Letters to the Editor

Lymphoma presenting with Addison's disease

Sir,

Several large autopsy series have shown that the adrenal glands are commonly involved in carcinomatosis.¹ Metastatic cancer presenting with Addison's disease is, however, rare.² In one series, 5 of 15 patients with bilateral adrenal involvement at computerized tomography (CT) had subnormal Synacthen tests.³ In another, 4 of 21 patients with adrenal masses at CT developed Addison's disease at some point in their illness.¹ In another, 7 of 173 cases of lymphoma had adrenal masses. Of these, 3 were detected at presentation. Three were bilateral, of which 2 were detected at presentation and the third at relapse.⁴ In another, 7 of 257 cases of non-Hodgkin's lymphoma had adrenal masses, of which 3 were bilateral. In these 7 the other organs involved were: none (3); kidneys (2); gut (1); kidneys, gut and pancreas (1); and retroperitoneal nodes (6).⁵ Cases of lymphoma presenting with Addison's disease due to adrenal involvement, but without evidence of dissemination, are very rare.^{6–10} We present one such case.

A 68 year old white male presented with a 9 month history of weakness, faintness, anorexia, dysgeusia and weight loss of 20 kg. The skin was pigmented on light-exposed areas, the palmar creases were dark and the nail beds pale. The pulse was 72 beats/min and the blood pressure 145/90 mmHg with no postural drop. There were no other abnormalities to find. There was a mild normochromic, normocytic anaemia. The erythrocyte sedimentation rate was 42 mm in the first hour. Plasma sodium was 132 mmol/l, potassium 4.2 mmol/l, urea 12.3 mmol/l and creatinine 190 µmol/l. Liver function tests and calcium were normal. The chest X-ray was clear. Pre-prandial blood sugar levels were in the range 1.9 to 3.8 mmol/l. The serum cortisol at midnight was 178 nmol/l, and at 9 a.m. 190 nmol/l. A short Synacthen test using 250 µg gave these results: serum cortisol at 0 min 199 nmol/l; at 20 min 203 nmol/l; and at 60 min 217 nmol/l. CT showed a smooth mass 10 cm across in the position of the right adrenal, and a similar one 8 cm across on the left. There were no other abnormalities seen in the abdomen or chest. A percutaneous needle biopsy of the right adrenal was done under ultrasound guidance. Microscopy showed tissue infiltrated by a high grade lymphoma of centroblastic type. Immunocytochemical studies confirmed a B cell immunotype. Trephine biopsy of iliac crest revealed normal bone marrow. Serum immunoglobulins were normal.

Treatment comprised saline, steroid replacement and entry into a trial of the chemotherapy regimen CAPOMeT, in which drugs are given in pairs at weekly intervals; cyclophosphamide with adriamycin, prednisolone with vincristine, methotrexate with folinic acid rescue and etoposide. His health improved. Four months later CT showed considerable reduction in size of both adrenal masses and no other deposits. He then received radiotherapy to both adrenal beds. A further scan at 9 months showed no change in size of the adrenal masses, but multiple deposits in the lungs.

The commonest cause of primary adrenal failure and shrunken adrenals is autoimmune adrenalitis. The same

clinical picture with adrenal masses is nowadays most commonly due to carcinomatous spread. Our case emphasizes the importance of obtaining tissue from patients such as these, where no primary lesion is apparent, as occasionally a treatable lymphoma will be found.

J. Gunn
R. Cuthbert
A. Trueman
City Hospital,
Hucknall Road,
Nottingham NG5 3PB, UK.

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Herpes simplex encephalitis without CSF leucocytosis

Sir,

Herpes simplex encephalitis (HSE) must be considered in the diagnosis of any acute encephalopathy, particularly if a fever or focal signs are present. Examination of the cerebrospinal fluid (CSF) is particularly important; a lymphocytic pleocytosis is a nearly constant feature of HSE¹ and strongly supports the diagnosis. Rare instances of HSE without a CSF leucocytosis have been explained by examination of the CSF at too early a stage of the illness.² However, we have observed a case of proven HSE in which no CSF leucocytosis was observed even at an advanced stage.

A 65 year old diabetic woman presented with a 2 week history of malaise and progressive sensory disturbance of the right arm. For 5 days there had been increasing confusion, drowsiness, right-sided limb weakness and involuntary jerking of the right arm. On examination,

there was no fever; the patient was stuporose and dysphasic. Memory was severely impaired but spatial skills appeared to be preserved. There was visual inattention and a hemiparesis on the right with absent joint position sense in the right hand. There were frequent right-sided focal motor seizures.

