Association between Clinical Features and Magnetic Resonance Imaging Findings in Patients with Temporal Lobe Epilepsy

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ABSTRACT

Background: Temporal lobe epilepsy (TLE) is the most common cause of partial seizures. However, there is a paucity of data on the correlation of clinical and semiological features of TLE with specific imaging findings on magnetic resonance imaging (MRI).

Objective: In this study, we sought to evaluate the association between the semiology of TLE with specific etiological findings as identified on MRI.

Materials and methods: This was a single-center, observational study in which consecutive patients presenting with clinical features diagnostic of TLE underwent a brain MRI on a 1.5 T scanner. The data collected from the various MR parameters were then correlated with history.

Results: A total of 90 patients were included in the study. The mean age of the study population was 29.1 years. Females comprised 45% of the study population. Mesial temporal sclerosis (MTS) was the most common imaging finding in about 60% of patients. Four out of five patients had aura whereas 70% had automatisms. The presence of aura in TLE patients was significantly associated with MTS on MRI (p = 0.042). The presence of automatism and history of childhood febrile seizure did not have a significant association with any specific etiological findings on MRI (p = 0.254 and 0.731, respectively). Drug-refractory epilepsy was commonly associated with the presence of MTS on MRI (p = 0.004). The presence of dual pathology on MRI was associated with drug-refractory epilepsy (p = 0.031).

Conclusions: The presence of aura and drug-refractory epilepsy point towards the presence of MTS. Dual pathology, on MRI, in TLE patients may be a risk factor for drug-refractory epilepsy.

KEY MESSAGE

The presence of aura and drug-refractory epilepsy predicts the presence of MTS as the cause of TLE and TLE patients with dual pathology on MRI are prone to drug-refractory epilepsy.

INTRODUCTION

Temporal lobe epilepsy is the most common cause of partial seizures in adults. It is clinically associated with cardinal semiologies like prodrome, aura, automatism, and altered consciousness. Patients usually have a family history of epilepsy and may also have a history of childhood-onset febrile seizures. Commonly, these seizures are refractory to drug therapy and may require surgery. MTS is the most common cause of TLE accounting for more than 80% of the cases.1 TLE can also be associated with numerous other causes like infections, malignancy, paraneoplastic syndromes, vascular malformations, or perinatal injury. Recognition of etiology is important for guided management strategy. MRI has revolutionized the detection and management of TLE and has an important role in guiding therapy.2 MRI features in TLE usually include a small hippocampus with hippocampal sclerosis (HS), a small temporal lobe, and an enlarged temporal horn.3 MRI can also be used to localize and characterize the lesions, help in predicting the etiology, and guide therapy.4

Studies on MRI findings on TLE have well described the various MRI features noted in this condition—the most common is HS.5-11 However, none of the studies have shown any correlation between imaging abnormalities and semiological features of TLE. In this study, our aim was to assess the correlation between specific clinical and semiological features of TLE with the etiology of TLE identified on MRI and other imaging findings.

MATERIALS AND METHODS

Our study was a single-center hospital-based observational study. Patients presenting with clinical features diagnostic of TLE were included in the study. Patients who had another neurological disease, who were not able to undergo imaging (claustrophobia, contrast allergy, and pacemaker implantation), and those who were not willing to take part in the study were excluded. The study period extended from January 2016 to January 2017. All patients were clinically evaluated for semiology and clinical characteristics of TLE including prodrome, aura, automatism, history of febrile seizures, drug history, and prior treatment history.1 Febrile seizure was defined in accordance with the International League Against Epilepsy as “a seizure occurring in childhood after one month of age associated with a febrile illness not caused by a central nervous system infection, without previous seizures, and not meeting the criteria for any other acute seizures.” All clinical data were recorded using a structured questionnaire. All study participants subsequently underwent brain MRI in a 1.5 T MR scanner (GE SIGNA). The routine protocol consisted of T1 weighted axial (slice thickness 5 mm) and sagittal, T2-weighted axial and sagittal, FLAIR axial and coronal, susceptibility-weighted imaging and diffusion-weighted imaging sequences, and postcontrast studies were performed in all patients following a standard epilepsy protocol. The data collected from the various imaging parameters were then analyzed to identify the underlying pathologies/etiologies. Increased hippocampal signal intensity and reduced size of the hippocampus were considered diagnostic of MTS. These imaging findings were then correlated with the history and clinical features of the patients in order to derive a clinical association.

