Letters

Depression of essential tremor by alpha-adrenergic blockade

Sir: Evidence exists that the alpha-adrenergic blocking drug thymoxamine (Opilon Forte) depresses activation of the dynamic gamma-motoneurone activity, both in animals1 and in man.2,3 As spindle activation may be of importance in the pathophysiology of tremors,4 we have tested the effect of intravenous thymoxamine, 0.15 mg/kg body weight, versus intravenous placebo on tremor patients not responding to conventional therapy.

After informed consent nine patients were tested by mechanomyographic recording of tremor frequency and amplitude before and 2-5 min after completion of the injection. Four of the patients suffered from static tremor judged as essential tremor and five resting tremor of Parkinsonian or senile type or both. Thymoxamine did not change tremor frequency in either group, but the tremor amplitude was reduced, as a mean to 18% of the pre-injection values, in patients with essential tremor (p < 0.01). No reduction of tremor amplitude was found in patients with Parkinsonian or senile tremor or both.

Alpha-adrenergic blocking drugs may thus be an alternative choice in the treatment of essential tremor. Further, our results indicate that spindle activation through dynamic gamma-motoneurones plays a role in the pathophysiology of essential tremor.

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References

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Hepatocellular carcinoma with cranial metastasis and hyperglobulinaemia

Sir: Hepatocellular carcinoma has a well established association with alcoholic cirrhosis of liver. Bony metastases have been reported in the past with an incidence of 3-12%.1 There has been only a single case report of multiple scattered asymptomatic osteolytic cranial metastases in the past.2 We report two patients of hepatocellular carcinoma diagnosed at necropsy, the first one presented with proptosis and total ophthalmoplegia on the right side, and the second had mild right monoparesis and dysphasia at presentation; both had diffuse serum hyperglobulinaemia.

Case 1: JH aged 65 yr, was admitted in 1979 with a three weeks history of diplopia, progressive right sided proptosis and ptosis, intermittent right temporal and facial pain and loss of sensation on the right side of the face. He had consumed alcohol in excess for 15 years. Multiple spider naevi were present on the shoulders but no other clinical features of hepatic cirrhosis were present. The left lobe of the liver was palpable 3 cm below the sternal angle. It was soft, non-tender and there was no bruising. On examination he was confused, but alert; he had total right ophthalmoplegia, and a pronounced non-pulsatile right-sided proptosis with marked conjunctival chemosis, there was no orbital bruising. Fundi were normal and visual acuity was reduced to N/48 in the right eye; field testing was unreliable. He had a sensory loss in the distribution of the first and second divisions of the right trigeminal nerve. Apart from a mild sensory neuropathy in the legs, the rest of the nervous system was normal. Other systems were clinically normal. Haematological profile showed macrocytosis and evidence of disseminated intravascular coagulation. Liver functions gave evidence of cholestasis and hepatocellular dysfunction. (Alkaline phosphatase raised to 399 IU/l, elevated SGOT and SGPT and reversal of albumin globin ratio.) Immunoelectrophoresis showed increased IgG (22-15 g/l); IgA (10-05 g/l) and IgM (3-1 g/l). Serum antinuclear factor was markedly raised. Blood VDRL and TPHA were negative. Sternal marrow aspirate showed marked plasmacytosis and the marrow was infiltrated with undifferentiated malignant cells of uncertain origin. Chest radiograph showed a soft tissue shadow at the left anterior second costochondral junction without bone destruction, radiographs of the skull were normal, but those of the lumbar spine done for persistent backache showed a doubtful osteolytic lesion in the fifth lumbar vertebra. Isotope brain scan showed minimal increase in the uptake on the right side in the anterioposterior projection but not the lateral views. A diagnosis of alcoholic cirrhosis with metastatic carcinoma of unknown origin, involving the right orbital apex was made. The patient died on the ninth day in hospital due to bronchopneumonia. At necropsy positive findings included evidence of mixed nodular cirrhosis of liver with antemortem tumour metastasis of the portal veins, metastatic deposits in the porta heptatis, and presence of a non-capsulated tumour (approximately 6 cm x 4 cm) in the left lobe of the liver with microscopic features of poorly differentiated hepatocellular carcinoma. In the skull, all the right extraocular muscles had tumour infiltration, the floor of the middle cranial fossa was eroded, the cavernous sinus was not thrombosed and cerebral parenchyma was not infiltrated. The metastasis was histologically identical to the liver primary.

