vasodilatation, hypoalbuminaemia, and venous pooling would be expected to stimulate the baroreceptors in the left atrium and carotid sinus. This would cause a decrease in vagal and glossopharyngeal inhibitory input to the midbrain and hypothalamus resulting in release of antidiuretic hormone and enhanced sympathetic nerve activity.³ For this physiological adjustment to occur the glossopharyngeal and vagus nerves must be functionally normal. Hence vagal damage, by decreasing the inhibitor influx to the hypothalamus, might be expected to cause an excessive secretion of antidiuretic hormone.

We did not find an increased incidence of hyponatraemia in our alcoholic patients with vagal neuropathy and no ascites. This agrees with the well known rarity of hyponatraemia in cirrhosis without ascites. In patients with vagal degeneration and ascites, however, we found a clear cut increase in the frequency of hyponatraemia.

FIG 2—Serum sodium concentrations in 64 patients with alcoholic and non-alcoholic cirrhosis and ascites. Shaded area represents normal range in our hospital.

Comparison between numbers in the two groups with concentrations below 135 mmol(mEq)/l: $p=0.006$ (Fisher's exact test).

Moreover, these patients had a higher heart rate than the group with a functionally normal vagus nerve, which might reflect, for instance, hypovolaemia or a lesion of the vagus nerve.

We emphasise that biochemical parameters of liver function were similar in the two groups except for a lower blood urea concentration in the alcoholics, which was probably related to a more frequent increase in the effective vascular volume in these patients.^{7,8} Since the hyponatraemia related to the syndrome of inappropriate secretion of antidiuretic hormone was not associated with abnormal vagal function in the five patients studied, it is unlikely that hyponatraemia by itself would have affected the tests of vagal function.

If the high incidence of vagal neuropathy in alcoholic cirrhosis plays a part in the inappropriate secretion of antidiuretic hormone we should expect to find a lower frequency of hyponatraemia in non-alcoholic cirrhosis—and that was indeed the case in our retrospective study. The discrepancy in the incidence of hyponatraemia between the alcoholic and non-alcoholic patients could not be explained by more severe liver failure in the first group as the biochemical findings were similar.

Before attributing increased sympathetic activity and excessive secretion of antidiuretic hormone to a decrease in blood volume in cirrhosis³ it seems important to exclude impaired vagal function, which may contribute to hyponatraemia independently of any contraction of effective blood volume.^{9,10}

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SHORT REPORTS

Effectiveness of intravenous acyclovir in immunocompetent patient with herpes zoster encephalitis

Herpes zoster associated encephalitis is a rare complication of a common cutaneous disorder. We report on an immunocompetent patient with herpes zoster associated encephalitis who responded rapidly to treatment with intravenous acyclovir.

Case report

A 69 year old widow was admitted with a two week history of severe left sided facial pain followed a few days later by left sided vesicular skin lesions on the face and ulcers on the left side of her tongue. She was anorectic, nauseated, and in great pain. She had had chickenpox at the age of 24 while pregnant with her third child; her son had developed severe neonatal varicella. She was healthy and was admitted primarily for rehydration and pain relief.

On admission she was unwell but afebrile, alert, and fully oriented with no meningism or abnormal neurological signs. She had a typical zoster rash in the

maxillary and mandibular divisions of the left trigeminal nerve and large whitish ulcers along the left border of her tongue and soft palate. The results of initial investigations showed normal haematological indices and concentrations of electrolytes and random blood glucose, but her erythrocyte sedimentation rate was 47 mm in the first hour and her blood urea concentration was increased (10.1 mmol/l (60.7 mg/100 ml)).

On the second evening after admission she first experienced severe visual hallucinations, continuous when her eyes were shut but suppressed when they were open, with delusions of paranoia and grandeur. A few hours later she developed unsteadiness of gait and vertigo. She became feverish (temperature 38.5°C) but remained conscious, with a mental test score of 10/10 on the modified Newcastle scale. Neurological examination showed complex nystagmus, gross truncal ataxia, bilateral abducent nerve palsies, complete left lower motor neurone facial weakness, sensorineural deafness in the left ear, hypoaesthesia of all three divisions of the left trigeminal nerve, and an absent left corneal reflex.

On lumbar puncture the cerebrospinal fluid contained 120 white blood cells/ml, with 95% lymphocytes. Cerebrospinal fluid glucose concentration was low (2.1 mmol/l (37.8 mg/100 ml)) compared with a simultaneous blood glucose concentration of 5.2 mmol/l (93.6 mg/100 ml), and cerebrospinal fluid protein concentration was increased at 1.29 (normal 0.3-0.5) g/l. The zoster titre was 1/16 in the cerebrospinal fluid and 1:1024 in serum. An electroencephalogram showed moderate generalised disorganisation consistent with encephalitis while a computed tomogram was normal. The results of Mantoux and candidal skin tests and serum immunoglobulin concentrations were normal. In view of these and her

good anti-herpes zoster virus antibody response she was thought to be immunocompetent. She was treated with intravenous acyclovir 10 mg/kg every eight hours for 10 days and improved rapidly. The pain from her skin lesions was greatly relieved, and after 48 hours of treatment she no longer had delusions or hallucinations and her ataxia was improving. After one week the skin lesions and ataxia had resolved, but partial abducent, facial, and vestibulocochlear palsies persisted.

