

Successful Treatment of Mesial Temporal Lobe Epilepsy with Bilateral Hippocampal Atrophy and False Temporal Scalp Ictal Onset: A case report

Kota KAGAWA¹⁾, Koji IIDA^{1,*}, Masaya KATAGIRI¹⁾, Takeshi NISHIMOTO¹⁾,
 Akira HASHIZUME¹⁾, Yoshihiro KIURA¹⁾, Ryosuke HANAYA²⁾,
 Kazunori ARITA²⁾ and Kaoru KURISU¹⁾

1) Department of Neurosurgery, Graduate School of Biomedical Sciences, Hiroshima University, Hiroshima 734-8551, Japan

2) Department of Neurosurgery, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, Japan

ABSTRACT

Patients with bilateral hippocampal atrophy (BHA) in a subgroup suffering from mesial temporal lobe epilepsy represent a therapeutic challenge. We achieved successful surgical treatment in a case with BHA and false lateralized ictal onset on video-scalp electroencephalogram (EEG). A 27-year-old male patient with seizures since the age of 15 years showed current seizures consisting of an epigastric aura, a feeling of difficulty in breathing and orolimentary automatism, which were frequently followed by secondary generalization with right-arm tonic extension. MRI showed BHA with hyperintensity on FLAIR and a slightly smaller volume in the left hippocampus on volumetry. Ictal EEG started from the left anterior temporal and subtemporal regions, spreading to the right anterior to middle temporal region. Interictal EEG was not lateralized, and showed independent spikes in the bilateral anterior temporal and subtemporal regions. The patient underwent chronic intracranial EEG-monitoring, revealing that the seizure onset originated from the right hippocampus with a rapid spread to the hippocampus and lateral temporal cortex on the left side. We performed a right anterior temporal lobectomy with amygdalohippocampectomy. Histological diagnosis was classic hippocampal sclerosis. The patient has since been seizure-free for 4 years. In this case, false lateralization may have been caused by an atypical seizure-propagating route to the contralateral temporal region via the dorsal hippocampal commissure instead of the usual pathway to the ipsilateral temporal neocortex. The technique of bilateral intracranial EEG-monitoring is advantageous to lateralize the actual side, particularly in BHA patients even with clearly and falsely lateralized ictal onset on scalp-EEG.

Key words: *Bilateral hippocampal atrophy, Intracranial EEG, Epilepsy surgery, False scalp ictal onset*

Signs of unilateral hippocampal atrophy detected by magnetic resonance imaging (MRI) imply the presence of mesial temporal sclerosis (MTS), thus indicating lateralization of mesial temporal lobe epilepsy (MTLE)⁴⁾. A subgroup of MTLE patients with bilateral hippocampal atrophy (BHA) poses a diagnostic and therapeutic challenge. Surgical outcomes in this group have been controversial: some establish favorable outcomes^{9,10,12)} while others continue to suffer from seizures^{4,13)}.

We achieved successful surgical treatment in a

BHA case with preoperative false lateralization on video-scalp EEG-monitoring, where ictal discharges were seen over the unilateral (left) anterior temporal and subtemporal regions, spreading to the right anterior to middle temporal regions. Intracranial EEG-monitoring revealed that the actual site of ictal onset was located in the right hippocampus, although MR volumetry indicated a slightly smaller volume in the left hippocampus. This atypical spread of ictal discharges is different from the pattern of bilateral independent mesial onsets on video-scalp

-EEG previously observed in BHA patients¹⁰). In fact, our case enhanced the significance of intracranial EEG-monitoring for surgical candidacy in terms of further seizure lateralization in BHA patients even with clearly lateralized ictal onset on video-scalp -EEG.

CASE REPORT

A 27-year-old right-handed male was referred to our hospital with intractable seizures since the age of 15 years. He was born by forceps delivery. His seizures had been poorly controlled even with multiple antiepileptic drugs. As the seizures began to increase in frequency and severity from the age of 25 years and had recently exacerbated, he was referred to our department for treatment.

