

Gelastic seizures due to right temporal cortical dysplasia

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ABSTRACT – Gelastic seizures are an uncommon seizure type. They are most frequently observed in patients with hypothalamic hamartoma. Their association with other types of cerebral lesions is rare. Depending on the location of the lesion, gelastic seizures may or may not be accompanied by a subjective feeling of mirth. The pathophysiological mechanisms of this type of seizure are still undefined, and little is known about which pathways promote laughter and its emotional content, mirth. We present a young man with drug-resistant, gelastic seizures due to focal cortical dysplasia of the right inferior temporal gyrus. The lesion was evident on cranial MRI. Interictal EEG displayed a right temporal focus, whereas ictal EEG was not informative. Ictal loss of consciousness precluded reporting of any possible emotional experience. The patient underwent surgical resection of the lesion and has been seizure-free with anti-epileptic medication for two years. Although various anatomical regions may elicit laughter, in view of the current literature it seems that the anterior cingulate region is involved in the motor aspects of laughter, while the basal temporal cortex is involved in the processing of mirth. The fact that the present case exhibited gelastic seizures stresses once more the importance of the baso-lateral temporal cortex in the genesis of this type of seizures.

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Gelastic seizures (GS) are a rare type of seizure. They can be cryptogenic, or symptomatic of a variety of cerebral lesions, most commonly hypothalamic hamartomas. Gelastic seizures associated with other types of cerebral lesions are exceedingly rare.

The pathophysiological mechanisms of this type of seizure are still undefined, and little is known about which pathways promote laughter and its emotional content, mirth (the subjective feeling of amusement). It has been claimed that mirth is dependent upon

the temporal and frontal neocortices (Papez 1937, Davison and Kelman 1939, Klüver and Bucy 1939, Terzian and Dalle 1955, Gerstenbrand *et al.* 1983, Mesulam 1985), while laughter is an automated motor program organised by the limbic system structures and the brainstem (Papez 1937, Mesulam 1985, Lopes *et al.* 1990).

We report a patient with GS related to cortical dysplasia of the temporal lobe. The patient underwent surgical resection of the lesion and the GS resolved following surgery.

Case report

A 22-year-old, right-handed man was admitted to the Neurology Department of our hospital for intractable seizures. He was the product of a non-consanguineous marriage and was born at term with no perinatal problems. He had two uncomplicated febrile convulsions at the age of two. When he was 14 years old, he started having secondarily generalized tonic clonic seizures with varying frequency (3-4 seizures/month, to once every two years). He was treated with carbamazepine without any significant improvement. At the age of 20, he began to experience laughter attacks, which occurred almost every day and lasted for 1-2 minutes. He generally experienced a loss of consciousness and postictal amnesia. He sometimes had an undescrivable feeling prior to seizures, but denied any subjective sensation of mirth. His physical and neurological examinations were normal. Personal and family histories were unremarkable except for febrile convulsions experienced by his cousins.

Outpatient EEGs indicated right temporal epileptic discharges. Gabapentine (1200 mg/day) was added to carbamazepine (800 mg/day), and he was admitted for video-EEG monitoring (VEEGM) a month later. EEG was recorded with scalp electrodes that were placed according to the 10-20 International System with additional T1-T2 electrodes. Within 24 hours he had two complex partial seizures that occurred during wakefulness. The onset of seizures was characterized by sudden, loud laughter lasting for 10-12 sec. The laughter seemed to be accompanied by a sensation of merriment, and was of a contagious nature. It was not just facial grimacing appearing as a forced smile. He failed to push the alarm button prior to seizures and was unconscious during the attacks. The laughter was followed by mild bilateral upper and lower extremity movements during the first seizure, and right hand automatisms with posturing of the left arm during the second one. Both seizures lasted for 1-2 minutes. His parents admitted that the seizures were exactly the same as those witnessed previously. Interictal scalp EEG revealed active spiking in the right temporal area, with phase reversal at T4. Ictal EEG was not informative. Short lasting, generalized slow waves were evident during the first seizure. The first ictal EEG change during the second seizure was 4-5 Hz slow wave discharges prominent on the anterior head regions (with a slight predominance in the right frontal area), and was followed by diffuse, polymorphic slow waves that ended abruptly after 30 seconds. Ictal EEG changes appeared 6-7 sec after the onset of laughter.

