Treatment of neurocysticercosis

J. JOUBERT, W. K. JENNI

Summary

The clinical and laboratory data of 88 black patients with computed tomographic (CT) evidence of active neurocysticercosis were analysed. The CT appearance of neurocysticercosis was distinctive in the majority. Seizures, chronic headache and neuropsychiatric changes were the most common clinical presentations. Hydrocephalus was diagnosed in 17 patients (9 obstructive and 8 communicating) and cerebral infarction with local neurological deficit occurred in 4 cases. All patients were treated with praziquantel (Biltricide; Bayer-Cilag). There was complete cyst clearance after two courses in 14 patients and in 16 cases the mean percentage reduction in cyst number was 85.68% and in cyst size 80.84%. In 1 patient there was no response to treatment. Although praziquantel was effective in parenchymal neurocysticercosis, it was ineffectual in the treatment of 5 patients with cysticercal meningitis. There were 2 deaths in the series.

Neurocysticercosis is the most common parasitic infestation of the central nervous system in man. It affects mainly young adults: it leaves in its wake a heavy socio-economic burden in terms of mortality and chronic morbidity. Recently there has been renewed interest in the condition because: (i) there is increased mobility of populations from endemic areas to previously non-endemic areas, especially in the USA; (ii) accurate diagnosis is now possible by computed tomography (CT); and (iii) an effective medical treatment is now available in praziquantel (Biltricide; Bayer-Miles), an acylated isoquinoline-pyrazine derivative.

Published reports contain a confusing multiplicity of clinical features associated with neurocysticercosis. There are, for instance, wide variations in the incidence of seizures and intracranial hypertension in different studies. Cysticercosis is endemic in southern Africa with a high prevalence in Transkei and Giselle. There is a high incidence of neurocysticercosis in black patients seen at Ga-Rankuwa Hospital, near Pretoria.

The clinical features and the results of medical and surgical management of 88 black South African patients with neurocysticercosis are described.

Patients and methods

Data from 88 adult black patients seen at Ga-Rankuwa Hospital between January 1984 and November 1986 with CT evidence of active neurocysticercosis were analysed. In only 2 cases was biopsy confirmation of the diagnosis necessary and obtained.

All the patients were treated with a standard regimen described previously. Praziquantel 50 mg/kg/d was administered in divided doses; the length of a course was 14 days. Prednisone in standard dosage was started 2 days before the praziquantel and continued throughout the course and for 2 days after the last dose of praziquantel. Anticonvulsants were administered to all patients and were continued indefinitely.

The decision to repeat a course of praziquantel depended upon the degree of resolution of the active cysts as seen on the CT that was performed routinely 2 weeks after the completion of a course. If viable cysts were present on CT, the course of praziquantel and corticosteroids was repeated.

Treatment courses were repeated according to the objective improvement observed on repeat CT. An average of two courses were given per patient. All patients with hydrocephalus had one or more courses of medical treatment and ventriculoperitoneal shunts were inserted in 11 cases.

CT of the head was performed with a Somatom 2 Siemens Corp. scanner. Routine 8 mm CT slices were taken. Intra-venous contrast medium was administered when considered necessary for diagnostic purposes. Of the 88 cases, 31 patients had two repeat CTs at monthly intervals. Fifty-seven patients did not return for repeat CT. The majority of patients were treated on an out-patient basis because of hospital bed shortage.

In the group of 31 patients who had repeat CT, the number of viable cysts and the diameter of each cyst was measured in each scan slice in the initial and subsequent CT. By comparing the total number of cysts and their mean diameter on initial CT with that of final CT, the mean percentage decrease in total cyst number as well as the mean percentage decrease in cyst diameter could be calculated in each patient. An objective assessment could thus be made of the effect of treatment.

Results

Only adult patients were studied; there were 54 men and 34 women, the majority of whom were in the fourth decade, with a peak at 35 years.