On admission, he had complex partial seizures (2-3 times a week) consisting of an epigastric aura, a feeling of difficulty in breathing, and oroalimentary automatism, which were frequently followed by secondary generalization. He was treated with valproic acid and carbamazepine.

Magnetic resonance imaging (MRI) with hyperintense fluid-attenuated inversion recovery (FLAIR) and T2-weighted images showed the BHA, slightly smaller on the left than on the right side (Fig. 1). The left (0.90 cm³) and right (1.05 cm³) hippocampal volumes measured by manual tracing was performed as previously described¹⁴). Interictal 18F-fluorodeoxyglucose (FDG)-positron emission tomography (PET) demonstrated attenuated metabolism in the bilateral mesial temporal structures.

We recorded 5 habitual seizures during 7-day video-scalp EEG-monitoring with sphenoid electrodes. All seizures were clinically and electrographically identical. The seizure semiology consisted of complex partial seizures followed by

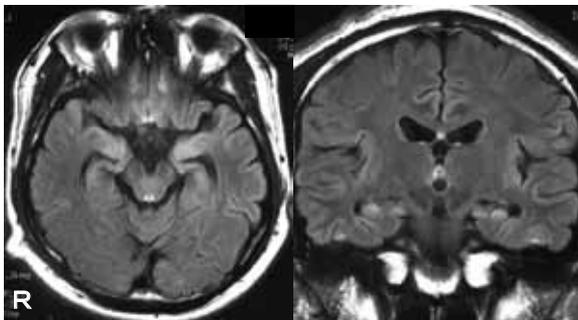


Fig. 1. Axial (left) and coronal (right) fluid-attenuated inversion recovery (FLAIR) and magnetic resonance imaging (MRI) performed in a 27-year-old right-handed male with intractable seizures since the age of 15 showed hypertensive bilateral hippocampal atrophies; the atrophy size is slightly smaller on the left than on the right side.

secondary generalization with right-arm tonic extension and left-arm flexion. Electrographically, the ictal onset was lateralized, and rhythmic delta activities originated from the left anterior to middle temporal regions and the subtemporal region (Fig. 2A). These discharges then altered to rhythmic theta activities in the same areas (Fig. 2B and 2C), and the right subtemporal and right lateral temporal regions appeared to be less involved (Fig. 2C). The seizure eventually spread to the right lateral temporal and the subtemporal regions, and then became generalized (Fig. 2D). The interictal video-scalp EEG demonstrated no lateralization, and synchronous spikes were observed in the bilateral subtemporal regions.

Considering that the seizure semiology consistently displayed a right-arm tonic extension



