe maxillofacial trauma, and another following maxillofacial surgery (Crowley & Venuto, 1980; Davis & Matukas, 1976; Cunningham *et al.*, 1976). We have seen two patients admitted for elective maxillofacial surgery in whom S.I.A.D.H. developed postoperatively, and in one of the cases this was confirmed by plasma antidiuretic hormone assay.

Case Reports

Case 1

An eight-year-old Caucasian girl presented with a history of restricted jaw opening that followed, according to her mother, an 'abscess' on the right side of her face at nineteen months of age. Her gape was 3 mm between the upper and lower central incisor teeth; her dental health was good. It had also been noticed that she had developed a facial asymmetry in the lower third of the face with deviation of the chin point towards the right side. Radiographs confirmed an ankylosis of the right temporomandibular joint. She was otherwise well with no relevant medical history; her weight was 22.1 Kg.

The child was premedicated with oral trimeprazine (44 mg) ninety minutes prior to induction. A sleep dose of sodium thiopentone (110 mg) was administered followed by nitrous oxide (67 per cent) and oxygen (33 per cent) and halothane (up to four per cent). She was intubated by blind nasal intubation (5.0 Porte cuffed tube). No muscle relaxants were employed. Anaesthesia was maintained using a similar nitrous oxide/oxygen mixture (Servo 900 B ventilator with a minute volume of 3.5 litres) and analgesia was supplemented with a fentanyl infusion. The fentanyl infusion consists of 2 mg fentanyl in 500 ml 5 per cent Dextrose and was given at a rate of 80 ml/hr throughout the operation (0.24 mic/Kg/min.).

The right condyle of the mandible was excised via a submandibular approach and a costo-chondral graft taken from the right seventh rib was inlaid to the lateral aspect

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of the right ascending ramus. The immediate opening obtained between the upper and lower incisor teeth was 15 mm.

Postoperatively the child was electively ventilated and intravenous fluid input was maintained at a total of 65 ml/hr providing 27 mmol/24 hr of sodium (Francis *et al.*, 1974). This fluid input consisted of a fentanyl infusion (2 mg in 500 ml 5 per cent Dextrose) given at a variable rate of 30 to 60 ml/hr as per analgesic requirements. In addition normal saline was added to make the total of 65 ml/hr. Twenty-four hours postoperatively, clinical examination revealed a level of consciousness varying between Grades II and IV on the Glasgow Coma Scale (Teasdale & Jennett, 1974) with bilateral extensor plantar responses. All other systems at this time were normal. Blood pressure and pulse were normal and there was no clinical evidence for dehydration with normal tissue turgor. There was neither peripheral oedema nor papilloedema. There was, however, marked hyponatraemia with an inappropriately high urinary osmolality compared to plasma osmolality and a random urinary sodium concentration of 90 mmol/l (table). On the basis of these findings a clinical diagnosis of S.I.A.D.H. was made. In view of the severity of the central nervous system signs, aggressive therapy was instituted including the use of intravenous mannitol and dexamethasone together with fluid restriction to 500 ml/24 hr.

A lumbar puncture performed twelve hours after starting treatment was normal. By the fourth postoperative day the child was fully orientated, her clinical and biochemical states were normal and ventilation was discontinued. She was discharged from hospital seven days postoperatively and has remained well. The initial operative opening of 15 mm has been maintained and increased to 17 mm between the upper and lower incisor teeth at six months post operation.

Plasma antidiuretic hormone (A.D.H.) concentration taken on the second postoperative day was 19.2 pg/ml (reference values 1 to 2.5 pg/ml) supporting the diagnosis of S.I.A.D.H.

Table
Biochemical findings in the two cases described

Investigation	Case	Postoperative time									
		12 hr	24 hr	36 hr	48 hr	60 hr	72 hr	84 hr	96 hr	108 hr	120 hr
Plasma Na+	I	119	120	—	118	124	134	135	135	—	—
Reference Range 134–143 mmol/l	II	139	—	125	115	114	110	112	126	127	133
Plasma K+	I	3.8	3.8	—	3.6	3.8	3.5	3.7	3.8	—	—
Reference Range 3.2–4.4 mmol/l	II	3.7	—	3.6	3.7	3.6	4.0	4.1	3.6	3.8	4.1
Plasma Urea	I	2.6	—	—	2.3	3.6	6.7	8.2	6.8	—	—
Reference Range 2.4–6.8 mmol/l	II	3.5	—	2.6	2.4	—	4.1	—	3.2	—	6.5
Plasma Osmolality	I	—	—	—	—	240	274	—	—	—	—
Reference Range 280–305 m0sm/kg	II	—	—	—	—	—	214	—	259	—	—
Urine Osmolality	I	—	—	—	—	538	948	—	—	—	—
m0sm/kg	II	—	—	—	—	—	411	—	193	—	—