In 58 patients (65.9%) a distinct onset of the symptoms of disease could be ascertained; the average duration being 56.78 weeks. In 5 patients symptoms had been present for > 10 years. The clinical presentation of the disease is shown in Table I.

Two patients with severe infestation died within 21 days of initiation of treatment. Apart from extensive neurocysticercosis, no cause for death was found at autopsy. Although there was flattening of cerebral gyri indicating cerebral oedema in both

<table>
<thead>
<tr>
<th>Symptom</th>
<th>% of patients</th>
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<tbody>
<tr>
<td>Seizures</td>
<td>72.7</td>
</tr>
<tr>
<td>Headache</td>
<td>17.0</td>
</tr>
<tr>
<td>Confusion</td>
<td>9.0</td>
</tr>
<tr>
<td>Meningitis</td>
<td>5.6</td>
</tr>
<tr>
<td>Ataxia</td>
<td>5.0</td>
</tr>
<tr>
<td>Hemiplegia</td>
<td>4.5</td>
</tr>
<tr>
<td>Raised intracranial pressure</td>
<td>4.5</td>
</tr>
<tr>
<td>Paraplegia</td>
<td>2.2</td>
</tr>
<tr>
<td>Chorea</td>
<td>1.1</td>
</tr>
</tbody>
</table>

TABLE I. PRESENTING SIGNS AND SYMPTOMS IN 88 PATIENTS

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cases, there was no other cerebral abnormality apart from neurocysticercosis. There was no evidence of tonsillar herniation.

Apart from transient mild headaches in some patients, no side-effects of drug treatment were noted. Haematological and biochemical indices, including liver function tests, remained essentially normal in all patients.

The initial and final CT of 31 patients with follow-up were analysed. The mean percentage decrease in cyst number, mean percentage decrease in cyst diameter and complete cyst clearance on CT after two courses of praziquantel are shown in Tables II - IV.

**TABLE II. REDUCTION IN CYST NUMBER PER PATIENT BEFORE AND AFTER TREATMENT (N = 31)**

<table>
<thead>
<tr>
<th></th>
<th>Before treatment</th>
<th>After treatment</th>
<th>Mean % decrease per scan after treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean number of cysts per scan</td>
<td>12.96</td>
<td>1.83</td>
<td>85.88%</td>
</tr>
</tbody>
</table>

**TABLE III. REDUCTION IN CYST DIAMETER BEFORE AND AFTER TREATMENT (N = 31)**

<table>
<thead>
<tr>
<th></th>
<th>Before treatment</th>
<th>After treatment</th>
<th>Mean % reduction in cyst size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean cyst diameter per patient</td>
<td>8.193</td>
<td>1.57</td>
<td>80.84%</td>
</tr>
</tbody>
</table>

**TABLE IV. CT EVALUATION OF PATIENTS AFTER TWO 14-DAY COURSES OF PRAZIQUANTEL (N = 31)**

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete cyst clearance</td>
<td>45.16% (N = 14)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decrease in cyst number and size</td>
<td>51.6% (N = 16)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No change</td>
<td>3.2% (N = 1)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

After two 14-day courses of praziquantel, there was complete clearance of cysts on CT in 14 patients (45.6%). In 16 patients (51.6%) complete clearance was not achieved but the mean percentage number of cysts was reduced by 85.88% and mean percentage reduction in cyst diameter was 80.84%. One patient showed no change in cyst number or size on CT after repeated courses of praziquantel.

**Discussion**

CT is undoubtedly one of the most accurate non-invasive methods for the diagnosis of neurocysticercosis. According to Rosas et al., the enzyme-linked immunosorbent assay (ELISA) is not a reliable test for the diagnosis of active neurocysticercosis. In serum, the sensitivity is 50% with a 70% specificity. However, ELISA done on cerebrospinal fluid is more accurate. In the great majority of patients with neurocysticercosis CT appearance is distinctive and examination of the cerebrospinal fluid as a diagnostic procedure may be unnecessary and, indeed, dangerous owing to the high incidence of raised intracranial pressure.

