Partial Corpus Callosotomy Beneficial for Lennox-Gastaut Syndrome

—Report of Two Cases—

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Abstract

Seizures in patients with Lennox-Gastaut syndrome are very resistant to drug therapy. Division of the anterior half of the corpus callosum was performed in two patients with Lennox-Gastaut syndrome incapacitated by frequent atonic seizures leading to sudden falls. Postoperatively, the atonic seizures were completely eliminated and their mental reactivities remarkably improved. It is clear that they have benefited from a lower frequency of seizures and reduced dosages of anticonvulsant medication, which outweigh the acquired disabilities.

Key words: Lennox-Gastaut syndrome, corpus callosum, atonic seizure

Introduction

Lennox-Gastaut syndrome was first described by Lennox and Davies¹³⁾ and later, more clearly by Gastaut *et al.*⁴⁾ The series of Lagenstein *et al.*¹²⁾ demonstrated cortical atrophy on computed tomographic (CT) scans in more than 50% of cases and neurological abnormality in 60%. Most patients suffer not only tonic seizures but also atypical absences and atonic seizures, which cause sudden falls and injuries. Such seizures incapacitate the patients in daily life and are very resistant to drug therapy. The characteristic electroencephalographic (EEG) findings are interictal diffuse slow spike and wave (2–2.5 Hz).

Van Wagenen and Herren²³⁾ introduced section of the corpus callosum to limit the bilateral spread of a convulsive wave in 1940. Since then, however, use of this promising technique has been limited, possibly because of the high operative morbidity reported. Recently, callosotomy has more frequently been used encouraged by the results of many authors.^{6,10,14,18–21,24)} We report here good results of corpus callosotomy in two patients with Lennox-Gastaut syndrome, with control of epileptic seizures and improvement in mental activity.

Case Reports

Case 1: A 28-year-old female first experienced seizures at 4 years of age. The seizures consisted of atypical absence attacks, atonic seizures, and generalized tonic seizures. She had contracted an infectious disease with high fever for 2 weeks prior to the onset of seizures. At 8 years old, a few, poorly documented nocturnal seizures occurred, and at 11 years old, a generalized tonic-clonic seizure was followed by a series of complex partial and absence seizures. These seizures were difficult to control with drug therapy and, at 12 years old, were considered part of Lennox-Gastaut syndrome. Anticonvulsants were tried in many hospitals but did not achieve seizure control. When she was 20 years old, the frequency of seizures increased despite administration of many anticonvulsants. Sudden falls during attacks occurred, due to a temporary complete loss of consciousness or an atonic state. The anticonvulsants then given were phenytoin, primidone, ethosuximide, and diazepam, with serum values within the therapeutic level.

On January 22, 1985, she was admitted for corpus callosotomy. Up to 10 atonic seizures and multiple atypical absence attacks were occurring every day. She had suffered several minor injuries during the atonic seizures. An EEG demonstrated the diffuse

Fig. 1 Case 1. Preoperative EEG, demonstrating bilaterally synchronous, diffuse slow spike and wave complex (2.5 Hz) discharges characteristic of the Lennox-Gastaut syndrome.

Fig. 2 Case 1. Preoperative CT scans, demonstrating no particular focal abnormality except moderate cerebral atrophy and calvarial thickening.

slow spike and wave complex (2.5 Hz) in the interictal phase (Fig. 1). Many atonic seizures were observed, during which she lost all body tone and fell to the floor. A Wechsler Adult Intelligence Scale-Revised (WAIS-R) test showed a full-scale intelli-

gence quotient (IQ) of 55, with a performance score of 51 and a verbal score of 68. A Wada test showed bihemispherical language function, with the left predominant. Memory was bilaterally decreased but definitely worse on the left after an injection of amytal sodium. A concurrent angiogram disclosed no abnormalities. A CT scan only demonstrated moderate cerebral atrophy (Fig. 2).

On February 15, 1985, a limited corpus callosotomy (anterior half) was performed using the operative microscope (Fig. 3). The mid-portion of the corpus callosum was identified by intraoperative skull x-ray. A large titanium clip was placed at the posterior margin of the divided corpus callosum to mark the exact position on postoperative x-ray films and in case total corpus callosotomy became necessary because of further seizure attacks. Postoperatively, she quickly recovered and showed no characteristic disconnection syndrome. By the second week, she could walk, eat, and dress unaided. No atonic seizures, atypical absence seizures, or sudden falls occurred. However, a new type of attack consisting of short-duration tonic seizures confined to the right upper extremity began to occur.

