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Postoperative changes in the brain: Assessment with serial T2WI/FLAIR MR images in non-neoplastic patients

Yoko Shigemoto[a], Noriko Sato[a,*], Yukio Kimura[a], Emiko Morimoto[a], Fumio Suzuki[a], Naoki Ikegaya[b,c], Masaki Iwasaki[b], Eiji Nakagawa[d], Hiroshi Matsuda[e]

[a] Department of Radiology, National Center Hospital, National Center of Neurology and Psychiatry, 4-1-1 Ogawa-Higashi, Kodaira, Tokyo 187-8551, Japan
[b] Department of Neurosurgery, National Center Hospital, National Center of Neurology and Psychiatry, 4-1-1 Ogawa-Higashi, Kodaira, Tokyo 187-8551, Japan
[c] Department of Neurosurgery, Yokohama City University, 3-9 Fukuura, Kanazawa, Yokohama 236-0004, Japan
[d] Department of Child Neurology, National Center Hospital, National Center of Neurology and Psychiatry, 4-1-1 Ogawa-Higashi, Kodaira, Tokyo 187-8551, Japan
[e] Integrative Brain Imaging Center, National Center Hospital, National Center of Neurology and Psychiatry, 4-1-1 Ogawa-Higashi, Kodaira, Tokyo 187-8551, Japan

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ABSTRACT

The aim of the current study was to investigate the postoperative changes of high-signal lesions at the surgical margin on serial T2WI/FLAIR images in non-neoplastic patients. Seventy-one postoperative MR images in 27 patients (17 focal cortical dysplasia and 10 hippocampal sclerosis) who underwent surgery for intractable epilepsy were evaluated. T2WI/FLAIR-high-signal lesions in size and shape were visually assessed using a 3-point grading system. Associations of postoperative seizures or electroencephalography(EEG)spikes with advancing grade were also evaluated. As a result, follow-up showed enlarged T2WI/FLAIR-high-signal lesions in 6 of 27 patients (22%). The presence of post-operative seizures or EEG spikes was significantly associated with enlargement of the T2WI/FLAIR-high-signal lesion. Enlargement of the T2WI/FLAIR-high-signal lesion was observed in some non-neoplastic patients, and this finding might be correlated with remnant epileptogenesis.

1. Introduction

Previous studies with T2WI/FLAIR images in epilepsy patients showed transient high-signal lesions in the splenium of the corpus callosum (Prilipko et al., 2005) and increasing cerebral white matter hyperintensities related to antiepileptic drugs (Mao et al., 2016). The postoperative T2WI/FLAIR high-signal lesions at the surgical margin are relatively common after epilepsy surgery, and we sometimes encounter the cases with enlargement of high-signal lesions. The enlargement of high-signal lesions may be caused by gliosis, minimal ischemia, antiepileptic drugs toxicity, abnormal electrical activity, or seizure recurrence. However, its time course and the association with recurrent seizure/EEG spikes have not been investigated precisely. Here, we investigate the time course of the postoperative changes in T2WI/FLAIR-high-signal lesions at the surgical margin in non-neoplastic patients.

2. Materials and methods

2.1. Participants

A retrospective review of our pathological database revealed 183 patients who underwent surgery due to intractable epilepsy from February 2012 to December 2016 in our institution. The patients who had neoplasms (n = 33), ulegyria (n = 2), tuberous sclerosis (n = 3), post-surgical infection or cerebrovascular disease (n = 7) were excluded. Patients who had undergone callosotomy or hemispherectomy (n = 44) or re-operation (n = 5) were also excluded. Patients who had only a single postoperative MR image (n = 65) were also excluded, because we evaluated serial MR images to observe the changes of T2WI/FLAIR-high-signal lesions at the surgical margin over time. Eventually, 27 patients (17.4 ± 13.2 years old) in total, which consisted of 17 focal cortical dysplasia (FCD) and 10 hippocampal sclerosis patients, were included in this study.

This retrospective study was approved by the institutional review board of the National Center of Neurology and Psychiatry, Japan, and the need for patient informed consent was waived due to its

Abbreviations: FCD, focal cortical dysplasia; EEG, electroencephalography

* Corresponding author.
E-mail address: snoriko@ncnp.go.jp (N. Sato).

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retrospective nature.

2.2. Clinical assessment

We assessed the postoperative seizure frequency, and scalp electroencephalography (EEG) findings. Postoperative assessment was evaluated one year after surgery.

