Childhood Neurocysticercosis: Issues in Diagnosis and Management

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Neurocysticercosis is the commonest parasitic disease of central nervous system (CNS)(1). It is caused by the larval form of *Taenia solium.* The preferred sites of involvement by these larval forms are brain, muscles, skin and eyes. Other body organs may also be involved. The presence of these cysticercus cysts in the brain and other parts of CNS is termed as "neurocysticercosis". Clinically it may manifest as epilepsy, increased intracranial tension (ICT), focal neurological deficits (stroke), hydrocephalus, and space occupying lesions(2,3).

In endemic areas like India neurocysticercosis is seen in all the age groups, particularly in children and young persons(4). In children the disease behaves differently in several aspects which have important implications in diagnosis, management and prognosis(4).

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Diagnosis

Accurate diagnosis of neurocysticercosis can be made with the help of recent imaging techniques *i.e.,* computerized tomographic (CT) scan, and magnetic resonance imaging (MRI) scan(2). CT scan is the most useful test for the diagnosis of neurocysticercosis. The parenchymal form which is seen in 60 to 75% of patients with cerebral cysticercosis is the commonest CT appearance(5). The larvae of neurocysticercosis most commonly appear as a hypodense cystic lesion with an asymmetrically located internal hyperintensity corresponding to dead and hyalinized scolex. Occasionally the lesion may also be isodense or hyperdense, depending on degree of organization and calcification of the cysts *(Fig.* 2). In addition, punctate calcificati6ns may also be seen within granuloma, as McCormick *et al.(5)* noted in 55% of their adult patients. The administration of contrast material on CT scanning characteristically demonstrates ring enhancement around the cysticercus cysts; nodular or homogenous enhancement of an organizing granulomatous cyst is equally common *(Fig. 2).* CT picture in patients with cysticercosis and those with a tuberculoma are remarkably similar in many cases, and it is exceedingly difficult to distinguish between them.

MRI appearance of the cysticerci also vary with the stage of development and with the area of involvement. MRI demonstrates a homogenous cerebrospinal fluid (CSF) like intensity on both long and short TR images except for a mural

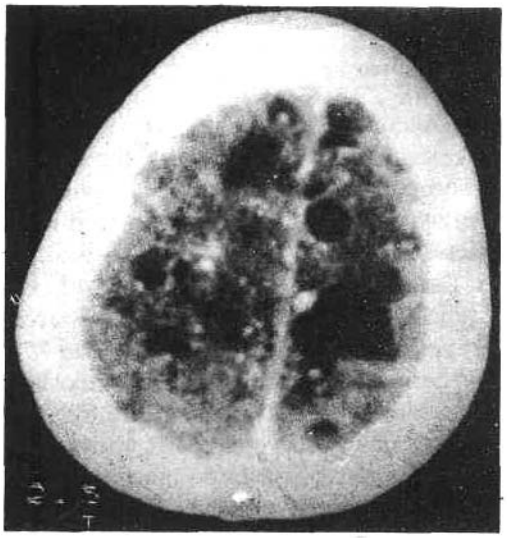

Fig. 1. Non-contrast enhanced cranial computerized tomographic scan showing multiple hypodense (cystic) lesions with eccentric hyperdensity representing scolices.

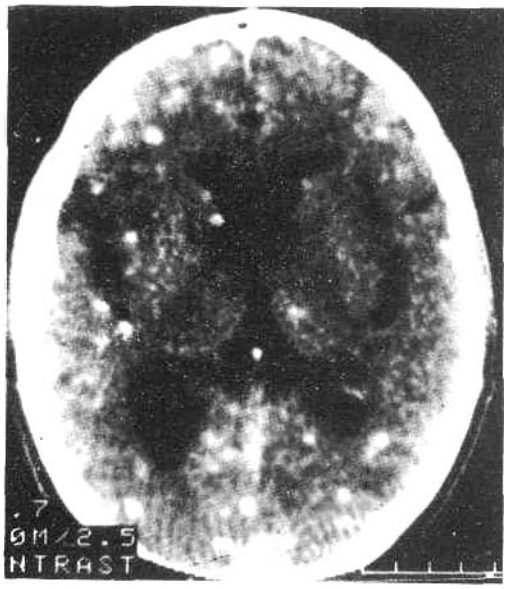

Fig. 2. Contrast enhanced cranial computerized tomographic scan showing multiple enhancing nodular lesions.

nodule which represents the scolex of larvae(6). CT is superior to MRI in the detection of calcified lesions but is far less sensitive in detection of early parenchymatous cysticerci, subarachnoid cysts and pericystic edema(7).

