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Letter to the Editor

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Epileptic Seizures with Mirthful Laughter

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Dear Editor,

Gelastic seizures (GS) are rare, short, unprovoked, and uncontrollable bouts of laughter (1,2). These attacks are often associated with other signs compatible with seizures and ictal and/or interictal abnormalities on electroencephalography (EEG) (1). GS may originate from the temporal, parietal or frontal lobes, but they predominantly originate from the hypothalamus (3). In the present study, we aimed to evaluate the typical features of GS with different foci and to investigate the brain parenchyma regions related to GS, utilizing video-EEG monitoring (VEM) in four patients with GS after obtaining their informed consents.

An 18-year-old female had mirthful laughter attacks that took place almost every day and that had started at 2 years of age. Her neurological examination (NE) was normal, but VEM revealed four GS and no ictal activity was distinguished apart from some artifacts on EEG. Brain magnetic resonance imaging (MRI) showed hypothalamic hamartoma (HH) (Figures 1a–c). The patient has been seizure-free since epilepsy surgery, which was performed 19 months ago.

A 64-year-old male had laughter bouts that started when he was 18 years old. He recently started to have epileptic seizures that included swearing and hypermotor movements as well as the feeling of fear. NE was normal, but VEM showed two GS during sleep, with a concurrent widespread low-amplitude activity on EEG. Brain MRI revealed bilateral cerebral atrophy. Because the patient declined to undergo epilepsy surgery, he uses a regimen of three antiepileptic drugs and has nocturnal seizures 1–2 times per week.

An 11-year-old male had a history of GS, with an onset at 7 years of age, which was sometimes accompanied by right-sided transient weakness. He underwent brain surgery twice during the neonatal period because of intracranial hemorrhage. He had three GS during VEM, and significant atrophy-encephalomalacia of the left cerebral hemisphere was detected in the brain MRI (Figures 1d–f). The frequency of seizures stayed the same (3–4 times a day) despite medication and vagal nervous stimulation (VNS); hence, hemispherectomy was planned.

A 38-year-old male underwent brain surgery because of a brain tumor, as he presented with epileptic seizures, which had started when he was 31 years old. Postoperatively, he was seizure-free for 6 years under diphenylhydantoin. However, since last year, he started to have uncontrollable laughter attacks as well as contractions originating from the left arm, occasionally spreading through the whole body, lasting approximately 3 min and taking place almost every day. He was using three antiepileptic drugs and had spastic paresis of the left arm. The pathology of the brain tumor, which was located in the right parietal lobe, was grade 3 anaplastic oligoastrocytoma. VEM revealed three GS, and due to the recurrence of brain tumor, he was not considered as a VNS candidate and reoperation was recommended.

In the first patient, VEM showed mirthful GS without any ictal electrophysiological EEG finding, and the patient had a diagnosis of HH, which is nearly always identified by GS. The epileptogenic region was easily determined in this patient. In the second patient, there were hypermotor seizures apart from the mirthful GS, and interictal EEG suggested the left basal frontal (anterior temporal) region, but there was no consistent lateralization/localization using ictal EEG. While the nocturnal and hypermotor features of attacks suggested the prefrontal area, some of the bouts with agitation and swearing indicated that the anterior cingulate gyrus was the epileptic focus. In the third patient, the epileptogenic area might have originated from the left hemisphere, where widespread encephalomalacia was located. The postepileptic right-sided Todd's paralysis the patient suffered might also support this hypothesis, but the ictal/interictal EEG findings suggest the contralateral frontal lobe as well. Thus, the probable epileptogenic origin is open to speculation for this patient. The last patient, who had a brain tumor located on the right parietal lobe, presented with different types of GS, some of them mirthful. The possible epileptogenic focus here was likely to comprise the networks, including the right parietal lobe (Table 1). For the last three patients, in order to make a more detailed evaluation, invasive EEG monitoring might be useful as the first step.

