Hashimoto's thyroiditis associated with acquired idiopathic demyelinating polyradiculoneuropathy

Sir,

Simultaneous presentation of acquired idiopathic demyelinating polyradiculoneuropathy (IDP) and Hashimoto's thyroiditis suggests that IDP has an autoimmune pathogenesis.

A 51 year old man presented with a 5-week history of weakness, initially in the legs and progressing to involve the arms. No recent viral infection or immunization had occurred. Two weeks before admission he had seen his general practitioner for the leg weakness and tiredness but had no other symptoms of hypothyroidism. At that time, thyroid stimulating hormone was raised (34.8 mU/l, normal range 0.4–6.0) and free thyroxine was within normal limits (10.4 pmol/l, normal range 8.8–23). There was no family history of thyroid or neurological disease and previously he had been healthy except for mild hypertension treated with atenolol. Thyroxine 50 µg/day was commenced one week prior to hospital admission but his weakness progressed. On examination, the cranial nerves were normal. The limbs displayed symmetrical, distally predominant weakness affecting the legs more than the arms, with areflexia and flexor plantar responses. He was unable to stand unaided. Light touch and pain sensation were decreased on the anterior aspects of both thighs. Forced vital capacity was 3.3 litres. The remainder of his examination, including the thyroid gland, was unremarkable. The cerebrospinal fluid (CSF) contained 2.24 g/l protein and 4×10^6 lymphocytes/l. Electrophysiology showed absent F waves in the right and left tibial nerves, with slight delay in the right median nerve (33.2 ms), and mild slowing of motor conduction velocity of 47 m/s in the right median nerve and 35 m/s in the right medial popliteal nerve. Sensory action potentials were normal in the right sural (12 µV) and radial (30 µV) nerves. Routine haematological and biochemical parameters were normal. Autoantibodies were found against thyroglobulin (titre > 1:5120) and thyroid microsomes (strongly positive). Antibodies against parietal cells, mitochondria, smooth muscle cells, reticulin and nuclei were absent. He was treated with prednisolone 60 mg/day and after 6 days the strength of his hands improved. Three months later he became able to walk 5 m without aid and has continued to improve whilst slowly decreasing the prednisolone. Four months after the onset he had not relapsed.

The clinical and neurophysiological picture and CSF results supported the diagnosis of an acquired IDP. The initial 5-week history of progressive weakness suggested a subacute form of acquired IDP rather than Guillain-Barré syndrome.¹ The occurrence of hypothyroidism with a high titre of antibodies to thyroid tissue is pathognomonic of Hashimoto's thyroiditis.² There has been one previous report of an association between 'autoimmune' hypothyroidism and chronic IDP,³ and three reports of hypothyroidism and Guillain-Barré syndrome.^{4–6}

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Fatal rupture of a subcapsular liver haematoma in a patient treated with anisoylated plasminogen streptokinase activated complex

Sir,

Haemorrhage is the major specific adverse effect of thrombolytic therapy.¹ In a recent AIMS Study² on the long term effects of intravenous (i.v.) anistreplase in acute myocardial infarction (AMI) bleeding was usually minor and related to venepuncture sites. This was easily controlled by minor pressure and in only 10 out of 1258 randomized patients was transfusion for such episodes necessary with no observed difference between treated and placebo groups. Major haemorrhagic complications associated with significant mortality are usually intracranial or intraperitoneal.^{1,3} We report a case of massive intraperitoneal bleeding from a spontaneous rupture of a subcapsular liver haematoma as a direct cause of death.

A 77 year old man was admitted (0 hours) with an acute inferior myocardial infarction and entered into ISIS 3.⁴ He was randomized to treatment with aspirin, heparin and anisoylated plasminogen streptokinase activator complex (APSAC). His clinical course was complicated in the initial 6 h by refractory chest pain which was successfully treated with 24 h of i.v. heparin and ventricular tachycardia which was controlled with lignocaine. Clotting screen during this time was normal. After 36 h he was well and ISIS heparin was reintroduced. Aspirin was stopped after 72 h for an episode of nausea, vomiting and abdominal pain. His subsequent clinical course was uneventful, he was mobilized and preparation for discharge was made. However, 120 h after admission he suffered a cardiac arrest from which resuscitation was unsuccessful.

