Opsoclonus as a presenting symptom in thymic carcinoma

Opsoclonus is a rare paraneoplastic syndrome accompanying some malignant tumours (carcinoma of the lung, uterus, breast, and neuroblastoma in children). We report a patient with opsoclonus combined with ataxia preceding the diagnosis of thymic carcinoma.

A 45-year-old man complained of dizziness and difficulties with walking before admission to hospital. This was followed by episodes of nocturnal sweating and diffuse abdominal pain. Medical, neurological and family history were non-contributory. On admission examination showed the patient to be in a good general condition. The neurological examination revealed normal consciousness; speech and cranial nerve functions were normal; no ataxia or dysmetria was noted. The patient was drowsy but orientated for time and place. The patient was referred to hospital with an established diagnosis of Opsoclonus and ataxia, which was not previously reported.

The patient's EEG was normal. Motor and sensory examinations were normal. The patient was referred to the neurophysiology department for further investigation.

The patient was treated with corticosteroids and lithium carbonate. He improved within 3 months, with a normalisation of his EEG. He was discharged, but readmitted again after 2 months for marked general and neurological deterioration, with severe ataxia, bilateral dysmetria, opsoclonus and chest pains. A trial treatment with clonazepam 2 mg/day orally for 2 weeks had no effect on the opsoclonus or ataxia, and this treatment was discontinued. His general condition deteriorated further and he died nine months after the onset of the symptoms of the disease. Permission for necropsy studies was also refused.

Opsoclonus may occur in encephalitis and as a remote effect of systemic malignancy, such as neuroblastoma in children, carcinoma of the lung, breast, uterus and thyroid. This phenomenon has previously been found in cases of demyelinating disease, brain glioblastoma, thalamic haemorrhage, hydrocephalus, Friedreich's ataxia, intoxication with lithium and chlorpromazine and hypothyroidism.1 In our patient, the opsoclonus was accompanied by truncal and limb ataxia. These symptoms were the first manifestation of carcinoma of the thymus. The association of opsoclonus and thymic carcinoma has not been previously reported. The site of the lesion that causes opsoclonus remains unclear. The association of myoclonus and a cerebellar syndrome in a few cases of opsoclonus has been described.2 In our patient, no evidence was found of a lesion in the dentate or in the cerebellar cortex.

In a few cases of opsoclonus and systemic carcinoma, the necropsy studies reported only inconsistent pathological findings of poor localising value, such as a mild loss of Purkinje cells, a peridental gliosis or slight gliosis in the cerebellum.3 However, there is no evidence that either a lesion in the dentate nuclei or in the cortex can produce opsoclonus by itself.

The pathophysiological mechanisms of the lesions that cause opsoclonus remain unknown. The occurrence of viral infection of the CNS (as in cases of opsoclonus in patients with encephalitis) or immunological dysfunction (as in demyelinating disease or in malignant disease) may be involved in the process. In support of the immunological theory are the elevated levels of CSF-IgG in some cases,4 the effective response to corticosteroid therapy in others5 and the presence of specific antibodies to the Purkinje cells that have been found in two patients with systemic malignancy.6 In opsoclonus caused by a paraneoplastic syndrome, neurological signs fail to improve after treatment. In certain cases, clonazepam and thiamine were effective.2 In our case, treatment with corticosteroids and clonazepam did not change or improve the evolution of the neurological signs.

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five patients. The EEG showed excess slow wave activity, of varied degree, in every case (table).

An abnormal EEG occurs frequently in SC. Diffuse slowing of spontaneous and wave occurring of behaviour activity is the commonest reported change, with an incidence of between 55 and 87 per cent.1 Its occurrence in all five of the patients in this series may reflect the fact that each exhibited disturbed behaviour at the time of study. Behavioural disorders occur frequently in SC2 and furnish an important diagnostic clue. They may be subtle and overlooked and distractibility or dysphoria contributed to chorea per se.

The absence of pathological change on CT brain scan has been a constant finding to date and is consistent with the presence of lesions seen on epilepsy scans.