Although serology may be useful in cases where atypical lesions are seen on CT, in our experience a therapeutic trial with praziquantel with repeat CT is of more value.

In this series, as in many other published reports, convulsions were the most common initial mode of presentation (72.7% in this study). Seizures, especially focal ones, in
patients living in an endemic area should always suggest the possibility of neurocysticercosis.

Chronic headache of a 'bursting' nature and characteristically present daily for long periods — many months and even years — was common in our patients (17%). Headache was often associated with hydrocephalus but also occurred in patients with CT evidence of only parenchymal cysts and no evidence of ventricular dilatation. Sotelo et al. have suggested that a form of subacute intracranial hypertension could be induced by relatively few viable cysts. Srinivas et al. emphasised the encephalitic features of neurocysticercosis; headache was a prominent feature in all patients in their series who had encephalitic features. At autopsy there was evidence of cerebral oedema with uncal and tonsillar herniation.

Keane reported 7 patients with neurocysticercosis who died unexpectedly owing to unsuspected obstructive hydrocephalus. All these patients had headaches of many months' duration, sometimes associated with vomiting. These headaches were often diagnosed as either migraine or tension headaches. There was little clinical indication of the gravity of the condition and papilloedema was absent. Thus, chronic persistent headache in a population in an endemic area, especially if associated with vomiting, should alert the clinician to the possibility of neurocysticercosis as an underlying cause.

Confusion and psychiatric changes were often associated with hydrocephalus and/or meningitis in our patients (9%). Psychiatric manifestations and personality changes have been documented in both adults and children. Sotelo et al. in a study of 753 cases documented intellectual deterioration in 15.8%. Torrealba have suggested that 12% of patients in their series had acute motor deficits and Thomson et al. found focal signs, chiefly hemiplegia, in 34% of a series of 61 South African children of all races. Facial signs, such as hemiparesis, were present in 9 of our patients (5.6%). In 1 woman it could be ascribed to compression by a large 40 mm diameter cyst in the parietal lobe, but in the other 8 there was CT evidence of cerebral infarction, presumably caused by granulomatous arteritis identical to that precipitated by tuberculosis or syphilis.

It is of interest that in both Torrealba et al. and McCormick et al. patients with cerebral arteritis, the occlusion occurred in a medium-sized artery — in both cases the suprachrondial internal carotid artery. Neurocysticercosis must therefore be considered as a possible underlying cause for focal neurological deficits, such as hemiparesis, presenting in unusual settings, for instance in children or young adults, in endemic areas.

Chronic cysticercal meningitis was diagnosed in 5 patients (5.6%) in our series. Since it is not our policy to perform lumbar puncture on all patients with cysticercosis, this figure may be an underestimation. The diagnosis in these cases was almost always incidental, since the symptoms were more in keeping with the commonly associated hydrocephalus than meningitis. Neck stiffness was present in only 1 case and in no patient was cranial nerve palsy present. This lack of clinical evidence of meningitis is an important distinction from the more well-known forms of chronic meningitis.

In spite of repeated courses of praziquantel and corticosteroids — sometimes as many as six — the cerebrospinal fluid abnormalities persisted in all our cases with cysticercal meningitis. Similarly, Sotelo et al. found that although praziquantel was highly effective in parenchymal cysticercosis (91% improvement) it was significantly less so in the meningeal form (47% remission). Thus cysticercal meningitis appears to be less amenable to treatment with praziquantel than the parenchymal form of neurocysticercosis.

