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Original article

Clinical profiles for seizure remission and developmental gains after total corpus callosotomy

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Abstract

Purpose: This study was aimed to determine what preoperative profiles were associated with seizure remission after corpus callosotomy and whether such seizure outcome was associated with the postoperative developmental outcome.

Methods: This retrospective study included 26 consecutive patients with childhood onset epilepsy who underwent one-stage total corpus callosotomy at our institution and were followed up for a minimum of 1 year. The age at surgery ranged from 13 months to 32 years (median 6 years). The association between postoperative seizure freedom and preoperative profiles, post-operative developmental gains was examined.

Results: Five patients achieved seizure freedom (Engel class I), and 10 patients achieved worthwhile reduction of seizures (class III), whereas the remaining patients had a class IV outcome. All five seizure-free patients had "lack of abnormal magnetic resonance imaging findings", "lack of proven etiology of seizures", and underwent "surgery at age 6 years or younger". These three factors were associated with seizure freedom ($p < 0.05$, Fisher exact test). Post-operative gains in developmental quotient were significantly better in patients with seizure freedom than in those without ($p < 0.05$, Mann Whitney U test).

Conclusion: Our study replicated the notion that seizure remission can be achieved after total corpus callosotomy in subsets of patients with medically-uncontrolled epilepsy, and suggested that a better developmental outcome can be expected in patients benefiting from seizure freedom.

Keywords: Corpus callosotomy; Seizure outcome; Pediatric epilepsy; Development; Generalized epilepsy; Infantile spasms

1. Introduction

Corpus callosotomy is an established palliative treatment for patients with intractable epilepsy who are not candidates for resective surgery, and is especially effective for suppressing drop attacks and generalized tonic clonic seizures, but seizure freedom is generally seen in less than 10% [1–3]. However, seizure freedom after total corpus callosotomy has been reported to be more common in pediatric patients than expected from surgical results in adult population [4,5]. Therefore, the clinical factors indicating such curative outcome are important to identify, because control of seizures can positively influence the development of such young

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patients [6]. The present study was aimed to determine what preoperative profiles were associated with seizure remission after total corpus callosotomy, and whether such seizure outcome was associated with the postoperative developmental outcome.

2. Methods

This retrospective study was approved by the Tohoku University School of Medicine institutional review board.

2.1. Study subjects

This study included 26 consecutive patients with childhood onset epilepsy who underwent one-stage total corpus callosotomy for alleviation of seizures between 2008 and 2013 at our institution and were followed up for a minimum of one year post-operatively. Thirteen patients were included in a previous report [5,7]. During the study period, a total of 28 patients underwent corpus callosotomy in our institution. One adult patient received anterior four third callosotomy. Another patient received second epilepsy surgery within 12 months of corpus callosotomy. These two cases were excluded from the present study. All patients underwent comprehensive evaluation for epilepsy at the department of pediatrics, including video-electroencephalography (EEG) monitoring, brain magnetic resonance (MR) imaging, and fluoro-deoxy-glucose positron emission tomography. Magnetoencephalography and ictal single photon emission computed tomography were performed as necessary. Metabolic screening, chromosomal analysis, and genetic screening were also performed as required.

All patients were qualified for surgery after patient management conference. The clinical characteristics are summarized in Table 1. The 26 patients were 12 males and 14 females aged at surgery from 13 months to 32 years (median 6 years, mean 8.8 years). Age at onset of epilepsy ranged from 11 days to 13 years (median 6 months, mean 16 months). Duration of epilepsy ranged from 5 months to 31 years (median 5 years, mean 7.5 years). Electro-clinical diagnosis of epilepsy at the onset of disease identified West syndrome in 16 patients. Pre-operative MR imaging detected no abnormalities in 12 patients and general atrophy without focal structural lesions in 5. The etiology of epilepsy was unknown in 13, tuberous sclerosis in 5, and chromosomal or genetic anomaly in 3 patients. Epileptic spasms or tonic seizures were the main seizure type in 22 patients. Atonic seizures were present in four patients. Drop attacks had occurred in 22 patients. Interictal EEG was characterized by generalized and/or multifocal epileptiform discharges in all patients. Focal ictal EEG onset was not seen in any patients. Adrenocorticotropic hormone therapy was performed previously in 16 patients. Ketogenic diet was tried in three patients. Previous resective epilepsy surgery was performed in two patients with tuberous sclerosis (Cases 20 and 21). The number of anti-epileptic drugs (AEDs) at the time of surgery ranged from 2 to 5 (median 3). The number of previously administered AEDs ranged from 5 to 15 (median 9). All patients showed developmental delay or mental retardation.

2.2. Corpus callosotomy and post-operative follow-up findings

One-stage total corpus callosotomy was performed by the same neurosurgeon (author MI) according to previous reports [5,8]. Post-operative MR imaging was performed to confirm complete section of the corpus callosum. Patients were followed up with continuation of antiepileptic medication by pediatric neurologists. Seizure outcome was evaluated at the outpatient clinic using Engel's classification [9] and the numbers of total seizures and drop attacks, both measured as reduction of the frequency relative to the preoperative state. Developmental age (DA) and developmental quotient (DQ) were evaluated immediately before surgery and one year post-operatively using the Kinder Infant Development Scale (KIDS) type T [10,11]. KIDS consists of approximately 130 Japanese questions answered by the parent, and evaluate the child's development in nine domains including motor function, manipulative function, receptive/expressive language functions, concept, social relationships with children/adults, discipline, and feeding. The KIDS type T is a special version for children with delayed mental development. Developmental assessment was started in May 2010 in this study, and performed in patients younger than 7 years old. The association between postoperative seizure freedom and preoperative profiles was examined with the Fisher exact test. Post-operative changes in DA and DQ were compared between groups with the Mann–Whitney U test. Statistical analysis was performed with R version 3.0.2 (The R Foundation for Statistical Computing).

3. Results

3.1. Seizure outcome

No hemorrhagic or ischemic complications were observed. Seizure freedom (Engel class I) was achieved in five patients (19.2%), worthwhile or greater than 50% reduction in seizure frequency (class III) in 10 patients, and no worthwhile reduction (class IV) in 11 patients (Table 1). Drop attacks no longer occurred in 15 of 22 patients (68.2%). No changes in seizure frequency were detected in seven patients, but appreciable