SHORT REPORTS

Hyponatraemia as a cause of reversible ataxia

Apart from ataxia induced by drugs or alcohol, reversible causes of cerebellar dysfunction are rare. We report on two patients with inappropriate antidiuretic hormone secretion as a result of bronchial carcinoma who presented with severe cerebellar ataxia that was fully reversible on correction of their serum sodium concentrations.

Case reports

CASE 1

A 64 year old man was admitted with a history of five weeks of unsteadiness and two days of slurred speech. His medical history was unremarkable. He had not been receiving any drugs, smoked five cigarettes a day, and rarely drank alcohol.

Neurological examination showed slight signs of confusion, which had not been noticed by his relatives. He had an obvious dysarthria and a noticeably ataxic gait and could not walk unaided. He had a bilateral intention tremor, and heel to shin coordination was poor. Fundi and cranial nerves were normal, and there was no nystagmus. Reflexes, strength, and sensation were also normal. Serum sodium concentrations were: 109 mmol(mEq)/l, potassium 4·2 mmol(mEq)/l, and urea 5·4 mmol(mEq)/l (32 mg/100 ml). Corrected serum calcium concentration was 2·16 mmol/l (8·6 mg/100 ml). Serum osmolality was 229 mmol(mosmol)/kg, and urinary osmolality was 628 mmol/kg. An x ray film of his chest showed left hilar lymphadenopathy. Bronchoscopy showed a tumour, which histological examination identified as a small cell carcinoma. The results of computed tomography of the skull, examination of cerebrospinal fluid, and an electroencephalogram were all normal. Thyroid function was normal, and results of treponemal serology were negative.

His fluid intake was restricted to 800 ml/day, and he received demeclocycline 600 mg/day. His serum sodium concentration rose over the next few days to 136 mmol/l, his cerebellar signs improved, and after one week there was no neurological deficit. He remained asymptomatic for three months but then deteriorated rapidly and died. An autopsy was not performed.

CASE 2

A 68 year old woman was admitted with a two week history of unsteadiness associated with a recent cough and anorexia. Medical history was unremarkable, and she was taking no drugs. She smoked 20 cigarettes a day and did not drink alcohol.

Examination showed poor heel to shin coordination and inability to walk unaided. There was some disorientation but no overt confusion. All reflexes were normal, and she showed no weakness or sensory loss. Fundi and cranial nerves were normal, and there was no nystagmus. Serum sodium concentration was 108 mmol/l, potassium 3·8 mmol/l and urea 4·7 mmol/l (27·2 mg/100 ml). Serum osmolality was 234 mmol/kg and urinary osmolality 702 mmol/kg. Corrected serum calcium concentration was 2·32 mmol/l (9·2 mg/100 ml). Radiography of the chest showed a mass in the right mid-zone with hilar lymphadenopathy. Cytology of sputum showed malignant cells of small cell type. A computed tomography scan of her skull and an electroencephalogram were normal. Thyroid function was normal and results of treponemal serology negative.

Her fluid intake was restricted to 700-800 ml/day, and her serum sodium concentration rose to 129 mmol/l with resolution of her ataxia. She remained well for six weeks but then developed pneumonia and died. Autopsy was not performed.

Comment

Hyponatraemia is associated with confusion and, at serum sodium concentrations of less than 120 mmol/l, with epilepsy and coma.[1,2] An almost pure cerebellar syndrome is not, however, a recognised feature. Ataxia coexisting with hyponatraemia has been reported in patients with carbamazepine toxicity and porphyria,[3,4] but in our patients ataxia was probably caused by the effect of the metabolic disorder on the central nervous system.

A subacute cerebellar degeneration is a recognised non-metastatic effect of bronchial carcinoma but is progressive and rarely reversible, even when the primary tumour is treated.[5] This therefore cannot explain the ataxia in these patients unless a subclinical, non-metastatic cerebellar syndrome had been greatly exacerbated by the low sodium concentrations.

We suggest that reversible cerebellar dysfunction should be recognised as a rare presenting feature of hyponatraemia in patients with inappropriate antidiuretic hormone secretion. Whether this occurs only when the syndrome is secondary to carcinoma is unknown.

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Finger clubbing in the Zollinger-Ellison syndrome

A case of the Zollinger-Ellison syndrome with clubbing of the fingers is described. So far as we know this association has not been reported before. The pathogenesis of clubbing is examined with particular reference to this case.