A postoperative EEG demonstrated marked qualitative decrease of spike and wave complex discharges from the right hemisphere. The slow spike and wave complexes still occurred in the left hemisphere, which corresponded to the postopera-

Fig. 3 Case 1. Intraoperative photographs of the corpus callosum section. Because of cerebral atrophy, the corpus callosum (arrowheads) was easily exposed under the operative microscope (left), and the anterior half divided (arrows) with microscissors and bipolar coagulator (right).

Fig. 4 Case 1. EEGs performed 35 days (*left*) and 4 years (*right*) postoperatively, showing a remarkable qualitative improvement in spike and wave complex discharges from the right hemisphere.

tive clinical features (Fig. 4 *left*). Presently, her medication is valproic acid and diazepam, but the attacks in the right upper extremity occur two to three times per month. Follow-up EEGs performed every 6 months after discharge demonstrated no significant changes (Fig. 4 *right*).

Case 2: A 33-year-old female began to suffer seizures at 3 years of age. The seizures were atypical absences, which began and ended gradually. Incomplete loss of consciousness and continued abstracted behavior occurred. When she was 10 years old, tonic-clonic seizures were recognized in addition to the atonic seizures. These seizures could not be controlled by phenytoin, primidone, ethosuximide, valproic acid, diazepam, phenobarbital, or mephobarbital in various strengths and combinations. When she was 13 years old, a left putaminotomy to decrease the frequency of epileptic attacks was performed but had no effect. Violent behavior began when she was 25 years old.

She was admitted in April, 1988. Despite administration of many anticonvulsants maintained within therapeutic serum levels, atonic seizures were occurring countless times each day, generalized tonic-clonic seizures at least every other day, and

complex partial seizures about three to four times a day. The last was characterized by aggressive behavior lasting for several minutes followed by urinary incontinence and drowsiness. Many injuries were evident on the face and head. EEGs showed bilaterally synchronous spikes and atypical spike and wave complexes throughout both hemispheres in the interictal state (Fig. 5 *left*). Prominent increases in the high-voltage spikes predominantly in the frontocentral area appeared in the ictal state (Fig. 5 *right*). Based on the clinical and EEG findings, the diagnosis was Lennox-Gastaut syndrome.

A plain skull x-ray film was normal except for calvarial thickening. A CT scan and a magnetic resonance (MR) image revealed moderate cerebral atrophy and a small porencephaly of the left putamen resulting from the previous putaminotomy (Fig. 6). A WAIS-R test showed a full-scale IQ of 71, with a performance score of 65 and a verbal score of 78. A Wada test performed in April, 1988 demonstrated bihemispherical language function, with the left predominant. Memory was bilaterally decreased but slightly worse on the right after an injection of amytal sodium. A concurrent angiogram showed no abnormalities.

Fig. 5 Case 2. Preoperative EEGs, demonstrating bilaterally synchronous spike and wave complex (2-2.5 Hz) discharges in the interictal state (*left*) and remarkable spike discharges in the ictal state (*right*).

Fig. 6 Case 2. Preoperative CT scan (*left*) and MR image (*right*), demonstrating moderate cerebral atrophy, small porencephaly at the left putamen (*arrows*) due to the previous putaminotomy, and calvarial thickening, but no other lesion initiating the frequent convulsive seizures.

The anterior half of the corpus callosum was divided on May 18, 1988. A large titanium clip was used to mark the posterior margin of the division. She

promptly recovered and showed no postoperative mutism. During convalescence, several partial motor seizures involving the left arm and left side of the face and lasting about 30 seconds occurred, but she was alert throughout. These seizures were controlled with valproic acid and carbamazepine.

From May 19, 1988 to November 24, 1989, no seizures inducing loss of consciousness occurred. At discharge on June 24, 1988, her personality had shown a remarkable improvement to friendliness and co-operation. MR images taken 1 year postoperatively showed a section at the mid-portion of the corpus callosum (Fig. 7). An EEG recorded on June 21, 1988 showed a qualitative improvement in spike and wave complex discharges from the left hemisphere. Spike and wave complexes were still seen in the left frontocentral region, but the potential was much lower than on the right (Fig. 8 *left*). An EEG recorded 17 months postoperatively demonstrated bilateral spike and wave complex discharges with right dominance, but there was no bilateral synchronization (Fig. 8 *right*).

Fig. 7 Case 2. Postoperative lateral (*left*) and coronal (*right*) MR images. Coronal sliced figure corresponding to F₃ (*arrowheads*) shows a section of the corpus callosum at the mid-portion (*arrow*).