Statistical Analysis

All the data were recorded in tabular format in Microsoft Excel. All statistical analysis was done using SPSS software v20. Data were divided into categorical and continuous variables. Student’s t-test and analysis

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of variance were used to study statistical significance between groups of continuous variables. Chi-square test was used to evaluate the relationship between categorical variables. 

\( p \)-value < 0.05 was considered to be significant.

**Results**

A total of 90 patients with clinical features of TLE were included in the study. The mean age of the study population was 29.1 years (range 3–62 years). Females comprised 45% of the study population. Most of the TLE cases occurred in the 20–39 years age group (young adult) (43.3%). Specific etiological findings on MRI were detected in 80% of the study population. MTS was the most common etiology of TLE (62.5%) followed by tumors (12.5%) (Table 1 and Figs 1A and B). Out of the nine cases of tumors, there were two cases of ganglioglioma, two cases of low-grade glioma, two cases of metastases (Figs 2A to D), one case each of high-grade glioma, pleomorphic xanthoastrocytoma, and dysembryoplastic neuroepithelial tumor. Infectious etiology was noted in around 10% (\( n = 7 \)) of the study group. Tuberculoma was detected in three cases whereas herpes encephalitis (\( n = 2 \)) (Figs 3A and B) and neurocysticercosis (\( n = 2 \)) (Figs 4A and B) were noted in others. Chronic infarct was the most common ischemic cause among adults and periventricular leukomalacia (PVL) was the most common ischemic cause among children in our study. About 4% (\( n = 3 \)) of the study patients were detected to have developmental abnormalities. Focal cortical dysplasia (FCD) was noted in two patients whereas gray matter heterotopia was found in one patient.

Table 2 shows the prevalence of various clinical parameters in the study population. Out of 90 cases, maximum cases had automatism (83.33%) and 71.11% of cases had aura. Fifty cases had both aura and automatism (55.56%) during seizures. About 15.56% of patients had a history of febrile seizures in childhood. About 46.66% of patients had refractory epilepsy.

Aura was noted in about 70% (\( n = 51 \)) of TLE patients who had specific etiological findings on MRI. MTS was the most common etiology (72.5%) noted in this group of patients (Table 3). A significant association was noted between the presence of aura and specific etiological findings on MRI (\( p = 0.042 \)). History of automatism was noted in about 85% of the study group with MTS being the most common associated etiology on MRI (Table 3). History of automatism had no significant association with the specific etiology of TLE (\( p = 0.254 \)).

Fourteen patients had a history of childhood febrile seizures and eight of them had abnormality on MRI. Six patients had a positive history of childhood-onset febrile seizures, however, no abnormality was found on MRI. There was no significant relationship between the history of childhood-onset febrile seizures with various etiologies of TLE (\( p = 0.731 \)) (Table 4). It was seen that the history of childhood-onset febrile seizures did

Figs 1A and B: Brain MRI T2/FLAIR image (A) in a patient with TLE showing hyperintensity and atrophy of the left hippocampus (white arrow). T1 axial image (B) shows dilatation of the temporal horn of the left lateral ventricle (white thick arrow)—features suggestive of MTS.
Association between Clinical Features and MRI Findings

not predict the occurrence of MTS in later life \((p = 0.561)\). Out of the 90 patients in the study population, 42 had drug-resistant epilepsy. There were only three patients in whom there was a positive history of refractory epilepsy, however, no abnormality was found on MRI, 39 patients had an MRI abnormality (Table 4). Drug-refractory seizures were most commonly associated with mesial temporal lobe sclerosis on MRI \((p = 0.004)\).

