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Case Report

A child with refractory complex partial seizures, right temporal ganglioglioma, contralateral continuous electrical status epilepticus, and a secondary Landau–Kleffner autistic syndrome

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ABSTRACT

A 7-year-old, right-handed girl started to have seizures at age 1 year 4 months. She developed normally until age 4 when she had worsening of seizures with auditory verbal agnosia, complete aphasia, and a behavioral disorder fulfilling the diagnostic criteria of autism. Medical therapy failed. MRI revealed a right temporal tumor. Video/EEG monitoring at age 7 showed contralateral electrical status epilepticus in wakefulness and sleep and ipsilateral onset of seizures. Resection (ganglioglioma with excessive inflammation) resulted in seizure freedom and marked reduction of the autistic features. This case is unique for being, to our knowledge, (1) the first in which a lesion located in the right, rather than left, temporal lobe resulted in secondary falsely localizing left temporal lobe electrical status epilepticus with a clinical picture of Landau–Kleffner syndrome and autism, and (2) the fourth reported patient with lesional Landau–Kleffner syndrome to respond to resective surgery.

1. Introduction

Landau–Kleffner syndrome (LKS) is an epilepsy syndrome involving progressive neuropsychological impairment related to the appearance of paroxysmal electroencephalographic activity. It is characterized by acquired aphasia and paroxysmal, sleep-activated electroencephalographic paroxysms predominating over the temporal or parieto-occipital regions. Secondary symptoms include psychomotor or behavioral disturbances and epilepsy [1–3].

Most of the literature on the surgical treatment of LKS is about multiple subpial transection [4–6]. Other surgical procedures including tumor resection and temporal lobectomy have been successfully used in the treatment of LKS, to our knowledge, in only five previously reported cases [7–10].

Inflammation of epileptic cortical tissue has been described in neuropathology after seizures in experimental models and in clinical cases of epilepsy, even in cases that clearly involve congenital lesions such as cortical dysplasia [11–13].

We describe here a girl with LKS who also fulfilled the criteria for autism with left temporal electrical status epilepticus, the underlying cause of which was a contralateral right temporal, excessively inflamed ganglioglioma; after surgical resection she became seizure free, with improvement of the autistic features, speech, and cognitive function.

2. Case report

Our patient is a 7-year-old girl with no family history of neurological disease and with nonconsanguineous parents. She was the product of a full-term pregnancy and normal vaginal delivery, with normal health and development until the age of 1 year 4 months, when she started to have seizures that usually lasted about 30 seconds and recurred about once every 15 days. The seizures, by report, consisted of initial cyanosis of the face and injection of the eyes followed by pallor, loss of consciousness, uprolling of the eyes with deviation to the left, turning of the head to the left side, and then generalized tonic–clonic movements with drooling and urination. The first EEG reportedly showed "epileptic discharges," for which she was started on carbamazepine. The seizures were not controlled and recurred at the same rate. Valproate, topiramate,

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lamotrigine, and clonazepam were given sequentially with no response. By the age of 3, seizures were occurring twice a week, but her development was still normal at that time. In January 2005, at the age of 4, she started having multiple seizures per day, and over the subsequent 2 months she became completely averbal with verbal auditory agnosia, behaving as if she were deaf. She could only occasionally understand very few simple phrases and inconsistently followed some single-step commands. She was given two doses of intravenous immunoglobulin, 1 g/kg per dose (25 g/day) over 2 consecutive days, followed by a course of steroids (prednisone 1 mg/kg/day (25 mg/day) for 4.5 months, which was then tapered gradually over 1.5 months). Following administration of intravenous immunoglobulin and steroids, her aphasia showed minimal improvement: she could follow two-step commands and became slightly more interactive and responsive to discipline; however, she continued to be averbal and ignored most speech directed to her. In December 2005 her EEG revealed bilateral independent left temporoparietal and right temporal epileptic discharges. Levetiracetam was initiated and increased up to 500 mg twice daily, eliciting some response with respect to the seizures, which decreased to once every 2 to 3 weeks. However, her speech and behavioral status did not improve and then subsequently regressed to her prior status. In May 2007, her EEG revealed continuous right temporoparietal spikes in sleep with no left-sided epileptic discharges.