Discussion

Lennox-Gastaut syndrome is known to be secondary to an undetermined encephalopathy. Evidence of cortical atrophy is found in more than 50% of cases examined by CT.¹²⁾ Many types of seizure may occur in

Lennox-Gastaut syndrome, but atonic, tonic, and clonic seizures are characteristic.⁴⁾ Many injuries to the face and head occur due to sudden falls caused by frequent atonic seizures.⁴⁾ Slow spike and wave complexes (2–2.5 Hz) in EEG are also important characteristics of this syndrome.⁴⁾ The seizures are very resistant to drug therapy, and even if an effective drug is found, it is only possible to control the seizures temporarily. Our patients displayed these pathognomonic features of Lennox-Gastaut syndrome.

Van Wagenen and Herren²³⁾ introduced the concept of corpus callosum section intended to prevent convulsive waves from spreading bilaterally based on the observation that epileptic patients who sustained a stroke involving the corpus callosum often showed improved seizure patterns. Various combinations of interhemispheric fiber tracts have been sectioned.^{2,6,10,14,18–21)} Most reports indicate that commissurotomy gives encouraging results in patients with intractable seizures. Concurrently with clinical applications of commissurotomy, experimental data have also been obtained. Erickson³⁾ demonstrated that the corpus callosum is the major factor in the

Fig. 8 Case 2. *left*: EEG performed 1 month after surgery, showing qualitative improvement in spike and wave complex discharges from the left hemisphere. *right*: EEG recorded 17 months postoperatively, demonstrating bilaterally independent spike and wave complex discharges with right dominance.

propagation of seizures in monkeys. Other experiments have also demonstrated the disruption of seizure spread by division of the commissure.^{11,15,16)} Such data have often been cited to support clinical application.

Although optimal selection criteria for commissurotomy are unresolved, early clinical results suggest better outcomes in patients with secondary generalized seizures.^{10,25,27)} In addition, atonic or akinetic seizures usually involving sudden falls also respond favorably to commissurotomy.^{5,6,18,20,21,28)} Williamson²⁴⁾ reviewed the surgical outcomes in various series and found sufficient improvement to justify surgical intervention in Lennox-Gastaut syndrome.

Whether a partial commissurotomy, as performed in our cases, is preferable to complete division as an initial procedure is less clear. Roberts²¹⁾ advocated partial commissurotomy in most patients, with division of the anterior half to two-thirds of the corpus callosum unless there is evidence of a predominantly posterior focus. Gates *et al.*⁵⁾ and Wilson *et al.*²⁷⁾ divided the corpus callosum totally, including the hippocampal commissure in their patients. However, total section of the corpus callosum may cause greater disconnection effects. An alteration in cognitive function after the section of the corpus callosum was reported by Akelaitis¹⁾ in 1944. More recently, Gazzaniga *et al.*^{7,8)} have demonstrated numerous disconnection effects by more advanced methods, although significant handicaps in these patients were unusual. Gates *et al.*⁶⁾ reported that neuropsychological testing showed no significant effects on daily life overall in a group of patients undergoing total corpus callosotomy. In Roberts' series,²¹⁾ five of 51 patients had decreased cognitive ability postoperatively.

In our patients, division of the anterior half of the corpus callosum was confirmed by postoperative x-ray films and MR images. Postoperative neuropsychological evaluation showed no new impairment in their cognitive function but marked improvement in response as a result of both diminished seizure activity and decreased anticonvulsant medication. Follow-up EEGs demonstrated only spike and wave complex discharges from the left hemisphere after 4 years in Case 1. Case 2 demonstrated independent spike and wave complex discharges from both hemispheres, although spike dominance was on the right. Bilateral synchronization of these waves was not observed. These EEG findings suggest that the preoperative epileptogenic focus in Case 1 was in the left hemisphere and in Case 2 in both hemispheres. The bilateral synchronous discharges leading to sud-

den falls in Case 2 were blocked by the corpus callosotomy.

Although favorable responses have been reported for complex partial seizures,^{10,18,19,22)} the mechanism suppressing attacks is much less obvious. Spectral EEG analysis with implanted electrodes⁹⁾ and depth recording¹⁷⁾ suggest a type of epileptic spread not involving the callosum in complex seizures.

Based on the present experiences and many previous reports,^{5,6,10,14,18,19,24,26)} we recommend a commissurotomy should be considered in Lennox-Gastaut syndrome cases in which seizures are mainly the atonic type, very resistant to the drug therapy, and actually incapacitate the patient.

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