Case 2

A 39-year-old Caucasian female (weight 58 Kg) presented with a skeletal Class III facial deformity which required treatment by sagittal split mandibular osteotomy and reduction genioplasty. These procedures were performed using a general anaesthetic technique essentially similar to the first case. Postoperatively the patient was ventilated electively and fluid input was maintained at a total of 125 ml/hr providing 60 mmol/24 hr sodium, using a regime similar to Case 1. Thirty-six hours postoperatively the patient became a little confused although her level of consciousness did not alter further. All other systems were normal; there was no evidence of dehydration and her blood pressure and pulse rate were normal. The hyponatraemia present did not respond to normal saline infusion, her serum sodium continued to fall and a diagnosis of S.I.A.D.H. was made (see Table). Treatment was instituted with mannitol and fluid restriction. Her confusion settled within twenty-four hours and within three days her serum and urinary biochemistry returned to normal; subsequent postoperative recovery was uneventful. The mandible was immobilised for a period of eight weeks and her subsequent progress has been uneventful.

Discussion

Bartter and Schwartz (1967) originally laid down the criteria for the diagnosis of S.I.A.D.H.: hyponatraemia with low plasma osmolality, inappropriately high urine osmolality with persistence of sodium in the urine and no evidence for dehydration, in the absence of renal or adrenal disease. Although adrenal function was not formally tested there was no evidence for this in either of the patients presented here. Both patients had the characteristics required for the diagnosis of S.I.A.D.H. and in one case the diagnosis was confirmed by radioimmunoassay for plasma A.D.H.

A very large number of causes for S.I.A.D.H. have been described (Kleeman & Vorherr, 1974). Possible causes in the two patients presented include anaesthesia, postoperative pain and intermittent positive pressure ventilation. Although it is not possible to exclude definitely these factors, either singly or in combination, as causes for S.I.A.D.H. in these patients, the influence of maxillofacial surgery must be considered. More than two hundred patients have been treated in the Intensive Care Unit of this hospital during the past year receiving similar perioperative management with reference to the type of anaesthesia, fluid balance and analgesic regimes and none have developed signs of S.I.A.D.H. By contrast two of our patients receiving major elective maxillofacial surgery during the last six months have developed clinical S.I.A.D.H. as described here.

Recently three patients have been described who developed S.I.A.D.H. following facial trauma or maxillofacial surgery (Cunningham *et al.*, 1976; Davis & Matukas, 1976; Crowley & Venuto, 1980). In the two patients in whom facial trauma was associated with S.I.A.D.H. there was also the possibility of cerebral injury, in one, clinical evidence for cerebral trauma was present in the form of concussion with unconsciousness (Davis & Matukas, 1976). She developed the syndrome spontaneously on the sixth day after the injury and before anaesthesia. In the other (Crowley & Venuto, 1980) cerebral trauma cannot be excluded by virtue of the occurrence of facial trauma in a road traffic accident. In this patient the syndrome developed after a meperidine and barbiturate general anaesthetic quite different from the technique in our cases. However, in both of these cases the over-riding clinical presentation was of facial injury. In the third patient (Cunningham *et al.*, 1976) as in the present cases, cerebral damage can be excluded since the S.I.A.D.H. followed relatively minor

elective maxillofacial surgery (mandibular vestibuloplasty); the anaesthetic agents used were nitrous oxide and a proprietary mixture of fentanyl and droperiodol (Innovar).

Known causes of S.I.A.D.H. involve one of four mechanisms: ectopic release of A.D.H., stimulus to pituitary release of A.D.H. by direct cerebral insults, drug induced release of pituitary A.D.H. and renal sensitization to the effects of A.D.H. None of these mechanisms apparently can explain the presence of S.I.A.D.H. following operative procedures involving the maxillofacial region. There is, however, a well defined tract from the trigeminal nerve to the midline nuclei in the floor of the third ventricle (the nucleus ventralis posterior medialis), the trigeminothalamic tract (Everett, 1965). It is possible that the intense stimulation of the trigeminal nerve occurring as a result of maxillofacial surgery may be sufficient via this tract and further intrahypothalamic relay neurones to stimulate release of A.D.H. through the paraventriculo-hypophyseal tract with subsequent development of S.I.A.D.H. Stimulation through humoral factors transported in the fluid of the third ventricle may also be possible (Collu, 1977).

It appears that maxillofacial surgery or trauma should be added to the list of cases of S.I.A.D.H.

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