LETTERS TO THE EDITOR

Insulinoma complicating tuberous sclerosis

A young man, known to have tuberous sclerosis, recently presented to us with tiredness and recurrent seizures after being fit for fifteen years. Removal of an insulinoma led to complete relief of symptoms which had for some time been attributed to the tuberous sclerosis.

The patient was a 23 year old man. Diagnosis of tuberous sclerosis was made in childhood. He had adenoma sebaceum and mild mental retardation. He had had generalised seizures up to the age of seven years and had then been free until 18 months before presentation. Seizures continued despite therapeutic levels of carbamazepine and primidone. He also complained of sleepiness after meals and an increased appetite for sweet foods. There was no family history of tuberous sclerosis. Apart from the typical skin changes and retardation there were no abnormal physical findings. His weight was normal for his height and there was no change in weight. CT scanning of the brain showed the typical intracerebral masses of tuberous sclerosis.

He was referred for investigation when a plasma glucose of 1.7 mmol/l (normal range 4.5–10 mmol/l) was noted following a seizure. Excess insulin excretion was demonstrated 9 hours into a fast when he suffered a generalised seizure with plasma glucose 1.2 mmol/l and insulin 55 mU/l (expected <10 in presence of hypoglycaemia). Whilst CT of the pancreas was unremarkable, coeliac angiography demonstrated a 3 cm blush in the inferior portion of the pancreatic head. A benign lesion was found and subsequently removed. He has remained seizure free and maintains a normal blood sugar without excess carbohydrates.

This is the first of two other reported cases of insulinoma complicating tuberous sclerosis and as in our patient the diagnosis was delayed. 1 A second patient has been reported with a non-functioning islet-cell tumour found at necropsy. She also had hypothyroidism as part of a multiple endocrine neoplasia. Her mother had a parathyroid adenoma and adenoma sebaceum, probably representing a forme fruste of tuberous sclerosis. 2

There may be a more than chance association between these two rare conditions. The incidence of insulinoma is estimated at one case per million per year 3 and the point prevalence of tuberous sclerosis at 1 in 10,000 100,000 persons in a community based study. 4 Insulinoma should be considered in patients with tuberous sclerosis who present with recurrent or uncontrollable fitting.

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The influence of head position upon head tremor

An alteration in head position influences hemiparetic line-of-stroke, 1 torticollis 2 and the amplitude of head tremor. 3 There is some conjecture as to whether this is due to: 1) a muscle spindle effect; 2) a consequence of altered muscle tone due to a change in loading of neck muscle when the head is in a dependent position; 3) a CNS effect related to the execution of a motor programme, as suggested in writing tremor 4 or 4) whether it is dependent upon vestibular mechanisms, with an alteration in the tonic discharge of the otolith receptors in response to gravity, 5 for example, in the modulation of downbeat nystagmus by head position.

Head tremor occurs in a variety of conditions including essential tremor, dystonia and cerebellar disease, though mechanisms underlying such head tremors are poorly understood. In some patients, the amplitude of head tremor changes considerably with head position. We describe in detail one of four such patients in whom this effect appears to be due to factors other than a vestibular mechanism.

A 48 year old woman developed increasing head tremor over a period of 20 years. It had first been noticeable on eating and drinking. Over the past three years tremor had affected her voice and arms. There was some improvement of tremor reduction but no family history of tremor in first degree relatives.

On examination, with the head upright, there was a marked tremor of the head in the planes of yaw (no-no) and pitch (yes-yes) which increased in amplitude on neck flexion. Her speech was interrupted by tremor though this did not affect the tongue at rest. Eye movements were normal. There was a variable head tilt and slight rotation of the head on attempted drinking. There was a postural and action tremor of the outstretched arms at 4·5 Hz similar to that of the head. Deep tendon reflexes were brisk with biceps and ankle clonus. She was mildly ataxic with poor heel-toe walking. There was no dystonic posturing of the limbs. Cortical somatosensory evoked potentials were delayed and CT scanning showed mild cerebral and cerebellar atrophy. CSF analysis was normal with no oligoclonal bands. There were no prolonged spasms or long bursts of EMG activity on surface EMG recording of splenius and sternocervicals, as may be typically seen in dystonia.

Influence of head position upon head tremor

<table>
<thead>
<tr>
<th>Patient sitting</th>
<th>Patient lying</th>
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<tbody>
<tr>
<td>head neutral</td>
<td>neck extended</td>
</tr>
<tr>
<td>Tremor amplitude</td>
<td>8°</td>
</tr>
<tr>
<td>Variables influencing tremor amplitude</td>
<td>+</td>
</tr>
<tr>
<td>Muscle spindles</td>
<td>+</td>
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<tr>
<td>Muscle tone</td>
<td>+</td>
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<tr>
<td>Vestibular</td>
<td>+</td>
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<tr>
<td>Motor programme</td>
<td>+</td>
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</tbody>
</table>

+ = increased or changed with respect to head neutral
+ = decreased or changed with respect to head neutral
[1 similar or opposite direction of otolith input]

Tremor amplitude refers to peak amplitude in degrees

Tremor frequency was similar in all instances (3·8–4·3 Hz).

The amplitude of head tremor was measured using an angular accelerometer (Schein-

The amplitude of head tremor was measured using an angular accelerometer (Scheinervelt, ASSAMP 80), with the patient sitting upright with the head in the neutral position and separately with the neck flexed and extended. Tremor amplitude during neck extension was measured from that in the neutral position. With neck flexion, tremor amplitude increased in magnitude eight-fold though the frequency did not change (table). This effect could be attributed to a change in either proprioceptive, muscle tone, the motor programme or vestibular input. To distinguish between these possibilities tremor was assessed with the patient lying prone and supine on a firm mattress. With the patient lying prone and supine on a firm mattress. With the patient lying prone (and with the face in the same position in relation to gravity as with the neck flexed) the amplitude of the tremor decreased slightly compared with head neutral (table). With the patient lying supine, the amplitude of head tremor was little changed, despite the head being similarly supported by the mattress (table). This argues against the criticism that the absence of an increase in amplitude of head tremor on lying prone was due to the head being partially supported on the mattress. Thus the marked change in amplitude of head tremor between head neutral and head prone, with a constant level of otolith input, implies that the head tremor was not influenced by otolith function, whose tonic firing is dependent upon their orientation to the gravity vector. Further, the absence of a major change in the amplitude of the head tremor while prone and supine also provides evidence against the head tremor being influenced by the otoliths in this patient.

Nystagmus that appears with the head in a static position, that is, otolith-dependent static positional nystagmus, may be accentuated with one ear down and lessened with the opposite ear down, reflecting the influence of gravity upon static otolith receptors. Using the same analogy, as tremor was maximal with the neck flexed, with “face down”, it would be expected that tremor would decrease in “face-up” positions (no change in extension or supine) if otolith mechanisms were involved. This was not the case, which suggests, that in this patient, the effect of head position in altering head tremor is likely to be due to an alteration in muscle spindle input, with altered stretch of muscles and/or altered muscle tone, with a change in the contractile force of different muscles when the head is in a different position and/or related to the execution of a motor pro-