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소아 간질 치료에서 뇌량 전체 절제술의 결과

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The Results of One stage Total Callosotomy in Pediatric Epilepsy

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Purpose : In the pediatric patients who have medically intractable epilepsy the callosotomy is useful to prevent the propagation of seizure from one hemisphere to the other. The indications of callosotomy are drop attack, life threatening primarily or secondarily generalized seizure, medically refractory mixed seizure types such as Lennox-Gastaut syndrome. In addition, the retarded children are not contraindicated. The anterior callosotomy is used to perform to control medically intractable epilepsy which is believed to have some advantages to total callosotomy. But, we propose that the anterior callosotomy does not seem to be superior to total callosotomy for the prevention of the propagation of seizure or complication. We describe a series of 21 patients with medically intractable epilepsy who underwent total callosotomy in one stage.

Methods : The diagnoses in these patients included Lennox-Gastaut syndrome, atonic seizure, infantile hemiplegia, and no obvious solitary seizure focus on chronic video/EEG monitoring to characterize seizures, electrographic activity, and postictal behaviors. Preoperatively 16 patients suffered from disabling drop attacks or intense head drop seizures which caused frequent physical injuries. Other types of seizures are 12 generalized tonic-clonic seizures, 7 complex partial seizures, 1 absence seizure, and 7 myoclonic seizures. Male : Female=14 : 7, Age : 2-22 years (Mean : 9.4 years). The follow-up period ranged from 0.8 to 3.8 years (median 2.4 years). Seizure outcome, parental assessment of daily function, and parental satisfaction with outcome were assessed postoperatively.

Results : Drop attacks disappeared completely during the entire follow-up period in 13 patients and decreased to less than 10% of baseline in five. The corpus callosum of the one patient were not completely sectioned in Diffusion Tensor Image, tractography. Other types of seizures resolved completely in 14 patients and decreased in 7. 2 patients experienced a transient disconnection syndrome, but completely resolved within four weeks. Overall daily function improved and parents were satisfied with the surgical outcome in all patients except three who experienced recurrent of drop attacks after operation. There was no sign of significant and persistent neurological deficits in any case.

Conclusion : Results of total callosotomy in patients with medically intractable epilepsy with diffuse epileptic foci were favorable in most cases. The procedure was particularly effective against drop attacks causing physical injuries and impaired quality of life in these patients. (J Korean Epilep Soc 2005;9(2):165-171)

KEY WORDS : Callosotomy · Drop attack · Atonic seizure · Lennox-Gastaut syndrome.

Introduction

In pediatric patients, early surgical intervention should be considered in terms of seizure control and prevention of neuronal deterioration. The common indication for callosotomy was medically refractory and generalized or partial seizure with a rapid secondarily generalized pattern without localized lesion. In particular, total callosotomy is effective for the treatment of drop attack, life threatening primarily or secondarily generalized seizure, medically refractory mixed seizure types such as Lennox-Gastaut syndrome, and has been considered most helpful in patient sustaining frequent injuries from epileptic falls, especially those resulting from atonic seizures. The callosotomy was first introduced as a surgical

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treatment for medically intractable epilepsy in 1939 by Van Wagenen and Herren.[1] Subsequent reports have confirmed the efficacy of the operation decreasing the frequency and severity of drop attacks or myoclonic seizures.[2,3] In addition to the reduction of seizure frequency, recent reports pointed out improved behavior and good parental satisfaction as important measures for evaluating this surgical intervention.[4,5] However, the benefit from the procedure was continued debate, particularly with respect to the effect of callosotomy in some seizure types and the extent of surgery. To identify the effect of total callosotomy on intractable generalized seizure and other seizure types, we report the result of 21 cases that underwent total callosotomy at Yonsei University Medical Center between Mar. 2001 and Jun 2005.