2.3. MR image acquisition

One hundred-four follow-up MR images were obtained in 27 patients from February 2012 to October 2017. Thirty- three images obtained less than 3 months after surgery were excluded because signal changes of postoperative reactive inflammation could often be observed (Sato et al., 1997). Eventually, 71 images in total were included in this study. The interval between surgery and imaging ranged from 3 months to 3.5 years. We used 6 periods to classify the MR images according to the time at which they were obtained after surgery: 3–6 months (13 images), 6–9 months (9 images), 9–12 months (14 images), 1–2 years (20 images), 2–3 years (12 images), and 3 years later (3 images).

All scans were performed using a 3-T MR imaging system with a 32-channel coil, either on a Philips Achieva (Achieva; Philips Medical Systems, Best, The Netherlands) or on a Siemens Verio (Verio; Siemens Healthcare, Erlangen, Germany). The imaging protocol included T2-weighted fast SE, FLAIR, and diffusion weighted imaging (DWI).

2.4. Image analyses

Findings of T2WI/FLAIR-high-signal lesions at the surgical margin were visually evaluated in size and shape. The degree of the high-signal lesions was assessed based on a three-point scale; grade 0 = none or minimal thin linear; grade 1 = band-like or patchy; grade 2 = thicker, and more extensive (Fig. 1). Two neuroradiologists (Y.S. and Y.K.) blinded to the patients' clinical data independently graded the T2WI/FLAIR images. When the grades assigned by the two readers were different, the final grade was determined by consensus. For the assessment of intra-rater reliability, the findings were rated again by one of the two raters at a second session one month after the first session. DWIs were evaluated to exclude acute cerebrovascular disease.

2.5. Statistical analyses

Fisher's exact test was used to examine the differences in postoperative seizures/EEG spikes with an advancing grade and those with a stable grade for the T2WI/FLAIR-high-signal lesion. A 2-sided $P < .05$ was considered statistically significant. Intra-observer and inter-observer agreements were tested using Cohen's κ statistics. All statistical analyses were performed using SPSS software ver. 25.0 (SPSS Japan, Tokyo).

3. Results

3.1. Demographic data

After surgery, 21 patients became seizure-free, whereas the remaining 6 patients experienced seizures a year after surgery. Postoperative EEG spikes were detected in only 4 of the 27 patients.

3.2. Inter-rater and intra-rater reliability

The κ value for inter-observer variability between the two reviewers was 0.85 and that for intra-observer variability was 0.96 for evaluating the T2WI/FLAIR-high-signal lesion at the surgical margin.

3.3. Evaluation of surgical marginal high intensity lesion

The grade of the T2WI/FLAIR-high-signal lesion seen at the surgical margin of all 71 MR studies was as follows; Grade 0 of 31, grade 1 of 29, and grade 2 of 11 MR studies, respectively. Of the 27 patients, 21 patients showed a stable grade, while the remaining six patients showed an advancing grade (Fig. 2), and no patients showed a decreased grade. The enlargement of the T2WI/FLAIR-high-signal lesion was first present as early as 6–9 months and as late as 3 years after surgery. The significant associations between the advancing grade and postoperative seizures ($p = 0.025$) / EEG spikes ($p = 0.004$) were detected.

Among 6 patients with postoperative seizures, 3 patients showed an advancing grade, while the remaining 3 showed a stable grade. Postoperative EEG spikes were observed in the advancing grade group, while not in the stable grade group (Fig. 3).

There were no high-signal abnormalities suggesting acute infarcts on DWIs.

4. Discussion

In this study, we demonstrated 22% of patients who showed an enlargement of T2WI/FLAIR-high-signal lesions at the surgical margin in non-neoplastic patients during follow-up, and these findings were associated with the presence of postoperative seizures/EEG spikes.

Among 6 patients who showed enlargement of high-signal lesions, there had been no clinical nor imaging findings suggesting acute inflammation or status epilepticus at the time of MR imaging. Furthermore, none of them showed a reduction during follow-up. Therefore, it seems acute effects of recurrent seizures or encephalitis are unlikely.

According to pathophysiological studies, central nervous system insults such as trauma, infection, stroke, and seizures induced an

