

Reversible Cortical Diffusion Restriction, Hyperperfusion and T2-Hyperintensity Caused by Two Different Types of Epileptic Seizure

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Introduction

Status epilepticus (SE) describes seizures that persist for a sufficient length of time or are repeated frequently enough that full recovery between the seizures does not occur. By contrast a series of epileptic seizures (SoES) is defined by separate and self-limiting seizures so that the patient recovers in between [1].

In the literature several studies have been reported concerning hemodynamic changes associated with ictal activity [2, 3] and areas of hyperperfusion have been identified with ictal single photon emission computed tomography (SPECT) in focal epilepsy [4]. Advances in magnetic resonance imaging (MRI) have opened opportunities for non-invasive identification of seizure-related neuronal dysfunction in affected areas [5]. By use of perfusion-weighted imaging (PWI), several authors have demonstrated ictal hyperperfusion in patients with focal epilepsy [6, 7]. With respect to diffusion-weighted imaging (DWI) transient reductions of the apparent diffusion coefficient (ADC) have been detected in experimental focal ischemia with peri-infarct depolarization and in models of spreading depression and models of epilepsy [8]. Diffusion-weighted imaging changes were found throughout the cerebral cortex, hippocampus, amygdala and medial thalamus in rat brains after 4 h of SE by Fabene et al. [9]. Several case studies have demonstrated decreased ADC values in patients with focal SE [10, 11]. With regard to the relationship between ictal activity and altered hemodynamic state, a study on the combined use of DWI and PWI in 10 patients presenting with complex partial SE revealed

that this combination can visualize transient hemodynamic and tissue changes also in the hippocampus, thalamus and affected cortical regions [7]. Beyond hemodynamic changes and altered cortical diffusivity, signal alterations both in T2 and fluid-attenuated inversion recovery (FLAIR) weighted imaging have been observed and have been interpreted as cortical swelling and edema [9, 12, 13].

To date no observations on the influence of continuous ictal activity on the development of distinct patterns of MRI signal alterations have been reported.

Case Reports and Technique

Case 1

A 55-year-old woman was admitted to hospital presenting with an acute loss of speech combined with unusual behaviour but without any loss of consciousness or convulsions, i.e. reactions to the environment were not less than before. Neurological examination was normal except for the speech disorder and apathy and neither laboratory investigations nor the results of a lumbar puncture revealed further pathological findings. The electroencephalography (EEG) showed a left frontal focal SE. Under EEG monitoring, the seizures could be temporarily suspended by intravenous (IV) application of lorazepam. With anticonvulsive treatment by use of phenytoin and levetiracetam, the patient fully recovered within 2 days. The history of the patient revealed a left-sided brain contusion 10 years ago.

The clinical MRI protocol consisted of T1 (precontrast and postcontrast), T2, T2* and FLAIR-weighted, DWI and ADC as well as PWI sequences, which were automatically computed and displayed as a time-to-peak (TTP) map by the scanner software and time-of-flight MR angiography (TOF-

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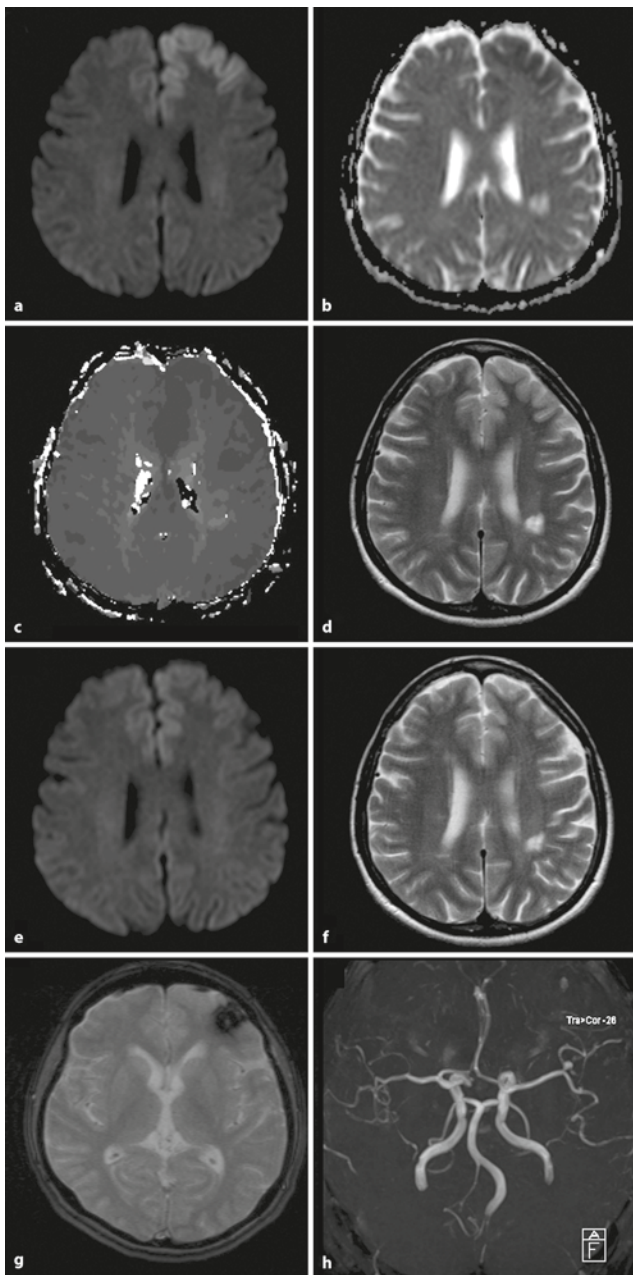