Methods and Materials

Patients

The records of all patients who underwent total callosotomy at Yonsei University Medical Center between Mar. 2001 to Jun. 2005 were retrospectively analyzed and followed for at least 8 months. Their ages ranged from 2 to 22 years (mean age : 9.4 years) and the male to female ratio was 14 : 7. Mean follow up duration was 2.4 years (ranging from 0.8 to 3.8 years) and the duration of seizure ranged from 0.9 to 20 years (mean 7 years). Our patients have had diverse causes of epilepsy, including neonatal complication, infantile spasm, cortical dysplasia, viral encephalitis, head trauma, and Down syndrome. Also, several patients have been diagnosed as Lennox-Gastaut syndrome secondary to various causative factors. The indications for total callosotomy in our series were as follows : 1) medical intractability of seizures (at least 3 years of intractable seizures with the attempted use of all standard anticonvulsant) ; 2) seizure type potentially amendable to callosotomy (particularly generalized atonic, tonic, or tonic-clonic seizures) ; 3) no single epileptiform focus identified. For preoperative work-up, continuous electroencephalogram (EEG) and video monitoring were performed to characterize seizure type in each patient. Brain magnetic resonance image (MRI) and EEG were performed pre- and postoperatively (Figure 1). 15 patients underwent neurophysiological test to evaluate their intelligence quotients (IQ) and cognitive deficits preoperatively and postoperatively. Other preoperative evaluations included interictal Single Photon Emission Computed Tomography (SPECT) in 2 patients, and Positron Emission Tomography (PET) study in 17. The completeness of callosal section was visually confirmed intraoperatively in all cases. Postoperative MR images were obtained in all patients, and the completeness of the callosal section was reconfirmed (Figure 1). There was no evidence of contusional, hemorrhagic, or ischemic changes of the brain around the surgical site in any case.

Types of seizure and surgical outcome

Seizures were classified into five types : general tonic-clonic seizure (GTC), complex partial seizure (CPS), absence

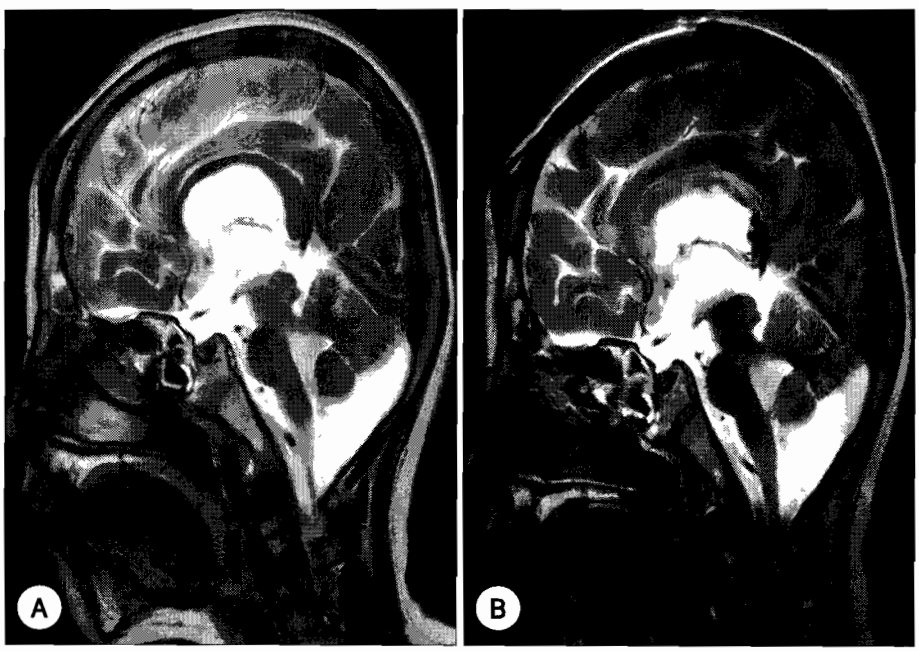

Figure 1. Preoperative (A) and postoperative (B) midsagittal MR images. Total callosotomy was performed in a one-stage operation.

Table 1. Classification of seizure outcome (modified Wyler's calssificaiton)

Class	Description
Class1	Free of seizure: when completely free of motor Seizure
Class2	Significantly improved: decrease in the frequency of the most disabling type of seizures, by at least 75%
Class3	Unchanged: Little or no change in seizure frequency or postoperative worsening of seizures

seizure, myoclonic seizure, and drop attack ; the last category included all atonic, akinetic, tonic or tonic-atonic seizure associated with abrupt falls. Seizure outcomes of each seizure type were evaluated according to modified Wyler's classifycation (Table 1).[6] Patients were followed-up for at least 8 months before they were classified as improved or seizure free. A patients was considered a failure if there was no improvement within the first 3 months of surgery. The significant improvement was defined as class 1 or class 2.

