

CONGRUENCE OF THE TOPOGRAPHY OF INTRACRANIAL CALCIFICATIONS AND EPILEPTIC FOCI

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SUMMARY - Nodular intracranial calcifications (NIC) are frequent findings in CT scans of epileptic patients in countries where granulomatous central nervous disease such as neurocysticercosis is endemic. In 34 consecutive epileptic patients with NIC submitted to EEG, CT and CSF analysis, the correlation between the electroclinical localization of the focus and the topography of the NIC was studied. Twenty-nine patients had partial (Group I) and 5 had primarily generalized seizures (Group II). Twenty group I and 1 group II patients showed abnormal EEGs. CSF abnormalities consisted of increased protein content (n=3) and positive Weinberg's reaction (n=2). In 2 cases, viable neurocysticercotic vesicles were seen. Twenty-one patients had single NICs. No correlation could be established in group II patients. Within group I, 15 patients had a positive and 14 a negative correlation. Sixty-six percent of the patients with single NICs had negative correlations. These findings strongly suggest that the calcifications themselves are not the epileptogenic lesions in at least 50% of the studied cases.

KEY WORDS: epilepsy, calcifications, CT, EEG.

Congruência da topografia de calcificações intracranianas e focos epilépticos

RESUMO - Calcificações nodulares intracranianas (CIN) representam achado frequente em pacientes epilépticos de países onde doenças granulomatosas do SNC (p.e.: neurocisticercose) são endêmicas. Trinta e quatro pacientes epilépticos consecutivos com CINs foram submetidos a exame de EEG, TC e LCR. A correlação entre a topografia do foco e das calcificações foi estudada em cada caso. Vinte e nove pacientes tinham crises parciais (Grupo I) e 5 crises primariamente generalizadas (Grupo II). Vinte pacientes do Grupo I e 1 do grupo II tinham EEGs anormais. Hiperproteorraquia (n=3) e reação de Weinberg positiva foram as alterações encontradas no LCR. Em 2 casos, vesículas neurocisticercóticas íntegras foram vistas na tomografia. Vinte e um pacientes possuíam CIN única. Não foi possível realizar a correlação clínica nos pacientes do Grupo II. No grupo I, 15 pacientes apresentaram correlação positiva e 14 negativa. Sessenta e quatro por cento dos pacientes com calcificação única apresentaram correlação negativa. Estes achados sugerem fortemente que as calcificações não são epileptogênicas em ao menos 50% dos casos estudados.

PALAVRAS-CHAVE: epilepsia, calcificações, TC, EEG.

The current basic workup of an epileptic patient when first seen in an out patient basis includes clinical, electroencephalographic, hematologic, cerebrospinal fluid (CSF) and neuroradiological studies. Computed tomography (CT) studies carried out in developed countries have reported brain tumors, vascular abnormalities and atrophies as the main findings in secondary epilepsies^{2,5,6}. On the other hand, in developing countries, brain lesions related to infectious diseases are common and neurocysticercosis is the main granulomatous disease in many countries^{10,21}. There are active and inactive forms of the disease¹⁴. Calcifications might represent the final stage of many central nervous system (CNS) infections and they are the hallmark of the cicatricial form of neurocysticercosis¹¹. They appear after the death and reabsorption of the parasite and by that time,

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immunological response to cysticercotic antigens is usually absent¹⁶. Mixed forms, where viable vesicles and calcified lesions could be noted, may also be seen.

In this paper it is discussed the putative epileptogenic role of the nodular intracranial calcifications suggestive of granulomatous involvement of the CNS found in CT scans of epileptic patients.

METHODS

Thirty-four consecutive epileptic patients (12 males; 22 females) from the epilepsy out-patient clinic with CT scans showing nodular intracranial calcifications were studied. Age ranged from 10 to 62 years (mean = 32). Clinical history, neuroradiological data, CSF analysis and electroencephalographic (EEG) studies were obtained in all patients.

The classification of the epileptic seizures was based on the ILAE 1981 Classification of the Epileptic Seizures. Twenty-nine patients had simple or complex partial seizures (Group I), secondarily generalized or not. In 5 patients (Group II), only generalized tonic-clonic (n=4) and absences (n=1) were noted.

Neuroradiological studies included skull X-rays (frontal and lateral views) and axial CT scanning using a third generation scanner. Slices were 6mm thick and 10mm apart, following the orbitomeatal axis.

Several 8-channel interictal EEG recordings (range 3-7; mean = 4) were obtained in all cases including either spontaneous or induced sleep.

CSF was obtained through a suboccipital puncture. Intracranial pressure (initial and closing pressure), protein, glucose, chloride and cellular contents were analysed. Complement fixation reaction for cysticercosis (Weinberg test) was carried out in the CSF of all patients.

The possible correlation of the electroclinical focus and the topography of the calcification was established. Ample matching criteria were accepted so that any bias would go towards better positive correlations. For instance, patients with temporal lobe epilepsy and calcifications anywhere within the temporal lobe of the same side were defined as having a positive correlation. Patients with multiple calcifications with at least one of those matching the correct topography were also considered as having a positive correlation.

