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 fit 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 had been 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 after he suffered a generalised seizure with plasma glucose 2·2 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 report is the second other reported case 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 year3 and the point prevalence of tuberous sclerosis at 10·6 per 100 000 persons in a community based study.2 Insulinoma should be considered in patients with tuberous sclerosis who present with recurrent or uncontrolled fitting.

PM DAVOREN
MT EPSTEIN
Royal Newcastle Hospital,
Newcastle, NSW, Australia


The influence of head position upon head tremor

An alteration in head position influences hemiparetic limb posture,4 torticollis5 and the amplitude of head tremor.6 There is some conjecture as to whether this is due to: 1) a muscle spindle effect,7 2) a consequence of altered muscle tone due to a change in loading of neck musculature when the head is in a dependent position; 3) a CNS effect related to the execution of a motor programme, as suggested in writing tremor6 or 4) whether it is dependent upon vestibular mechanisms, with an alteration in the tonic discharge of the otolith receptors in response to gravity,8 for example, in the modulation of downbeat nystagmus by head position.

Head tremor was seen 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 considerabily 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 and also of the patient's speech when he sat with his neck flexed and extended. She had had adenoma sebaceum since childhood. She had been observed to have dystonic movements of the head, arms and legs, with an increased amplitude of 20 mm. On examination, there was a marked tremor of the head in the planes of yaw (no-no) and pitch (yes-yes) where it varied 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, patellar and ankle plantars. She was mildly ataxic with poor heel-to-toe walking. There was no dystonic posturing of the limbs. Cortical somatosensory evoked potentials were delayed and CT scanning showed mild cerebellar 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 sternomastoids, as may be typically seen in dystonia.

Influence of head position upon head tremor

Patient sitting

Tremor amplitude

head neutral neck extended neck flexed prone supine

Variables influencing tremor amplitude

Muscle spindle

+ + + +

Muscle tone

+ + + +

Vestibular

+ + + +

Motor programme

+ + + +

+ increased or changed with respect to head neutral

- decreased or changed with respect to head neutral

[] 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 (Schatzvet, ASAMP-50), with the subject lying prone and supine on a firm mattress. The head was orientated in the horizontal plane and 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 head flexed. 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 neck flexion and extension, 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 otolithic 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 (neck flexion or 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-
program. This is in keeping with the tremor of other body parts, for example the wing-beating arm tremor of Wilson's disease and task-specific tremors such as writing and other occupational tremors.5

We have examined clinically, three other patients with clear dystonic head tremor in whom head tremor was altered by the position of the head in the anterior-posterior plane. In none of the others could we demonstrate a vestibular (otolith) mechanism. Despite these negative observations for a clear oto-lingual influence upon head tremor electrophysiological measurements have shown that oto-lingual reflexes may be modulated by both head and body position.6 Thus there still remains the possibility that a change in head or body position may in itself modify vestibular influences upon body movement.

S MOSSMAN
L CLEEVES
L FINDLEY
MRC Human Movement and Balance Unit,
Section of Neuro-otology,
National Hospital for Neurology and Neurosurgery,
London, UK.

Correspondence to: Dr Mossman, Department of Neurology, Wellington Hospital, Private Bag, Wel-lington South, Wellington, New Zealand.


