Additional value of contrast injection in brain MRI of patients with epilepsy

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Aims and objectives

INTRODUCTION

As defined by international league against epilepsy and the national Bureau for epilepsy (IBE) in 2005, epilepsy is characterized by an enduring predisposition to generate epileptic seizures. History of at least one episode of seizure and its associated neurobiological, cognitive, psychological and social disturbances are regarded as the other essential elements of epilepsy definition [1].

Epilepsy can be categorized on the basis of presence or absence of structural brain abnormality. Epileptic seizure can occur in those with structural brain abnormality, or in those whose brain appears structurally normal, but develop seizure because of microstructural changes or biochemical or genetic predispositions [2]. Epilepsy can be further classified into partial or complex, depending on the site of the triggering focus or foci. Partial seizure originates from a specific region of the brain, whereas, diffuse epileptic discharges are responsible for generalized type of epilepsy [3].

Epilepsy is a relatively common disorder, affecting approximately 0.4% to 1% of the population [4].

The advent of electroencephalography (EEG) and brain imaging in the past century were the two major advances in the diagnosis and treatment of epilepsy. By introducing x-ray in 1895, a new era in medical history was started. Since then, many advances had been made in the imaging of the nervous system, but perhaps one of the most influencing was the invention of computed tomography (CT), which for years was the mainstay of neuroimaging and in particular imaging of epilepsy. It still has some roles in investigation of new onset seizure in the emergent setting [5], but it has been superseded by more novel imaging techniques in recent years.

With new developments in techniques, previously undetectable subtle structural abnormalities are now routinely demonstrated by magnetic resonance imaging (MRI).

As compared with CT, MR imaging, with its higher sensitivity, superior spatial resolution, excellent soft tissue contrast, multiplanar imaging capability, and lack of ionizing radiation has emerged as primary modality of choice in the evaluation of patients with epilepsy.

Despite widespread application of MRI in the routine evaluation of those with epilepsy and extensive research in this field, the role of contrast injection in primary evaluation of epileptic patients is still controversial. Several articles have studied the role of contrast injection in patients with partial epilepsy, but there is still a large number of contrast enhanced MRIs, being performed each year as the primary workup for different types of epilepsy. American College of Radiology (ACR) has proposed a guideline to determine
the appropriate method of neuroimaging in the context of seizure and epilepsy [6]. Considering the ACR appropriateness criteria, the epileptic patients are classified into seven different categories based on the factors such as age, type of epilepsy, medical response, history of trauma and drug. In all seven groups, contrast enhanced MRI has been recommended as a high priority neuroimaging method. On the other hand, there are increasing reports in literature regarding the adverse effects of gadolinium based agents, the most well-known, being nephrogenic systemic sclerosis (NFS) [7]. NFS is a systemic fibrosing process, with occasional fatal outcomes [8], which limits the application of gadolinium to justifiable indications.

In this study, we explore the expanding role of MRI in the diagnosis of patients with various types of epilepsy and evaluate the additional value of contrast injection in this regard.
Methods and materials

MATERIALS AND METHODS

PATIENTS

Pre and post-contrast Brain MRI of 180 epileptic patients, referred to Namazi and Faghihi hospitals - two major hospitals affiliated to Shiraz University of Medical Sciences - over a 12 months period, were reviewed. Inclusion criteria were those referring for primary evaluation of new onset or refractory epilepsy. Those with a known history of neoplastic, infective, metabolic disorder or those with prior history of acute trauma, or positive previous brain imaging findings were excluded from our study.

MRI PROTOCOLS

MRI was performed according to our dedicated epilepsy protocol, on two 1.5 T scanners: Philips Gyroscan Intera (ACS-II, Philips Medical Systems, Best, Netherlands) in Namazi hospital and Siemens Magnetum Avanto (I-class, Siemens, Erlangen, Germany) in Faghihi hospital using a standard head coil.

The brain MRI protocol was consisted of axial T1, T2 and FLAIR; coronal T1, T2, FLAIR; sagittal T1 sequences and post contrast axial, coronal and sagittal planes.

The injected contrast was either Gadopentate Dimeglumine (Magnevist, Bayer Schering Pharma AG, Germany) or Gadoterate (Dotarem, Guerbet, Roissy, France), which was administered at the dose of 0.1 mmol/kg. Post contrast images were taken approximately 5 minutes after the injection.

