Structural Brain Lesions in Epilepsy Patients: An Experience from Northeast India

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Abstract

Objectives The aim of this article was to study the various structural causes and role of magnetic resonance imaging (MRI) in epilepsy patients.

Materials and Methods A 4-year retrospective cross-sectional study was conducted in Northeast India. The MRI brain findings of epilepsy patient were collected and analyzed for the years 2017 to 2020.

Result A total of 630 patients of epilepsy underwent MRI brain with normal findings noted in 280 patients (44.4%). The other groups of 350 epilepsy patients (55.5%) had abnormal MRI brain findings and were included in the study with a minimum age of 2-month old and a maximum of 80 years. The most common abnormal MRI finding belongs to the infectious group (33.7%), with neurocysticercosis being the most common infectious etiology (p-value < 0.001). Gliosis was seen in 57 patients (16.3%), mostly in the middle-aged group. Vascular etiology was seen in 44 patients (12.6%), mostly in the middle-aged group. Features of hypoxic brain injury was seen in 26 patients (7.4%), mostly among patients of < 18 years age. Mesial temporal lobe epilepsy was seen in 45 patients (12.9%), mostly seen in the adolescent. Neuronal migration defect was seen in 23 patients (6.5%), mostly among adolescent and young adults. Other abnormal MRI findings were tumor in 8 patients (2.3%), diffuse gyral swelling in 11 patients (3.1%), Rasmussen encephalitis in 4 patients (1.1%), neurocutaneous syndrome in 4 patients (1.1%), radiation necrosis and cyst in 1 patient each, Dyke-Davidoff-Masson syndrome in 3 patients, moyamoya disease in 1 patient, posterior reversible encephalopathy syndrome in 2 patients, and vasculitis in 4 patients.

Conclusion MRI brain is the key investigation to identify the epileptic focus in epilepsy patients helping in their further treatment and prognosis.
**Key Message**

Magnetic resonance imaging of brain with a dedicated epilepsy protocol has a higher rate of detecting epileptogenic focus. It helps to understand the epileptic focus, prognosticate patients and offer the various treatment pillars.

**Introduction**

Epilepsy is a chronic neurological disorder with an estimated lifetime prevalence of around 10%. However, the prevalence rates in India vary widely, that is, ranging between 1.3 and 11.9 per 1,000 population. Etiological classification is known, with structural brain lesion being an important cause. Epilepsy patients once diagnosed clinically need an etiological cause to be labeled. Clinical diagnosis is based on age, seizure semiology, and electroencephalogram (EEG) findings. For the identification of a structural lesion (which is the seizure focus, helping us to label specific epilepsy syndrome), neuroimaging is required. The chance of recurrence after a first seizure remains an important concern. Detection of the underlying structural lesion by neuroimaging helps in all aspects of diagnosis, treatment, and predicting recurrence or prognosis. A computed tomography (CT) imaging can detect gross abnormality like tumors and infarct but magnetic resonance imaging (MRI) allows the detection of subtle parenchyma abnormality like focal cortical dysplasia (FCD) and hippocampal sclerosis. An unusual cause or atypical clinic-radiological finding brings a challenge, but appropriate use of the various MRI sequence helps us to detect the foci. The risk of recurrence is poorly predicted by EEG, but the presence of abnormal MRI findings helps in predicting the risk of recurrence, thus it should be considered as a routine test for epilepsy.

With this background, we aim to:

- Evaluate the various abnormal MRI neuroimaging findings in our epilepsy patients.
- Find out the most common etiology with age-wise distribution.

**Materials and Methods**

This was a retrospective study performed by the departments of neurology and radiology in a referral center in Northeast India. All the abnormal neuroimaging (MRI brain) of epilepsy patients who underwent MRI in our radiology department were taken as data from the years 2017 to 2020. These epilepsy patients were from different age groups, sex, and departments. The division of age groups was as follows:

- Infant and toddlers: <2 years
- Preschool age group: 2 to 6 years
- School age group: 6 to 12 years
- Adolescent: 12 to 18 years
- Young adults: 18 to 25 years
- Adult: 25 to 40 years
- Middle-aged adult: 41 to 60 years
- Aged: >60 years

Data like age, sex, abnormal MRI findings, and clinical seizure semiology of the patients were included with an aim of understanding and correlating the various structural abnormal neuroimaging finding. The MRI examination was performed on a 1.5 Tesla machine. The standard protocol used included axial T1, T2, fluid-attenuated inversion recovery, diffusion-weighted imaging, susceptibility-weighted imaging (SWI), gradient-recalled echo (GRE), sagittal and coronal T2, and specific epilepsy protocol, and T1 contrast gadolinium was administered when required as decided by the radiologist.