Dual pathology on MRI was noted in about 8\% \((n = 7)\) of the study population. MTS was found in all seven patients associated with FCD in four patients (Figs 5A and B). Heterotopia, PVL, and cavernous malformation were noted in the other three patients. The presence of dual pathology on MRI was significantly associated with drug-resistant epilepsy \((p = 0.031)\).

Among the broad etiological groups causing TLE, the lateralization of temporal lobe abnormalities was studied and the result was not statistically significant, that is, the lesions had no preferred lateralization—left or right. Among the MTS group, 25 (55.56\%) patients had lesion on the left side, 14 patients on the right side, and six patients had lesions bilaterally. No significant difference was noted among the groups \((p = 0.644)\).

Six MRI features of MTS were specifically evaluated: (1) increased signal intensity of the hippocampus, (2) reduced size of the hippocampus, (3) atrophy of the white matter of the ipsilateral hippocampus, (4) enlarged temporal horn of the ipsilateral side, (5) reduced gray-white matter demarcation in the temporal lobe, and (6) decreased size of the temporal lobe. In our study, we used the increased signal intensity of the hippocampus and reduced size of the hippocampus as prerequisites for defining cases of “hippocampal/mesial temporal sclerosis.” There were 45 cases which fulfilled these criteria. Table 5 shows the prevalence of various imaging features of MTS. Out of 90 patients, six had cerebellar atrophy on imaging and all six cases of cerebellar atrophy were found in those patients who had an imaging diagnosis of MTS. Cerebellar atrophy was significantly associated with the presence of MTS in our study \((p = 0.048)\).

**Discussion**

Our study showed that MRI has a sensitivity of 80\% in the detection of the etiology of TLE. The study conducted by Lehéricy et al. also showed that in TLE, no specific abnormality was found on MRI in 20\% of the cases. Another study also mentioned the sensitivity of MRI in the detection of structural temporal lobe lesions like tumors, vascular malformations, etc. to be 90\%.

![Figs 2A to D: Brain MRI in a patient with epileptic seizures](image)

![Figs 3A and B: MRI brain in a follow-up patient with herpes encephalitis](image)
the present study, MTS was the most common etiology of TLE comprising 62.5%, followed by tumors (12.5%), similar to previously published studies.5,6 Lehéricy et al. showed that HS was the most common cause in patients with TLE (50–70%), followed by tumors (10–15%), developmental abnormalities (5–7%), vascular malformations (mostly cavernous malformations, 1–5%), and traumatic scars (5–10%).

The prevalence of aura and automatism in our study population was 71 and 83%, respectively. In a previous study, a large number of patients with TLE demonstrated or described an aura, which was typically of short duration. About 40–80% of the patients in this study had automatisms during a seizure.12 MTS emerged to be the most common etiology in patients describing aura or automatism in our study group.

In the present study, there was no significant relationship between the history of childhood febrile seizures with various etiologies of TLE or with the occurrence of MTS in later life. Our findings correlate well with the study by Tarkka et al. which showed that the relationship of MTS with febrile seizures is controversial. Up to one-third of patients with refractory TLE have a history of febrile seizures. Follow-up of the children with a history of febrile seizures did not demonstrate a statistically significant increase in the incidence of TLE in this study.13 Another study by Labate et al., however, showed that febrile seizures were more frequent in patients with MTS detected on MRI (36%) as compared with those with normal MRI (22.7%), but again, this difference was not significant.14

In our study, out of 90 subjects, 42 had drug-refractory epilepsy. Previous studies have described the prevalence of drug-refractory

