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Original article

Dysembryoplastic neuroepithelial tumors in pediatric patients

Jeehun Lee [a], Bo Lyun Lee [a], Eun Yeon Joo [b], Dae Won Seo [b], Seung Bong Hong [b], Seung-Chyul Hong [c], Yeon-Lim Suh [d], Munhyang Lee [a,*]

[a] *Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Ilwon-dong, Gangnam-gu, Seoul 135-710, Republic of Korea*
[b] *Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea*
[c] *Department of Neurosurgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea*
[d] *Department of Pathology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea*

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Abstract

Objective: Dysembryoplastic neuroepithelial tumors (DNTs) are benign cortical tumors that are frequently associated with the medically intractable focal epilepsy. In this study, the authors delineate the clinical characteristics of DNTs in children and evaluate the role of cortical dysplasia (CD) in the epileptogenicity to find out the optimum surgical strategy. *Methods:* A retrospective analysis was performed for clinical data of children with DNT, who underwent surgery between 1996 and 2006. The adopted surgical methods were uniform according to the tumor location and included intraoperative electrocorticography (ECoG)-guided resection. The prognostic factors were evaluated for the two prognostic group categorized by the seizure outcome at one year after surgery. *Results:* Of 22 patients, the overall seizure free rate was 90.9% and the other two patients belonged to Engel class II during the mean follow-up period of 44.1 months. There was no worsening of the seizure after one year of surgery. Associated CD was found in 18 cases (81.8%) and in the 80% (8 of 10 cases) of the additionally resected areas according to the electrophysiologic studies. *Conclusions:* The CD associated with DNT appears to have its own epileptogenicity. Therefore, complete removal of the CD with tumor itself is important for patient outcome. A thorough surgical approach can be accomplished by comprehensive presurgical evaluations and extensive surgery with the aid of the intraoperative ECoG or intracranial recording.

Keywords: Dysembryoplastic neuroepithelial tumor; Cortical dysplasia; Electrocorticography; Epilepsy surgery; Seizure outcome; Children

1. Introduction

Dysembryoplastic neuroepithelial tumors (DNTs) are benign cortical tumors that are frequently associated with the medically intractable focal epilepsy in childhood and early adult life [1–3]. The mainstay of treatment has been surgical resection of the tumor. The outcome after surgery has proved to be favorable for the affected patients [2–5]. Pathologically these tumors have a disorganized arrangement of neuronal and glial elements without significant cytological atypia; they characteristically are accompanied by foci of cortical dysplasia (CD), initially described by Daumas-Duport [2].

A long duration of epilepsy, older age at surgery, and incomplete resection of the tumor have been suggested as poor prognostic factors [6–9]. However, the prognostic factors associated with the method of resection have not been well established, especially in pediatric patients. In addition the epileptogenic mechanisms associated with DNT have not been fully identified. The intrinsic epileptogenicity and irritation of adjacent cortex have been postulated as possible causes [10]. The association

* Corresponding author. Tel.: +82 2 3410 3539x0910; fax: +82 2 3410 0043.
E-mail address: sy0429@skku.edu (M. Lee).

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of CD with DNT and the intrinsic epileptogenicity of CD may provide some insight into treatment strategies. Previously we reported on the association of CD with the area of epileptogenicity in a mixed population of adults and children with DNT, and suggested that the complete resection of the tumor itself and the associated dysplastic tissue might be associated with a more favorable outcome [11].

The objectives of this study were (1) to delineate the clinical characteristics of the pediatric DNTs, (2) to assess the prognostic factors associated with post-operative seizure control, and (3) to determine the association of CD with the epileptogenicity of DNT and the optimum surgical strategy for treatment.

2. Patients and methods

Twenty-two children with focal epilepsy who underwent surgery at Samsung Medical Center (Seoul, Republic of Korea) between March 1996 and April 2006 were included. All of the children were less than 18 years of age at the time of the surgery and were pathologically confirmed to have DNTs. Written parental consent was obtained for all patients before surgery. This study was approved by the Samsung Medical Center Institutional Review Board.