Daily function and satisfaction

Changes in daily function and parent satisfaction with surgical outcome was obtained during follow-up admission, out patient evaluation, and consultation. Daily function was assessed in terms of changes in attention, emotional well-being, daily activity and hyperactivity. Changes in overall daily function were categorized as improved, unchanged, and impaired. Parental satisfaction was assessed as excellent, moderate, and poor. In addition, parents were interviewed to ascertain changes in daily function and their satisfaction.

Results

Demographic data

21 patients were included in this study ; 14 patients were male and 7 were female. The age of patients at the time of onset of seizures ranged from birth to 20 years with a mean of 2.8 years. The mean age at the time of surgery was 9.4 years with a ranged of 2 to 22 years. Although the follow-up period was short, no patient was followed for less than 9 months.

Seizure types

21 patients demonstrated either drop attack or mixed seizure. Of 5 patients with mixed seizures, one had three seizure types, and four had two seizure types. The seizure types represented in the mixed group included : generalized tonic-clonic seizure in 12 cases ; complex partial in 7 ; absence in 1 ; myoclonic in 7. The frequency of seizure was variable from 2/day to 150/day. During chronic video/EEG monitoring, the common type of drop attack was a tonic seizure in chronic video/EEG monitoring.

Table 2. Surgical outcome of callosotomy according to the seizure types in 21 patients

Type of seizure	Class 1	Class 2	Class 3
Drop attack	13	5	3
GTC	6	4	2
CPS	4	1	2
Abscenc	1	0	0
Myoclonic	3	2	2
Total (cases)	7	10	4

GTC, generalized tonic-clonic seizure; CPS, complex partial seizure

Seizure outcome

7 patients (30%) became seizure free ; of these, five had drop attack, one had complex partial seizure, one had absence seizure. Four of 21 patients unchanged : two had generalized tonic-clonic seizure, one had complex partial seizure, and one had myoclonic seizure. After at least 9 post-operative months, the outcome of total callosotomy was evaluated. Significant improvement was defined as class 1 or 2. Overall outcomes were : 7 case of class 1, 10 of class 2 and 4 cases of class 3 (Table 2). The surgical outcomes were variable according to types of seizures. Drop attack was dramatically improved after total callosotomy. Among 21 cases with drop attacks, there were 13 of class 1, 5 of class 2 and 3 of class 3. Significant improvements were 85.7% in drop attack. However, significant improvement in CPS and myoclonic seizure were much lower than those of drop attack or GTC (Table 2). One patient underwent hemispherotomy as a second step to control intractable seizures originating from unilateral hemispheric lesion. After the second operation, the patient became class 1. After the total callosotomy, one patient developed a new type of seizure with a localized focal spike wave. In the patient, GTC newly developed after total callosotomy. With respect to operative complication, the disconnection syndrome was observed in 2 patients with total callosotomy but it gradually improved and became non-problematic within 4 weeks.

Changes in daily function and satisfaction

The parent assessed the overall daily function as improved in 57% of patients and impaired in 23% (Table 3). Satisfaction after total callosotomy was achieved in parent of 71% of the patients (Table 4). Postoperative changes in daily function

Table 3. Assessment of overall daily function

	Overall daily function		
	Improved	Unchanged	Impaired
Infant patients (2-8 yr) (n=10)	7	1	2
Adolescent patients (9-22 yr) (n=11)	5	3	3
Total (n=21)	12	4	5

Table 4. Parent satisfaction

	Satisfaction		
	Excellent	Moderate	Poor
Infant patients (2-8 yr) (n=10)	7	2	1
Adolescent patients (9-22 yr) (n=11)	3	3	5
Total (n=21)	10	5	6

Table 5. Seizure control and changes of EEG pattern after callosotomy in 21 patients

Changes of synchronous spike wave	Class 1	Class 2	Class 3
Totally abolished	6		
Marked decreased (75%<)	2	4	5
Unchanged		2	2

All patients in our series had preoperatively bilateral synchronous spike wave by scalp EEG and EEG video monitoring

found in attention, emotional well-being, daily activity, and hyperactivity. Improvement was most often seen in attention and emotional well-being. However, As a usual, parent complained of hyperactivity and slight stammering.

