

Experience with neurocysticercosis in the UK: correct diagnosis and neurosurgical management of the small enhancing brain lesion

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Abstract

Neurocysticercosis is a major cause of epilepsy and other neurological morbidity in endemic areas of the world but is exceptionally rare in the West. We have recently had experience of eight patients with this condition, seven presenting with epilepsy and single or multiple small, enhancing parenchymal lesions and one with hydrocephalus caused by a midbrain lesion. One lesion was stereotactically excised after it persisted, but in five other cases spontaneous cyst resolution was observed during expectant management with anticonvulsants. Two patients with multiple lesions were referred to us for further management but were free of active infection. Recent studies show that neurocysticercosis may often be diagnosed based upon the clinical, epidemiological and radiological features. Spontaneous cyst resolution is to be expected in this condition and suspected patients should be carefully observed and surgery avoided. We believe that this disease presents more commonly than has been appreciated in the UK and propose a protocol for management.

Key words: Diagnostic criteria, epilepsy, expectant management, neurocysticercosis, spontaneous resolution.

Introduction

Neurocysticercosis is a disease that is unlikely to be familiar or even known to most clinicians in the UK and Western Europe. Despite being the most common parasitic disease of the central nervous system worldwide and a major cause of epilepsy and death in endemic areas such as Mexico and India.¹⁻¹² With perhaps the exception of the South-Western USA,^{1,4,13} it is exceptionally rare for it to present in developed countries.^{4,5,13,14,15} The condition is caused by the encysted larval stage, Cysticercus cellulosae, of the pork tapeworm Taenia solium. Man is the usual final host, but may unwittingly become the intermediate host, rather than the pig by ingesting the ova shed in the faeces.⁵ Serious neurological sequelae may result when the subsequent larvae preferentially settle in the brain, and more rarely the spinal cord. The solitary parenchymal lesion is the most common form¹⁷ and the presenting symptom in 52-94% of cases is epilepsy,^{1,3,5,9,11,12} but the lesions may be multiple and cause mass effect, hydrocephalus, basal arachnoiditis and cerebral infarction.^{1,5,9,10}

It is now known that parenchymal cysts usually lie dormant for many years and symptoms usually coincide with larval death and an intense inflammatory reaction elicited by the release of larval antigens. The cyst then shrinks, and the resulting granuloma calcifies or disappears completely.^{3,5,16-19} This clinicopathological pattern of spontaneous resolution has important implications for the correct diagnosis and treatment of the disease.

Clinical material

Patient data are summarized in Table I.

A total of eight patients were admitted to the Regional Neurosciences Service at Charing Cross Hospital during a period of just under 2 years, between August 1995 and May 1997, in whom a definitive diagnosis of cerebral cysticercosis was made. Five patients were urgent neurosurgical referrals from district general hospitals with enhancing cerebral lesions initially diagnosed by a radiologist as tumours (4) or tuberculoma (1) and three patients were referred to the neurology service, two for further management with multiple lesions and a previous diagnosis of neurocysticercosis and one with a single enhancing lesion, initially diagnosed as a tuberculoma, in whom joint consultation was effected. There were three male patients and five female patients with a mean age of 32 years (range 19-69).