Data were then collected and analyzed using SPSS-23 software. A nonparametric chi-squared test of independence was used to find out the significance among the various variables.

**Result**

A total of 630 epilepsy patients from various departments underwent MRI brain consecutively within the span of 4 years. Normal MRI brain findings were noted in 280 patients (44.4%) while the rest 350 epilepsy patients (55.5%) had abnormal MRI brain findings. These epilepsy patients with abnormal MRI findings were included as the study group of interest. The minimum age included was 2 months while the maximum was 80 years with a mean of 26.40 ± 16.87. The maximum numbers of patients were in the adult age groups (24%) of 26 to 40 years followed by the adolescent age group (19.4%) of 12 to 18 years. The aged (>60 years) group had the least number, with 13 patients (3.7%). Males (61%) were more in number in the study group as compared with females (39%), as given in Table 1. The seizure semiology was equaled between focal and generalized onset, but this could be biased on history taking and eye witness availability.

Several abnormal MRI brain findings were noted among our epilepsy patients (Fig. 7). The most common finding is the infectious group seen in 33.7%, mostly in the adult age group. Here, the most common was neurocysticercosis (NCC) in 79 patients (66.9%), followed by tuberculosis in 31 patients (28%). The other infections noted were Japanese encephalitis, herpes meningoencephalitis, cytomegalovirus, hydatid cyst, and neurosyphilis (Table 2). The next common MRI finding was gliotic scar seen in 57 patients (16.3%), mostly in the middle-aged adult group. Vascular etiology was seen in 44 patients (12.6%), mostly in the middle-aged group. This vascular etiology included infarct (23 patients), cortical venous thrombosis in six patients, cavernoma in four patients, vasculitis in four patients, arteriovenous malformation (AVM) in two patients, dural sinus malformation in one patient, posterior reversible encephalopathy syndrome (PRES) in two patients, and traumatic intracranial bleed (intracerebral hemorrhage) in one patient. The patients of vascular etiology and meningoencephalitis who presented with seizure developed epilepsy as a sequelae to the acute insult. Features suggestive of hypoxic brain injury was seen in 26 patients (7.4%), mostly distributed among adolescence and children of <18 years; these included mostly perinatal
Epilepsy is an illness of the brain characterized by its ability to generate abnormal electrical activity leading to recurrent seizure, and cognitive, psychological, and social consequences. Epilepsy is defined by International League of Epilepsy (ILAE; 1993) as a condition characterized by recurrent (two or more) epileptic seizures, unprovoked by any immediate identified cause. Eighty percent of the worldwide epilepsy patients reside in the developing countries, out of which 10 million live in India. Its prevalence is ranged widely from 17 to 91%.

Table 1 Base line variables among our epilepsy patients

<table>
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<tr>
<th>Age groups</th>
<th>Count (n = 350)</th>
<th>%</th>
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<tr>
<td>Infant and toddlers</td>
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<td>4.9</td>
</tr>
<tr>
<td>Preschool children</td>
<td>13/350</td>
<td>3.7</td>
</tr>
<tr>
<td>School children</td>
<td>39/350</td>
<td>11.1</td>
</tr>
<tr>
<td>Adolescent</td>
<td>68/350</td>
<td>19.4</td>
</tr>
<tr>
<td>Young adult</td>
<td>59/350</td>
<td>16.9</td>
</tr>
<tr>
<td>Adult</td>
<td>84/350</td>
<td>24.0</td>
</tr>
<tr>
<td>Middle-aged adult</td>
<td>57/350</td>
<td>16.3</td>
</tr>
<tr>
<td>Aged</td>
<td>13/350</td>
<td>3.7</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>212/350</td>
<td>60.6</td>
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<tr>
<td>Female</td>
<td>138/350</td>
<td>39.4</td>
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<tr>
<td>Seizure semiology</td>
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<td></td>
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<tr>
<td>Generalized</td>
<td>179/350</td>
<td>51.1</td>
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<tr>
<td>tonic-clonic seizure</td>
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<td></td>
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<tr>
<td>Focal</td>
<td>171/350</td>
<td>48.9</td>
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Table 2 Various infectious etiologies noted on MRI brain among the epilepsy patients

