Otosclonus as a presenting symptom in thymic carcinoma

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

The patient 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 orofacial movements were normal. The most relevant finding was the patient’s eye movements; there were rapid, chaotic and conjugate saccades of the eyes in all directions, considerably exacerbated by attention. The eye movements were normal in size, reactive to light and accommodation and the funduscopy showed normal optic discs. The examination of the rest of the cranial nerves was normal. Myoclonic seizures were not seen. Systematic and deep reflex testing did not reveal any abnormalities.

Motor and sensory examinations were normal except for his gait which showed mild truncal ataxia. Findings on the test, heel-to-toe and rapid alternating manoeuvres were within normal limits. The values of the laboratory tests including blood glucose, electrolytes, urea, uric acid, bilirubin, creatinine, serum albumin and globulin, calcium, phosphate, SGOT, alkaline phosphatase, ESR, haemoglobin and leukocytes were within normal limits. Beta-human chorionic gonadotropin in the blood; alpha-feto-protein and 5-hydroxy-indole acetic acid in the urine were also within normal limits. The level of blood immunoglobulins was normal. Serological tests for syphilis were negative. X-ray chest and radiological examination of the abdomen were normal.

One month after admission the patient had a right anterior mediastinotomy for biopsy of the mass. The histology revealed thymic carcinoma (lymphoepithelioma type, poorly differentiated squamous cell carcinoma) with pleural metastases. The patient was treated with a combined chemotherapy regime which is used in the treatment of malignant thymoma. Three weeks later there was a further deterioration in the patient’s general condition. Chest radiograph showed no change and CT scan of the brain was within normal limits. Chemotherapy treatment was continued with no subjective or objective change.

Following the failure of chemotherapy, the patient was treated with radiotherapy but with little improvement. The patient was discharged, but readmitted again after two months for marked general and neurological deterioration, with severe ataxia, bilateral dysmetria, otosclonus and chest pains. A trial treatment with clonazepam 2 mg/day orally for two weeks had no effect on the otosclonus 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 was not available.

Otosclonus 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 been reported in cases of demyelinating disease, brain glioblastoma, thalamic haemorrhage, hydrocephalus, Friedreich’s ataxia, intoxication with lithium and chronic alcoholism, and aceto-glycemic states. In our patient, the otosclonus was accompanied by truncal and limb ataxia. These symptoms were the first manifestation of carcinoma of the thymus. The association of otosclonus with thymic carcinoma has not been previously reported. The site of the lesion that causes otosclonus remains unclear. The association of myoclonus and a cerebellar syndrome in a few cases, which are a mild loss of Purkinje cells, in the inferior olive, red nuclei and the dentate nuclei. However, there is no evidence that either a lesion in the dentate nuclei or in the red nuclei produces otosclonus by itself.

In a few cases of otosclonus and systemic carcinoma, the necropsy studies reported only inconsistent pathological findings of poor or localising value, such as a mild loss of Purkinje cells, a peridental glial or slight loss of myelin in the cerebellum. In other patients, perivascular infiltrates and gliosis in the pons, midbrain and hypothalamus were described. In a few patients necropsy studies had no demonstrable pathology in the brain or cerebellum.

The pathophysiological mechanisms of the lesions that cause otosclonus remain unknown. The association of viral infection with the CNS (as in cases of otosclonus 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, the effective response to corticosteroid therapy in others and the presence of specific antibodies to the Purkinje cells that have been found in two patients with systemic malignancy. In otosclonus caused by a paraneoplastic syndrome, neurological signs fail to improve after treatment. In certain cases, clonazepam and thiamine were effective. In our case, treatment with corticosteroids and clonazepam did not change or improve the evolution of the neurological signs.

M SCHWARTZ
B SHARF
Department of Neurology, Brai Zion Medical Center, Faculty of Medicine, Technion, Haifa, Israel
ZIDAN
Department of Oncology, Rambam University Hospital, Haifa, Israel

Standard neurodiagnostic tests in Sydenham’s chorea

The recent resurgence of acute rheumatic fever in the United States has served to focus attention on the procedures for diagnosing Sydenham’s chorea (SC). No single test is available for this purpose and it is widely agreed that the criteria for this condition often cannot be established with certainty at the time of presentation of chorea. In the era when acute rheumatic fever in the developed world was sufficiently common for large numbers of patients with SC to be collected, standard neurodiagnostic tests were limited to electroencephalography (EEG) and analysis of cerebrospinal fluid (CSF) for total protein and white cell count. Futhermore, few alternative causes of chorea were sought. We report here the results of a series of contemporary neurodiagnostic tests in a prospective study of SC.

The subject group comprised five consecutive cases seen by one of the authors at Kafalofg Hospital over a period of three years (January 1985 to December 1987). Kafalofg is a general hospital on the outskirts of Pretoria serving the black community. All the patients were females, their ages ranging from seven to 16 years. Serologic evidence of recent streptococcal infection (antistrep-tolysin-o titre > 200) was present in 70% of cases.

We report here the results of a series of contemporary neurodiagnostic tests in a prospective study of SC.

The subject group comprised five consecutive cases seen by one of the authors at Kafalofg Hospital over a period of three years (January 1985 to December 1987). Kafalofg is a general hospital on the outskirts of Pretoria serving the black community. All the patients were females, their ages ranging from seven to 16 years. Serologic evidence of recent streptococcal infection (antistrep-tolysin-o titre > 200) was present in 70% of cases.