IMAGE REVIEW

In each patient pre-contrast images were reviewed by two radiologists for detecting any abnormal findings. Post contrast images were then scrutinized in the same session for any abnormal contrast enhancement, classified either as elucidation of previously unrecognized pathology or enhancement of a detectable pathology in pre-contrast images. When possible the most likely diagnosis based on the imaging was made. Pre-contrast and post-contrast findings were recorded and compared to see if contrast added any more information to the pre-contrast study i.e. either showing a lesion which was not detected in the pre-contrast study or a typical pattern of enhancement aiding in better characterization of the pathology. Contrast enhancement was also categorized as non-enhancing (or minimally enhanced), moderate and significantly enhancing lesion.

STATISTICAL ANALYSIS

Page 4 of 16
Data were analyzed using SPSS 13. The inter-observer agreement was assessed by kappa coefficient.

For comparing the proportions, chi-square test was used and p-value < 0.05 was regarded as significant.
<table>
<thead>
<tr>
<th>Kappa value</th>
<th>Degree of agreement</th>
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<tbody>
<tr>
<td>&lt;0</td>
<td>No agreement</td>
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<tr>
<td>0-0.20</td>
<td>Slight agreement</td>
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<tr>
<td>0.21-0.40</td>
<td>Fair agreement</td>
</tr>
<tr>
<td>0.41-0.60</td>
<td>Moderate agreement</td>
</tr>
<tr>
<td>0.61-0.80</td>
<td>Substantial agreement</td>
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<tr>
<td>0.81-1</td>
<td>Perfect agreement</td>
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**Table 1:** Guideline for interpretation of kappa value

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Results

Out of 180 brain MRI performed, 93 (51.7%) were normal in pre-contrast studies and contrast injection did not appear to reveal any pathology. Of the remaining 87 cases, 21 (11.7%) patients (mean age of 42.5 years), showed non-specific white matter changes or ischemia represented by multiple small well defined hyperintense lesions on T2 and FLAIR, distributed in subcortical and periventricular white matter. These lesions did not show contrast enhancement as these white matter changes are not associated with breakdown of blood-brain barrier.

Possibility of mesial temporal sclerosis was suggested in 10 (5.6%), based on signal intensity, cortical atrophy or both.

In 7 (3.9%) patients, developmental anomalies were detected as heterotopia (2 cases), pachygyria (1 case), and agenesis of corpus callosum (2 cases) and focal cortical dysplasia (2 cases).

Vascular malformations were seen in 5 (2.8%) cases, four of which were cavernous angioma and one was venous angioma. We were able to make definite diagnosis according to precontrast images in these cases, and contrast injection further improved visualization of venous angioma and confirmed our diagnosis according to the typical pattern of enhancement.

Tumoral process was diagnosed as the most likely diagnosis in 12 (6.7%) patients (mean age of 30.1 years). Considering the location of the lesions, temporal lobe was the most frequent (7 cases) followed by frontal and parietal lobe (3 and 2 cases respectively).

Significant contrast enhancement was detected in 5 (2.8 %) patients. 3 cases were in the tumor group and 2 cases in the vascular category. Mild to moderate degree of enhancement was detected in 6 (3.4%) cases. Of these, five patients had brain tumor and one showed vascular abnormality. 4 cases with the diagnosis of brain tumor did not show any contrast enhancement. In this group, the lack of enhancement, may suggest a hypovascular or less aggressive nature, although this is not absolute.

There was perfect agreement between the two radiologists for detection of any lesion in the brain. (κ=1.00). Contrast injection did not change the primary radiological diagnosis in any of the cases; however, it was helpful in better delineation of the margins, extent, grade or nature of suspected neoplasm in 8 (3.9%) cases. Contrast was helpful in confirming the preliminary diagnosis in two patients one with venous angioma and the other with dural sinus thrombosis.

One of our cases presented with intracerebral hemorrhage. We found no enhancement in this case, suggesting that the possibility of underlying tumor is less likely.
Tuberous sclerosis, the most important among the miscellaneous group, was diagnosed as the cause of epilepsy in 2 (1.2%) patients. Cortical tubers were easily detected in both cases using T1, T2 and Flair sequences and typical subependymal nodules were also detected in one case, in which nonenhancement was used as a diagnostic criteria in differentiating a nontumorous subependymal tuber from giant cell astrocytoma.

Arachnoid cyst, usually an incidental finding may result in epileptic seizure. We found two cases of arachnoid cysts in temporal lobes and two in posterior fossa. The definite diagnosis was readily made based on precontrast images and contrast studies added no more diagnostic information.

One patient with the diagnosis of multiple sclerosis was detected. Epilepsy although not common, can be an initial presentation of MS. Enhancement was helpful to identify the active plaques.

