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Review

Controversies in the treatment of seizures associated with neurocysticercosis

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ABSTRACT

Seizures are the commonest manifestation of brain parenchymal cysticercosis. In terms of pathophysiological basis and prognostic significance of the seizures, a distinction might be applied between viable cysts, solitary cysticercus granuloma and calcific cysticerci. A number of uncertainties shroud the management of seizures in people with neurocysticercosis (NCC). Although antihelminthic treatment is effective in eliminating viable cysts and possibly cysticercus granulomas, its effect on seizure outcome remains uncertain. Corticosteroids and combinations of antihelminthic and corticosteroid treatments reduce the incidence of seizures in the short term at least. Although antiepileptic drugs (AEDs) are routinely employed in the treatment of seizures associated with NCC, there is no clear consensus regarding the choice and optimal duration of AED treatment. Long-term AED treatment is warranted in people with calcific residue following involution of brain parenchymal cysticercosis.

This article is part of a Special Issue entitled "Neurocysticercosis and Epilepsy".

1. Introduction

Human infestation with the larval stage of the pork tapeworm, *Taenia solium* is known as neurocysticercosis (NCC). It is the putative cause of nearly one-third of epilepsies in *T. solium*-endemic regions of the world [1]. A meta-analysis revealed that 80% of people with NCC present with epileptic seizures [2]. The seizure outcome following a first seizure associated with NCC is quite unpredictable and probably depends upon the location, number and stage of the cysticercus. A follow-up study revealed that roughly a third of those with a first seizure will have a second seizure [3]. From a historical standpoint, seizures continued to occur till death in 34 out of 45 people British military personnel who acquired cysticercosis during overseas service in India [4]. Mortality in eight (24%) was attributed to status epilepticus. Treatment of seizures in those days comprised of bromides, phenobarbital and in some patients, Epanutin. The authors noted that while the antiepileptic drugs (AEDs) were able to control seizures to an extent, the prognosis of the disorder was not altered by treatment in any case. At that time, there was no specific (antihelminthic) treatment of cysticercosis.

Over the time elapsed since, highly effective antihelminthic drugs have been rendered available for the treatment of NCC [5,6]. In addition to antihelminthic drugs, corticosteroids are often administered on a short-term basis in order to ameliorate some of the symptoms of NCC. Finally, a range of AEDs apart from the three mentioned hitherto, are now available for the prevention of seizures in people with NCC. The availability of a range of modern medications notwithstanding, the treatment of NCC continues to be dogged with controversies. Among the controversies are whether treatment with antihelminthic agents is associated with any change in seizure outcome? Likewise, another question relates to the impact of corticosteroid administration on seizure control. Finally, a question that is rather difficult to answer because of lack of evidence relates to the choice and duration of AED therapy in NCC. We attempt to address these three questions in this brief review.

2. The basis of seizures in NCC: Relationship to evolutionary stages

Seizures are typically a manifestation of parenchymal cysticercosis (Fig. 1). Other anatomical sites, e.g., intraventricular and basal meningeal cysticercosis do not typically present with seizures [7,8]. One exception is a cysticercus located in the subarachnoid space in the depths of sulci in close relation to the cerebral cortex [9]. Presumably, degeneration of a cyst in subarachnoid space in the sulci leads to irritation of the subjacent cortex and hence, seizures.

In the cerebral parenchyma, the cysticercus proceeds through a series of evolutionary stages [9,10]. These stages have been described elegantly in pathological studies but are also quite clearly discerned in modern imaging studies, particularly magnetic resonance imaging (Fig. 2a–c). The imaging studies demonstrate a viable (live, also known as vesicular stage on pathological studies) cysticercus as hypodense (on computed tomography; CT) or T1-hypointense and T2-hyperintense cystic lesion/s with an eccentric scolex within but

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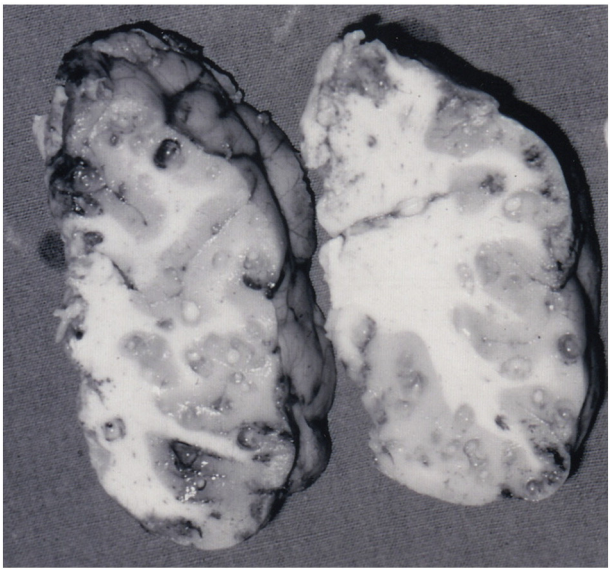

Fig. 1. Parenchymal cysticercosis: Multiple cysticerci located at the junction of the cerebral cortex and underlying white matter in post-mortem axial pathological sections of the brain.

