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A prospective study of diffusion weighted magnetic resonance imaging abnormalities in patients with cluster of seizures and status epilepticus

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ABSTRACT

Objective: To study the frequency, imaging characteristics, and clinical predictors for development of periictal diffusion weighted MRI abnormalities.
Methods: We prospectively analyzed electro clinical and imaging characteristic of adult patients with cluster of seizures or status epilepticus between November 2013 and November 2015, in whom the diffusion weighted imaging was done within 24 h after the end of last seizure (clinical or electrographic).
Results: There were thirty patients who fulfilled the inclusion and exclusion criteria. Twenty patients (66%) had periictal MRI abnormalities. Nine patients (34%) did not have any MRI abnormality. All the patients with PMA had abnormalities on diffusion weighted imaging (DWI). Hippocampal abnormalities were seen in nine (53%), perisylvian in two (11.7%), thalamic in five (30%), splenium involvement in two (11.7%) and cortical involvement (temporo-occipital, parieto-occipital, temporo-parietal, fronto-parietal and fronto-temporal) in sixteen (94.1%) patients. Complete reversal of DWI changes was noted in sixteen (80%) patients and four (20%) patients showed partial resolution of MRI abnormalities. Mean duration of seizures was significantly higher among patients with PMA (59.11 + 20.97 h) compared to those without MRI changes (27.33 + 9.33 h) ($p < 0.001$).
Conclusions: Diffusion abnormalities on MRI are common in patients with cluster of seizures and status epilepticus and were highly concordant with clinical semiology and EEG activity. Patients with longer duration of seizures/status were more likely to have PMA.

1. Introduction

Imaging of postictal patients is performed to investigate causes of seizure, such as space-occupying lesions or other "structural" processes. However, abnormalities may be found, that reflect physiological or pathologic alterations due to seizure activity, and are called periictal MRI abnormalities (PMA) [1]. These changes are caused by factors such as increased metabolic activity, hyperperfusion associated with ictal activity, postictal hypoperfusion and transient ultrastructural pathologic alterations, all of which reflect the sustained electrical activity of epileptic neurons. Lee and Goldberg performed angiographic studies initially and described a blush associated with ictal activity [2]. This was later corroborated by ictal 99mTc-HMPAO single photon emission computed tomography (SPECT) studies (e.g., [4]), which demonstrated ictal hyperperfusion in patients with focal epilepsy [3]. Since then, there have been many case reports, small series, and animal studies showing reversible and irreversible periictal MRI findings. Several MRI techniques including diffusion weighted MRI (DWMRI), perfusion MRI (PMRI), functional MRI (fMRI) recognized similar changes in several case studies [3,5–7]. In addition to localized hyperperfusion, reported changes include contrast enhancement, increased T2 fluid-attenuated inversion recovery (FLAIR), and

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diffusion weighted imaging (DWI) signals, and a variable degree of reduction in the apparent diffusion coefficient (ADC) [8–12]. All these studies were retrospective and hence it is still unclear why only few patients have these changes. The precise incidence and factors responsible for development of MRI changes are not known. We designed a prospective study assessing MRI abnormalities, focusing on diffusion weighted imaging in patients with cluster of seizures and status epilepticus (convulsive and non-convulsive). Aim of the study was to know the incidence of PMA, their imaging characteristics and their clinical predictors.

2. Patients and methods

This was a prospective study conducted at a tertiary referral hospital in southern India. This study was approved by Institutional review board and was conducted over 24 months from November 2013 to November 2015.

3. Inclusion criteria

Consecutive adult patients, (age > 12 years) who were admitted in the hospital, either with cluster of seizures or status epilepticus, (convulsive (CSE) or nonconvulsive (NCSE)) well documented by EEG were included in this study.

4. Exclusion criteria

[1] Patients in whom DWI alterations were suspected to be related to underlying structural acute brain pathology.
[2] Patients who had any evidence of CNS infection in the form of CSF abnormalities were excluded.

4.1. EEG study

According to the inclusion criteria, all patients underwent video-EEG or continuous EEG monitoring with polygraphic channels (Telefactor System, 21 channels, International 10–20 System). During hospitalization, we clinically assessed all patients and treated them as per standard guidelines, with EEG monitoring and documented their responses to treatment.