Case 2: WG aged 55 years was admitted with a three months history of tiredness, anorexia and loss of 20 pounds (9 kg) in weight. Three years previously a diagnosis of alcoholic cirrhosis had been made. On examination he was jaundiced, drowsy, with multiple spider naevi, clubbing and palmar erythema but no oedema. He had a soft non-tender, non-pulsatile fixed swelling of approximately 5 cm x 7 cm over the left fronto-parietal region. The liver was enlarged 4-5 cm, was hard, non-tender and non-nodular; the spleenic tip was just palpable and there was no ascites. On initial examination he was drowsy but orientated, and dysphasic, but over the next three days he became progressively confused and agitated and developed slight weakness of right upper limb. Other systems were normal. Blood count was normal. Liver function tests showed evidence of chole-
tasis and hepatocellular dysfunction (elevated alkaline phosphatase 1124 IU/l, elevated SGOT and SGPT and reversal of albumin globulin ratio). Immuno-electrophoresis showed raised IgG (26-10 g/l), IgM (1-95 g/l) and IgA 8-60 g/l). The chest radiograph was normal; skull radiographs showed a massive osteolytic lesion in the left parietal bone corresponding with the clinically palpable scalp swelling. On the basis of above findings a diagnosis of cirrhosis of liver with metastatic carcinoma of unknown origin was made. The patient lapsed into coma and died on the seventh day. At necropsy the positive findings included severe bronchopneumonia, diffuse micro-nodular cirrhosis of liver with antemortem portal vein thrombosis and total replacement of the right lobe of liver by a necrotic haemorrhagic tumour with microscopic features of undifferentiated hepatocellular carcinoma, along with multiple small separate foci of hepatocellular carcinoma. The skull vault deposit was not infiltrating but was compressing the underlying left fronto-parietal cerebral hemisphere, and had microscopic similarities to the hepatic primary. Additional tumour deposits were present in the left sixth rib and left adrenal gland.

The subject of elevated immunoglobins in patients with hepatoma has been studied in detail by Ipp et al.2 Hepatic carcinoma can present with metastatic deposits, the common sites being lung, bones and lymph nodes. Al-Sarraf et al4 reported that 30-70% of patients with liver cancer had metastasis at the time of clinical diagnosis, although it is unclear what percentage of these secondaries were symptomatic. Amongst the neurological complications reported are vertebral metastases with cord compression5 and cerebral gigantism in a child.6 There has been a solitary case report in the literature7 of a 62-year-old lady, who repeatedly presented for nine years with multiple osteolytic deposits including an asymptomatic skull vault deposit and who at necropsy suffering cerebral bleeding due to hypertension, was shown to have metastatic hepatocellular carcinoma.

The syndromes of upper cranial nerve palsy as in our first patient and mild right hemiparesis in the second patient owing to metastases from hepatocellular carcinoma has not, to our knowledge, been previously reported. There has been no report of metastasis actually in the cerebral tissue, and in the case cited above and in both our patients there was no infiltration of cerebral parenchyma, and it is possible that this reflects a peculiarity of this tumour. We suggest that, when investigating patients with suspected cranial secondaries particularly if there is a bony involvement, serum alpha fetoprotein and hepatic ultrasound should be carried out as screening procedures.

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Muscular inhibitory and excitatory phenomena during spike-and-wave discharges: effect of posture

SIR: In 1886 Hughlings Jackson observed that an epileptic patient suffering from falling fits due to loss of tone during standing could also show sudden jerks of the limbs while lying supine (cited in Janz 1969). Gastaut et al noticed that spike-and-wave discharges can cause both myoclonic jerks and atonic drops.2 In an epileptic child we observed spike-and-wave discharges that had different clinical manifestations depending upon posture. Myoclonic jerks were present when the patient was at rest, whereas atonic fits without myoclonus were evident during maintenance of posture.

A nine-year-old boy born post-term by caesarean section, had a first tonic seizure at 11 months and three more similar attacks during the following months. He then remained seizure-free until aged two and a half years, when absences appeared several times a day. They lasted a few seconds and were often associated with myoclonic jerks of the head and arms. No falling fits were reported. Neurological examination and IQ were normal. A polygraphic recording was carried out which included electroencephalogram, electrooculogram, electromyogram of neck, chin and deltoid muscles, electrocardiogram and thoracic respirogram. The patient’s clinical manifestations were monitored simultaneously with the polygraphic recording by means of an audiovisual videotape system. The EEG showed a normal background activity with generalised 3-5 Hz, spike-and-wave discharges, each one lasting 2 to 5 s. Some discharges did not induce any clinical phenomena, whereas others had a clinical manifestation which depended upon the posture of the patient: (a) when the patient was at rest, sitting with his arms along his body, the spike-and-wave discharge was associated with myoclonic jerks of the head and upper limbs, which sometimes spread to the lower limbs as well. These jerks observed in the neck and deltoid muscles were synchronous with the spike of the spike-and-wave complexes (fig a). (b) When the patient held the arms outstretched, the spike-and-wave discharge was associated instead with a sudden drop of his head and arms. The drop was due to a loss of tone, recorded in the neck and deltoid muscles and synchronous with the wave of the spike-and-wave complex. It usually lasted 100 to 200 ms, the next spike marking then the reappearance of the tonic muscular activity (fig b), with myoclonus now being absent.

This case demonstrates that, on the same pool of motoneurons, an excitatory influence related to the spike may prevail during muscular rest, whereas an inhibitory influence related to the wave
Hepatocellular carcinoma with cranial metastasis and hyperglobulinaemia.
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