Fig. 1 Initial magnetic resonance imaging findings in patient 1 with left frontal status epilepticus for 4 h. Diffusion (**a**) and T2-weighted images (**d**) showed extensive strictly cortical located hyperintense signal alterations within the left frontal brain, exceeding the arterial territory of the anterior cerebral artery and a hypointense cortical signal was observed in ADC maps (**b**). Perfusion-weighted imaging detected hyperperfusion of the affected cortical areas (**c**). Follow-up brain scans of patient 1 at day 10 (**e, f**) including cortical diffusivity (**e**) and T2-hyperintensity (**f**) showed delayed normalization after termination of the status epilepticus. Additional magnetic resonance imaging findings demonstrated a left frontal contusion area with residual hemosiderin in T2*-weighted images (**g**) and an incidental aneurysm of the left medial cerebral artery in the time-of-flight magnetic resonance angiography (**h**)

MRA). Approximately 4 h after onset of clinical symptoms MRI showed extensive signal alterations encompassing hyperintensity in DWI, T2 and FLAIR-weighted imaging and hypointensity in the ADC maps as well as hyperperfusion in PWI (Fig. 1a–d; FLAIR images not displayed). All pathological findings were restricted to left frontal cortical areas and follow-up MRI scans showed progressive normalization (day 10: Fig. 1e, f). The contusion was located in the left frontal lobe and showed residual hemosiderin in T2*-weighted images (Fig. 1g). Retrospectively, this lesion has to be considered causative for the status epilepticus. The TOF-MRA was normal except for the incidental detection of a medial cerebral artery aneurysm (Fig. 1h) while further MRI abnormalities, e.g. parenchymal or meningeal contrast enhancement, were not observed (data not displayed).

