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SHORT RESEARCH ARTICLES

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Intermittent perilesional edema and contrast enhancement in epilepsy with calcified neurocysticercosis may help to identify the seizure focus

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Abstract

Neurocysticercosis is a frequent cause of seizures in endemic countries. It is caused by the larvae of the tapeworm *Taenia solium*. The larvae once hosted in the cerebral parenchyma evolve into viable cysts, called the vesicular stage (with little or no inflammatory reaction), and may remain at this stage for years, or may enter in an inflammatory-degenerative process (colloidal phase) that ends with calcified nodules. Edema and MRI contrast enhancement associated with these calcifications have been described, suggesting that it may be associated with seizures. However, most of these reports were either cross-sectional case-control series or case reports with a single time point MRI. Therefore, the clinical significance of recurring perilesional edema and contrast enhancement around calcified lesions is still uncertain. Here, we describe repeated MRIs of a patient with calcified neurocysticercosis over 4 years. The seizures were associated with edema and contrast enhancement that disappeared in the seizure-free periods, occurring only around one calcified nodule that coincided with the EEG findings and seizure semiology, although he had three additional calcifications. These findings support the association between pericalcification contrast enhancement and edema with recent seizures. This MRI finding may be a marker to define the epileptogenic focus in epilepsies with calcified neurocysticercosis.

KEYWORDS

brain calcifications, computed tomography, focal seizures, magnetic resonance imaging, neurocysticercosis

1 | INTRODUCTION

Neurocysticercosis (NC) is the most common helminth infection of the central nervous system (CNS) and a frequent cause of seizures in endemic countries.[1,2] It is the result of infection by the larval stage of the tapeworm *Taenia solium*, which occurs when eggs excreted in the feces of an individual carrying the parasite are ingested through contaminated food and directly from a carrier via the oral-fecal route.[1–4] The natural course of brain injury of neurocysticercosis can be divided into four stages: vesicular, colloidal, nodular, and calcified.[2,3]

The larvae of the *Taenia solium* once hosted in the cerebral parenchyma evolve into viable cysts, called the vesicular stage, that may cause little or no inflammatory reaction. It may remain at this stage for years or may enter, as a result of a host immune attack in an inflammatory-degenerative

process, called colloidal phase, that ends with its transformation into mineralized nodules (calcification phase).[1–7]

Perilesional edema and contrast edema around calcified NC have been well described.[7–14] Postgadolinium MRI-enhancing calcified lesions are more likely to show perilesional edema and be associated with the occurrence of seizures.[8–10] However, the clinical significance of recurring perilesional edema associated with calcified lesions is still unclear.

2 | CASE REPORT

A 22-year-old man was followed since the age of two, due to recurrent focal and bilateral tonic-clonic seizures. He was healthy until April 1997, when he presented a seizure characterized by forced cephalic deviation and forced deviation of the gaze to the right, followed by clonic movements with right-sided predominance. He had a computed tomography (CT, 04/15/97), with a diagnosis of NC in the degenerative phase (not shown here). He was treated with albendazole for ten days and put on phenobarbital, with clinical improvement. In the years that followed, he had rare convulsive episodes. Subsequent CTs revealed calcified lesions in the right lentiform nucleus, right occipital lobe, left frontal and left precentral region, with contrast enhancement. In 2014, he had an MRI, which showed punctiform hypointense lesions (calcifications) without perilesional edema. In 2015, he had new convulsive seizures (similar semiology), with MRI (September 25, 2015) showing perilesional edema and contrast enhancement around the left precentral calcification (Figure 1). He was put on oxcarbazepine. Eleven months later (August 19, 2016), he had a new MRI that showed complete improvement of the perilesional edema and no significant contrast enhancement, during which time he was asymptomatic. One year later, he had a new lateralized convulsive seizure (similar semiology), and the MRI was performed five days after the event (August 9, 2017), again showing perilesional edema and contrast enhancement around the lesion in the left precentral region (Figure 1). Repeated electroencephalograms (EEGs) showed slow waves and epileptiform