Comment

Herpes zoster associated encephalitis was diagnosed in this patient from clinical features and the typical cerebrospinal fluid and electroencephalographic findings. Six months later she remained well, with no evidence of immunosuppression. Her abducent and facial nerve palsies resolved but the deafness in her left ear remained. Serum zoster titres decreased to 1/8.

Intravenous acyclovir has been effective in the treatment of severe cutaneous zoster in immunocompetent¹ and immunocompromised² adults. It has also proved effective in treating herpes simplex encephalitis.³ There has not to our knowledge been a study of the use of acyclovir in herpes zoster associated encephalitis. Six patients with disseminated malignancy or other profound immunosuppression all improved dramatically within 24 hours of starting treatment with acyclovir.^{4,5}

Our patient had no evidence of immunosuppression at diagnosis or afterwards and the dramatic clinical improvement was temporally related to the start of treatment with acyclovir.

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Resolution of diabetic cheiroarthropathy

We report on two patients with diabetic sclerosis or cheiroarthropathy in whom both skin and joint changes resolved completely. In one case this improvement seemed to be related to better diabetic control. This is the first time such improvement has been reported.

Case reports

The flexion contractures of the interphalangeal joints of the hands were assessed in the two patients by the method of Grgic *et al.*,¹ which we use routinely in evaluating such diabetic patients. The patient's hands are placed palm down on a table top with fingers spread. These fingers are then viewed by the examiner at table level and the contact of the fingers with the table determined. Normally the entire palmar surface of the fingers makes contact. Patients are classified as having stage 1 disease if they are unable to make contact with some portion of one finger and stage 2 disease if unable to make contact with two or more fingers.

Skin thickness was assessed over the fingers as outlined by Siebold²: 0=R normal; 1+ = slight but definite thickening with inability to tent the skin between the examiner's thumbs; 2+ = mild to moderate changes; 3+ = severe thickening; 4+ = extreme thickening.

Glycosylated haemoglobin concentration was estimated using electrophoresis on cellulose matrix (Glyco-Phore, Gelman Sciences Ltd) (normal range up to 8.5%).

Case 1—A 16 year old girl with an 11 year history of insulin dependent diabetes mellitus developed limited movement of all interphalangeal joints in her hands with associated tightening and thickening of overlying skin. She was classified as having stage 2 disease and skin thickness 2+. The symptoms developed after three months of poor diabetic control when she had a persistently raised blood glucose concentration and a haemoglobin A₁ concentration of 11%. With improved diabetic control the hand changes resolved completely over five weeks. She did not have any evidence of microvascular diabetic complications.

Case 2—A 58 year old man (interestingly, the father of the patient in case 1) with a 12 year history of insulin dependent diabetes mellitus developed a clinical picture similar to that of his daughter. He was classified as having stage 2 disease

and skin thickness 2+. The symptoms occurred after five months of erratic diabetic control, although the haemoglobin A₁ concentration was only 9.7%. With improved diabetic control the hand changes resolved completely over five months. He did not have any microvascular complications.

Comment

Flexion contractures of interphalangeal joints are well described in insulin dependent diabetics, various series suggesting an incidence of 20-30%.^{1,3} In some these contractures are associated with skin that is waxy or has a sclerodermatous appearance, and the terms diabetic sclerosis and diabetic cheiroarthropathy have been used to describe this.

Interest in the pathogenesis of this condition is heightened by suggestions that those who develop joint contractures are at an increased risk of developing microvascular diabetic complications.³ Joint contractures, and more recently skin thickness, in these patients have been correlated with the duration of diabetes. Workers have suggested that these clinical changes reflect abnormal non-enzymatic glycosylation of collagen, and it has been shown experimentally in rats that these changes in liver, kidney, and haemoglobin are reversible. Such reversibility was not shown to occur in collagen.⁴ This contrasts with the findings in our patients, in whom apparently typical skin and joint changes resolved completely. Resolution of joint contractures has not previously been described, although in a small study skin thickness measured by ultrasonography decreased with improved diabetic control.⁵

Any theory that is advanced to explain diabetic cheiroarthropathy must take account of the potential reversibility of these changes. Observations need to be performed on several occasions in affected patients to evaluate the clinical course more fully.

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Alveolitis and haemolytic anaemia induced by azapropazone

Increasing numbers of drugs have been identified as causing pulmonary disease.¹ Non-steroidal anti-inflammatory drugs may seriously depress haemopoiesis, and immune haemolytic anaemia has also been reported.^{2,3} We report three cases of both reversible pulmonary infiltration and haemolytic anaemia in patients who had been taking azapropazone for nine to 18 months.

Case reports

Case 1—A 60 year old woman with an 18 month history of rheumatoid arthritis was treated initially with azapropazone and indomethacin, but both drugs were stopped when a rash developed. After a short course of prednisolone azapropazone was restarted. Eight months later she was admitted to hospital with haemolytic anaemia, breathlessness, and widespread pulmonary crackles. Haemoglobin concentration was 98 g/l and reticulocyte count 22%. A direct Coombs test yielded a positive result. A chest x ray film showed bilateral pulmonary infiltrates. Azapropazone was stopped, and she recovered fully after treatment with corticosteroids. Fifteen months later azapropazone was restarted, but after three weeks she again became breathless with fresh pulmonary infiltration. She responded well to corticosteroid treatment after azapropazone was stopped, and one month later there were no abnormal clinical or radiological signs.

Case 2—A 70 year old woman presented with a three week history of breathlessness. She had received azapropazone 600 mg twice daily for nine months because of a painful osteoarthritic knee. She was breathless at rest, with