

normal but electroencephalography revealed non-specific widespread slow-wave activity without focal features or triphasic complexes. The first CSF examination was acellular with an elevated protein of 0.93 g/l. A traumatic repeat lumbar puncture two days later, revealed 13,000 red blood cells, 280 white cells (90% polymorphs) and a protein of 2.7 g/l, the CSF/serum glucose ratio remaining normal. Bacteriological and viral cultures from a variety of sites were unhelpful and examination of paired serum and CSF revealed no rise in complement fixing antibodies to HSV1. He continued to deteriorate and developed right sided focal seizures. A further electroencephalogram 12 days after admission revealed sharp activity in the left temporal lobe while a CT scan showed a large area of low attenuation in the left frontal and temporal lobes with considerable mass effect. He was started on intravenous dexamethasone and acyclovir but died the same day.

At necropsy, the heart was unremarkable, the coronary and intracranial vessels were patent and histological examination of the sinus node, the AV node and bundle of His showed no abnormality. The brain was swollen with evidence of softening of both temporal lobes and superficial petechial haemorrhages were seen both over the inferior aspect of the temporal lobes and the diencephalon. Histological examination revealed neuronal loss, perivascular lymphocytic cuffing, necrosis and the presence of macrophages and reactive astrocytes. These changes, typical of a viral encephalitis, were most marked in the temporal lobes but were also present in the diencephalon, hypothalamus and to a lesser extent in the brainstem. Positive immunoperoxidase stains for HSV1 were obtained from both the temporal lobes and the pons, the causative agent being confirmed when the virus was isolated from the left temporal lobe.

This patient with proven herpes simplex encephalitis ultimately developed typical radiological and pathological evidence of temporal lobe involvement. The case is of interest, however, because of the unusual presentation and progression of the illness. The presence of coma with intact respiration and brain stem reflexes but small reactive pupils strongly suggests that the infection initially affected the diencephalon and mid-brain only. This may also be the explanation for the low serum sodium concentration since damage to the hypothalamus is a cause of inappropriate secretion of anti-diuretic hormone. Disturbance of cardiovascular control is a well recognised feature of diencephalic syndromes⁴ and there has been

a recent report of herpetic brainstem encephalitis with recovery⁵ in which labile hypertension, marked tachycardia, profuse sweating and mild hypothermia were attributed to diencephalic involvement. No primary cardiac cause for the arrhythmia could be demonstrated and in the absence of early temporal or brainstem involvement it seems probable that the attacks of asystole which precipitated admission were caused by herpetic encephalitis involving the diencephalon.

There is a further point of interest. The CSF cellular response to HSV1 though variable in size is predominantly lymphocytic for both supratentorial and brainstem presentations. The differential count seen in this case cannot be explained by traumatic tap and it would appear that the presence of a predominantly polymorphonuclear pleocytosis in the CSF does not exclude HSV encephalitis.

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Aseptic meningitis due to trimethoprim-sulfamethoxazole

Sir: Aseptic meningitis has been described in association with the administration of anti-inflammatory drugs, including ibuprofen,

sulindac and tolmetin, and azathioprine.¹⁻⁴ We have recently seen a case of this adverse reaction caused by trimethoprim-sulfamethoxazole.

A 46-year-old woman was admitted because of chills, fever, headache and confusion. A diagnosis of systemic lupus erythematosus was made 12 years previously. Two days before her admission a urinary tract infection was detected and she was started on trimethoprim-sulfamethoxazole therapy. Half an hour after taking the first dose she began to experience chills, dizziness, fever, headache and confusion. On examination she was confused and had mild stiff neck. Her temperature was 40°C. Spinal fluid was turbid with 1070 leucocytes/mm³ (80% polynuclear, 20% lymphocytes). Spinal fluid protein was 1.38 g/l and glucose 3.7 mmol/l. Blood and spinal fluid cultures were negative. The patient was initially treated with intravenous cefotaxime and ampicillin. On the second day a dramatic improvement occurred; her temperature was 37°C. A second lumbar puncture revealed clear spinal fluid with 150 leucocytes/mm³ (32% polynuclear, 68% lymphocytes), protein concentration was 1.28 g/l and glucose 4.4 mmol/l. An adverse reaction to trimethoprim-sulfamethoxazole was suspected and antimicrobial drugs were withdrawn. A challenge test, after obtaining fully informed consent, was performed on the fifth day of admission. Thirty minutes after a dose of trimethoprim-sulfamethoxazole (80 and 400 mg respectively) was given by mouth she developed vomiting, chills, fever, dizziness, confusion, and combativeness. Confusion and nuchal rigidity was present. Three hours after the challenge test her spinal fluid leucocyte count was 284/mm³ (98% polynuclear, 2% lymphocytes) and protein concentration of 1.18 g/l. Mannitol and dexamethasone were given by vein and 5 days later she was discharged well.