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Case	M/F	Age (years)	Presentation	Epidemiology	CT/MRI	X-ray thighs	Serology	Stools (ova)	Referral diagnosis	Management	Follow up
1	Male	69	Hydrocephalus	India M. East (Travel)	Single enhancing cyst brainstem scolex	Negative	Negative	Negative	Tumour	VP Shunt Follow-up scans	MRI 4 months Lesion disappeared Symptom free 2 years
0	Female	19	Epilepsy	India (Travel)	Single enhancing cyst L. temporal scolex	Negative	Negative	Negative	Tumour	Anticonvulsants Follow-up scans	MR12 months: no resolution Stereotactic excision (Neurocvaticercosis)
Ś	Female	53	Epilepsy	India (Born, UK 3 years)	Single enhancing cyst L. frontal, scolex Multiple calcifications	Positive Calcifications	Negative	Negative	Tumour	Anticonvulsants Follow-up scans	Scizure 3/12 MRI: resolution but new cyst R frontal MRI 14/12: disappeared stopped anticonvuls 18/12 scizure-free 1 year later
4	Female	21	Epilepsy	India Malawi (Travel)	Single enhancing cyst R. temporal scolex	Negative	Negative	Negative	Tuberculom a	Anticonvulsants Follow-up scans	MRI 8/12: disappeared stopped anticonvuls seizure-free 2 years
Ŋ	Male	27	Epilepsy	India (Born, UK 3 years)	Single enhancing cyst R. frontal scolex	Negative	Positive (1994) Negative (1996)	Negative	Tuberculoma	Anticonvulsants Follow-up scans	MRI 4/12: resolving MRI 16/12: disappeared seizure-free 18/12
Q	Female	31	Epilepsy (1994) Recurrent seizures (1996)	South America (Travel)	Multiple calcifications & enhancing cysts (1994–1996)	Positive Calcifications	Positive	Negative (1995 & 1998)	Neurocysticercosis (1994)	Change anticonvulsants Follow-up scans	MRI 9/12: no new cysts all lesions calcified seizure free 9/12
2	Male	23	Epilepsy	India (Travel)	Single enhancing cyst R. frontal scolex	Negative	Negative	Negative	Tumour	Anticonvulsants Follow-up scans	MRI 3/12: resolving MRI 18/12: disappeared stopped anticonvuls 1 year seizure-free 18/12
∞	Female	45	Epilepsy (1985) Recurrent seizures (1997)	Thailand (Born & Travel)	Multiple cerebral calcifications	Positive Calcifications	Positive (1985) Negative (1997)	Negative (1997)	Neurocysticercosis (1985) Neurocysticercosis inactive (1997)	Restart anticonvulsants Follow-up scans	Seizure-free 1 year stop anticonvulsants if seizure-free 2 years

Presentation was with focal and/or generalised epilepsy in seven and obstructive hydrocephalus in one. Only one patient experienced prodromal symptoms of headaches for several weeks. No patients with epileptic seizures had a demonstrable neurological deficit upon presentation. The first patient in the series, who presented with hydrocephalus, had experienced 6 months of erratic driving and 10 days of progressive gait disturbance and confusion.

All eight patients had a history of travel to or had been born in endemic areas for cysticercosis (Table I). The country common to six patients was India: two patients were born in India and had both been resident in the UK for 3 years prior to presentation.

Results

Radiological features

All patients underwent contrast CT and MRI of the brain, either at the referring hospital or after admission. All cases demonstrated the cause of the symptoms as a spherical ring-enhancing cystic lesion between 8 and 12 mm in diameter. In five patients the lesion was single (Fig. 1); one patient showed a single enhancing lesion with additional multiple cerebral calcifications (Fig. 2), and two patients with previous diagnosis of neurocysticercosis а demonstrated multiple lesions, one of mixed enhancing and calcified cysts, and one of multiple calcifications only. All enhancing cortical cysticerci elicited a marked degree of surrounding oedema, particularly well demonstrated on T2 MR sequences (Fig. 2B,C).

In the six patients with a solitary cysticercus the

larval scolex was clearly demonstrated on MRI and sometimes also on CT, as a characteristic 'spot' irregularity within the cyst wall (Fig. 4). In the five presenting with epilepsy the lesion was cortical or subcortical. The first patient, who presented with obstructive hydrocephalus, harboured a single cysticercus that was visible on CT and MRI situated within the midbrain, causing aqueductal obstruction (Fig. 1A).

Further investigations

All patients were questioned for a history of, or contact with, tuberculosis. This was negative in all cases and all patients had normal chest radiographs. There was no clinical or laboratory evidence of systemic or intracranial bacterial infection in any case.