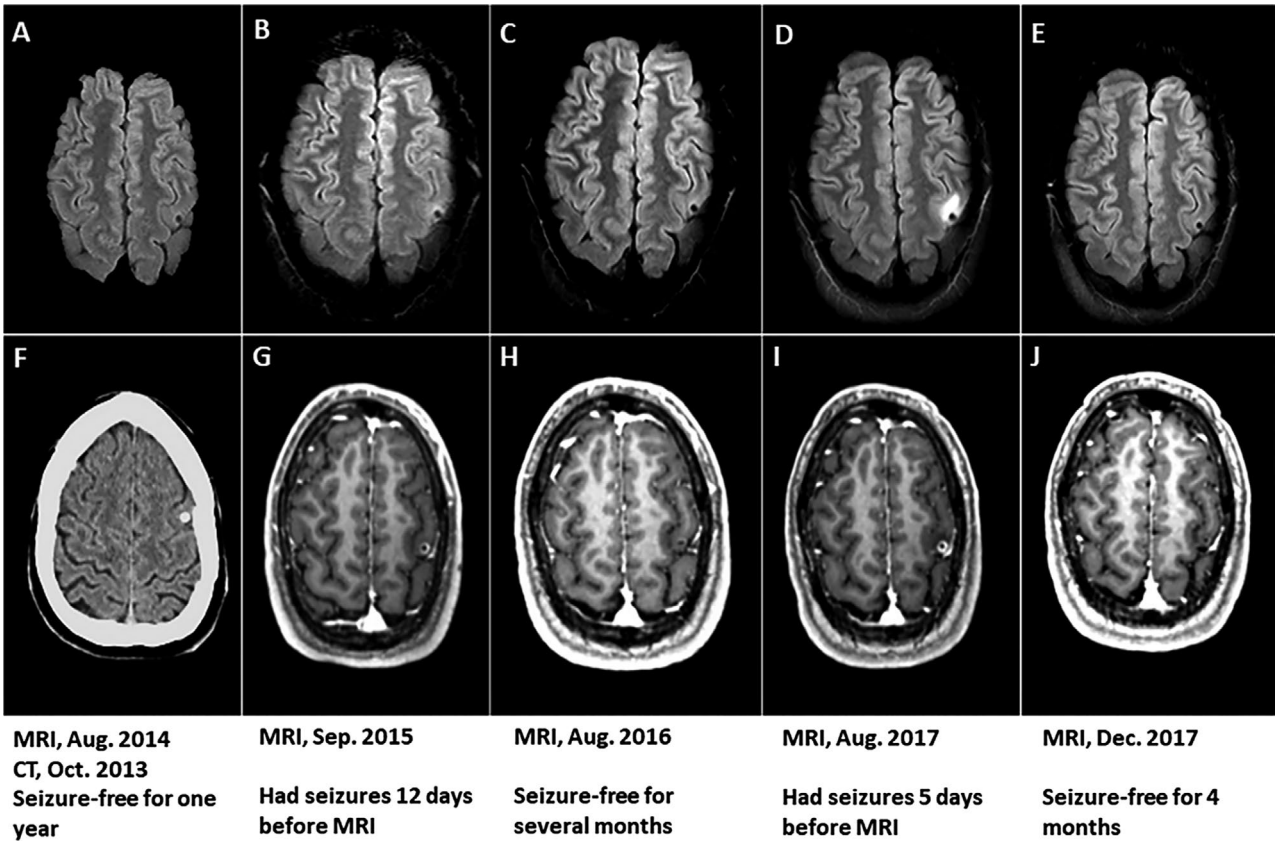

FIGURE 1 MRI and clinical evolution of calcified neurocysticercosis. A, C, E, Axial fluid-attenuated inversion recovery (FLAIR) MRI images are showing left precentral calcification (confirmed by CT scan, shown in F) without perilesional edema (August 29, 2014; August 19, 2016; December 7, 2017). B and D, FLAIR MRI showing the same left precentral calcification with perilesional edema (September 25, 2015; August 9, 2017). G and I, Postgadolinium T1-weighted spin echo images showing contrast enhancement around the left precentral calcification (September 25, 2015; August 9, 2017). H and J, Postgadolinium T1-weighted spin echo images are showing the left precentral calcification without significant contrast enhancement

discharges over the left centrotemporal area (Figure S1). At this time, the patient reported weight gain and opted to replace oxcarbazepine with lamotrigine (400 mg/day). Seizures were controlled, and in December 2017, the MRI did not show perilesional edema or contrast enhancement (Figure 1).