no contrast enhancement or edema in the surrounding parenchyma (Fig. 2a). As the viable cysticercus begins to degenerate, the scolex loses its distinctive appearance and cystic contents are rendered less hypointense on T1 or less hyperintense on T2 images. In addition, the cyst wall begins to enhance following contrast administration and there appears edema in the surrounding parenchyma (Fig. 2b). In pathological studies, this stage is known as the colloidal stage as distinct from the subsequent granular-nodular stage (Fig. 2c). The latter is characterized by a nearly complete degeneration of the scolex and a granuloma like appearance on imaging studies. The colloidal and granular-nodular pathological stages together comprise the degenerating or involuting stages of the cysticercus, but with a fundamental difference as outlined below. The cysticercus eventually involutes to a fibro-calcified nodule with little surrounding inflammation, if any (Fig. 2d). This stage is traditionally known as the inactive or 'dead' stage of the cysticercus.

From the standpoint of the role of antihelminthic treatment, the cysticercus might be considered either viable (as long as the scolex within is clearly discernable) or non-viable (with no visible scolex). The viable stage thus might include the vesicular (or live, active) and colloidal stage. The scolex is nearly completely degenerate in the granular-nodular and more so in the fibro-calcified stages. From an intuitive standpoint, antihelminthic treatment is appealing in the viable stage.

Seizures occur during all involutional stages of the parenchymal cysticercus including the vesicular and fibro-calcified stages. Seizures

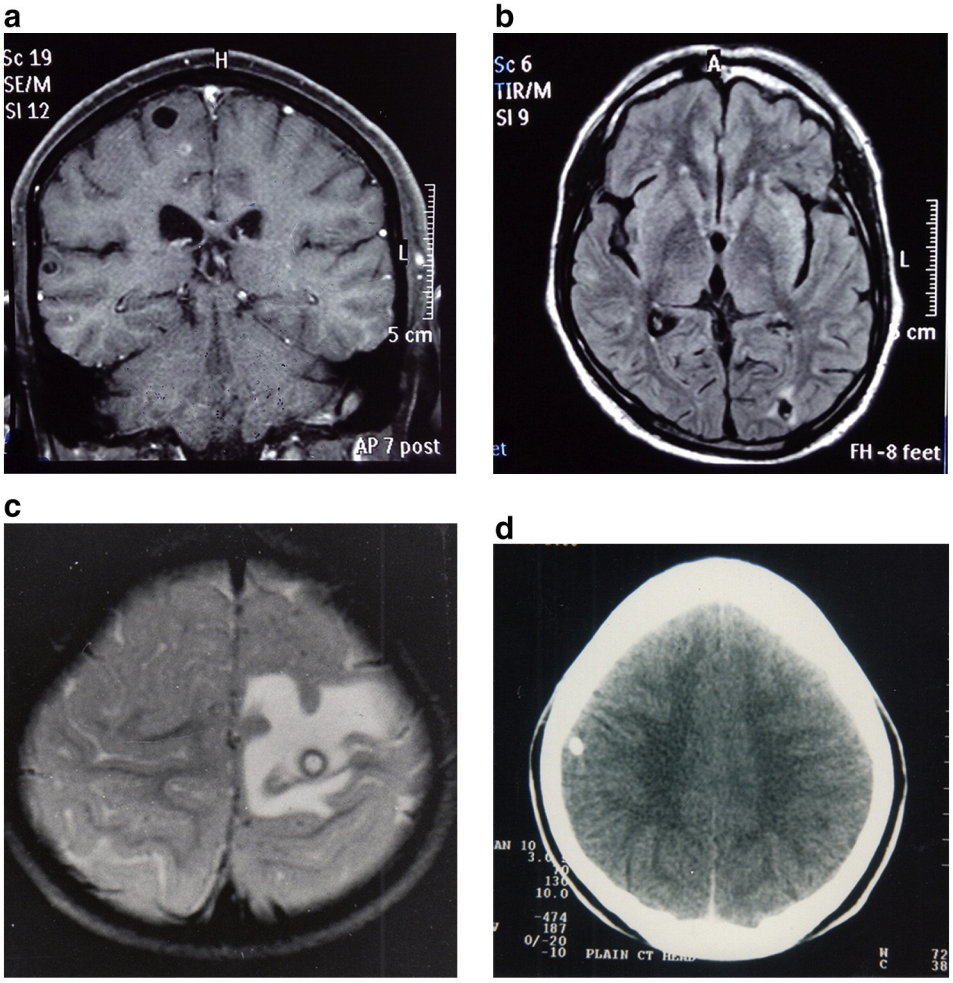

Fig. 2. Evolutionary stages of the cysticerci on imaging studies: (a) Vesicular stage (arrow) with eccentric scolex and no surrounding edema on a post-contrast (Gadolinium) T1 MR image; (b) Colloidal stage a cystic lesion with surrounding edema on an axial FLAIR image (Note the discernable scolex); (c) Granular-nodular stage on T2 MR image (Note the absence of the visualizable scolex); and (d) calcified stage on CT image.

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