Serological tests of serum or CSF for anticysticercal antibodies were performed in all cases: enzyme-linked immunosorbent assay (ELISA) or the enzyme-linked immunotransfer blot (immunoblot), or both. Serology was negative in five cases and positive in three. Of the three patients with positive serology, only one had a single enhancing lesion. The other two harboured multiple lesions; both had positive serology at original diagnosis, but negative tests at referral.

Three patients with multiple cerebral lesions were seen to have 'cigar-shaped' calcifications caused by larvae in the thigh muscles visible upon plain radiography (Fig. 3). Stool examination was performed in all cases to search for ova (proglottids) to rule out co-existing taeniasis (gut tapeworms) and thus the possibility of continuing auto-infection. This was negative in all eight cases.

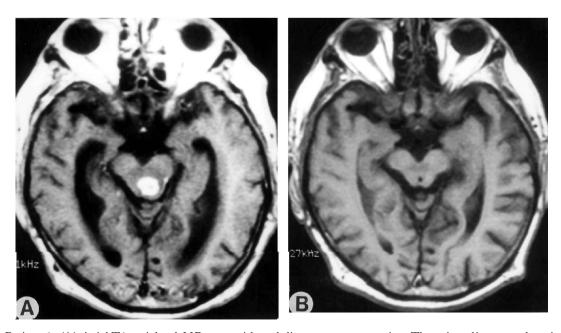


FIG. 1. Patient 1. (A) Axial T1-weighted MR scan with gadolineum at presentation. There is a discrete enhancing lesion within the midbrain and obvious hydrocephalus. The scolex of the cysticercus is visible as an irregularity within the wall of the cyst. (B) Axial T1-weighted MRI scan with gadolineum at 4 months and after VP shunt insertion. There has been spontaneous and complete resolution of the midbrain lesion and the cerebral aqueduct is clearly visible and patent.

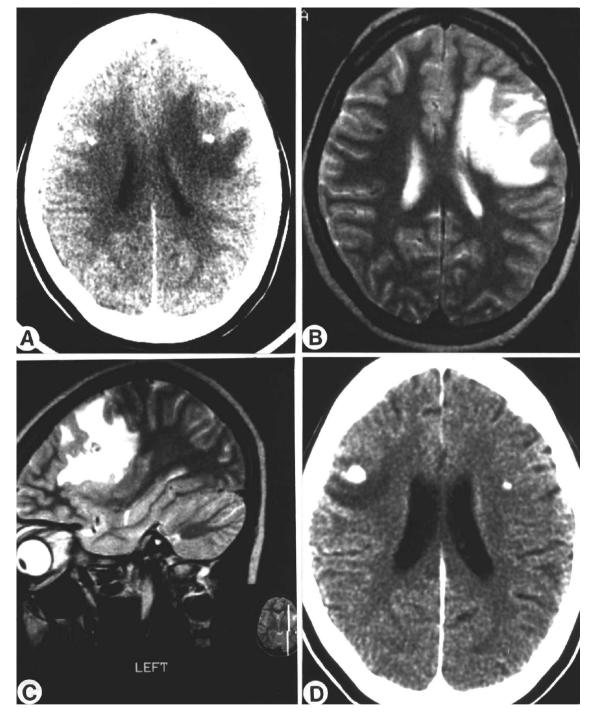


FIG. 2. Patient 3. (A) Axial CT scan with contrast after presentation with grand mal seizures. There is a small left frontal enhancing lesion with a considerable amount of surrounding oedema. There are also two small calcifications in the opposite frontal lobe, but without oedema. (B) Axial and (C) sagittal T2-weighted MR scans demonstrate very well the oedema surrounding the cysticercus and the 'dot and spot' appearance of the larval scolex is clearly appreciated. (D) Enhanced CT scan at 3 months after a further generalized seizure. The previous left frontal lesion has almost disappeared, but there is a new cysticercus with surrounding oedema in the right frontal lobe.