High resolution cranial MRI disclosed a lesion in the right inferior temporal gyrus, in close proximity to the fusiform gyrus (figure 1), which suggested cortical dysplasia. The intracarotid amobarbital test was performed prior to surgery and revealed left hemispheric speech dominance as well as an impaired memory function on the affected side.

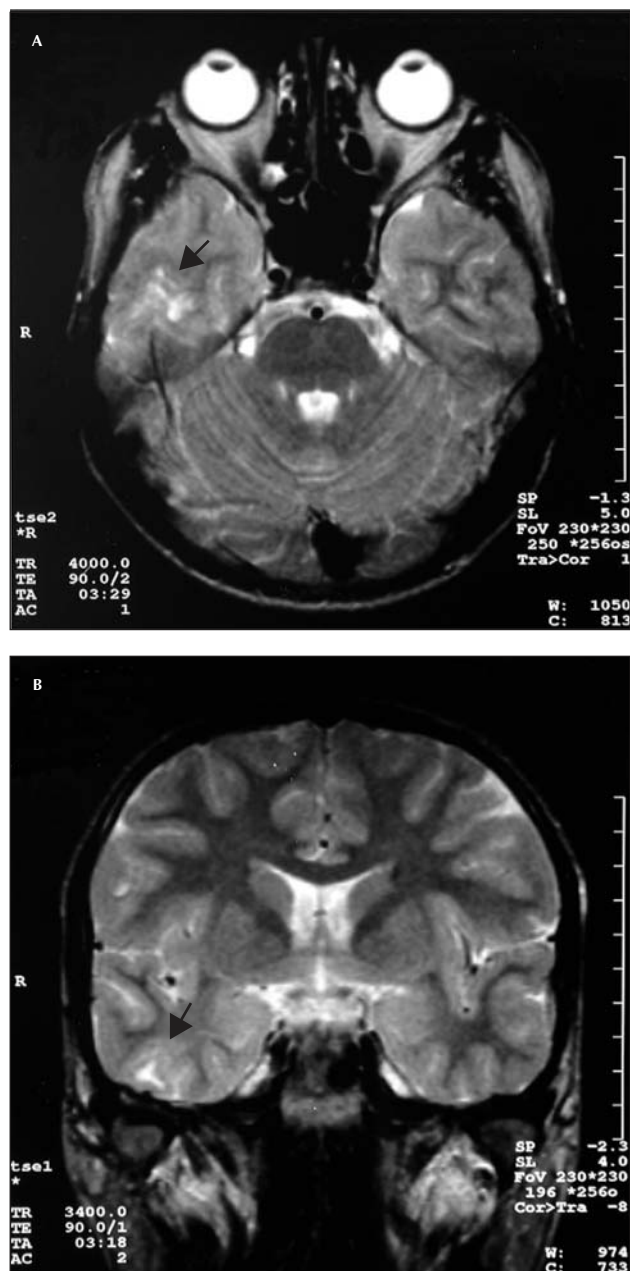


Figure 1. Axial (A) and coronal (B) T2-weighted images indicate a hyperintense lesion with minimal mass effect in the right inferior temporal gyrus (arrows).

The limits of what we considered to be a dysplastic lesion were not well delineated on MRI. For this reason a simple lesionectomy encounter the risk of leaving part of the epileptogenic zone in place. Investigation with invasive monitoring would probably provide a clearer definition of the zone to be resected. However, at that time, we had no invasive monitoring facilities, and the patient felt really handicapped by his seizures. With his consent it was decided to proceed to a right temporal lobectomy with