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<th>Infectious group</th>
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<th>Column (%)</th>
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<tr>
<td>NCC</td>
<td>79/118</td>
<td>66.9</td>
</tr>
<tr>
<td>TBM</td>
<td>4/118</td>
<td>3.4</td>
</tr>
<tr>
<td>Tuberculoma</td>
<td>29/118</td>
<td>24.6</td>
</tr>
<tr>
<td>Herpes</td>
<td>1/118</td>
<td>0.8</td>
</tr>
<tr>
<td>Hydatid cyst</td>
<td>1/118</td>
<td>0.8</td>
</tr>
<tr>
<td>JE</td>
<td>2/118</td>
<td>1.7</td>
</tr>
<tr>
<td>Neurosyphilis</td>
<td>1/118</td>
<td>0.8</td>
</tr>
<tr>
<td>CMV</td>
<td>1/118</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Abbreviations: CMV, cytomegalovirus; JE, Japanese encephalitis; MRI, magnetic resonance imaging; NCC, neurocysticercosis; TBM, tubercular meningitis.

Note: p-Value < 0.001.

In an acute setting, CT brain is the first-line tool due to its rapid availability, and faster and less motion artifact. It rapidly rules out mass or a hemorrhage, which requires urgent neurosurgery intervention. It is adequate to detect encephalomalacia and infections, and can also contribute to diagnosis as an abnormal CT in a seizure patient predicts a high chance of recurrence in the next 6 months. CT brain used to be the neuroimaging of choice in most health care settings due to resource reasons and culture. However, now that has been overruled by MRI brain. MRI brain in a negative CT helps to detect a subtler lesion that accounts for seizure. MRI brain has a higher diagnostic yield in epilepsy as compared with CT brain. The diagnostic yield of MRI in focal epilepsy patients ranged widely from 17 to 91%. MRI brain in epilepsy patients has to be performed with proper epilepsy protocols and optimization of the various sequences in mind. A correlation of seizure semiology, and EEG finding by a radiologist help to minimize the MRI negative patients. MRI protocol has been recommended and published. For the detection of
hippocampal sclerosis, thin (<3 mm) images parallel to the hippocampal plane, volumetric T1-weighted images, and others are a must. Neuroimaging is done in all epilepsy patients unless a specific clinical and electro-diagnosis of idiopathic epilepsy is made. Refractory epilepsy has around 80% abnormal MRI findings and 20% among first unprovoked seizure. Thin slice of 3 mm with no interspace gap is used to detect cortical and subcortical signal changes. Cortical thickening, gray–white matter interface blurring, and associated signal abnormalities may be more apparent on coronal than on axial images.\textsuperscript{25} Calcification, hemorrhage, or an occult vascular abnormality is picked up better by using the T2-weighted GRE or SWI sequence.\textsuperscript{26} Tumors account for 25 to 35% of pathologic specimens obtained from operation centers for epilepsy. The common tumors are gangliogliomas,
Fig. 5  (A, B) Magnetic resonance imaging (MRI) brain axial fluid-attenuated inversion recovery (FLAIR) and T2-weighted imaging showing diffuse atrophy of the left cerebral hemisphere with periventricular cystic encephalomalacia and ex-vacuo dilatation of left lateral ventricle. Enlargement of the left frontal sinus, and mastoid antrum with ipsilateral calvarial thickening. (C) Coronal FLAIR showing hyperintensities in right hippocampus with mild atrophy. (D, E) MRI brain axial and coronal FLAIR showing right sphenoid wing hypoplasia, dilated cerebrospinal fluid spaces in middle cranial fossa, and anterior displacement of right temporal lobe. (F) MRI brain axial T1-weighted imaging postcontrast study showing a well-defined ring enhancing lesion in right frontal lobe.