Management

The changing management of the patients in this series from the second case onwards reflects our growing experience and the evolution of a defined management protocol for patients presenting with epilepsy and small enhancing cerebral lesions or calcifications. Patient 1, the only patient not to present with epilepsy, underwent ventriculoperitoneal shunting for obstructive hydrocephalus and made a rapid recovery. Follow-up MRI at 4 months surprisingly showed complete resolution of the initial midbrain cyst. The diagnosis was initially uncertain, but in the light of the complete disappearance of the lesion and review of the radiology a retrospective diagnosis of cerebral cysticercosis was made. No further treatment was necessary and he was well at review 2 years later.

The second patient presented with a similar single enhancing lesion, in a subcortical position in the left temporal lobe. It was decided to treat with **RIGHTSLINKO**



FIG. 3. Patient 3. Plain radiograph of the thighs. Three 'cigar-shaped' calcifications are clearly demonstrated within the thigh muscles (arrows).

anti-epileptic drugs (AEDs) in the light of the history of recent travel to rural India. The lesion persisted at 8 weeks, however, and it was therefore excised. Histological features of the cyst showed a chronic encapsulated inflammatory process in keeping with a cysticercus, but unfortunately the central pearly white scolex seen at surgery was lost in the laboratory. In hindsight it was felt that a longer period should have been allowed before deciding upon surgery.

From the third case onwards, we felt confident about the typical CT and MRI appearances of the lesions of neurocysticercosis. A defined management protocol was aided by the recent diagnostic criteria formulated by Del Brutto *et al.*⁸

In this way the four remaining patients who were referred as emergencies to our service with small enhancing lesions and epilepsy were managed with AEDs alone and repeat imaging at follow-up. In all cases this observant approach was justified by complete disappearance of the enhancing lesions at intervals of between 8 and 18 months. Patient 3 was interesting in that a further seizure at 3 months resulted in repeat MRI, which showed that the initial cysticercus had resolved but a new lesion had appeared in the opposite frontal lobe (Fig. 3a-d). The patient was continued on AEDs and this second lesion had resolved at 14 months. Subsequently, all four of these patients remained seizure-free, at follow-up intervals between 18 months and 2 years. AEDs were successfully stopped in three patients after cyst resolution. Patients 6 and 8 were different in that they were referred for further management with multiple cerebral lesions and a previous diagnosis of neurocysticercosis. Both were considered to be free of live cysticerci during follow-up and repeat serology was negative having been positive in the past. Anticysticercal treatment was not required.

Discussion

Although cerebral cysticercosis is a disease that has been recognized in endemic areas since the middle of the last century, it is really only since the advent of modern neuroimaging with CT and MRI that the natural history, and true prevalence of this infestation have been realized.

The most worrying concern with such small enhancing lesions is that they might represent primary or metastatic malignancy, and is the reason why stereotactic biopsy or excision may initially be advocated unless thought is given to alternative conditions. Other lesions that might present with similar radiological features are bacterial abscess, mycotic granuloma, toxoplasmosis, hydatid cyst, larva migrans and sarcoidosis.

A controversy since CT became widely available is the distinction between the lesions of neurocysticercosis and cerebral tuberculoma.^{17,18,20-23} This is because both diseases are common in endemic areas, may coexist in the same patient and may both present with epilepsy. Recent studies from India^{17,18} have revealed that the majority of small enhancing lesions in epileptic patients disappear spontaneously on AEDs alone and are actually cysticerci. Rajshekar¹⁸ has found that cysticerci are usually round in shape, 20 mm or less in size with ring enhancement or a visible scolex, and midline shift or neurological deficit are never seen. Tuberculomas by contrast are usually irregular, solid, greater than 2 cm in size, usually with shift and presenting with a progressive deficit. This distinction is an important issue since parenchymal cysticercosis is a benign and self-limiting condition, whereas a tuberculoma is an active infection that requires prolonged therapy with potentially toxic drugs.17,18