Case report

A 15 year old boy was referred in 1983 with a three year history of diarrhoea and episodic epigastric pain. There had been a severe bout of haematemesis and melaena three months previously. There was no relevant past medical history or family history of illness, including pachydermatoperiostosis.

Examination showed no abnormality other than clubbing of all the fingers. Facial features and skin were normal. Results of a barium meal study and endoscopy were normal apart from an ulcer in the first part of the duodenum. Radiographs of chest and hands were normal. Serum gastrin concentration was 1350 pmol/l (upper limit of normal 30 pmol/l); vasoactive intestinal peptide, pancreatic polypeptide, glucagon, and neurotensin values were not raised. Full blood count and urea and electrolyte, glucose, calcium, and phosphate concentrations were normal. Thyroid and adrenal functions were normal.

Computed tomography detected a tumour in the superior aspect of the head of the pancreas, which was confirmed by a coeliac axis angiogram. At operation a 3 cm trilobulated tumour on the superior aspect of the head of the pancreas was removed. No metastases were seen. Histologically the tumour consisted of sheets and clusters of regular polyhedral cells with a little eosinophilic cytoplasm and regular vesicular nuclei, consistent with a G cell tumour of pancreatic origin. Postoperative recovery was uneventful. Within a year of operation the finger clubbing had disappeared. Three years later the patient was well and the serum gastrin concentration had remained normal.

Comment

Many intrathoracic conditions are known to be associated with finger clubbing, including bronchial and oesophageal carcinoma, mesothelioma, bronchiectasis, lung abscesses, empyema, fibrotic lung diseases, subacute bacterial endocarditis, and cyanotic heart disease. Extrathoracic causes of clubbing include tumours of the upper gastrointestinal tract, ulcerative colitis, Crohn's disease, achalasia of the cardia, polyarteritis nodosa, α chain disease, Hodgkin's disease, and cirrhosis of the liver. The causative mechanism of this phenomenon remains uncertain.

Similar changes may be induced in dogs by the surgical production of a cardiac right to left shunt. It may be that substances capable of producing these changes are produced by various organs of the body but are normally inactivated in the pulmonary vasculature. Shunting results in their presence in the general circulation with consequent clubbing. Ferritin, a substance inactivated by the lungs, has been found in arterial blood only of patients who have clubbing[1]; this has not, however, been confirmed experimentally. A similar mechanism affecting the liver might account for the association of clubbing with liver disease.

A neurogenic explanation has also been advanced. Increased vascularity of the diseased organ may initiate a neural reflex, the afferent limb of which is vagal. This is supported by reports that clubbing may disappear after vagotomy.[2]

That the efferent limb of the "clubbing reflex" may be humoral is suggested by observations of hormonal factors being associated with clubbing. Patients with bronchial carcinoma and hypertrophic pulmonary osteoarthropathy have been reported to have raised concentrations of growth hormone.[3] Clubbing has also been described in association with a case of thyroid carcinoma and primary hyperparathyroidism.[4] Lam *et al* reported two cases (in brothers) with pachydermatoperiostosis, hypertrophic gastropathy, and complicated duodenal ulcers.[5] In these cases the serum concentrations of gastrin were normal but concentrations of pepsinogen 1 and 2 were raised.

The clubbing associated with the Zollinger-Ellison syndrome in our patient, which regressed after resection of the tumour, was probably due to some substance produced by the tumour. Gastrin itself was unlikely to be the substance, as vagotomy, which may abolish clubbing, is often associated with raised serum concentrations of gastrin. Moreover, tumours such as gastrinomas, which are from the APUD cell series, are known to secrete many peptides, only some of which have been characterised.

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Neuropsychiatric complications related to use of prazosin in patients with renal failure

Although postural hypotension and syncope are well known side effects of prazosin, neuropsychiatric complications have rarely been recorded. We report on three neuropsychiatric patients who recovered completely after the drug was withdrawn.

Case reports

Case 1—A 63 year old housewife who had been receiving continuous ambulatory peritoneal dialysis for one year for diabetic renal failure was admitted because of impaired drainage of peritoneal dialysate. She also had hypertension, diabetic retinopathy, and peripheral and autonomic neuropathy. Her blood pressure was not well controlled despite treatment with metoprolol, and prazosin was started and increased to 2 mg three times daily. Over the next four weeks she became confused and suffered from visual hallucinations and paranoid ideas. No significant biochemical changes occurred, however, and her autonomic dysfunction did not change. An electroencephalogram showed intermittent diffuse slow wave abnormality, which was consistent with metabolic encephalopathy. Prazosin was stopped, and she recovered over eight weeks.