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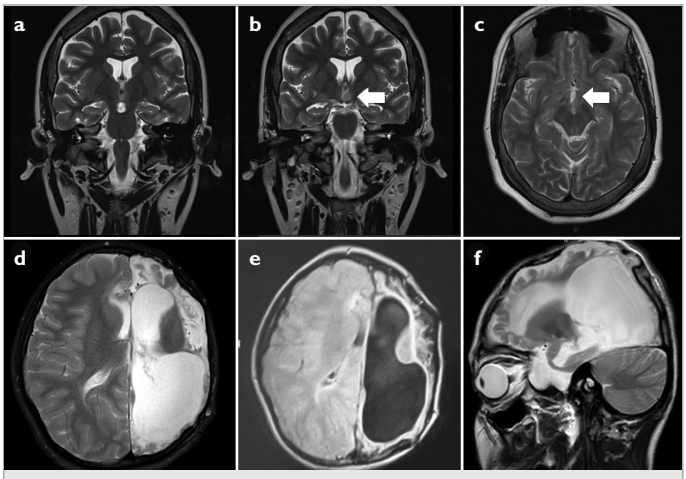


Figure 1. a-f. Case 1: Hypothalamic hamartoma and brain MRI; T2 coronal (a, b) and axial (c) planes. Case 3: Extensive atrophy and encephalomalacia of the left hemisphere, and brain MRI T2 axial (d), T2-flair axial (e), and T2 sagittal (f) planes.

Table 1. Video EEG monitoring and brain MRI features of the patients

	Patient 1	Patient 2	Patient 3	Patient 4
Interictal EEG	No sign of epileptiform discharges	Sharp wave at F7	Multifocal EEG	Sharp-slow wave activity at T5-P3
Ictal EEG	Undetermined	Generalized fast activity	Fast rhythms starting from the right F4	Undetermined
Aura	+	-	-	-
Mirth associating gelastic seizure	+	+	+	+/-
Non-gelastic seizure	+	+	+	+/-
Brain MRG	Hypothalamic hamartoma	Bilateral cerebral atrophy	Encephalomalacia of the left hemisphere	Right parietal anaplastic oligoastrocytoma

EEG: electroencephalography; MRI: magnetic resonance imaging

The definition of gelastic seizure does not indicate a certain anatomic localization. HH, which is a rare, non-neoplastic, developmental lesion originating from the hypothalamus, is the most common localization of GS (4). On the other hand, GS originating from the foci of the frontal lobe are infrequently seen. The common feature of frontal lobe GS is laughter of an artificial nature and without emotions such as humor (5). Patients with preserved consciousness during GS originating from the frontal lobe have reported a lack of simultaneous emotion or motivation (3). The second most common focus for patients who have GS is the temporal lobe (6). These patients usually report that they lose contact during GS, which often start during childhood and which can be natural, unmotivated, or associated with a feeling (5).

In a study involving dipole analysis for epileptic foci, the relationship between the clinical features of cryptogenic GS and the electrical generators that they originate from was analyzed (7,8). In two patients with subjective mirth, the suggested localization was the medio-basal temporal region, while in a patient with GS without any emotion, the focus was found to be the right frontal lobe (8). The structures that generate "emotionally driven" laughter movement are the amygdala, fusiform gyrus, parahippocampal gyrus, thalamus, hypothalamus, subthalamic regions and the dorsal tegmental brainstem (9). In the formation of laughter without emotion, the anterior cingulate, premotor frontal, and opercular areas connect with the ventral brainstem via the motor cortex and pyramidal tract (9). It is also emphasized that the neuronal activity in the hippocampal region serves an important role in the generation of mirthful GS and that the cingulate gyrus functions as a key element in the motor movement of laughter (8).

In conclusion, although the correlation between GS and HH can be made easily, GS may also originate from various other regions of the brain parenchyma. To identify structures playing crucial roles in the generation of GS, more detailed studies, including invasive EEG monitoring, should be conducted.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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