Representative cases of more important categories are shown in Figs 1 to 4.
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**Table 1:** Guideline for interpretation of kappa value

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<table>
<thead>
<tr>
<th>FINDINGS</th>
<th>No. of Cases</th>
<th>Percent</th>
<th>Mean Age(+/− SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>93</td>
<td>51.7</td>
<td>25.7 (9.5)</td>
</tr>
<tr>
<td>White matter changes or Ischemia</td>
<td>21</td>
<td>11.7</td>
<td>42.5 (12.2)</td>
</tr>
<tr>
<td>Neoplasm</td>
<td>12</td>
<td>6.7</td>
<td>30.1 (16.1)</td>
</tr>
<tr>
<td>MTS†</td>
<td>10</td>
<td>5.6</td>
<td>22.4 (10.3)</td>
</tr>
<tr>
<td>Vascular Anomaly</td>
<td>5</td>
<td>2.8</td>
<td>33 (14.8)</td>
</tr>
<tr>
<td>Developmental Anomaly</td>
<td>7</td>
<td>3.9</td>
<td>20 (5.8)</td>
</tr>
<tr>
<td>Dural Sinus Thrombosis</td>
<td>1</td>
<td>0.6</td>
<td></td>
</tr>
<tr>
<td>Sinusitis</td>
<td>18</td>
<td>10</td>
<td>26.7 (14.4)</td>
</tr>
<tr>
<td>Post Traumatic</td>
<td>3</td>
<td>1.7</td>
<td>32.3 (14.4)</td>
</tr>
<tr>
<td>Miscellaneous‡</td>
<td>10</td>
<td>5.6</td>
<td>30.8 (19.5)</td>
</tr>
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</table>

†Mesial temporal sclerosis
‡Tuberous sclerosis: 2, Multiple sclerosis: 1, Prominent Virchow Robin space: 2, Arachnoid cyst: 4, ICH: 1

**Table 2:** Frequency of various brain MRI findings in 180 epileptic patients

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**Fig. 1:** Axial T1w pre and post contrast images show a hypersignal nonenhancing lesion in medial aspect of right temporal lobe. A cystic component was evident in other slices. No edema was detected. A low grade glioma was the most possible diagnosis and pathology proved the mass to be a low grade astrocytoma.

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**Fig. 2:** A) Isosignal cortically based tumor in lateral aspect of left temporal lobe. B) No enhancement is seen in post contrast images. C, D) Flair and T2 coronal images show the mentioned lesion as being hypersignal with tiny cystic changes and no significant edema. Considering the MR findings a low grade tumor such as DNET was suggested.
Fig. 3: A,B) Axial pre and post contrast images show an extra-axial isosignal mass with avid contrast enhancement. Findings are typical for meningioma.
Fig. 4: A) Tubular flow void structure in left cerebellar hemisphere. B) Coronal section after contrast injection clearly demonstrates stellate vessels converging on a collector vein, typical for venous angioma.

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Conclusion

Numerous researches have been performed to propose the best protocols for evaluation of seizure. Different protocols are suggested according to the type of seizure; although this policy proves to be useful in many cases, appropriate clinical data is missing in a considerable number. One of the questions radiologist may face is whether contrast injection is necessary in the primary evaluation of a patient with the general term of epilepsy being the only available information. Few articles have studied the usefulness of contrast injection in epileptic patients.

we found all the important pathologies to be detectable without the injection of gadolinium.

With regard to contrast enhancement, no significant change was observed in our differential list for tumoral lesions, although as it was expected, contrast was beneficial in increasing diagnostic confidence, improving demarcation of tumoral margin and suggesting indolent or aggressive nature.

Vascular malformations were all detectable in pre-contrast studies. Three of the cases showing typical appearance of cavernoma, located in temporal and frontal lobes. The other case showed the typical appearance of venous angioma best elucidated on contrast enhanced images, although still well detected on non contrast films too.

Malformations of cortical development as a cause for epilepsy are well known. Of utmost importance are neuronal heterotopia and focal cortical dysplasia which constituted 2.2% of our cases. Contrast failed to provide additional information in these cases.

Overall, contrast injection did not change the primary radiological diagnosis in any of the 180 cases; Contrast administration added additional diagnostic information in 16 (8.8%) cases, of these, 12 (75%) cases were those with tumoral pathologies.

Although according to ACR appropriateness criteria, brain MRI without and with contrast agent has a high priority among various available imaging modalities, additional economic burden of contrast administration is a problem in some societies, such as Iran, where the out of pocket cost of MRI with contrast injection sums up to a substantial amount. Therefore based on our results, stratifying guidelines according to different healthcare systems for prioritizing the use of contrast agent and to make the best use of available resources in a cost-effective manner appears to be justifiable.
Personal information

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References