Case 2—A 70 year old woman with a 15 year history of diabetes mellitus stabilised by glibenclamide was admitted after three weeks of intermittent drowsiness, confusion, and uninhibited behaviour such as undressing. She also had longstanding hypertension, treated initially with methyldopa, but prazosin 5 mg three times daily had been started six weeks previously for better control. Over the past year she had developed diabetic renal failure, with urea concentration 19·6 (normal 3-8) mmol/l (117·6 (18-48) mg/100 ml) and creatinine concentration 280 (50-120) μmol/l (3·17 (0·57-1·36) mg/100 ml). She was afebrile and had no focal neurological deficit. There was no evidence of hypoglycaemia or postural hypotension, and cerebrospinal fluid composition and results of other biochemical investigations were normal. Over the next few days her mental state fluctuated, and an electroencephalogram was performed, which showed diffusely abnormal trace with no focal features. We suspected that this might be related to prazosin, which was stopped over the next three days; her mental state improved dramatically. Two months after discharge her mental state and behaviour were normal, and a repeat electroencephalogram showed great improvement.

Case 3—A 40 year old man with a 20 year history of insulin dependent diabetes and hypertension was admitted because of sudden left hemiparesis. Computed tomography of his head showed a lacunar infarct in the right internal capsule. While in hospital he had two grand mal seizures, controlled with phenytoin. Prazosin 2 mg three times daily was also started because his blood pressure was not well controlled with methyldopa alone. His hemiparesis improved gradually and he returned home. He was readmitted two weeks later, however, because of psychotic behaviour. He was paranoid, with signs of organic psychosis, strong delusions of grandeur, and hallucinations. There was no biochemical evidence of hypoglycaemia or phenytoin toxicity, and an electroencephalogram showed intermittent slow waves over the right hemisphere, compatible with the vascular lesion. His renal function was mildly impaired, but it remained stable throughout his psychosis. Prazosin was stopped and the hypertension controlled with metoprolol. The psychosis was settled with a short course of chlorpromazine and trifluoperazine. Eight months after discharge and withdrawal of the major tranquilliser paranoia had not recurred.

Comment

We think that the increased abnormalities in the central nervous system in our three patients were due to prazosin, because their chronic renal failure might have affected the clearance of prazosin.

The results of pharmacokinetic studies in chronic renal failure are not yet consistent,[1 2] though the 50% increase in the free fraction of prazosin observed in patients with chronic renal failure[3] might explain the apparent association of central nervous system toxicity with renal failure. Animal studies also support the observation that prazosin could be responsible for the abnormal symptoms of the central nervous system.[4 5]

We advise the cautious use of prazosin in patients with renal failure. The Committee on Safety of Medicines and the drug manufacturer have told us about one notification of paranoia and five of hallucination since 1974.

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Epidural methadone for preoperative analgesia in patients with proximal femoral fractures

Proximal femoral fracture in elderly patients is one of the most common fractures seen in the orthopaedic department. The treatment of choice is internal fixation, and a delay in performing the operation or contraindication to surgery creates problems in the nursing of patients. The optimal time for preoperative assessment, preparation, and medical stabilisation of these patients is about 12 to 24 hours.[1] Before and after surgery such patients are prone to pain, pressure sores, pneumonia, thromboembolic phenomena, and central depression caused by systemic narcotics.

Epidural analgesia induced by opiates is an accepted method of pain relief after surgical orthopaedic intervention.[2] Epidural methadone has the same analgesic potency as morphine but fewer complications; urinary retention is rarely seen, and respiratory depression has not been reported. We evaluated prospectively the effect of continuous epidural analgesia induced by methadone in patients with fractures of the femoral neck.

Patients, methods, and results

Twelve patients (seven women and five men, age range 21-93 (mean 68·9)) sustained proximal femoral fractures and were treated surgically by hemiarthroplasty or Richard's sliding compression nail. Epidural analgesia was started soon after clinical and radiological evaluation in the emergency room. We added 4 ml of methadone hydrochloride 0·1% to 6 ml of saline and injected this through the epidural catheter. The severity of the pain was evaluated subjectively before and two hours after the injection as follows: no pain=0, mild pain=1, and severe