EEG findings

Preoperatively, the predominant interictal pattern in patients was bilateral synchronous spike and wave by scalp EEG and chronic video/EEG monitoring. Other EEG findings included diffuse slow spike and wave complex, or polyspike and wave, or multifocal spike and slow wave. Typically, EEG findings of drop attack due to tonic seizure were a generalized irregular theta/delta burst or diffuse back ground suppression proceeding low amplitude fasting activity with rhythmic activity (4-6 Hz). Postoperative EEG revealed completely abolished bilateral synchronous polyspikes and waves in 6 cases that were classified as class 1, bilateral synchronous polyspikes and waves diminished by more than 75% in 11 cases, unchanged in 4 cases (Table 5). Among 11 cases with bilateral synchronous polyspikes and waves diminished by more than 75%, there were 2 of class 1, 4 of class 2 and 5 of class 3. A reduction in the number of spike and wave complexes and the persistence of occasional bursts of synchronous discharges were observed in all patients with significant improvement.

Functional outcome and prognotic factors

We compared the surgical outcomes of 10 infant patients (age ≤8 years) with those of 11 adolescent (age >8). Among 10 infants, there were 7 in Class 1, 2 in Class 2, and 1 in Class 3, while among 11 adolescents ; there were 3 in Class 1, 3 in Class 2, and 5 in Class 3. These results indicated the age factors might be influenced the surgical outcome. Also, younger patient was to predict improvement in overall daily function. In overall daily function and parent satisfaction, younger patients obtained a superior outcome. Finally we suggested that the superior postoperative satisfaction in the younger patients may have been due to the significantly better functional outcome observed in the younger patients. 15 patients underwent a pre-and postoperative neuropsychological assessment. Mild mental retardation (55-70) was noted in 7 patients, severe mental retardation (40-55) in 2 patients, and profound mental retardation (<40) in 6 patients. In our series, children with mental retardation had a good outcome. Significant improvement was found in 5 of the 7 (71.4%) patients with mild mental retardation, and 5 of the 6 (83%) patients with profound mental retardation. Intelligence quotients (IQ) and cognitive deficits were not correlated with outcome. Generally mental retardation can be a manifestation of pervasive cortical dysfunction, these patients may have a lower threshold for epileptogenesis and poor prognosis. Therefore, we did not consider mental retardation to be a contraindication to total callosotomy.

Discussion

Total callosotomy has been proposed for patients with severe developmental delay and various seizure types.[7,8] Children with medically intractable seizures often show severe developmental delay because of brain abnormalities and persistent seizures. Therefore, early surgical intervention has been reported to be very important because developmental defects are minimized if seizures are controlled by operation.[9-11] Cerebral hemispheres connect with six midline commissural structures : anterior commissure, posterior commissure, corpus callosum, hippocampal commissure, massa intermedia of thalamus, and fornix. More than 60% of corpus callosum, which contains about 300 million fibers, are fast-conduction myeli-

nated fibers. The rationale for callosotomy was based on the hypothesis that the corpus callosum is the most important pathway for the interhemispheric spread of seizure activity, especially in secondarily generalized seizures. Crowell and Ajomone reported that experimentally induced cortical epileptic activities of one hemisphere were also found in the homotopic area of the opposite hemisphere.[12] Therefore, they suggested that a cortical epileptic discharge in one hemisphere is transferred to the other to induce epileptic synchronization. Several experimental observations corroborate division of the corpus callosum to treat seizures : 1) The corpus callosum is a major pathway for interhemispheric generalization of seizures in monkeys.[13] 2) The callosotomy can disrupt interictal bilateral synchronous spike and wave activity in cats.[14] and in human.[15] 3) The corpus callosum may exert a tonic influence on seizure foci by inhibiting kindled seizures in rhesus monkeys, but facilitating the same process in the baboon Papio papio.[16]