The patient signed an informed consent approved by the Ethics Committee of the University of Campinas.

3 | DISCUSSION

In this case, the acute onset of seizures was related to the degenerative phase of the NC lesions, which is already well established in the literature.[1–7]

Recent data show that calcified cysticerci are not completely inert as some of them they may cause recurrent seizures.[1–6] When parasitic antigens are trapped in the calcium matrix, they are exposed to the host immune system due to a calcification remodeling process.[5]

After the initial treatment, our patient remained asymptomatic for many years. The lesions were calcified years later (confirmed by CT). Repeated MRIs showed that the intermittent seizures were associated with the presence of perilesional edema and contrast enhancement that disappeared in the seizure-free periods.

In a study carried out to determine whether the calcified lesions received contrast after nodular involution and complete calcification, the authors observed that in some cases, the calcified lesions continued to present contrast enhancement for at least one year and concluded that this abnormality might be a risk factor for future seizures.[8] These results, in part, differ from the present case, because as we have seen, the injury was observed in the degenerative phase about 20 years earlier. One hypothesis that supports the persistence of enhancement in calcified lesions is that it may represent an injury that is not at full resolution, thus with local reactive cellular activity. It is possible that the persistent enhancement of calcified lesions is an additional risk factor for seizures.[4,7,9,10] However, its significance, potential, and clinical characteristics are still not well defined, since in some cases, symptomatic patients with perilesional edema around calcification are commonly diagnosed as refractory neurocysticercosis and treated unnecessarily with anthelmintics.[9]

Histopathological examination of inflammation associated with perilesional edema of calcified NC revealed significant extracellular fluid, which supports the concept that perilesional edema is inflammatory.[14] Some authors argue that perilesional edema is the result of an inflammatory process directed to the sequestered parasite antigen, so they advocate specific measures to limit the inflammation process, which can be used to treat or prevent complications.[9] Histological reports of calcified NC associated with episodes of perilesional edema on MRI showed intense inflammation with intracystic and intense capsular inflammatory response, consisting of mononuclear cells, plasma cells, and eosinophils around the degenerated cysticercus with a surrounding capsule.[14]

Another hypothesis is that perilesional edema occurs because of seizure activity.[10] However, there are differences between edema associated with seizures and calcified NC perilesional edema, the first being more diffuse, with no defined maximum area of activity, presumably of cytogenic origin.[5,6,10] In endemic regions, the number of patients with epilepsy and NC calcification is high;[1,4] however, not all calcifications present perilesional edema or enhancement contrast, as shown in our case. A plausible explanation is that not all calcified lesions are the same and may differ in their epileptogenic nature, as well as the amount of calcium deposition, the degree of antigens recognized by the host, the level of residual inflammation, or the proximity of a blood vessel,[9] leading to the occurrence of perilesional edema or enhancement contrast.

4 | CONCLUSION

This report demonstrates that some calcified cysts may have epileptogenic characteristics and that intermittent perilesional edema combined with contrast enhancement on MRI may serve as a marker of the seizure onset region when performed close to the occurrence of seizures. The edema and contrast enhancement around a calcified lesion may help to identify the seizure focus in patients with pharmacoresistant focal seizures associated with calcified NC.

DISCLOSURES

The authors have nothing to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

AUTHOR CONTRIBUTION

JMCJA: study concept, design, acquisition, analysis, interpretation of clinical data and drafting of the manuscript. FC: study concept, design, acquisition, analysis, interpretation of clinical data, revising the manuscript and supervision.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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