We report here the results of a series of contemporary neurodiagnostic tests in a prospective study of SC.

Each patient fulfilled the following criteria, anamnestic details being provided or corroborated, by a parent or close relative. 1) Involuntary movements typical of chorea developing insidiously in the setting of previously good health. 2) Alert mental state. 3) Absence within the family of members with a progressively disabling disorder. 4) Negative history for drug ingestion preceding, or concurrent with, the onset of chorea. 5) Normal test values for thyroid, renal and hepatic function. 6) Normal full blood count and red cell morphology. 7) Normal plasma glucose and serum sodium, calcium and phosphate. 8) Absence of Kayser-Fleischer rings, normal serum copper and ceruloplasmin, and normal radiographs of the auricles. 9) Negative tests for rheumatoid factor, anti-nuclear antibodies, rheumatoid factor, specific and non-specific. 10) Negative pregnancy tests (where indicated).

Cerebrospinal fluid analysis, contrast enhanced computed tomography (CT) brain scan and upper (median nerve) and lower limb (tibial nerve) cortical somatosensory evoked potentials (SEPs) were normal in all


5 Bolshauer E, Donna T, Hirt HR. Myoclonus and encephalopathy of infants with the syndrome. Helv Paediatr Acta 1979;34:119.


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 activity is the commonest reported change, with an incidence of between 55 and 87 percent.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 attributed to chorea per se.

The absence of pathologcal change on CT brain scan has been a constant finding to date and is consistent with the poverty of lesions seen at autopsy.

We are not aware of a published account documenting a series of cases of SC, SEP 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 in 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 an 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 demonstrating 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 somatosensory 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.3 Normal results in SC stand in contrast to the situation in Huntington's disease, where the early cortical components are either reduced in size or absent.7 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,8 whereas results in benign hereditary chorea9 and chorea gravidarum (personal observations) have been normal.

The results of this study emphasise that EEG abnormalities and associated behavioural disturbances found in frequent concomitants 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 neuroradiologic tests to be of some discriminatory value.

We thank Professor P Bartel for scientific advice, Mr Y Chetty, Dr RA Dupont and Mrs J Bester provided technical help.

RG LEDGILL
Division of Neurology,
Department of Internal Medicine,
University of Pretoria and Kalafong Hospital,
South Africa
PD THOMPSON
University Department of Clinical Neurology,
Institute of Neurology,
Queen Square, London

Correspondence to: Dr R F Gedgill, Neurosciences Department, Rashid Hospital, PO Box 4545, Dubai, United Arab Emirates.


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>1</td>
<td>7</td>
<td>Diffuse excess theta</td>
<td>1*</td>
<td>0-10</td>
</tr>
<tr>
<td>2</td>
<td>11</td>
<td>Excess theta with posterior dominance</td>
<td>3*</td>
<td>0-22</td>
</tr>
<tr>
<td>3</td>
<td>11</td>
<td>Excess theta with right dominance</td>
<td>2</td>
<td>0-13</td>
</tr>
<tr>
<td>4</td>
<td>16</td>
<td>Diffuse excess theta</td>
<td>3</td>
<td>0-20</td>
</tr>
<tr>
<td>5</td>
<td>13</td>
<td>Diffuse delta and excess theta</td>
<td>2</td>
<td>0-20</td>
</tr>
</tbody>
</table>

* CSF: White cells (x 10^6/L), Total # protein (g/L), Oligoclonal IgG bands

---

MATTERS ARISING

Outpatient referrals

I was astonished to read that among 7836 successive new outpatient referrals analysed by G D Perkins,1 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 Perkins 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.

E A A NIEMAN,
St Mary's Hospital, London, United Kingdom

Dr Perkins replies:

The criteria that I use for the diagnosis of conversion hysteria are the presence of physical signs which by their nature can only be explained on the basis of an elaborated disability on the part of the patient. I would disagree that the condition is rare. The cases that I discussed were seldom, if ever, referred by the psychiatrists. They appear to share Dr Niemann's view about the scarcity of the problem. I have analysed some of this data in greater detail elsewhere,1 where, I found that approximately half the patients with features of conversion hysteria had the additional characteristics of Briquet's syndrome. That particular syndrome with or without evidence of conversion hysteria has been found remarkably frequently in those patients who are frequent attenders of medical outpatient clinics.

I find Dr Niemann's use of the word "should" in the last but one line of his comment, a curious one. It almost suggests a compulsive need on the part of the neurologist to make a diagnosis in his patients. Indeed that compulsive need, I suspect, often produces spurious diagnoses which may possibly help the doctor but do little to assist the patient. It may be that all patients who develop gidiness on turning their head have vertebro-basilari insufficiency. I rather doubt it and because of this doubt, this would be one category of patients that I would leave undiagnosed in many circumstances. If, on
Standard neurodiagnostic tests in Sydenham's chorea.

R F Gledhill and P D Thompson

J Neurol Neurosurg Psychiatry 1990 53: 534-535
doi: 10.1136/jnnp.53.6.534-a

Updated information and services can be found at:
http://jnnp.bmj.com/content/53/6/534.2.citation

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/