Case 2

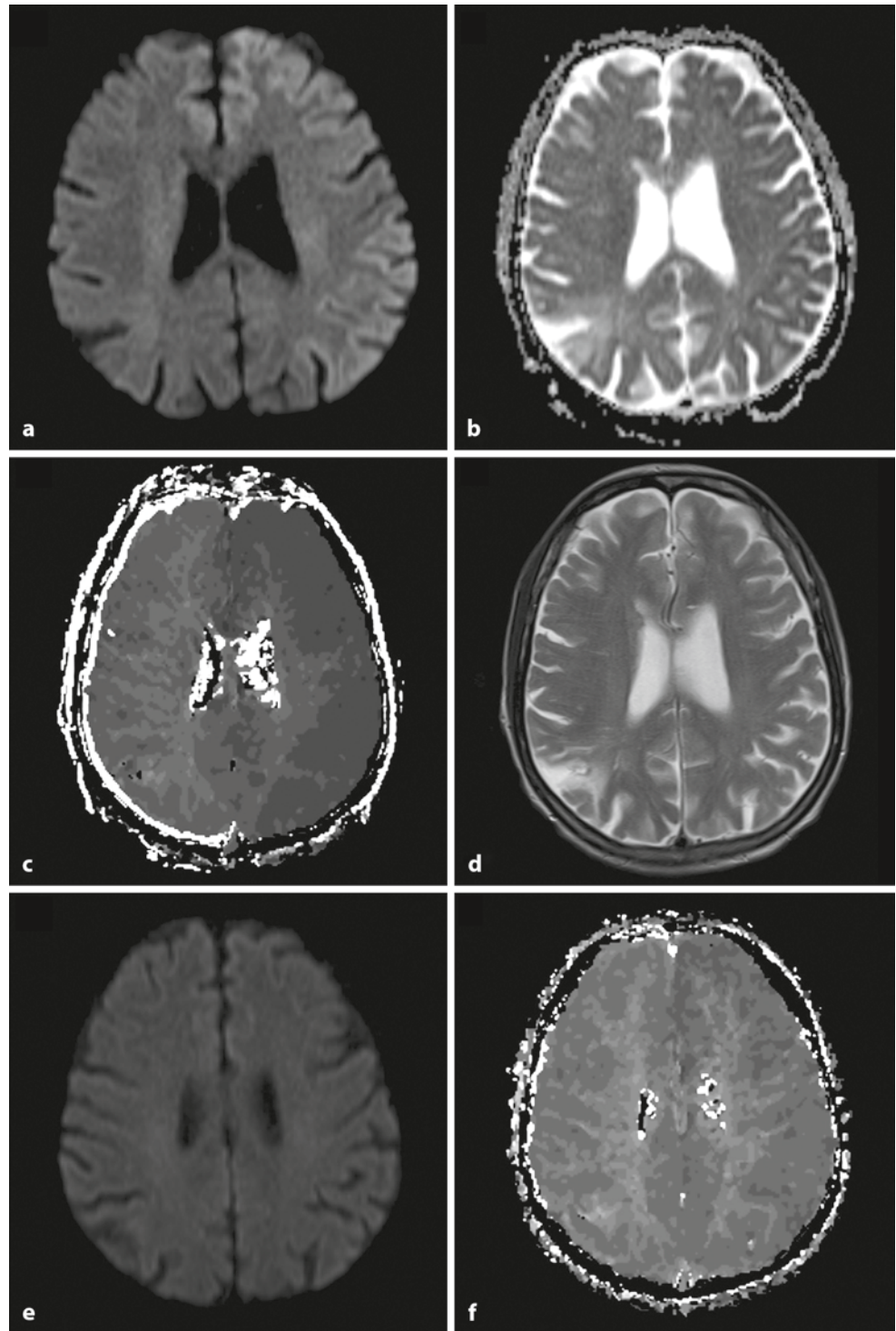
A 62-year-old female was admitted to hospital presenting with fluctuating aphasia (i.e. reduced speech fluency and paraphasia) combined with fluctuating vigilance for about 3 h. The clinical examination also showed no additional neurological deficits and laboratory results and a lumbar puncture showed negative results. The EEG demonstrated short-term epileptic discharges with left frontotemporal predominance in terms of a SoES. The patient was already pre-treated with levetiracetam due to symptomatic epilepsy after a left temporal middle cerebral artery (MCA) stroke 2 years ago but medication was discontinued 2 days prior to admittance. After initiation of IV administration of levetiracetam the fluctuating clinical deficits disappeared and the patient fully recovered until the next day.

The MRI was acquired approximately 3 h after symptom onset. It similarly showed both extensive cortical hyperintensity in DWI and corresponding hypointense signal alterations in the ADC map (Fig. 2a, b) and the TTP map of the PWI revealed hyperperfusion of cortical areas of the left hemisphere (Fig. 2c). In contrast to case 1, no cortical T2-hyperintensities (Fig. 2d) or FLAIR changes were observed. No further pathologic MRI findings except from the old stroke lesion could be detected. In the follow-up MRI scan 36 h post admittance, both altered cortical diffusivity and perfusion were normalized (Fig. 2e, f).

Technique

All data were acquired on a 1.5 T Magnetom Siemens Symphony total imaging matrix system (TIM; Siemens, Erlangen, Germany) by use of standard Siemens sequences and perfusion data were provided by the standard Siemens SYNGO scanner software. All PWI raw data were subjected to a semi-quantitative evaluation of the bolus peak ratio (BPR) as proposed by Leonhardt et al. [14] to diffe-

Fig. 2 Initial magnetic resonance imaging of patient 2 with a series of complex focal seizures for 3.5 h. Similar to the findings in patient 1 but to a larger extent, cortical hyperintensity within the left hemisphere in diffusion-weighted images (**a**) along with decreased cortical signal in the ADC map (**b**) and hyperperfusion of the affected cortical areas in perfusion-weighted imaging (**c**) were observed. Notably no cortical signal alteration in the T2-weighted images could be detected (**d**). The follow-up magnetic resonance imaging at day 2 showed almost complete normalization of each cortical diffusivity (**e**) and brain perfusion (**f**)