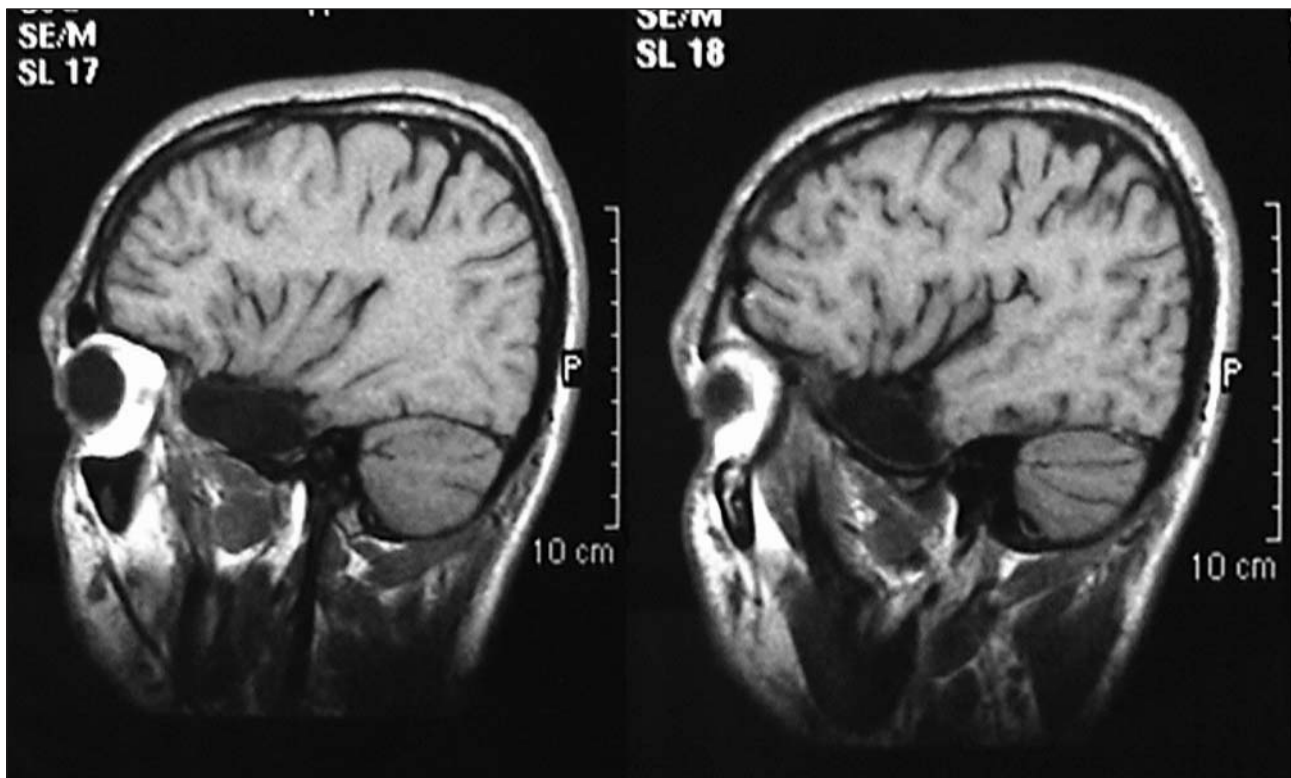


Figure 2. T1-weighted postoperative MRI in the sagittal plane disclosing the margins of resection.

amygdalo-hippocampectomy to obtain a satisfactory resection of the structurally and electrophysiologically abnormal cortex. Mesial structures were included in the resection because Flair MRI was suggestive of mesial involvement.

Pathological examination of the resected specimen was consistent with cortical dysplasia. Examination of the hippocampus did not reveal the overt cell loss consistent with hippocampal sclerosis. The anticonvulsants were not changed after surgery and the patient has been seizure-free for two years (*figure 2*).

Discussion

Gelastic seizures are characterized by inappropriate, stereotyped ictal laughter which is not precipitated by a stimulus. They account for less than 1% of all epilepsies (Chen and Forster 1973, Assal *et al.* 1993). The most common cause is hypothalamic hamartoma, where GS and other seizure types are usually accompanied by precocious puberty and behavioural disturbances (Berkovic *et al.* 1988, Tassinari *et al.* 1997, Arzimanoglou *et al.* 2003, Berkovic *et al.* 2003). Symptomatic GS, secondary to brain structural lesions outside the hypothalamus, are very rare. Although seizure control has been achieved in some patients with various anti-epileptic medications

(Ilanetti *et al.* 1997, Coria *et al.* 2000, Garcia *et al.* 2000), GS are frequently difficult to control. Few patients in the literature have undergone surgical interventions due to GS associated with lesions outside the hypothalamus (Bancaud *et al.* 1974, Arroyo *et al.* 1993, Taniguchi *et al.* 1994, Kurle and Sheth 2000, Chassagnon *et al.* 2003). The postoperative outcomes are reported to be excellent.