Fig. 2A

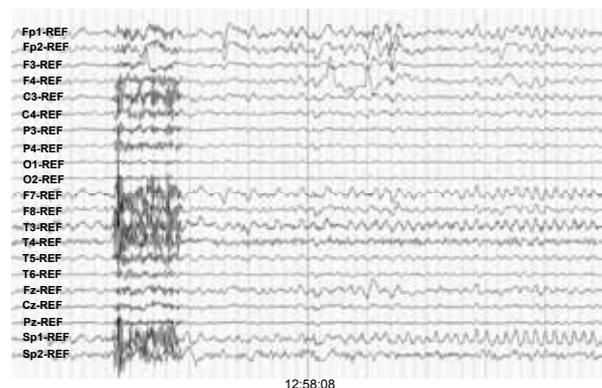


Fig. 2B

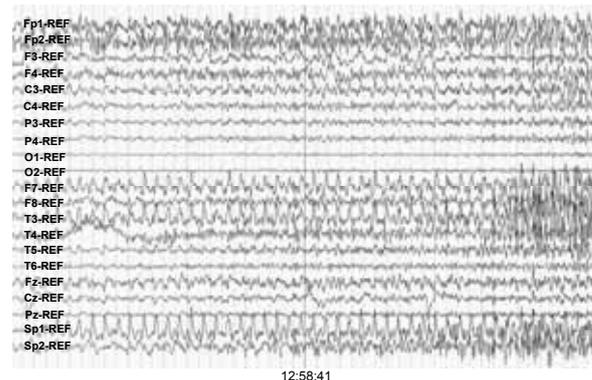


Fig. 2C

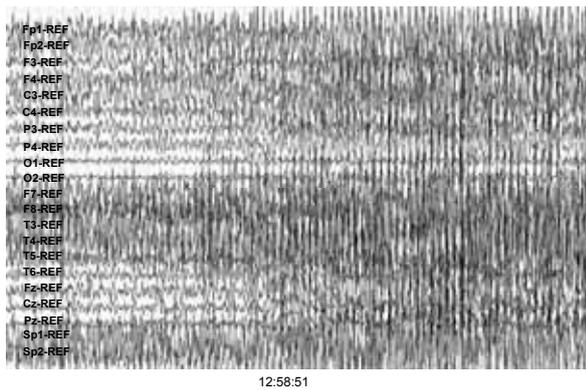


Fig. 2D

Fig. 2. Sequential ictal scalp-sphenoidal EEG-recording. (A) Electrographic onset appeared to originate from the left anterior to middle temporal (F7 and T3) and the subtemporal regions (Sp1) with rhythmic delta wave activities (arrows). (B) Following delta wave activity, rhythmic theta activity appeared, building up in the left temporal and subtemporal regions. (C) Theta activities evolved into rhythmic spike-waves in the same area with less involvement of the right temporal region. (D) The seizure eventually spread to the right subtemporal (Sp2) and the lateral temporal (F8 and T4) regions, and then became generalized with high amplitude polyspike-waves.

and MRI findings of a slightly smaller hippocampus on the left (vs the right) side, these seizures could have originated from the left side. We then adopted chronic intracranial EEG-monitoring for precise seizure lateralization. We performed a left craniotomy covering the entire temporal lobe, basal temporal region and mesial structures by placement of subdural, strip and depth electrodes. On the right side, we made a burr-hole to place two depth electrodes directly into the hippocampal head and body. However, we failed to implant the strip electrodes for the basal and lateral temporal coverage due to insufficient subdural space from the burr-hole. We recorded 35 habitual seizures with (4) or without (31) secondary generalization during the 4-day intracranial EEG-monitoring. All seizures were electrographically identical, and originated from the right hippocampus (Fig. 3A). The ictal discharges first dispersed to the left anterior basal temporal and mesial temporal regions, and then extended to the left lateral temporal cortex before reaching the left frontal cortex (Fig. 3B).

Eventually, we diagnosed his seizures as right MTLE, and the patient underwent right anterior temporal lobectomy (ATL) with amygdalohippocampectomy. A tailored hippocampal resection was performed to confirm the absence/presence of residual spike activity in the posterior

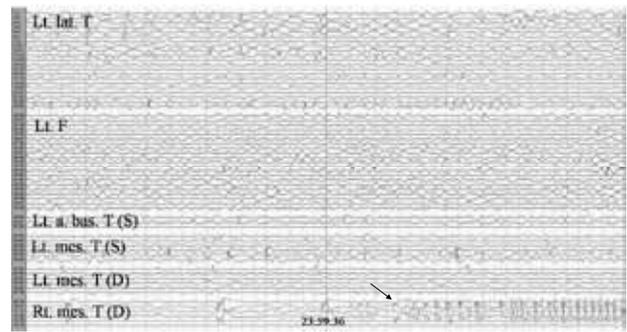


Fig. 3A

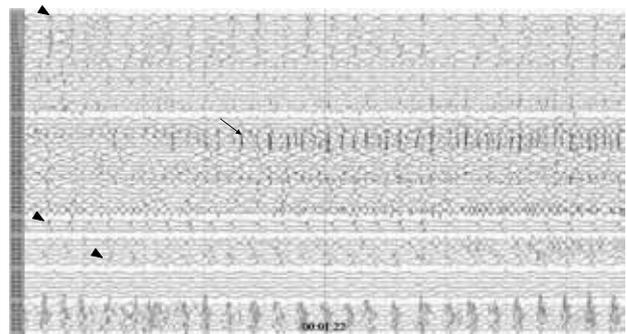


Fig. 3B

Fig. 3. Sequential intracranial ictal EEG-recording using strip electrodes (S) and depth electrodes (D).