4.2. MRI data acquisition and analysis

Cranial MRI was performed in all thirty patients. MR imaging was performed on a WIPRO GE 1.5 Tesla LXi system with a 5-mm slice thickness acquiring axial T1-weighted spin echo (TR/TE: 620/9.7), T2-weighted (TR/TE 4000/85.6), fluid-attenuated inversion recovery (FLAIR) (TR/TE:7800/161) and DWI (TR/TE: 8999/128) images. The ADC maps were obtained from the diffusion images. Regions of interest of a uniform shape and size were chosen and drawn by a neuroradiologist. Diffusion gradients were applied along the three principal orthogonal axes using single-shot spin-echo echo-planar sequences. ADC maps were also generated and analyzed directly on the DWI images (b values of 0 s/mm^2).

Perfusion MRI brain was done in 5 patients. Follow up DWI imaging was obtained (3 days–16 weeks) in all. An experienced neuroradiologist visually reviewed the images and reported all MRI abnormalities and opined if the MRI abnormality was possibly due to seizures. MRI abnormalities were attributed to postictal changes, if they did not appear to represent strokes, tumors, encephalitis and their location corresponded to the EEG abnormality or seizure semiology.

5. Results

Thirty patients (seventeen men), with a mean age of 46.8 years (age range 13–84 years) were included. The patient population was divided into two groups, those with periictal MRI abnormalities (PMA) and patients without PMA. There were 20 patients who showed PMA (12 were male and 8 were female with a mean age of 51.5 years) and 9 patients without PMA (5 were male and 4 were female with a mean age of 41.1years). One patient was excluded from the study because the MRI changes were attributed to mitochondrial disease which was confirmed later on investigations. The clinical and electroencephalographic findings of patients with and without PMA are given in Tables 1 and 2 respectively. Patients with and without such changes did not differ significantly with regard to mean age, sex distribution or time to MRI.

5.1. Electroclinical findings

History of epilepsy was present in 7/20 (35%) patients with PMA and in 2/9 (22.22%) patients without MRI changes.

The clinical seizures in patients with PMA comprised of complex partial seizures in 13, simple partial in 2 patients and generalized tonic clonic seizures in 5 patients. In patients without MRI changes, 6 had complex partial seizures and 3 had generalized tonic clinical seizure.

In patients with PMA, ten had NCSE (50%), five CSE (25%), five patients had cluster of seizures (25%) and among nine patients without MRI changes, five had NCSE (55.55%), three had CSE (33.33%), and one had cluster of seizures (11.11%). The duration of seizures ranged from 12 to 96 h in all patients. Mean duration of seizures was significantly higher among patients with PMA (59.11 + 20.97 h) compared to those without MRI changes (27.33 + 9.33 h) ($p < 0.001$).

5.2. Etiology

Eleven patients (55%) with PMA had unknown etiology, one (5%) had tumor, two (10%) were posttraumatic, three had post stroke epilepsy (10%) and the remaining three patients (15%) had metabolic, vascular and autoimmune etiology respectively. Among nine patients without MRI changes, six (66.66%) had unknown etiology, two had vascular etiology (22.22%) and one had alcohol withdrawal seizures (11.11%).

5.3. Reversible peri-ictal diffusion imaging and follow-up

Among the 20 patients with PMA, hippocampal abnormalities were seen in 10 (50%), perisylvian involvement in 2 (10%), thalamic involvement in 4 (20%), splenium involvement in two (10%) and cortical involvement in sixteen (80%) patients. Cortical regions involved were temporo-occipital, parieto-occipital, temporo-parietal, fronto-parital and fronto-temporal. MR perfusion imaging was performed in only 5 patient and documented hyperperfusion in the corresponding areas seen on DWI images in all the 5 patients.

Follow up MRI was done in all patients. The signal abnormalities observed in the acute phase largely resolved (completely or partially) in all patients and the DWI signals returned to normal between 2 and 45 days after the index event. Complete reversal of MRI changes was noted in 16 of 20 (80%) patients and 4/20 (20%) patients showed partial resolution of MRI abnormalities (Table 3).

Fig. 1 depicts the details of illustrative cases during the acute and follow up phase (Table 4 and Fig. 1).