Modern neuroimaging has clearly established the pattern of larval death that leads to inflammation and oedema and the onset of symptoms, followed by spontaneous granuloma resorption or calcification.^{3,5,9,13,17,18} Miller¹³ documented this phenomenon and questioned the need for surgical intervention. It is known that cerebral larvae may lie dormant with no symptoms for 10 years or more^{3,5,13} and although the period from presentation to spontaneous resolution is variable,¹⁷ 65% of lesions disappear within 12–16 weeks¹⁸ and 85% by 6–8 months.¹⁹

As well as clearly delineating the different stages of the disease described above, CT and MRI has also been used to identify the characteristic radiological features of the individual parenchymal cysticercus.^{1,8,9,11,17,24} Although live asymptomatic cysts may be several centimetres in diameter, dying enhancing

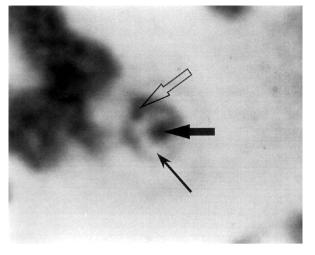


FIG. 4. Enlarged view of cysticercus from T2-weighted MR scan to highlight the characteristic appearance of the larval scolex. The scolex is seen as the 'spot' irregularity in the cyst wall (black arrow), the cyst wall itself (hollow arrow) and the cyst fluid which is of high intensity in the T2 sequence (headed arrow).

cysticercus granulomas are always 20 mm or less in size.¹⁸ In most cases the scolex may be seen within the cyst wall as an eccentric, enhancing hyperdense spot on T1 sequences and is regarded as a pathognemonic feature^{1,5,8,11} (Fig. 4). There is usually marked oedema surrounding the cyst and contrast enhancement during the transitional phase,²⁴ which diminishes during resolution. In 65% of cases with multiple lesions small calcifications will also be seen,¹ although each cysticercus may not necessarily calcify before resolution.

The two principal serological tests in use are the enzyme-linked immunosorbent assay (ELISA) and the enzyme-linked immunotransfer blot (immunoblot, EITB). The immunoblot is regarded as more reliable, with a specificity of 100% and a sensitivity of up to 97% in both blood and CSF.^{5,16} However, it is recognized that these tests display poor sensitivity in detecting antibodies in cases of solitary lesions^{5,17,18} when the sensitivity drops to 18-46%.¹⁶ Positive tests may help to confirm the diagnosis, but a negative test cannot be used to exclude neurocysticercosis.^{8,16}

Two anticisticercal drugs are widely used in endemic areas: praziquantel and albendazole.^{5-7,12} It is our policy not to use these drugs with single lesions since the enhancing cysticerci demonstrated upon imaging are by definition dying anyway and will spontaneously resolve, a view shared by others.^{5,11,18,17,21} These drugs may accelerate cyst resolution and some authors advocate their use even with solitary lesions.

The mainstay of treatment in this patient group during observation has been seizure control with AEDs. Seizures caused by a single cysticercus are generally very well controlled^{5,7,11} and Rajshekhar¹⁹ found that 58 of 62 patients with solitary lesions remained seizure-free in the long term after AED withdrawal between 2 and 4 weeks after cyst disappearance. The principal indications for surgical intervention in neurocysticercosis are the treatment of hydrocephalus, the removal of mobile intraventricular cysts, spinal cysts, accessible racemose cysts in the basal cisterns and large supratentorial cysts causing mass effect.^{1,3-6,12,19,20,25} Small cortical granulomas such as those in this series should not be biopsied or removed since the parasite is dying and will disappear spontaneously.^{1,7,8,10,18,25}

Additionally, stereotactic biopsy may be difficult owing to the toughness and mobility of the cysticercus, and hazardous owing to the usual site of lesions at the grey-white matter junction with the subsequent risk of haemorrhage.¹⁷ In the rare situation where a cyst enlarges or causes increasing neurological deficit we would treat with anticisticercal therapy in the first instance if the diagnosis is definite. If the lesion still does not respond to this therapy then surgery is inevitable.