(A) Seizures demonstrated onset in the right mesial temporal contacts and portrayed maximum levels with the hippocampal electrodes (contact 73-74; arrow). (B) Seizures propagated to the contralateral anterior basal temporal site, mesial temporal regions, and temporal cortex (contacts 49-50, 50-51, 58-59, 59-60, 1-2, 2-3; arrowheads). The seizures thereafter propagated to the frontal cortex (contacts 28-29, 29-30, 30-31). Lt, left; Rt, right; T, temporal; F, frontal; a. bas., anterior basal; mes, mesial; lat, lateral.

hippocampus (the absence of spike activity implied successful surgical intervention). Histological findings indicated hippocampal sclerosis. The postoperative course was uneventful and the patient has since remained seizure-free for 4 years with continued medication. Postoperative 4-year EEG presented no interictal activities on the right side and remained occasional sharp and wave discharges over the left anterior temporal region.

DISCUSSION

Bitemporal abnormalities on imaging studies or scalp-EEG complicate lateralizing the epileptogenic zone in MTLE patients, and surgical outcomes in this group have been controversial. Cendes et al have reported poor outcomes in patients with bilateral mesial temporal atrophy and bitemporal independent excitability on scalp-

EEG, suggesting the significance of mesial temporal atrophy in relation to intracranial stereo-EEG⁴). Accordingly, they concluded as follows: unilateral mesial atrophy predicts ipsilateral mesial stereo-EEG seizure onset despite the presence of bitemporal scalp-EEG foci. However, in patients (n=8) with significant bilateral mesial atrophy, stereo-EEG seizure may originate from either side, even with significant asymmetry. Of these 8 patients with significant bilateral mesial atrophy, 5 of 7 patients (surgery was not performed in a patient with symmetrical severe bilateral atrophy) with bilateral and significant asymmetry in mesial atrophy underwent surgery on the more atrophic side concordant with certain predominance of seizure onset, and none were seizure-free after a post-operative period of 18 to 49 months. Surgery was not done in the other 2 patients; one had seizures from only the contralateral side to the more atrophic side, while the other experienced seizures equally from both sides.

However, King et al have suggested that favorable outcomes can be achieved in BHA patients, although success depends on intracranial EEG documentation of the side with a predominant ictal onset¹⁰. Five of 53 patients who underwent temporal lobectomy for MTLE indicated BHA. Of 4 patients (1 died of postoperative status epilepticus), 3 (with symmetric BHA) and 1 (with asymmetric bilateral atrophy) were seizure-free after surgery for follow-up periods of 12-50 months. Surgery was performed on the side (regardless of the hippocampal volume lateralization), which was determined by intracranial EEG with completely unilateral seizure onset in 3 and predominant right-sided onset in 2 patients. One of the latter 2 patients (with predominantly right-sided onset) died of status epilepticus in the postoperative period.