There are two previous reports of aseptic meningitis due to trimethoprim-sulfamethoxazole^{5,6} and another case caused by trimethoprim alone.⁷ In our case, as in those reported previously, the spinal fluid glucose concentration was normal. The precise mechanism of this extremely rare adverse reaction remains unclear, although an immediate hypersensitivity reaction seems the most plausible. We believe that trimethoprim-sulfamethoxazole should be considered in the differential diagnosis of aseptic meningitis.

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Severe sensorimotor neuropathy after cisplatin therapy

Sir: Cisplatin (Cis-dichlorodiammine platinum (II)) is a chemotherapeutic agent which is used in the treatment of head and neck, ovarian, bladder and testicular cancers. Its main toxic effects are renal, gastrointestinal

and hematological.¹² The most frequent neurological complication is neurosensory hearing loss.¹³ Some cases of sensory neuropathy have been published.⁴⁻⁸ However, a severe sensorimotor neuropathy, as in the case described here, is unusual.

A 48-year-old woman was operated on the 5 January 1983 for a left ovarian cystadenocarcinoma, measuring 15 × 8 cm. Chemotherapy was instituted with adriamycin (40 mg/m²), cyclophosphamide (300 mg/m²) and cisplatin (100 mg/m²). Each course was administered during 4 days, cisplatin being given on the fourth day. Six courses were given from February to September 1983, with a cumulated dose of 240 mg/m² adriamycin, 1,800 mg/m² cyclophosphamide and 600 mg/m² cisplatin. Eight days after the 5th course, the patient experienced acute pains like electric discharges in the legs. They became more severe after the 6th course and also involved the fingers. Simultaneously, the patient had paresthesiae in hand and feet. She became unable to climb stairs and was admitted in November.

Physical examination revealed a proximal and distal paresis of lower limbs with amyotrophy. Muscle strength was normal in upper limbs. The pressure on muscles elicited pain but there was no sensory disturbance. Osteotendinous reflexes were all abolished. EMG revealed signs of peripheral neuropathy, with motor unit potentials firing at rapid rates in muscles of both upper and lower limbs. Motor conduction veloci-

ties were normal except in the peroneal nerve (33 m/s). A right sural nerve biopsy was performed at the level of the ankle, but the patient refused a lumbar puncture.

The treatment was interrupted after the 6th course and there was a slowly progressive improvement of clinical signs during the following months. The patient recovered a normal muscle strength and became able to climb stairs on April 1984. Pains became less severe and totally disappeared by October 1984. A new examination on November 1984 revealed neither sensory nor motor disturbances. Deep tendon reflexes had remained abolished, but there was no amyotrophy. The patient refused a new needle EMG, but measurement of motor nerve conduction by cutaneous electrodes showed values within the normal range.

The nerve biopsy specimen was studied with morphometric, optic and electron microscope methods. On morphometric studies, there was a severe loss of myelinated (2,780/mm²; normal: 5 to 9,000/mm²) and unmyelinated (15,000/mm²; normal: 18,000 to 65,000/mm²) fibres. Size fibre histogram of myelinated fibres revealed a decrease of the largest fibres (fig. 1). On optic microscope study, many myelin ovoids were seen (fig. 2). Electron microscope study revealed severe degenerative lesions of myelin sheets and axons, with Schwann cells filled with myelin debris. Some of them were invaded by macrophages.

The toxic nature of this neuropathy may

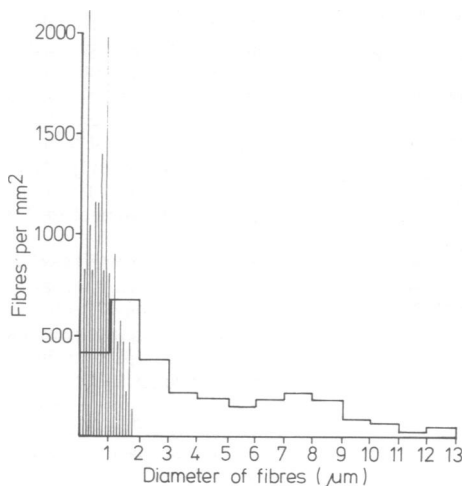


Fig. 1 Size fibre histogram of myelinated (thick line) and unmyelinated fibres (thin lines) of the sural nerve.

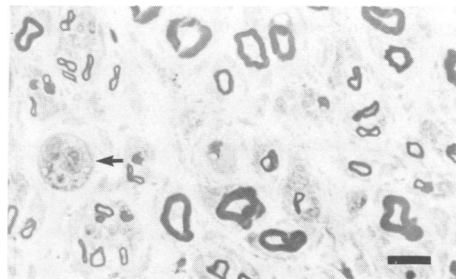


Fig. 2 Semi thin section, toluidine blue. Loss of myelinated fibres; a degenerating fibre is seen on the left (arrow). Bar = 10 µm.