At autopsy there was a haemoperitoneum which was due to a rupture of one of several subcapsular liver haematomas. Death was thought to be due to primary rupture rather than resuscitation since the quantity of blood in the abdominal cavity was too large to be accounted for by the size of the haematoma. The remaining abdominal viscera were normal with no other evidence of haemorrhage.

This is the first reported case of formation and rupture of subcapsular liver haematomas resulting in death in a patient receiving APSAC and should be considered in patients with unexplained gastrointestinal symptoms, anaemia or haemodynamic changes post-thrombolysis. It has also been stated that lethal complications of thrombolysis may have been under reported¹ and therefore this case may not be as unique as it appears, again stressing the importance of the autopsy.⁵

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Advances in understanding alcohol withdrawal states

Sir,

Chronic ethanol treatment lowers levels of GABA (gamma-amino butyric acid) as well as increasing the number of GABA receptors in the brains of alcoholics.¹ GABA-mimicking agents, and those which increase GABA levels alleviate the alcohol withdrawal in animals.^{1,2} Gamma-hydroxybutyrate is both precursor and a metabolite of GABA as well as being classified as a possible GABA agonist.³ Recently, oral gamma-hydroxybutyric acid has proved therapeutic in treating the alcoholic withdrawal state in man.⁴ The proposed mode of action of the latter medication suggested by these authors was via its GABA-like action, since drugs which are clinically effective in treating alcohol withdrawal have all been found to have some direct or indirect GABA-like-effect in the nervous system.² This also applies to analgesic nitrous oxide, in that a nitrous oxide-diazepam interaction has been demonstrated, possibly with both drugs acting at the same site. This conclusion was reached because their mutual effect was reversed by flumazenil, an inverse benzodiazepine agonist. These workers also suggested that opioid activity could influence the affinity of benzodiazepine binding sites.⁴

Analgesic nitrous oxide is used clinically in alcohol withdrawal states for distinguishing those patients requiring intensive in-patient care from those that do not.⁵ Some of the factors responsible for this difference may include the degrees of liver pathology and of organic brain damage.

Patients with cirrhosis without overt hepatic insufficiency seem to tolerate morphine reasonably well,⁶ and even those with cirrhosis who have had hepatic coma do not have serious reactions following a single therapeutic dose of morphine,⁶ this despite the fact that the duration of morphine's action would be expected to be prolonged thereby causing cumulative effects.⁶ Although morphine produces marked sedation in normal subjects, this same dosage in cirrhotics only produced mild sedation.⁷ This may explain the previous findings which show the relative safety of morphine in cases of chronic liver disease.⁶ Since analgesic nitrous oxide has opioid agonist properties,⁸ it is possible that its lack of effect in the severe cases of alcohol withdrawal might be related to decreased opioid sensitivity in the central nervous system associated with chronic liver disease. This factor clearly requires further investigation.

From the point of view of organic brain damage in chronic alcoholism, ethanol can modify opioid receptors and levels of brain opioid peptides.⁹ In view of this, it is conceivable that the more intense and prolonged the alcohol abuse has been, the more likely it is that the ensuing organic brain damage would be associated with marked alterations in affinity of opioid receptors. This would possibly cause impairment of the therapeutic effect of nitrous oxide in such cases when they present in withdrawal.

This proposed mechanism explaining the failure of analgesic nitrous oxide to ameliorate the condition in some severe cases is being investigated. It is possible that a combination of chronic liver and brain pathology would both contribute substantially to the therapeutic failure with analgesic nitrous oxide found in the minority of cases of alcohol withdrawal.

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