RESULTS

Twenty group I patients showed abnormal focal interictal EEG findings. The nine group I patients with no EEG abnormalities had simple partial motor seizures which presumably arised from the rolandic area, thus allowing the study of possible topographical correlations. All group II patients with generalized tonic-clonic seizures had normal EEGs and in the patient with absences, 3 Hz spike and wave complexes were recorded.

CSF abnormalities consisted of isolated increased protein content (n=3) and positive Weinberg's reaction (n=2).

CT abnormalities other than nodular intracranial calcification were also noted: in 2 patients focal atrophy was present and in another 2 cases viable cysticercotic vesicles were detected. The latter corresponded to the 2 cases with positive Weinberg's reaction.

Twenty-one patients had a single intracranial calcification but in 13, 2 or more lesions were detected. Only 2 patients had subcortical calcifications. The other calcifications had a cortical projection.

Table 1. Summary of the relationships found between the electroclinical localization and the topography of the calcification (s) in Group I patients and in the cases where a single nodular calcification was found.

	Group I N = 29	Single calcifications N = 21
Positive correlation	15	7
Negative correlation	14	14

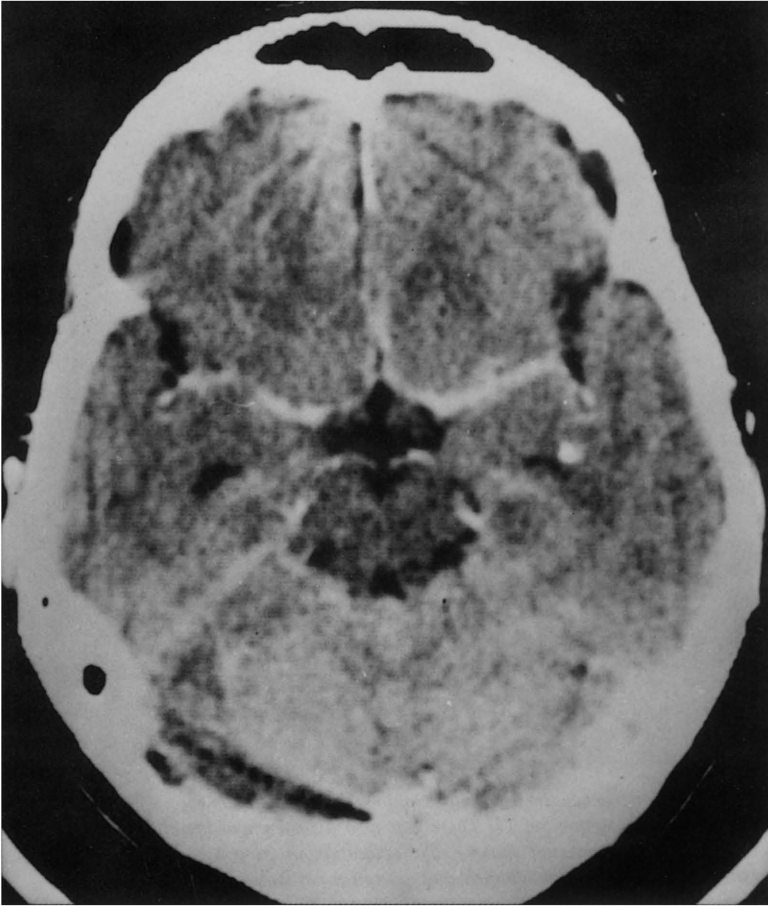


Fig 1. CT scan showing a LEFT hippocampal nodular calcification in a patient with an extremely active RIGHT temporal focus.

No correlation could be established in the patients with primarily generalized seizures. Within the 29 patients with simple or complex partial seizures (Table 1), 15 had a positive and 14 a negative correlation between the electroclinical localization and the topography of the calcification (Fig 1 and 2). Seventy-three percent of the patients with a positive and 64% of the patients with a negative correlation had an abnormal EEG.

Two of the 21 patients with a single intracranial calcification had basal ganglia lesions. In this group (n=21), 14 patients (including those 2 with subcortical calcifications) had a negative and 7 had a positive correlation .

COMMENTS

A high rate of negative correlations between the electroclinical localization and the topography of intracranial calcification was found in this study. This was true in approximately 50% of the cases. In patients with a single calcification, this rate was even higher: 66%. It should be emphasized that there was a strong bias towards a better positive correlation, so that these already high rates of negative correlation might actually be underestimated. These findings strongly suggest that the calcifications themselves are not necessarily the epileptogenic lesions in these patients.