We saw her for the first time in July 2007, at which time she was admitted to our Epilepsy Monitoring Unit for continuous long-term video/EEG monitoring and investigations. At that time she was aphasic (averbal), exhibited markedly impaired eye contact, and was agitated and irritable all the time. She was not interested in playing with toys or with people. She was preoccupied with arranging things in her own way (she was particularly fixated on repeatedly stacking audio cassettes on top of each other). She had no or, rarely, a slight facial expression when talked to or given commands. She ignored speech directed to her; was nonresponsive to almost all commands; could follow, on rare occasions and after repeated trials, very few single-step commands; and shouted or uttered idiosyncratic sounds and syllables repetitively. She screamed for no reason. She clapped her hands frequently and repetitively, and would not hold a pen or scribble. A clinical psychologist (U.Y. Ph.D.), who is certified by the British Society of Clinical Psychology, performed a formal neuropsychological assessment in which the patient showed very poor concentration, was unable to understand instructions even after demonstration, and was assessed to be similar mentally to a 12- to 14-month-old child. Her severe impairments precluded the use of neuropsychological instruments that are used in less impaired or normal children of her age and necessitated use of the Bayley Scales of Infant Development (2nd ed.). At that time she also fulfilled the diagnostic criteria for 299.00 Autistic Disorder from DSM-IV. Table 1 summarizes the criteria applicable to our patient. The difference between her and patients with autism is that her autistic syndrome occurred after normal development.

On physical examination, the patient was conscious but noncooperative. Mental status was as described above. She was still right-handed, and otherwise her neurological examination and general physical examination were both normal. The brainstem auditory evoked response test was normal. MRI of the brain revealed a right temporal lobe enhancing lesion. The differential diagnosis included oligodendroglioma, ganglioglioma, and astrocytoma (Fig. 1).

Her EEG on July 27, 2007, was markedly abnormal because of essentially continuous left temporal spikes and spikes and slow waves in wakefulness, with further activation in drowsiness. There was some spread to the contralateral hemisphere. In addition the background was diffusely slow (Fig. 2).

During long-term video/EEG monitoring (VLTM) (July 27, 6:00 PM to August 2, 11:00 AM), the presence of electrical status epilepticus in wakefulness and in sleep was demonstrated throughout the monitoring period. This consisted of very frequent, essentially continuous left temporal focal sharp waves and spikes repeating every 1–2 seconds. In addition, there were right parietal and right posterior temporal focal spikes and sharp waves, but these were less frequent than those on the left; the left:right ratio was approximately 5:1. The patient had seven clinical seizure events similar to those described above. The semiology of these seizures was considered to be consistent with right temporal- or right frontal-type seizures with secondary generalization. Interictal SPECT showed hypoperfusion of the right medial inferior temporal lobe and hyperperfusion of the right superior temporal lobe, and ictal SPECT showed relative hyperperfusion of the right temporal lobe (Fig. 3).

The epileptogenic zone was thus judged to be right temporal, and surgery was performed on August 13, 2007. This consisted of resection of the right mesial temporal tumor along with resection of the involved amygdala and the hippocampus. The patient was discharged on levetiracetam and phenytoin. She has been seizure free since.

Neuropathological examination revealed that the lesion was a ganglioglioma involving the parahippocampal gyrus and amygdala with a marked inflammatory response greater than is usually seen in such lesions (Fig. 4). The inflammatory cells consisted of polymorphonuclear cells and lymphocytes (mostly B cells with some T cells and very few natural killer cells and helper T cells indicating active acute and chronic inflammation).

Postoperatively, two sleep-deprived routine EEGs (September 2007 and February 2008) and a 6-hour (2 hours awake and 4 hours asleep) video/EEG monitoring session (May 2008) revealed complete resolution of the left hemisphere electrical status epilepticus. This complete resolution was never seen on review of all her preoperative routine and continuous long-term EEGs. In the EEGs from

Table 1
Clinical characteristics of our patient fulfilling the diagnostic criteria for 299.00 Autistic Disorder from DSM-IV

(A) Quality impairment in social interaction	(B)Quality impairment in communication	(C) Restricted repetitive and stereotyped patterns of behavior, interests, and activites
1. Marked impairments in the use of multiple nonverbal behaviors such as eye-to-eye gaze, facial expression, body posture, and gestures to regulate social interaction	1. Total lack of spoken language	1. Encompassing preoccupation with one or more stereotyped and restricted patterns of interest that is abnormal in either intensity or focus (e.g., she arranged things, cassettes, in her own way)
2. Failure to develop peer relationships appropriate to developmental level	2. Stereotyped and repetitive use of language or idiosyncratic language	2. Stereotyped and repetitive motor mannerisms (e.g., she clapped her hands and shouted in a similar pattern repetitively)
	3. Lack of varied, spontaneous make-believe play or social imitative play appropriate to developmental level	3. Persistent preoccupation with parts of objects (she touched specific parts of her toys repetitively)