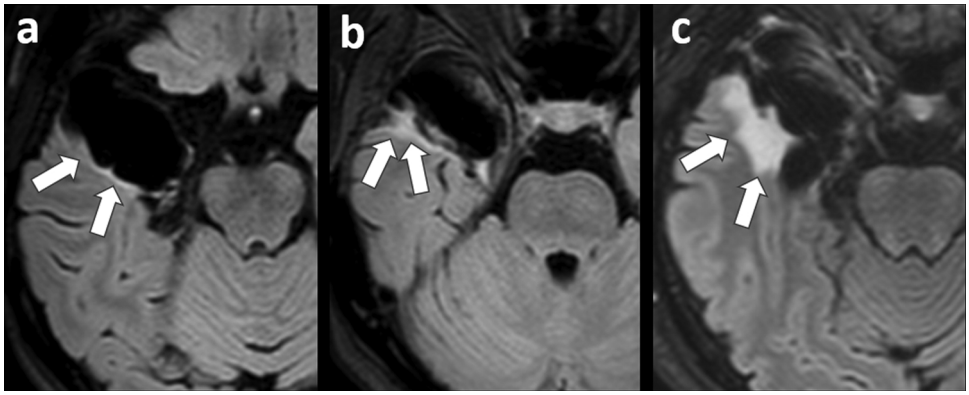

Fig. 1. Grading system for F T2WI/LAIR-high-signal lesions at the surgical margin. (a) Grade 0 = none or minimal thin linear pattern (arrows). (b) Grade 1 = band-like or patchy pattern (arrows). (c) Grade 2 = thicker, and more extensive pattern (arrows).

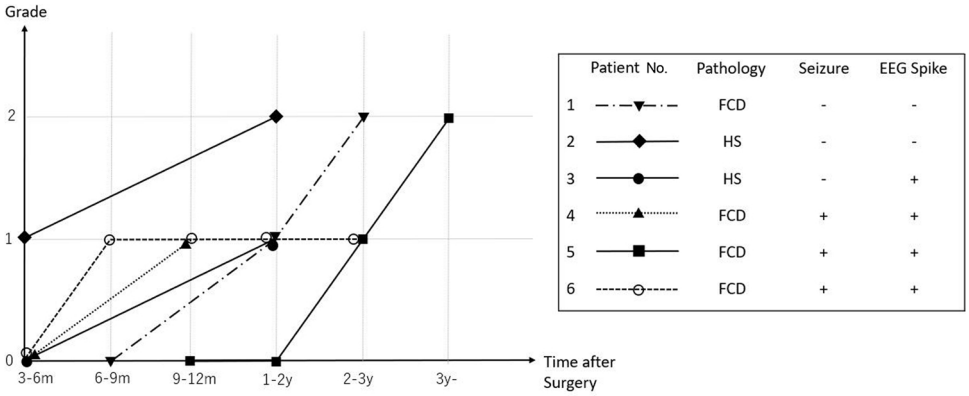

Fig. 2. Advancing grade over time in six patients.

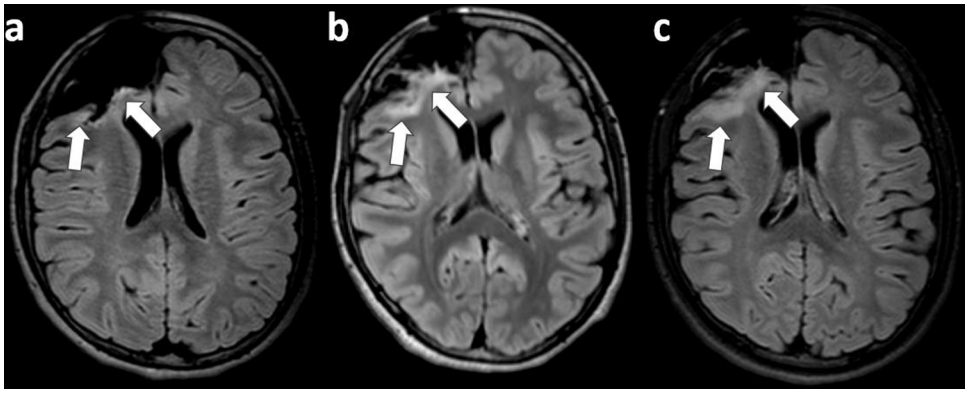

Fig. 3. Advancing grade (G0→G1→G2). Patient number 1 from Fig. 2. An 11-year-old boy who underwent resection of FCD in the right frontal lobe. (a) An axial FLAIR image obtained 8 months after surgery shows a thin-linear high-signal lesion at the surgical margin (arrow). (b) On an MR image taken 1 year after surgery, the high-signal lesion have enlarged to a band-like pattern (arrow). (c) On an MR image taken 2 years after surgery, the high-signal lesion has further enlarged (arrow).

inflammatory response of astrocytic and microglial activation (Sofroniew et al., 2015). These activated glias usually become inactivated by a normal feedback mechanism. However, when the feedback mechanisms fail, chronically activated astrocytes can form a glial scar and promote neuronal injury, seizures, and epileptogenesis (Devinsky et al., 2013). Our results raised the possibility that postoperative seizures may induce activated glias and cause the enlargement of high-signal lesions.

This study has several limitations. First, the number of patients was not large. Second, this study lacked a pathology at the enlarged T2WI/FLAIR-high-signal lesions. Third, we need to consider the patients' selection bias. To prove our hypothesis of the association between T2WI/FLAIR enlargement and postoperative seizures, further studies are needed to compare the serial MR images in the patients with and without seizure recurrences.

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