We adopted nearly the same protocol for the presurgical evaluations and the surgical procedure used in our previous study (11). The presurgical evaluations included clinical history and examination, routine scalp electroencephalography (EEG) (32 channels with sphenoidal leads), brain magnetic resonance imaging (MRI), interictal single-photon emission computed tomography (SPECT), ^{18}F-fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET), and neuropsychological evaluation. The patients were then admitted to the epilepsy-monitoring unit (Vangard system, Cleveland, OH) for long-term video-EEG monitoring. The seizure semiology and ictal EEG were analyzed. Ictal SPECT was performed and ictal–interictal subtraction images were coregistered on MRI whenever possible. Wada's test (with sodium amytal) was performed in patients with temporal lobe DNT. Intracranial recordings with subdural electrodes were performed if necessary.

During the surgical procedure the goal was to remove the entire epileptogenic zone including the DNT. We defined the epileptogenic zone as the peritumor regions with interictal spikes on the intraoperative ECoG, and/or ictal-onset EEG activity on the intracranial recordings. In all patients, we performed either an intraoperative ECoG to detect interictal spikes before resection or intracranial recording using subdural electrodes (two-stage operation). The ECoG was performed again after resection of the tumors and at epileptic foci in all cases during surgery. We defined positive ECoG results as the interictal spikes, sharp waves or polyspikes that were consistently observed more than one time per minute during a 5-min recording.

A standard temporal lobectomy (STL: anterior temporal lobectomy with tailored amygdalohippocampectomy) including the tumor was performed in patients with lesions located medial to the rhinal/collateral sulcus on MRI and in whom the preoperative scalp EEG showed that the location of the epileptogenic zone was in the medial temporal lobe (ictal and/or interictal spikes arose from the ipsilateral sphenoidal or anterobasal temporal electrodes). Lesionectomy was performed in 11 patients whose lesions were located in the lateral temporal or extratemporal areas and in one patient with a lesion in the medial temporal area. We defined the lesionectomy as a subpial resection of the lesion, in which the lesion and the surrounding normal-looking brain tissue were included within the boundary of the surrounding sulci. Additional resection beyond the sulcal margin, of the lesion, was performed in six cases according to the results of the intraoperative ECoG before and after the resection, or the intracranial recording, similar to cases with additional resection in the STL.

The pathological specimens were reviewed by one pathologist (Suh, YL) and the classification of the associated CD was graded according to the classification of the Mischel et al.[12]: Severe (III), presence of balloon cells and/or neuronal cytomegaly (cytoskeletal abnormalities); moderate (II), presence of polymicrogyria and/or white matter neuronal heterotopia but no evidence of balloon cells or neuronal cytomegaly; and mild (I), cortical laminar disorganization and/or presence of single heterotopic white matter neurons but no evidence of balloon cells, neuronal cytomegaly, polymicrogyria, or white matter neuronal heterotopia.

After the surgery, antiepileptic drugs were administered for 1–2 years and tapered over 6-months if the patient was seizure free for over at least 1 year. The post-operative seizure outcome was graded as class I through IV according to the Engel classification [13].

Statistical analysis was performed using the χ^2 test and the Fisher's exact test to evaluate the association of the clinical, neurophysiological, radiological, and pathological data with the patient prognosis. The results were considered significant at a probability value of less than 0.05.

3. Results

3.1. Clinical data

The clinical data are summarized in Tables 1 and 2. All of the patients enrolled in this study underwent epilepsy surgery as described above and were pathologically confirmed to have DNTs. The mean age of seizure onset was 8.1 years (2 months–14 years, SD = 4.3) and surgery was performed at a mean age of 12.4 years (3.25–18.5 years, SD = 3.6). The mean interval from seizure onset