Further confirmation of diagnosis can be made with the help of serological studies. A number of workers have utilized a variety of serological techniques to detect antibodies in serum and CSF of patients with cerebral cysticercosis. Most of these techniques showed lack of specificity(1). In particular, cross reactions with various forms of other *Taenia* species and tissue parasites have been noted. The use of cyst fluid in the enzyme linked immunosorbent assay (ELISA) technique has recently been documented to provide more reliable serological data for the diagnosis of ne'urocysticercosis and indicate greater specificity when compared to studies using whole cysticercal preparations. Rosas *et al.(8)* reported 50% sensitivity with 70% specificity in serum, and 87% sensitivity with 95% specificity in CSF for diagnosis of active neurocysticercosis. The newer enzyme linked immuno-electrotransfer blot (EITB) assay developed by Tsang *et al.(9)* is reported to be 98% sensitive and 100% specific. Wilson *et al.* (10) reported further experience with the test performed on specimens from 50 patients and more than 100 patients with clinically suspected disease. In patients with two or more intracranial lesions the test was 94% sensitive, but in those who had only single lesion the sensitivity ranged from 28 to 78%.

Histopathology of biopsied subcutaneous nodule or other tissue specimen establishes the diagnosis(2).

Natural Course

Initially, cysticercal infection develop into a viable cyst representing larval form of the disease. For a variable period of time these cysts remain unchanged and exhibit a state of immune tolerance with the host(ll). Patient may have seizures, or may remain asymptomatic. CT scan shows circumscribed hypodense cystic lesions(12) *(Fig. 1)*. Eventually these cysts are attacked by the body immune defence mechanisms(13). the cysts now show signs of inflammation around them. In contrast-enhanced CT scan the lesions appear as nodular or ring lesions, along with surrounding edema *(Fig.* 2). So, these lesions represent dying cysts which are no more viable. At this stage patients have a much greater likelihood of being symptomatic(14). Ultimately, these lesions either disappear or heal by calcification. Calcified lesions are seen as small punctate hyperdense nodules on the plain CT scan(12). Calcified lesions may be a persistent focus for seizures recurrence. Few lesions may heal with tissue scarring(15).

Cysticercotic Encephalitis

Cysticercotic encephalitis is a peculiar variety of parenchyma! brain cysticercosis, much more likely to affect children and young adults(16-18).It produces a severe and frequently fatal neurological disorder. It is due to severe inflammatory reaction in brain parenchyma around innumerable cysts(16,17). As a result of diffuse brain-edema the patients develop intracranial hypertension, and deterioration of visual functions secondary to optic nerve damage(16-18). The condition represents an unusual response of host against dying cysts, rather than mere physical presence of viable cysts. It is more common in young females. An interaction between gender and HLA antigen present on cyst wall, has also been demonstrated^). The nature of the treatment in this condition is unsettled. Anticysticercal drugs are largely contraindicated due to high risk of exacerbation of manifestations which may be life-threatening. Patient may require gluco-corticoids along with other edema reducing measures. Few patients may even need shunt surgery(4,14,18).

Antihelminthic Treatment for Neurocysticercosis: Is it Required?

The, pediatric data regarding the untreated natural course of neurocysticercosis indicates that all patients given enough time may have improvement in CT appearances(14). The lesions either calcify or disappear spontaneously. Upto 55% of individual lesions may disappear(19). Moreover, the treatment with antihelminthic drugs (albendazole and praziquantel) is not free of side effects (headache, nausea, vomiting and seizures)(l,4,20). Antihelminthic drugs, probably, expedite the natural course of disease, and the chances of calcification or local scarring, are increased(20). Furthermore, intense inflammatory changes following antihelminthic treatment may lead to brain damage, and patient may be left with long-term sequelae in forms of dementia, blindness, and focal neurological deficits(21). The benefits of antihelminthic treatment are not conclusively proved, especially in children and

young adults who are more prone to develop adverse reactions(4,22).