Fig. 6  Magnetic resonance imaging brain axial T2-weighted imaging, T1-weighted imaging, fluid-attenuated inversion recovery, and sagittal T2-weighted imaging showing a loss of deep white matter volume evidenced by thinning of gyri and prominent sulcal spaces in bilateral cerebral hemispheres resulting in diffuse cerebral atrophy. Resultant dilatation of the ventricular system noted. There is severe thinning of corpus callosum.

Fig. 7  Radiological classification of abnormal magnetic resonance imaging brain findings in our epilepsy patients (p-Value < 0.001). MTLE, mesial temporal lobe epilepsy.
dysembryoplastic neuroepithelial tumors, and pleomorphic xanthoastrocytomas. Other epilepsy-associated tumors are low-grade gliomas (oligodendrogliomas and astrocytoma) and low-grade mixed glial tumors and mixed glial-glioneuronal tumors.27

When epilepsy-dedicated MRIs were compared with standard protocol, it showed that standard MRI fails to detect abnormality in almost 57% of patients.20 Other studies also confirm it, showing the importance of epilepsy-dedicated protocol MRI.28 The diagnostic yield of neuroimaging in patients with first-onset seizures is reported up to 67%.29,30 A comparable diagnostic yield of MRI with newly diagnosed epilepsy of around 35% is reported from the United Kingdom.31 Our present study could detect a structural etiology in 55% of epilepsy patients, which is quite similar to another study from India having a diagnostic structural cause of seizure in 51.3% of their patients;32 some other Indian study reported a higher detection rate of >60%.33

Infection and inflammation are the most common structural causes of epilepsy in developing countries.30 NCC is the leading cause of acquired epilepsy worldwide and also responsible for higher prevalence of epilepsy in developing countries.34 The present study also shows infectious group as the most common etiology, with NCC in 66.9% followed by tuberculosis of the brain in 28%, which is statistically significant. An Indian study noted that tuberculosis causes seizure in ~50% of children and 5% of adults, and recurrence is common in this group.35 A higher rate of epilepsy in the developing countries is probably due to the method of the study, although overall NCC is the most frequent cause of epilepsy.36 Most studies noted that infections with NCC is the leading cause of epilepsy among the younger age group.32

The association of epilepsy and reactive astrogliosis is a known fact. A gliotic scar can induce an epileptic seizure and also lead to drug-resistant state.37 Our present study noted gliotic scar in 57 patients (16.3%). It was seen mostly in the middle-aged adult group and it was also noted that gliotic scar can lead to drug-resistant epilepsy.38 Kaushik and Manmohan also noted that gliosis was a common structural lesion in both younger age and the aged, having infarct with gliosis.32

In 1960, the prevalence of temporal lobe epilepsy was 1.7 per 1,000 people but surgical centers reported a higher rate.39–41 In India, 728 patients were operated for epilepsy; temporal lobe resection was the most common surgery done followed by hemispherectomy.42,43 Mesial temporal lobe sclerosis incidence is like previous studies ranging from 8 to 30%.44 In the present study, MTLE was seen in 45 patients (12.9%), mostly in the adolescent age group.

A written review by the ILAE subcommittee on pediatric neuroimaging notified that it is abnormal in one-half of the children with new-onset focal seizures, with epileptic focus localization in 15 to 20%.45 Another pediatric epilepsy study revealed positive MRI findings up to more than 50%.24,46 Amirsalari et al reported abnormal MRI findings in 28.5% of their epileptic children, with brain atrophy, tumors, vascular abnormality, benign cyst, and high signal white matter changes as their findings.47 Significant proportion of pediatric patient has an abnormal MRI finding relating to developmental brain abnormalities, like leukodystrophy, arachnoid cyst, agenesis of corpus callosum, AVM, cyst (porencephalic) gliosis, tuberculoma, meningitis, and encephalitis in different proportions.37,48 An Indian study on children with refractory epilepsy concluded that perinatal insult was the most common etiology. Onset below 2 years of age, presence of a neurological abnormality, certain seizure type, and male sex were the important risk factors.49 In the present study, the most common etiology noted was hypoxic injury in 23% and infections in 23%. Others were tumor (7.2%), autoimmune (1.4%), cortical malformation (8.6%), vascular (5.7%), MTLE (11%), gliosis (2.8%), metabolic cause (1.4%), and postictal changes (1.4%).