A CT scan of the brain revealed only a small lacunar infarct in the left lentiform nucleus, an electroencephalogram showed left-sided slow waves and bilateral frontal intermittent rhythmic delta activity. The CSF contained 15 red cells/ μ l and no leucocytes, protein 0.81 g/l and glucose 14.1 mmol/l.

The patient was given intravenous acyclovir, phenytoin and insulin. After 5 days, the CSF contained 3 lymphocytes/ μ l, protein 0.46 g/l and glucose 5.6 mmol/l (blood glucose 12.5 mmol/l). High affinity antibodies to Herpes simplex virus type 1 were detected in the CSF (and not the serum) by ELISA³ and antibody heterogeneity was confirmed by agarose gel isoelectric focusing and antigen immunoblotting with immunoperoxidase staining on polyvinyl difluoride membranes.⁴ The patient made a good recovery over the next two weeks.

This case demonstrates that a raised CSF cell count may be absent in advanced HSE. Previously, one other case without a CSF pleocytosis on the first, second and eighth days of proven HSE was reported.² In our patient, both CSF specimens were taken even later after the onset of HSE.

HSE is a serious disease; without treatment, many patients die and few survivors are neurologically intact.¹ Antiviral therapy is effective in HSE⁵ but results are better with early treatment. For this reason, when HSE is suspected, empirical treatment with acyclovir is advisable without waiting for laboratory confirmation which cannot be achieved in the early stages of the illness. In this situation, we wish to emphasize that the absence of a cellular response in the CSF does not exclude HSE, even after more than two weeks from the onset.

N.A. Fletcher
M. Sharief
R.S. Kocen

National Hospital for Neurology and Neurosurgery,
Queen Square,
London WC1N 3BG, UK.

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Cerebellar ataxia due to hyponatraemia

Sir,

Hyponatraemia, a common electrolyte disorder in the medical setting, has protean causes and clinical manifestations,¹ but cerebellar symptoms and signs are extremely rare.² We describe two cases of reversible cerebellar ataxia, induced by severe hyponatraemia.

Case 1

A 35 year old male patient was admitted with progressive weakness, pallor and purpura of 3 months duration shown to be aplastic anaemia. On the 7th day of his hospital stay he developed severe watery diarrhoea and became drowsy. He had received 80 mg intravenous frusemide with blood transfusion the previous night. Examination revealed moderately severe volume depletion, slurred speech, bilateral intention tremors, past pointing, impaired knee–heel test and ataxia. Serum sodium was 96 mmol/l. Other biochemical investigations and computed tomographic scan of the head were normal. His hyponatraemia was corrected over a period of 3 days, during which his cerebellar signs rapidly diminished and disappeared over the following 2 days.

Case 2

A 15 year old boy presented with intermittent fever, anorexia and recurrent vomiting for 10 days, unsteadiness of gait and head bobbing of 2 days duration prior to the admission. He had received a 7-day course of ampicillin before admission. He was febrile, moderately dehydrated and had soft splenomegaly. Neurological evaluation revealed striking dysynergia, marked truncal ataxia, impaired coordination, broad-based ataxic gait and scanning speech. Investigations showed a positive Widal test, serum sodium 110 mmol/l, serum potassium 3.5 mmol/l and sterile blood culture. He was given intravenous ciprofloxacin and volume depletion was corrected with saline. His neurological symptoms rapidly improved within 24 h of hospitalization. He achieved complete neurological recovery within 3 days and became afebrile on the 5th day after admission.

Various authors have highlighted aphasia, hypo- and hyperreflexia, generalized rigidity, hemiparesis, focal weakness and unilateral Babinski sign in hyponatraemia reports.¹ Ataxia with hyponatraemia has been described with the use of carbamazepine,³ in acute intermittent porphyria⁴ and associated with bronchogenic carcinoma.² Indeed, a pure cerebellar syndrome has only been described in the last setting, thus re-emphasizing the rarity of this manifestation. In both the cases described in this report, gross cerebellar signs were observed, though absence of nystagmus was noteworthy. Volume depletion was the triggering mechanism of hyponatraemia, a fact not described earlier in connection with hyponatraemia and cerebellar syndrome. Although cerebellar ataxia has been noted as a rare feature of enteric fever,^{5,6} it is slowly reversible over weeks to months, if at all, making it an unlikely possibility in the second case.

Thus, in an appropriate clinical setting, it may be worth