Role of Glucocorticoids Along with Antihelminthic Therapy

Antihelminthics rapidly lead to parasite death producing exacerbations of symptoms. Patients may experience severe headache, nausea, vomiting and seizures. These symptoms are relieved by administration of glucocorticoids and other anti-edema measures(l,2,23). Few deaths due to increased intracranial pressure, following antihelminthic treatment have been reported(4,22). Instances of cerebral infarct in adults due to vasculitis precipitated by praziquantel despite premedication with dexamethasone has also been reported(24). It has also been shown that simultaneous administration of dexamethasone can reduce plasma levels of praziquantel by 50%, but may increase levels of albendazole(25). In Latin American countries glucbcorticoids are given till symptoms abate. However, in India it is recommended that all patients, especially children, receiving antiparasitic treatment should receive dexamethasone(4,l 1,26,27).

Single Enhancing Ring Lesions in Patients of Epilepsy

Single lesions that are enhanced in ring form after contrast administration, in CT scan, are frequent finding in children with epilepsy(28) *(Fig. 3).* The exact pathogenesis of these lesions is controversial. Previously, these lesions were considered as tuberculomas(29,30). However, several serological and brain biopsy based studies have shown that neurocysticercosis is the most likely cause of such lesions(31,32). In Latin American countries similar lesions are considered as a manifestation of neurocysticercosis(33). Until recently majority of such lesions were treated with antituberculous drugs(29,30). Some physicians avoid treating these enhancing lesions as they tend to disappear spontaneously(34,35). Treatment with antihelminthic drugs is recommended since these lesions are considered manifestations of neurocysticercosis(36,37). However, the role of antihelminthic treatment is doubtful because these lesions represent a dying cyst which do not require any definitive treatment(12,20). The underlying etiology in patients showing a persistent lesion is not well identified. In one recent uncontrolled study, Rajshekhar(36) showed that a course of albendazole led to early resplution of these persisting lesions. However, in a controlled double blind study which included both pediatric and adult patients, Padma *et al.(37)* could not demonstrate a benefecial effect of albendazole on the resolution of these lesions.

Anti-Epileptic Treatment in Patients of Neurocysticercosis

Other important issues in the management of neurocysticercosis are, how long should anti-convulsants be given? Does antihelminthic treatment help in curing the epilepsy in these patients? Studies done in Latin American countries suggest that antihelminthic treatment does affect the short term prognosis of epilepsy(38,39). Del Brutto *et al.(38)* observed that despite the excellent control of seizures with anticonvulsants following antihelminthic therapy, withdrawal of the former caused relapses of seizures. Another

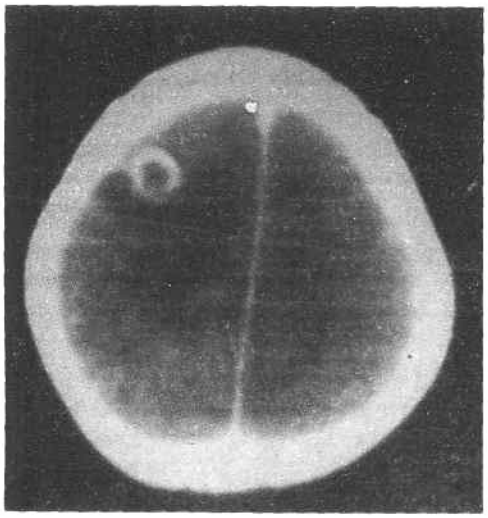

Fig. 3. *Contrast enhanced cranial CT scan showing 'single small enhancing ring lesion'.*

study(40) demonstrated that patients with residual calcification and those with multiple cystic lesions had a high rate of relapse after withdrawal of anticonvulsants despite having received a course of albendazole therapy. So if one has to take antiepileptic treatment (bearing its cost and adverse effects), probably there is little justification for costly antihelminthic therapy.

Conclusions

A mere improvement in CT picture and symptoms and signs does not represent a cure of disease. In asymptomatic subjects, treatment may present with complications, or even sudden death after long uneventful periods. In the current state of knowledge, it may be wise to leave the disease to follow it's natural course rather than artificially modifying it with antihelminthic drugs. Antihelminthic therapy is potentially risky and costly. The real solution of this serious problem lies primarily in the prevention of the disease.

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