Probable cases of Mast syndrome in a non-Amish family

Complicated forms of hereditary spastic paraplegia are rare. A 58 year old Amish woman was admitted with a clinical picture of slowly progressive spastic paraplegia, dysarthria, presenile dementia and mild athetosis. At the age of 16 her gait became shuffling. Before the age of 30 she used a walking stick, since the age of 35 she has needed a walking frame and from the age of 40 she has become wheelchair bound. During the third decade (maybe earlier) dystharia, ataxia and negativism appeared. Towards her 45th year, urinary incontinence began. On admission, aged 48, significant bradyphrenia and comprehension difficulties were noted and during the following years she presented a further mental deterioration. She is now bedridden and her speech restricted to rare, usually inappropriate single syllable aphasia, which are sometimes repeated. She has difficulty swallowing fluids. She often shows spontaneous repeated slow turning of the head to the right and left and mild tortuous movements of the shoulders. Except for a divergent strabismus there are neither oculo-motor abnormalities, nor fundoscopic anomalies. There is a slight bilateral facial weakness. The fine motor hand skills are lost without clear paresis of the upper limbs. The strength of leg muscles measures about 1 to 2/5. There were neither sensory deficits nor cerebellar signs. Deep tendon reflexes in the upper limbs were increased slightly. Knee jerks were unusually brisk and without clonus; ankle jerks were absent. Plantar responses were extensor. Snout reflex and bilateral palrnumental reflexes were present whilst corneomandibular reflexes were absent.

The following laboratory investigations showed no significant abnormalities: routine blood examination (except for intermittent elevation of glucose with normal haemoglobin A1C), creatine kinase, copper, lipids, very long chain fatty acids ratio C24/C22 and C26/C22, vitamin E, vitamin B12, folate, cortisol, adrenocorticotropic hormone, thyroid hormones, arylsulfatase A and hexosaminidase A + B; the CSF protein was 590 mg/ml with normal electrographic pattern.

The EEG showed mild general slowing. Nerve conduction studies and needle electromyography showed a mild axonal polyneuropathy. The somato-sensory evoked potentials demonstrated a slightly prolonged central conduction time. An electrocardiogram was normal. MRI of the brain showed diffuse cortico-subcortical atrophy, periventricular hypointensities, thin corpus callosum and less marked atrophy of the brainstem and cerebellum. Light microscopic and electron microscopic examination of conjunctiva and skin showed some membranous cytoplasmic body-like inclusions (Professor J J Martin, Dr C Ceuterick-de Groote, University Hospital Antwerp).

The family history revealed two similar cases (figure). There was no known consanguinity.

The monozygotic twin has an almost identical medical history and clinical picture. She is able to stammer a few simple words. Her answers are sometimes slightly more appropriate, particularly for old memories. Her knee jerks and ankle jerks are both unusually brisk, and the plantar responses are extensor. One brother died at the age of 53. The medical records and relatives described difficulties with walking from the age of 20 (maybe earlier). During the following decades he presented a progressive spastic paraparesis, dystharia, mental deterioration and urinary and faecal incontinence; no deficits of sensation or coordination were demonstrated. There were jerks in his last years. Death was due to pneumonia.


Ultrasonic TSH assay and anti-Parkinsonian treatment with levodopa

We have recently reported the association of Parkinson’s disease and hyperthyroidism in a group of 10 patients.1 In that report, symptoms of Parkinson’s disease were always significantly exacerbated by the development of hyperthyroidism and improved by its successful treatment.2 We proposed that hyperthyroidism should be suspected in all Parkinsonian patients when their condition deteriorates.3 Since clinical diagnosis of thyrotoxicosis is difficult in Parkinsonian patients, they should have a comprehensive thyroid examination and, if there is the slightest suspicion of hyperthyroidism, a hormonal evaluation of thyroid function (free T3, ultrasonic TSH).

Thyroid hormone levels (T3 and T4) have been found to be normal in Parkinsonian patients untreated or treated with levodopa.4 However, a decreased response of thyrotropin (TSH) after stimulation by TRH (thyrropin releasing hormone) has been reported in Parkinsonian patients treated with levodopa.5 Such a decreased TSH response after TRH stimulation is observed during hyperthyroidism, and is sometimes the only hormonal abnormality, especially in elderly patients with autonomous thyroid nodules. Thus the decreased TSH response after TRH-stimulation in patients treated with levodopa could be responsible for a false diagnosis of hyperthyroidism. These results, however, were obtained before the ultrasonic TSH determination with a monoclonal antibody assay was available. A low ultrasonic TSH level has the same significance as a decreased TSH response to TRH, indicating an increased negative feed-