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SURGICAL NEUROLOGY INTERNATIONAL

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Editor: **Sandi Lam**, M.D. Baylor College of Medicine; Houston, TX, USA

SNI: Pediatric Neurosurgery, a supplement to *Surgical Neurology International*

Case Report

Volumetric growth analysis of an insular dysembryoplastic neuroepithelial tumor over a 10-year follow-up

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Received: 31 January 16 Accepted: 23 July 16 Published: 28 December 16

Abstract

Background: Dysembryoplastic neuroepithelial tumors (DNETs) are benign tumors characterized by a cortical location; they result in symptoms of drug-resistant partial seizures in children. The development of DNETs is poorly understood because most of them are resected immediately upon diagnosis without any observation period owing to the intractable seizures.

Case Description: We report the first DNET case with the growth rate analyzed in the natural course of development for a period of 10 years. The patient was a right-handed man who was initially referred to another hospital with mild head injury when he was 8 years old. A tumor located in the right insular cortex was incidentally detected on magnetic resonance imaging (MRI) and followed-up with annual MRI for 10 years.

Conclusion: In this case, the volume of the DNET increased in direct proportion to the length of time in its clinical course. The tumor doubling time was approximately 10 years. This case suggests DNET is a slow-growing but not stable tumor.

Key Words: Dysembryoplastic neuroepithelial tumor, insular, growth analysis

Access this article online

Website: www.surgicalneurologyint.com

DOI: 10.4103/2152-7806.196931

Quick Response Code:

INTRODUCTION

Dysembryoplastic neuroepithelial tumors (DNETs) are benign, hamartomatous tumors thought to arise from the cortical gray matter. They are mixed neuronal-glial tumors, classified as grade I by the World Health Organization (WHO). Progression or post-surgical recurrence of DNETs is perceived to be extremely rare. DNETs typically cause intractable seizures in children, and are removed surgically without observation.[1,10] Therefore, the natural course and development of DNETs is poorly understood. The DNET case reported here was observed for 10 years without surgery because of the absence of symptoms. The lesion demonstrated gradual growth. We report an analysis of the DNET growth rate for the first time.

CASE REPORT

Our patient was initially referred to another hospital with mild head injury when he was 8 years old. An intra-axial tumor located in the right insular cortex was incidentally

How to cite this article: Uno T, Kinoshita M, Furuta T, Miyashita K, Sabit H, Nakada M. Volumetric growth analysis of an insular dysembryoplastic neuroepithelial tumor over a 10-year follow-up. Surg Neurol Int 2016;7:1154-7.
http://surgicalneurologyint.com/Volumetric-growth-analysis-of-an-insular-dysembryoplastic-neuroepithelial-tumor-over-a-10-year-follow-up/

detected on MRI. Surgical resection was waived and followed-up for 10 years until the patient was 18 years old because of slowly growing tumor without symptoms. At the end of the observation period, the tumor size was measured to be one and a half times the diameter measured on the first MRI scan. After the end of the follow-up period, he visited our hospital for intensive examination and treatment.

The patient had no neurological deficit. Computed tomography (CT) imaging showed a low-density lesion with no calcification located in the right insular cortex [Figure 1a]. T1-weighted MRI demonstrated a hypointense lesion in the right insular cortex [Figure 1b]. T2-weighted MRI showed a hyperintense lesion that corresponded with the hypointensity on the T1-weighted image [Figure 1c]. T1-weighted MRI with gadolinium administration did not show any enhanced lesions [Figure 1d and e]. Arterial spin labeling study suggested decreased blood flow at the lesion [Figure 1f].

The lesion located in the right insular cortex demonstrated gradual growth for 10 years [Figure 2a-d]. The change in lesion volume was assessed using polygonal tracing with fusion. Fluid-attenuated inversion recovery (FLAIR) signals were assessed using the DICOM image viewer OsiriX (®) (v. 7.0; Pixmeo SARL, Bernex, Switzerland) by slice-by-slice region of interest tracings. The growth rate of this lesion was found to be almost directly proportional to time [Figure 2e].

In order to remove the lesion and obtain histopathological diagnosis, an awake craniotomy was performed using cortical and subcortical stimulation mapping with a bipolar direct electrical stimulator at 3.5 mA/60 Hz biphasic current to monitor motor and somatosensory response, speech or language difficulties, and other higher brain functions.[6] An anarthria was induced by stimulation of the ventral precentral gyrus [Figure 3a]. Tumor resection was performed via a transopercular approach. Intraoperatively, the nature of the tumor was gray, soft, and jelly-like tissue with clear boundaries. Fiber structures in the peripheral zone were relatively well-defined and we promoted excision of the tumor using an ultrasonic surgical aspirator. A postoperative MRI showed gross total resection of the tumor [Figure 3b]. Postoperative course was uneventful without neurological deficits. No recurrence was recognized postoperatively for 12 months.