Table 4: Number of cases with a history of febrile seizures and refractory epilepsy among the etiological groups

| Etiologies detected on MRI | Number of cases with a history of febrile seizures in childhood (percentage) | Number of cases with refractory epilepsy (percentage) |
|---------------------------|------------------------------------------------------------------------------|-----------------------------------------------------|
| MTS                       | 6 (75%)                                                                      | 27 (69.2%)                                          |
| Tumors                    | 1 (12.5%) (high-grade glioma)                                                | 7 (17.9%)                                           |
| Developmental             | 1 (12.5%) (heterotopia)                                                     | 3 (7.7%) (FCD = 2 and heterotopia = 1)              |
| Ischemic                  | 0                                                                            | 1 (2.6%) (chronic infarct)                          |
| Vascular malformation     | 0                                                                            | 1 (2.6%) (cavernoma)                                |
| Total                     | 8 (100%)                                                                     | 39 (100%)                                           |

Table 5: The prevalence of various imaging features of MTS

| Serial number | Imaging finding                                         | Number of patients (n = 45) | %   |
|---------------|---------------------------------------------------------|-----------------------------|-----|
| 1             | Increased hippocampal signal intensity (essential criteria) | 45                          | 100 |
| 2             | Reduced hippocampal size (essential criteria)           | 45                          | 100 |
| 3             | Atrophy of the ipsilateral hippocampal collateral white matter | 35                          | 77.77 |
| 4             | Enlarged ipsilateral temporal horn                      | 44                          | 97.77 |
| 5             | Reduced gray-white matter demarcation in the temporal lobe | 27                          | 60.00 |
| 6             | Decreased temporal lobe size                            | 20                          | 44.44 |
epilepsy to be 40% among patients with TLE. We observed that those patients who have refractory epilepsy are more likely to have an abnormality on MRI than those who do not. This finding is in agreement with the study by Lehéricy et al. which showed that only 8.5% of cases of refractory epilepsy did not demonstrate any specific abnormality on MRI.

Cendes et al. showed that MTS is associated with other extrahippocampal anomalies which could be epileptogenic in 15% of cases. The presence of such dual pathologies was associated with a poor postoperative prognosis and refractory epilepsy in their study. Indeed in our population also, similar findings were noted.

The term mesial temporal sclerosis was coined by Falconer et al. to describe a lesion with gliosis and neuronal loss involving mainly the amygdala and the hippocampus, or both, but sometimes involving other temporal lobe components or even the whole temporal lobe, leading to generalized atrophy and gliosis. T2/FLAIR hyperintensity of the hippocampus and hippocampal atrophy were the most prevalent findings in our population. Enlarged ipsilateral temporal horn was found in 97.77%. Various studies propose that the FLAIR sequence is ideal to identify hippocampal signal abnormalities since water content increases with gliosis which appears as an increased signal on T2-weighted MRI. The FLAIR sequence nulls the bright signal because of the cerebrospinal fluid, hence, the increased signal of the hippocampus is more apparent.

In our study, there was a significant association between the occurrence of cerebellar atrophy and the presence of MTS. However, this is in contrast to a study published by Hagemann et al. in which the results did not support the concept that cerebellar atrophy predisposes to epilepsy rather, the authors were of the view that cerebellar atrophy is the result of epileptic seizures or antiseizure drugs. The current study has inherent limitations. As the present study was conducted in a tertiary level center, the study population may not be representative of the general population with TLE. So, to further support our results and observations, studies with more sample size are warranted. Many patients were lost to follow-up. Many newer technologies could not be utilized in our study like spectroscopy and volumetry. Histopathological confirmation also could not be obtained for most of the cases.

**Conclusion**

The presence of aura and drug-refractory epilepsy predicts the presence of MTS as the cause of TLE. The presence of automatism and history of childhood-onset febrile seizures did not predict the etiology of TLE in our study. TLE patients with dual pathology on MRI are prone to drug-refractory epilepsy.

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