We are not aware of a published account documenting a series of cases of SC, SEPs recordings or analysis of CSF for oligoclonal immunoglobulin (Ig) G bands. It is generally accepted that value for CSF total protein and white cell count in SC are normal,3 although the evidence for this is not well documented. Our findings substantiate this traditional doctrine. The absence of oligoclonal bands is somewhat at variance with the result of an apparent selective increase in CSF IgG reported previously.4 In this case, however, the evidence for local CSF IgG synthesis was based on elevated IgG/total protein ratio where spuriously high values may be found when, as happened in that patient, there exists an abnormally high serum IgG. The detection of oligoclonal bands is an accurate method for diagnosing intrathecal synthesis of IgG. The negative result in all of our patients tested argues against a primarily antibody mediated pathologic immune reaction within the central nervous system being responsible.

What role cortical SEP results may have in the differential diagnosis of chorea has yet to be determined. Our findings differ from those in a recent report of a single case of SC in which central sensory conduction time was prolonged.6 However, this patient exhibited psychomotor retardation, tonic gaze deviation, facial weakness, hyperactive deep tendon reflexes and the plantar response was extensor, all of which are atypical signs for SC.7 Normal results in SC condition in contrast to the situation in Huntington's disease, where the early cortical components are either reduced in size or absent.8 This disparity may be explained by differences in the pathologic anatomy of the two diseases. Cortical SEPs also have been reported to reveal abnormalities in patients with Wilson's disease,9 whereas results in benign hereditary chorea10 and chorea gravidarum (personal observations) have been normal.

The results of this study emphasise that EEG abnormalities and associated behavioural disturbances are frequent companions to chorea in patients with SC. While clinical features remain the cornerstone in diagnosing SC, our experience suggests that the stereotyped pattern of results may allow standard neurodiagnostic tests to be of some discriminatory value.

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Table Results of neurodiagnostic tests

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (y)</th>
<th>Duration of chorea (mo)</th>
<th>EEG</th>
<th>CSF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>7</td>
<td>½</td>
<td>Diffuse excess theta</td>
<td>Neg</td>
</tr>
<tr>
<td>2</td>
<td>12</td>
<td></td>
<td>Excess theta with posterior dominance</td>
<td>0-10</td>
</tr>
<tr>
<td>3</td>
<td>11</td>
<td>3</td>
<td>Excess theta with right dominance</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>16</td>
<td>9</td>
<td>Diffuse excess theta</td>
<td>Neg</td>
</tr>
<tr>
<td>5</td>
<td>13</td>
<td>12</td>
<td>Diffuse delta and excess theta</td>
<td>Neg</td>
</tr>
</tbody>
</table>

# 95 per cent reference range (black adults): 0 to 10 g/L.
# µ Two or more bands, not present in serum, identification by agar gel electrophoresis with silver stain.
* Lymphocytes.
Neg = Negative.

MATTERS ARISING

Outpatient referrals

I was astonished to read that among 7836 successive new outpatient referrals analysed by G D Perkin, that "conversion hysteria" with 297 examples in ten years was number six in the top twenty of his diagnoses and constituted 3.8% of the referrals. Moreover, conversion hysteria was twice as common as either Parkinson's or post traumatic syndrome and almost three times as common as depression. In my experience, depression is a very common symptom and presents in many guises often with somatic symptoms. Conversion hysteria is, by contrast, a very rare disorder and I do not think that I make this diagnosis more than once a year in the whole of my clinical practice. Does Dr Perkin have special criteria for the diagnosis of conversion hysteria or is his outpatient practice biased heavily by referrals from psychiatric colleagues?

I was also surprised that no diagnosis was made in 26-5% of patients—surely an unusually high percentage. I should have thought that 5— would be nearer the mark. I recognise that in an outpatient clinic one may make an inaccurate diagnosis but I do not think that one should make no diagnosis at all in more than a quarter of the patients.

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Standard neurodiagnostic tests in Sydenham's chorea.

R F Gledhill and P D Thompson

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