Histological examination of the hypointense area on T1-weighted MRI showed multiple cystic structures with myxomatous background and proliferation of oligodendroglia-like cells with oval nuclei in the wall of the cystic spaces [Figure 4a]. Neuronal elements featuring "floating neurons" were observed, indicating a glioneuronal lesion within the cystic cavity [Figure 4b]. Immunohistochemical analysis revealed intense positive staining for Olig2, S-100 and synaptophysin, and less reactivity for IDH-1 [Figure 4c]. The Ki-67 staining

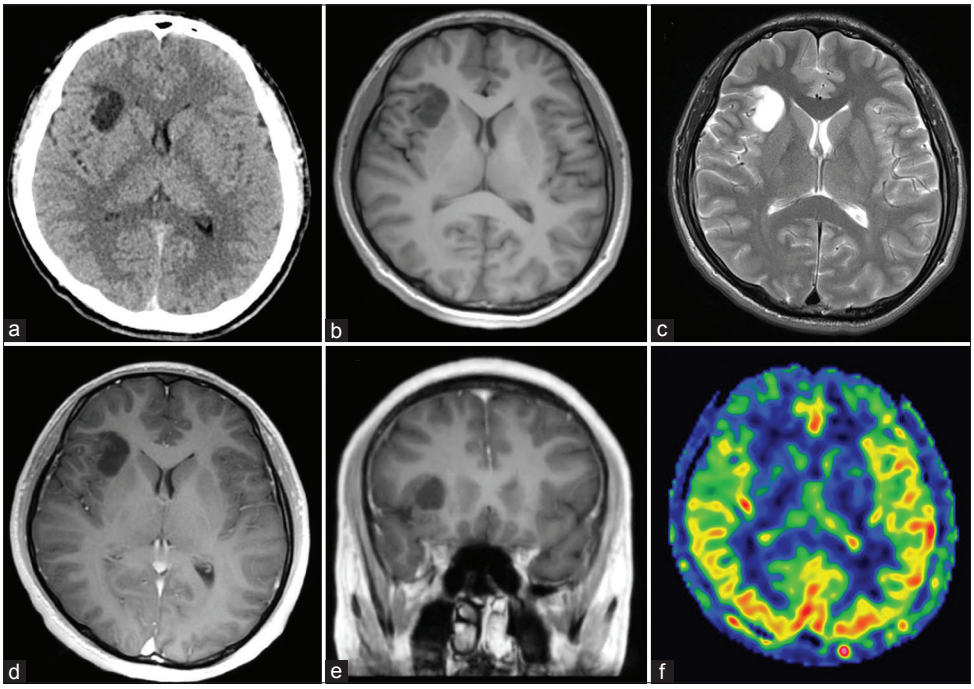

Figure 1: Axial computed tomography (CT) (a) and magnetic resonance imaging (MRI) scans (b-d, f) and coronal MRI scan (e). (a) CT scan shows a low-density lesion in right insular cortex with no calcification. (b) T1-weighted MRI demonstrates a hypointense lesion. (c) T2-weighted MRI shows a hyperintense lesion that corresponds with the hypointensity on the T1-weighted MRI image. (d, e) T1-weighted MRI with gadolinium administration did not demonstrate any enhanced lesion. (f) Arterial spin labeling study shows decreased blood flow at the lesion

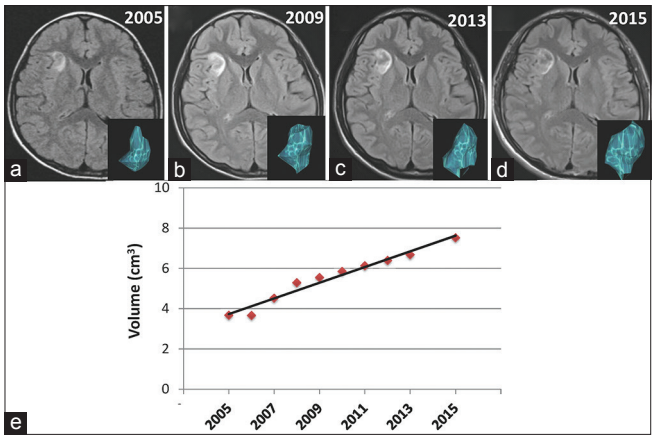

Figure 2: (a-d) T2-FLAIR MRI scans in the axial plane from age 8 to 18 years show gradual growth. An inserted picture in the corner of images is a three-dimensional reconstructed model of the tumor in each figure. (e) A dot graph with an almost straight line shows that the increase in tumor volume is directly proportional to time

index (SI) was 1% [Figure 4d]. A combined deletion of 1p and 19q chromosomes was absent. The histological diagnosis was WHO grade I DNET.

DISCUSSION

This rare case of DNET was followed for 10 years with annual MRI. Our statistical analysis of growth rate showed that the tumor volume gradually increased in direct proportion to time. According to this analysis, the tumor doubling time was determined to be approximately 3473 days. To date, only a few studies on DNET growth pattern have been reported.[3,4] We report the first case of DNET growth rate analysis in its natural course over a period of 10 years.