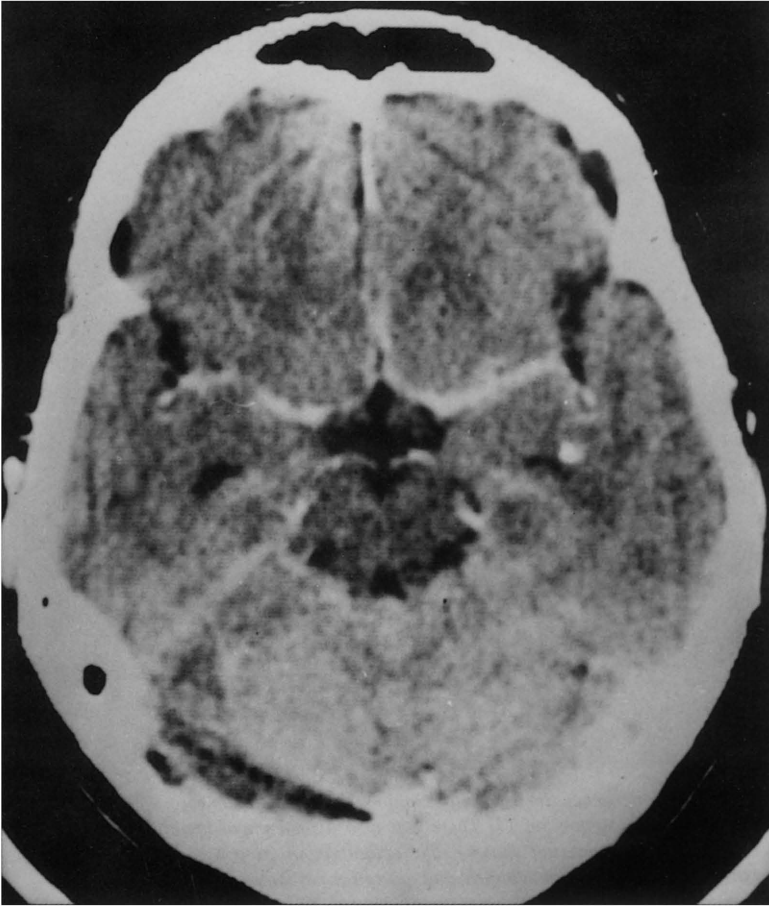


Fig 1. CT scan showing a LEFT hippocampal nodular calcification in a patient with an extremely active RIGHT temporal focus.

Routine 8-channel EEG recordings have a limited sensitivity in detecting epileptic abnormalities, ranging from approximately 100% in typical absences to around 40-70% in the simple and complex partial seizures.

In cases of partial seizures with a negative EEG, seizure's semiologic features (e.g., jacksonian march etc) may be used for the electroclinical localization. On the other hand, in patients with clinically primarily generalized seizures, semiology could not contribute to clinical localization.

CT is the best imaging method to detect intracranial calcifications^{3,9}. Very small calcifications could theoretically be missed by routine scanning but it is unlikely that this would happen with the nodular calcifications seen in neurocysticercosis.

MRI scanning was able to detect abnormalities in 70-90% of the epileptic patients with normal CT scans^{7,13}. The main findings were mesial temporal sclerosis, focal atrophies and gliosis^{1,17,18}. On the other hand, MRI diagnostic rate for small calcifications is poor⁸. Although there is no doubt that MRI is superior to CT in the diagnostic approach of the epilepsies, CT might represent the best technique in the detection of intracranial calcifications in countries where neurocysticercosis is endemic.

Several CNS diseases could yield intracranial calcifications as end-stage lesions. In developing countries, CNS infection/parasitosis are major causes of intracranial calcifications, especially in

neurocysticercosis^{4,15}. Discrepancies found between the topography of the calcifications and the electroclinical localization may be explained by several factors. Non-calcified scars, and not the calcifications may represent the actual epileptogenic zone. Coexistence of CNS parasitosis and other epileptogenic lesions, such as mesial temporal sclerosis and tumors is also possible. Multiple infestation is also an alternative explanation, since intact or dead parasites may appear isodense to the brain in CT scanning before calcifying or disappearing. Cisterna magna injections of cysticercotic antigens alone (derived from dead cysticercii) is able to trigger partial motor seizures in dogs (Machado and Cukiert, personal communication), suggesting that the immunologic response is per se able to stimulate focal epileptogenesis. We have treated cases of refractory temporal lobe epilepsy in whom CT has shown multiple calcifications but MRI has found clearcut mesial temporal sclerosis (Fig 1 and 2). Many of these cases, in whom the clinical symptomatology derived from the hippocampal pathology, were submitted to cortical and hippocampal resections disregarding the topography of the calcifications and were rendered seizure free by the procedure. Basal ganglia¹² and other massive cerebral calcifications^{19,20} are not epileptogenic.

In the process of epileptogenesis there is a latency for a lesion to produce enough functional abnormalities to trigger an epileptic seizure. Furthermore, the affected cortex has an epileptogenic threshold that depends both on the inhibition ability of the surrounding areas and the existence of pathways for seizure spreading.

In summary, even though intracranial calcifications may be gross cortical lesions, they are not the epileptogenic lesion in at least 50% of the studied cases. The cases in which 2 or more calcifications were noted and in whom only one of them was in agreement with the electroclinical localization are good examples of how similar lesions have a different epileptogenic behaviour depending on their topography. The mesial surface of the temporal and frontal lobes have lower epileptogenic thresholds when compared to other cortical areas.

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