Focal brain lesions associated with GS are most commonly located in the frontal or temporal region. Different location of the lesions associated with GS may account for the variety of accompanying clinical manifestations. The lesion was located in the right inferior temporal gyrus and some ictal characteristics were consistent with temporal lobe seizures in our case. Interictal EEG displayed a right temporal focus. Ictal EEG however was not informative.

Striano *et al.* (1999) have also reported that ictal EEG was not informative in some of their patients since only a brief ictal depression of background rhythms was observed during seizures. It was decided to proceed for resective surgery based on cranial MRI findings and VEEGM studies with scalp electrodes. The fact that the patient has been seizure free for 2 years proves that the resected lesion was indeed responsible for the GS observed. To the best of our knowledge, this is the first reported case of GS secondary to a focal cortical dysplasia of the inferior temporal gyrus.

The neurological basis of mirth and laughter is debated. It is believed that mirth and laughter are separate functions and can be neurologically dissociated. In their elegant paper where they discuss the anatomical and physiological basis of laughter in detail, Arroyo *et al.* (1993) report on their experience with three patients. One of the patients had a lesion in the left, superior mesial frontal region. Her GS were not accompanied by a subjective feeling of mirth. Ictal subdural electrode recordings showed the seizure onset to be in the left anterior cingulate gyrus. The other two patients had complex partial seizures of temporal lobe origin. However, ictal laughter or a sensation of mirth were not part of their seizures. Electrical stimulation of the fusiform and parahippocampal gyri produced bursts of laughter accompanied by a feeling of mirth. The authors concluded that the anterior cingulate region is involved in the motor aspects of laughter, while the basal temporal cortex is involved in the processing of mirth.

Coria *et al.* (2000) have reported a patient with isolated GS secondary to entrapment of the lateral horn. The right, basolateral temporal cortex was damaged due to progressive cystic enlargement of the temporal horn in this case. During the attacks the patient was conscious and had a feeling of mirth.

In a recently published paper by Iwasa *et al.* (2002), dipole source localization corresponding to interictal spikes, were estimated using EEG dipole tracing with a realistic, three-shell head model in three patients with cryptogenic, gelastic epilepsy. In one patient who did not experience a sensation of mirth, the dipole sources were localized in the right, frontal region corresponding to the anterior cingulate. In two patients whose GS were accompanied by a subjective feeling of mirth, the dipole sources were estimated in the right or left mesio-basal temporal regions. On the other hand, Fried *et al.* (1998) reported that electrical stimulation in the anterior part of the human supplementary motor area can elicit laughter, which is accompanied by a sensation of mirth (laughter did not accompany the patient's own seizures). The duration and intensity of laughter however, were influenced by the level of stimulation current. At low currents, only a smile was present, while at higher currents a robust, contagious laughter was induced. However, cortical stimulation may have both local and more remote effects, and the possibility of temporal lobe involvement with higher currents can not be ruled out.

Chassagnon *et al.* (2003) recently reported a young male patient with cryptogenic, partial epilepsy, whose seizures were characterized by dyskinetic behavior and ictal laughter. The epileptogenic zone was circumscribed in the anterior and ventral part of the supplementary motor area and the underlying dorsal cingulate cortex. There was no or only little spreading to neighboring cortical areas. The patient remained conscious during the attacks and did not describe any subjective feeling of cheerfulness. Based on these findings, the authors stated that, by contrast to the

case of electrically-induced laughter reported by Fried *et al.*, the present case did not have the appropriate affective tone.

Although various anatomical regions such as the hypothalamus, anterior cingulate gyrus, the orbitofrontal cortex, the baso-lateral temporal cortex and the supplementary motor area may elicit laughter, in view of the current literature it seems that the anterior cingulate region is involved in the motor aspects of laughter, while the basal temporal cortex is involved in processing of mirth. The motor and emotional contents of laughter are probably represented in a large neuronal network where stimulation of any of its constituent units may activate the network entirely or in part thus leading to GS that may or may not be accompanied by a subjective feeling of mirth. The laughter in our patient was of a contagious nature. The patient *seemed* to be amused; however, ictal loss of consciousness precluded reporting of the emotional experience, if there had been any. The fact that the present case exhibited GS, stresses once more the importance of the baso-lateral temporal cortex in the genesis of this type of seizure. □

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