DNETs are usually stable tumors. However, malignant transformation in DNETs results in rapid growth rates.[3,10] It is still debated whether DNET is stable at birth or exhibits gradual growth in cases without malignant transformation. Jensen *et al.* reported a case of DNET that was stable for 15 years.[7] Conversely, Alexander *et al.* reported a case of DNET in which the occipital lobe grew from 5.2 cm to approximately 10.4 cm, accompanied by the appearance of enhanced tumor lesions on MRI for 10 years.[1] In our patient, the volume of DNET increased in direct proportion to the length of time without the appearance of enhanced lesions on MRI during its clinical course.

The lesion was located in the right insular cortex in our patient. DNETs typically occur in the temporal lobe in 62%, the frontal lobe in 31%, the parietal and/or occipital lobe in 7% of cases,[4] and rarely in the periventricular white matter, basal ganglia, thalamus, brainstem, and cerebellum[12] including the pons and third ventricle.[8]

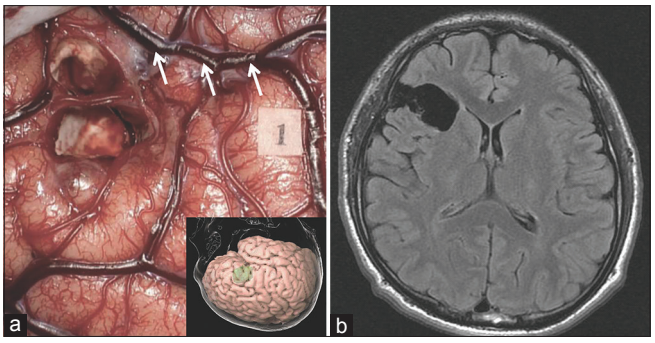

Figure 3: Intraoperative (a) and postoperative (b) images. (a) Intraoperative view after tumor resection during awake surgery. Tag 1 suggests the area where anarthria was induced on the ventral precentral gyrus by direct electrical stimulation. An inserted picture is the three-dimensional cortical view. (b) Fluid-attenuated inversion recovery magnetic resonance imaging performed 3 months after the operation shows gross total resection. Arrows indicate the Sylvian fissure

To the best of our knowledge, this is the first report of DNET located in the insular cortex.

DNET is generally positive for Olig2, S-100, and synaptophysin. The genetic background of DNETs has not been systemically investigated. Loss of heterozygosity at 1p/19q and *TP53*[5] or *IDH1*[2] mutations were not detected in DNETs. However, Maria *et al.* reported a case with 1p/19q chromosomal deletion and *IDH1* mutation.[11] Most DNETs show very low proliferative activity and Ki-67 SIs lower than 1%.[9] Our results agreed with these findings.

The patient underwent an awake craniotomy. Gross total resection of the lesion was achieved. We expected an extremely low risk of tumor recurrence.[11] This case indicated that partial resection of DNETs might result in the regrowth of residual lesion in direct proportion to the length of time. Therefore, we suggest that patients with partial or subtotal resection of DNET be followed-up for longer time after surgery.

Despite being recognized for only less than three decades, DNETs are becoming an important part of epilepsy neurosurgical practice. However, their natural growth rate remains poorly understood. We present this case to increase the knowledge related to the growth pattern of these tumors, and to suggest that the growth rate of DNETs is directly proportional to time.

Acknowledgments
We thank Erika Komura for assistance with preparation of the immunohistochemistry.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

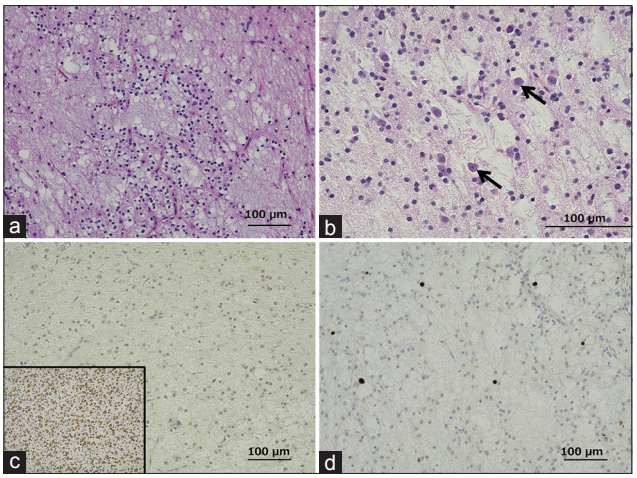

Figure 4: Photomicrographs of the surgical specimen showing the hypointense lesion on T1-weighted magnetic resonance imaging. (a) Multiple cystic structures are observed on a mucinous background. Hematoxylin and eosin (H and E) staining, original magnification ×100. (b) High-power view of a, showing floating neurons (arrows) scattered in the cystic structure. H and E staining, ×200. (c) Negative staining for *IDH1* mutation, ×100. Inset: Positive control (d) The Ki-67 staining index was 1%, ×100

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