Our case had severe BHA, although the volume was slightly smaller on the left than the right side when measured by MR volumetry¹⁴). Many studies have previously shown volume reduction of the hippocampus ipsilateral to the side of seizure onset in MTLE patients^{1,3,5,7}). Cascino et al have observed the right hippocampus volume minus the left hippocampal volume (designated DHF) for the presence of unilateral atrophy in MTLE patients³). According to their criteria, the DHF values (less than -0.2 cm^3 or greater than 0.6 cm^3) correctly lateralized the temporal lobe resected, and indeterminate DHF values (between -0.2 cm^3 and 0.6 cm^3) did not permit lateralization. Cook et al have described the ratios of right-left hippocampal volumes for convenience expressed as smaller to greater in 20 patients with well-lateralized temporal lobe epilepsy⁵). All 20 patients had asymmetric hippocampal volume loss, corresponding to the side of clinical and EEG seizure lateralization, with a ratio of hippocampal

volumes between 0.59 and 0.95 compared to >0.96 in normal subjects⁵). The ratio of hippocampal volume in our case was 0.86, indicating asymmetric volume loss of hippocampus on the left side. In addition to observations of the seizure semiology consistently with a right-arm tonic extension and video-scalp EEG-monitoring with lateralized ictal onset on the left side, we thought his seizures might have originated from the left side. Ictal symptomatology has demonstrated highly lateralizing value of unilateral tonic posturing to the contralateral side⁶).

Successful surgical treatment was established in our case, because we could lateralize all the seizure onsets to the right side by intracranial EEG-monitoring. This situation was similar to those of patients reported by King et al¹⁰). However, the preoperative scalp EEG-monitoring in our case showed a false lateralized ictal onset different from that observed in patients with bilateral mesial atrophy characterized by bilateral independent mesial onsets or unilateral onset concordant to the intracranial EEG¹⁰). The scalp ictal discharges were observed on the left anterior to middle temporal and subtemporal regions, spreading to the right anterior to middle temporal regions. Intracranial EEG-monitoring revealed that all seizures arising from the right hippocampus propagated to the temporal regions and frontal cortex on the contralateral side. As we failed to cover the right temporal cortex with intracranial electrodes, we were not able to evaluate the extent of seizure propagation to the right temporal cortex. Taking the ictal scalp-EEG findings and seizure semiology together, we hypothesized that his seizures displayed an atypical propagation route: viz., spreading not to the ipsilateral temporal cortex but to the contralateral temporal regions and frontal cortex.

According to a review by Gloor et al on depth-electrode recordings in 53 patients, they observed a large majority featuring propagation from the mesial temporal structures to the neighboring neocortex, usually in the temporal cortex⁸). However, propagation occurring directly from one mesial temporal region to the contralateral neocortex without involvement of the ipsilateral neocortex was observed in a smaller number of seizures. Additionally, some seizures spread from one mesial temporal region to the contralateral mesial and lateral temporal cortex simultaneously prior to involvement of the ipsilateral neocortex⁸). Thus, they postulated the route through the dorsal hippocampal commissure as an atypical seizure-propagating pathway to the contralateral hemisphere⁸). We have noted that such seizures might have a falsely lateralized scalp ictal EEG, because the initial mesial temporal discharge may remain undetected^{8,11}). Mintzer et al have described a rare but important phenomenon

(referred to as the “burned-out hippocampus” syndrome) in which a possibly atypical spread of ictal discharges could result in an apparent gross discordance between imaging and scalp ictal recording¹¹).

The brainstem may be responsible for this atypical pathway of ictal discharges originating from the mesial temporal region²). Based on a correlation study of ictal activities²), the cingulate gyri and anterior thalamic nuclei have also been postulated as possible pathways for the contralateral discharge propagation. Although there are insufficient data on the precise mechanism associated with the atypical seizure-propagating pathway to the contralateral hemisphere, from our present findings we speculated that the pathway through the dorsal hippocampal commissure might play an important role in structuring this crossed pattern of seizure propagation from the unilateral hippocampus to the contralateral hemisphere.

We provided successful surgical treatment for a BHA case with preoperative false lateralization on the ictal video-scalp EEG. In this case, the favorable clinical outcome was established probably because we appropriated evaluations of surgical candidacy and adopted bilateral intracranial EEG-monitoring for seizure lateralization in a BHA patient even with clearly lateralized ictal onsets on scalp-EEG.

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