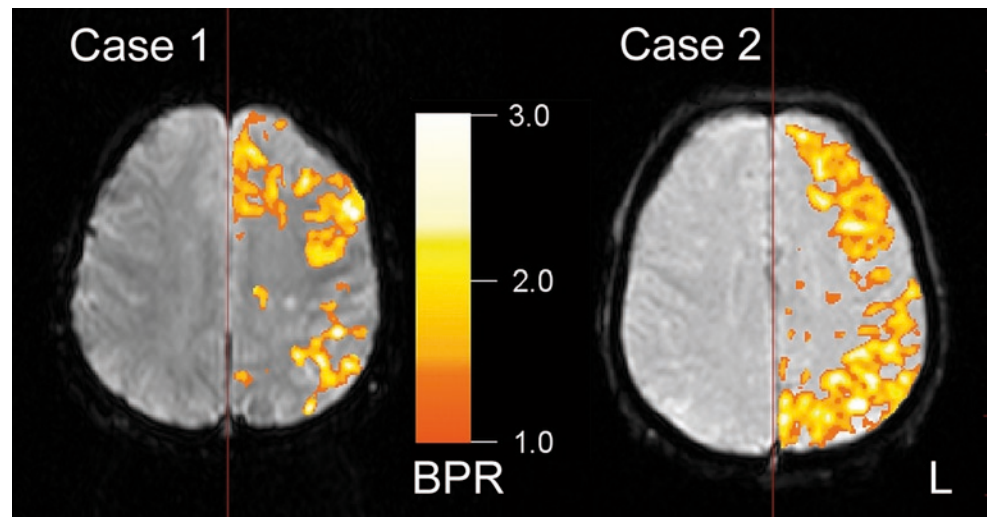


rennate between hyperperfusion and hypoperfusion within the respective cortical brain areas. Here, clear evidence for hyperperfusion was found as the bolus peak ratio (BPR) was above 1 in the cortical brain areas of the 2 cases during the prolonged epileptic seizures at day 1 (Fig. 3).

Discussion

In these two patients with prolonged ictal activity, i.e. left frontal SE and left hemispheric SoES (complex focal), respectively, distinct patterns of transient MRI signal alterations were found. With respect to the underlying pathophysiological background DWI alterations are considered a correlate of cytotoxic effects or vasogenic edema in ictally

Fig. 3 The bolus-peak-ratio (BPR) was calculated for the perfusion-weighted images (PWI) of both patients. In each PWI sequence cortical hyperperfusion could be confirmed by a BPR > 1 (see *centered colour bar*), for case 1 (*left*) within areas of the left frontal brain, for case 2 (*right*) within extensive areas of the left hemisphere (L left hemisphere)



affected neurons [10, 12, 15]. A large variation in the occurrence of cortical diffusivity changes and its correlation with T2-hyperintensity was reported in previous case series [7, 16, 17]. A possible explanation for the variable extent of MRI changes during continued epileptic activity might be the interindividual predisposition for brain tissue edema. A more systematic approach could be the suggestion of a functional cascade caused by epileptic brain activity in the context of time-dependency for the interpretation of MRI findings. In single epileptic seizures, no change of diffusivity or T2-hyperintensity could be observed except for one report of transient ADC changes [18] which might be explained by the short-lasting neuronal affectation, not long enough to cause visible damage. The findings of cortical DWI alterations in terms of altered diffusivity during SE might be considered a result of membrane function breakdown due to ictal activity. The MRI correlate of longer lasting damage mechanisms, i.e. the development of vasogenic edema, might be T2 hyperintensity within the affected cortical regions similar to the interpretation of time-dependent damage visualization in stroke imaging [19]. Finally, residual lesions with enduring cortical dysfunction after prolonged SE might be observed as persisting T2 hyperintensity [15, 17, 20].

Conclusion

Cortical MRI signal changes are not only a relevant differential diagnosis of diffusion restrictions beyond stroke but also transient or persisting T2-hyperintensity might be interpreted as a time-dependent morphological correlate of focal vasogenic edema in the course of prolonged ictal activity or persisting lesions after SE.

Conflict of Interest The authors declare that there is no actual or potential conflict of interest in relation to this article.

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