A study from India on neuroimaging in new-onset seizure among elderly patients noted cerebral atrophy as the most common finding, followed by vascular findings such as infarct, hemorrhage, and white matter changes. Others noted were focal lesion, granuloma, gliosis, tumor, hemispheric atrophy, diffuse edema, dilated Virchow-Robin spare, and other unidentified bright objects.50 The present study included a very small number of 13 elderly patients whose abnormal MRI findings are similar to other studies.

An important cause of epilepsy among elderly patients is cerebrovascular disease.51 Development of poststroke seizure within 5 years of stroke is seen in 11.5% in one study, which is comparable to other studies.52 In a recent review of poststroke seizure, although 5 to 20% develop seizure at some stage after stroke, but only a few develop epilepsy.53 The present study noted that vascular etiology was the third most common etiology overall seen in 44 patients (12.6%). Out of these patients, most of them belong to the adult group (18–60 years) seen in 72.7%, elderly (>60 years) patients seen in 11.4%, adolescent seen in 6.8%, and children (<12 years) in 9%.

A Saudi Arabia study that included 245 adults with refractory epilepsy noted structural MRI abnormality in all patients. Hippocampal sclerosis was the most common in 86 (35%) patients followed by tumors in 76 patients (30%). Other pathologies that were noted were cortical developmental malformation, vascular malformation, gliotic scar, and dual pathology in 12 patients (5%).54 In the present study, among the young and middle-aged adults, which included 200 patients (57.2%), infectious etiology was the most common abnormality seen in 35%, gliosis in 20%, vascular in 16%, and MTLE in 12%. Other abnormalities noted were cortical malformation (6.5%), hypoxic changes, tumor, and postictal changes.

Cortical dysplasia is the abnormal development of cells and organization within brain parenchyma, which becomes a seizure focus. In the present study, neuronal migration defect was seen in 24 patients (6%) among all age groups, predominantly affecting adolescents and young adults (—Table 3). The most common type was FCD (33.3%); others were microgyria (16.7%), porencephaly (12.5%), schizencephaly (8.3%), pachygria (8.3%), heterotopia (4.2%), polymicrogyria (4.2%), and corpus callosum agenesis (4.2%). Another study on epilepsy noted that 13 patients (4.3%) of their study group had neuronal...
migration defect. The lesion included schizencephaly, heterotopia, pachy/polymicrogyrias, and hemimegalencephaly.55

DDMS in three patients, Rasmussen encephalitis in four patients, moyamoya disease in one patient, PRES in two patients, vasculitis in four patients, and neurofibromatosis type 1 in two patients were noted in the present study, which is more common in western countries as compared with ours. Recurrent focal seizure, hemiplegia, facial asymmetry, and mental retardation are its clinical features.56,57

Conclusion

Neuroimaging is important in an epilepsy patient for diagnosing a structural etiology. It helps in prognosticating patients and further change of treatment protocol from medical therapy to surgical therapy.

Limitations

- Proper follow-up of patients could not be done as it was a retrospective study.
- The base line number of epilepsy patients being referred for all neuroimaging (CT brain and/or MRI brain) by all departments is also not available, limiting our information for comparison.

Note

This study was conducted in North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, Meghalaya, India.

Table 3 Age-wise distribution of the various etiological classifications based on neuroimaging

<table>
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<tr>
<th></th>
<th>Infants and toddler</th>
<th>Preschool children</th>
<th>School children</th>
<th>Adolescent</th>
<th>Young adult</th>
<th>Adults</th>
<th>Middle-aged adult</th>
<th>Aged</th>
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<tbody>
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<td>Autoimmune</td>
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<td>3</td>
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<td>5</td>
<td>9</td>
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Conflict of Interest
None declared

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