It is possible that the form of cysticercal meningitis that does not respond to praziquantel may be caused by Cysticercus racemossus. In this abortive form of cysticercus the cyst contains no scolex. It is typically found in grape-like clusters around

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**TABLE V. CLINICAL AND LABORATORY FEATURES OF 9 PATIENTS WITH HYDROCEPHALUS**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Type of hydrocephalus</th>
<th>Presenting symptoms</th>
<th>Clinical signs</th>
<th>Cerebrospinal fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>32</td>
<td>M</td>
<td>Communicating</td>
<td>Epilepsy, dementia, gait disturbance</td>
<td>Papilloedema, ataxia</td>
<td>Normal</td>
</tr>
<tr>
<td>2</td>
<td>29</td>
<td>M</td>
<td>Obstructive</td>
<td>Chronic headache, decreased vision</td>
<td>Papilloedema, hyperreflexia</td>
<td>Normal</td>
</tr>
<tr>
<td>3</td>
<td>40</td>
<td>M</td>
<td>Communicating</td>
<td>Dementia, epilepsy</td>
<td>Papilloedema, stupor, hyperreflexia</td>
<td>Abnormal</td>
</tr>
<tr>
<td>4</td>
<td>44</td>
<td>M</td>
<td>Obstructive</td>
<td>Epilepsy, confusion, chronic headache</td>
<td>Mild nuchal rigidity, confusion</td>
<td>Abnormal</td>
</tr>
<tr>
<td>5</td>
<td>58</td>
<td>F</td>
<td>Communicating</td>
<td>Headache, decreased vision, gait disturbance</td>
<td>Optic atrophy, urinary incontinence, hyperreflexia</td>
<td>Abnormal</td>
</tr>
<tr>
<td>6</td>
<td>49</td>
<td>M</td>
<td>Obstructive</td>
<td>Dementia, chronic headache, gait disturbance</td>
<td>Dementia, papilloedema, ataxia</td>
<td>Abnormal</td>
</tr>
<tr>
<td>7</td>
<td>35</td>
<td>M</td>
<td>Communicating</td>
<td>Confusion, gait disturbance</td>
<td>Mental dullness, frontal lobe signs, ataxia</td>
<td>Abnormal</td>
</tr>
<tr>
<td>8</td>
<td>31</td>
<td>M</td>
<td>Obstructive</td>
<td>Chronic headache, psychiatric changes, decreased vision, gait disturbance</td>
<td>Dementia, hyperreflexia</td>
<td>Abnormal</td>
</tr>
<tr>
<td>9</td>
<td>45</td>
<td>M</td>
<td>Communicating</td>
<td>Gait disturbance</td>
<td>Papilloedema, ataxia</td>
<td>Abnormal</td>
</tr>
</tbody>
</table>
the base of the brain, and excites a marked granulomatous inflammation. According to McCormick et al., an antigenic stimulus from the cyst may produce a pronounced arachnoiditis without fever, neck stiffness or cranial nerve palsy. Meningitis caused by *C. cellulosae* would possibly be amenable to treatment with praziquantel, but *C. racemosa* is less responsive to treatment, presenting as a chronic sterile arachnoiditis without the clinical signs of meningitis but causing obstruction to cerebrospinal fluid flow thus resulting in the development of hydrocephalus.

Hydrocephalus was diagnosed on CT in 17 cases. Nine patients had obstructive and 8 communicating hydrocephalus. In 3 of the patients with obstructive hydrocephalus, intraventricular cysts were visible (lateral and third ventricles). The most frequent symptoms in patients with hydrocephalus were gait disturbance, mental changes and headache, while the most common neurological signs were papilloedema, optic atrophy and spasticity (Table VI). In patients with hydrocephalus, the results of treatment, even after ventriculoperitoneal shunting, were poor. Only one-third of patients showed even moderate improvement.

**Conclusion**

Thus, in our setting the diagnosis of neurocysticercosis may be suspected because of relatively few, clearly defined clinical syndromes, such as epilepsy, headache, insidious psychiatric changes and hydrocephalus.

The efficacy of praziquantel as a larvicide has recently been documented by Sotelo et al., who showed that 91% of patients with parenchymal cysts improved after treatment.

**REFERENCES**