The common indication for callosotomy was medically refractory and generalized or partial seizure with a rapid secondary generalized pattern without localized lesion. There is still no universal agreement on indications for callosotomy. Many reports support the idea that callosotomy would benefit patients with intractable seizures, especially those who suffer with epileptic falls from generalized seizures, such as tonic, tonic-clonic, clonic, and atonic seizures.[17] In some reports, satisfactory outcomes with more than 50% reduction of seizures were recorded in patients with generalized tonic-clonic seizures (38−86%), generalized tonic seizures (43−60%), atonic seizures (60−83%), and complex partial seizures (50−51%).[6,18,19] Our result indicate that one stage total callosotomy provided more seizure control and less complication than does other callosotomy. In our experience, the best outcome was achieved in drop attacks (85.7%), generalized tonic-clonic seizures (83.3%), and complex partial seizures (71.4%). The issue of the required extent of resection has been a subject of considerable controversy. Previous studies support the view that a total callosotomy controls seizures more effectively than an anterior callosotomy.[1,20,21] Spencer et al. concluded that a total callosotomy was twice as effective as an anterior callosotomy in controlling seizures,[22] and more seizure type, lower verbal IQ scores, and diffuse ictal EEG patterns were significantly more common in case of anterior callosotomy failures.[8] Pinard et al. demonstrated that partial callosotomy for drop attacks was effective only in 3 (27%) of 11 children after West syndrome, whereas total callosal section was effective in 8 (89%) of 9 children.[7] In our opinion, the anterior callosotomy does not seem to be superior to total callosotomy in the prevention of the propagation of seizure or complication. However, contrary to our opinion, Purves, et al., supported the contention that anterior callosotomy may be sufficient for many patients, reporting that this procedure resulted in improvement in 75% of their series.[3] Seven of 24 patients developed a truncated disconnection syndrome marked by mutism and left hemiataxia, but these disturbances cleared over a few days. Murro, et al., reported that 17 (68%) of 25 patients experienced significant reduction of generalized tonic-clonic seizures following anterior callosotomy.[23] These discrepancies in multiple studies ascribed to difference in the patient selection and the definition of successful surgery, in addition to the extent of callosal section. Callosotomy is usually performed in two stages in most epilepsy centers.[8,24] The reason for two stages callosotomy was that neuropsychological sequela may be less pronounced. Previously, we conducted two-staged callosotomy in patients with medically refractory seizures, but we have shifted to one-stage total callosotomy for children with drop attack and intractable GTC. The change in surgical procedure was impelled by our experience and the studies by Lassonde and Sauerwein,[25] and Lassonde, et al.[26] Interhemispheric communication was not impaired in cases in which the corpus callosum was absent early in life, whether for congenital reasons or due to surgery.[26] The most appropriate time for considering surgery for medical intractable seizure has not been clearly defined. However, we advocate performing total callosotomy before puberty because of the greater gains in cognitive function and social adjustment as well as the reduced risk of neuropsychological deficits.[25,27] One of the possible explanations for the superior functional outcome in children is that congenital or early functional absence of transcallosal projections may lead to the development alteration and/or selective reinforcement of connections that would not have been formed or reinforced under normal circumstances. The use of subcortical pathways, such as the intercollicular or the posterior commissures, has also been invoked to explain the excellent transfer abilities of acallosal and young callosotomized patients.[28] Drop attacks are the most severe seizure type and place a severe burden on both patients and their families. In our series, 85% of patients had daily or weekly drop attacks before the surgery, they still could be expected to face a considerable risk of physiological injury and their families would still have to provide continuous stressful care. Seizure types that responded best to corpus

callosum were atonic and tonic, which often result in abrupt and violent falls and commonly termed drop attack. Outcome of total callosotomy in drop attack was favorable in 80.9% of the case. In our study, we selected the assessment of overall daily function and familial satisfaction. Parents were interviewed to ascertain changes in their daily function and their satisfaction. We found that the younger patients had signifycantly better outcome in overall daily function, with improvements noted in 70% of patients aged ≤8 years old. However, overall daily function was impaired in 20% of patients aged at least 8. Claverie et al. statistically demonstrated that younger patients had better outcome in daily life and better psychosocial adjustment.[29] The improvements in hyperactivity and emotional well-being found have already been stressed as additional benefits in callosotomy for children.[4,5] We found that 71% of parents were satisfied with this surgical procedure. This rate is as high as that reported in other recent series.[5] Also, Our results suggested that the superior postoperative satisfaction in the younger patients may have been due to the significantly better functional outcome observed in the children. The most frequent operative complications of callosotomy include hydrocephalus, aseptic meningitis, sagittal sinus tearing with bleeding, cerebral edema, venous infarction, and epidural hematoma. But in our 21 cases, we did not have any of these complications. Neurological complications of callosotomy were seen in only 2 patients in whom disconnection syndrome was suspected. In addition to the aforementioned chronic sequela developing after total callosotomy, acute and transient disconnection syndrome, represented by mutism and apraxia in the nondominant limbs, has also been shown to be independent of whether callosotomy was complete or partial.[24]

We found that total callosotomy was particularly effective against drop attacks causing physical injuries and impaired quality of life in these patients. In pediatric patient, dramatic improvement of daily function and family satisfaction was observed.

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