In the light of the above information, how may a confident diagnosis of neurocysticercosis be made from the presenting clinical evidence and the radiological findings? This controversy has recently been addressed by an international panel led by Del Brutto⁸ which has summarized diagnostic criteria and degrees of diagnostic certainty (Tables II and III). The criteria are subdivided into separate categories according to the weight attached to each feature: absolute, major, minor and epidemiological. Interpretation of the cumulative criteria in each patient allow the calculation of three degrees of diagnostic certainty: definitive, probable and possible. Since spontaneous cyst resolution is typical of this

Absolute	1. Histological demonstration of parasite.
	2. Fundoscopic visualization of parasite.
	3. Cystic lesions with scolex on CT or MRI.
Major	1. Lesions suggestive of neurocysticercosis on CT or MRI.
	2. Positive anticysticercal antibodies in serum or CSF.
	3. Calcifications on plain X-rays of thighs.
Minor	1. Subcutaneous nodules.
	2. Clinical manifestations suggestive of cysticercosis.
	3. Disappearance of brain lesions with anticysticercal therapy.
Epidemiological	1. Immigration from or living in endemic area.
	2. Travel to endemic area.
	3. Household contact with T. solium infection.

TABLE II. Diagnostic criteria (after Del Brutto)⁸

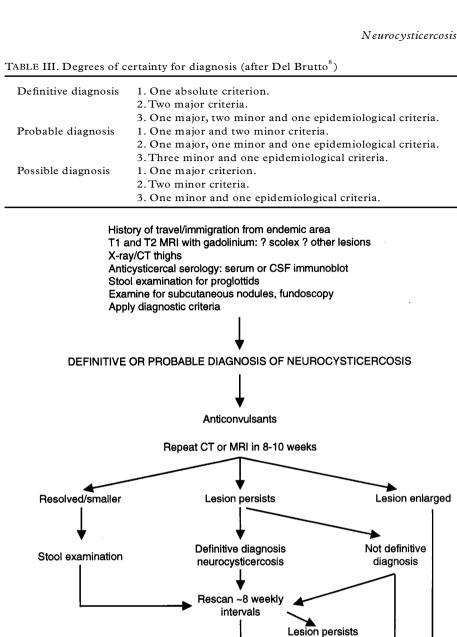


FIG. 5. Management protocol of a patient presenting with epilepsy and small enhancing lesion(s).

LESION RESOLUTION

condition, it might be suggested that this is also included as a minor criterion. In all cases in our series the criteria accumulated permitted a definitive diagnosis to be made. With increasing experience during the series described we have adopted a coherent management strategy for patients presenting with small enhancing cerebral lesions and epilepsy (Fig. 5). For patients with a definitive or probable diagnosis after investigation, the management should be expectant with AEDs alone and repeat imaging initially at 8–10 weeks. Stereotactic or image guided excision should be reserved for lesions that enlarge or persist despite additional anticysticercal treatment or when the diagnosis is not certain.

Conclusions

We have aimed to highlight a new clinical problem that must be considered as a differential diagnosis in industrialised nations in the era of modern travel and immigration from endemic areas. Lesions such as those described may have been mistakenly biopsied or removed in the past when thought to be tuberculomas or small tumours, resulting in non-specific histological findings. Correct differential diagnosis with other ring-enhancing lesions is essential, since neurocysticercosis with a solitary or a small number of cerebral lesions is a self-limiting disease, and unnecessary surgery or prolonged therapy with potentially toxic drugs should be avoided since the pattern is of spontaneous cyst resolution.

STEREOTACTIC OR IMAGE GUIDED EXCISION

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