

## BRIEF COMMUNICATION

# Atypical presentations of dysembryoplastic neuroepithelial tumors

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## Summary

Dysembryoplastic neuroepithelial tumors (DNETs) are World Health Organization grade 1 neoplasms, typically present as isolated cortical lesions with no associated edema. We present 3 rare cases of DNETs that were atypical in location (all were subcortical and 1 was bilateral), 2 of which displayed substantial growth over time. All 3 cases presented with seizures that were not well controlled on medications, followed by a successful cure of the epilepsy when these lesions were removed. These cases uniquely illustrate that DNETs can be present throughout the brain and may generate seizures even in a subcortical location, possibly due to containing neurons with the potential for aberrant microcircuitry. The slow, nonmalignant proliferation of these lesions may engage epileptogenic networks, leading to the onset of seizures. These cases carry implications for the management of these surgically treatable lesions. Thus far, there have only been a handful of cases of growth reported in nonmalignant DNETs, and 2 of these cases displayed growth over the interval of monitoring.

## KEYWORDS

dysembryoplastic neuroepithelial tumor, epilepsy, seizures, subcortical

## 1 | INTRODUCTION

Dysembryoplastic neuroepithelial tumors (DNETs) were first described in 1988 by Daumas-Duport as supratentorial cortical mixed glial-neuronal neoplasms with a multinodular architecture and a heterogeneous cellular composition.<sup>1</sup> They are typically located in the temporal lobe or supratentorial cortical areas in children and young adults<sup>2</sup> <20 years old. DNETs are typically isolated lesions that do not enlarge in any substantial fashion.<sup>3,4</sup> The most common presentation is seizures, in part from their typical location in the temporal lobe; however, this paper illustrates that DNETs can cause seizures in subcortical locations, possibly due to the possession of neurons with the potential for

aberrant microcircuitry or cortical dysplasia adjacent to the lesions.<sup>5</sup> Although rare, progression and recurrence has been observed in these tumors; however, this is almost solely reported in the presence of malignant transformation.<sup>4</sup>

These tumors and the related epilepsy are curable by excision, with >80% Engel class I outcomes following complete resection.<sup>6</sup> Thus, an accurate diagnosis is essential, as aggressive and early surgical treatment for epilepsy outweighs the risks of uncontrolled seizures.<sup>7</sup> Magnetic resonance imaging (MRI) has characteristic findings of T2 hyperintense multicystic heterogeneous lesions with no edema.<sup>3</sup> On fluid-attenuated inversion recovery imaging, DNETs classically have a hyperintense rim surrounding

hypo- or isointense signal. Atypical DNETs have been described, although no case reports have shown subcortical DNETs with progression in the setting of no malignant features (see Table 1).<sup>4,8–11</sup> This case series comprises 3 young women with poorly controlled epilepsy found to have lesions that were unusual in location, being subcortical in all 3 cases, with the last one even more unusual in that it was bilateral. The first 2 subcortical DNETs showed clear progression over time and were causally associated with seizures despite their subcortical location, and pathology revealed DNET with no malignant or atypical features in all 3 cases.

## 2 | CASE ONE

This patient was a 19-year-old female with a history of seizures since age 6 years who had previously undergone a left anterior temporal lobectomy with sparing of the amygdala and hippocampus (due to her high-performance status and to preserve her excellent verbal memory) after an intracranial evaluation for refractory epilepsy at age 15 years. At the time, she was experiencing absence seizures with déjà vu and auras described as nose tingling. The surgical specimen revealed subpial gliosis and cortical dysplasia. After her initial resection, she was weaned off her anticonvulsants (lacosamide and zonisamide), but 2½ years postresection, her seizures recurred and she was started back on the same medications at the same dosage, with no resolution of these seizures. At the time of her second presentation to us, she was having approximately 1–2 seizures per month on medications characterized by auras and focal impaired awareness seizures. Saliently, she had been noted to have a small right subcortical lesion contralateral to her previous anterior temporal lobectomy on her routine postoperative imaging, which had grown in size over the past 4 years (Figure 1 1.A–C).

Given the progressive nature of the lesion, and its deep location, we elected to proceed with a stereotactic biopsy

and concomitant laser ablation of the lesion. The preoperative diagnosis was that this was likely a low-grade glial neoplasm and that surgical intervention would likely not have any beneficial effects on her epilepsy.

Surgical intervention was uneventful and post-laser ablation contrasted T1-weighted imaging sequences confirmed that the lesion was completely ablated. Histopathology revealed a dysembryoplastic neuroepithelial tumor; multiple clusters of round, uniform, oligodendroglialike cells were seen in a mucinous background. Synaptophysin, neurofilament, and glial fibrillary acidic protein (GFAP) were positive in the expected cellular component, with p53 negative in the neoplastic cells. The MIB-1 labeling index was low, around 3%. The patient had no further seizures at her 1-year follow-up visit, and is now pursuing an undergraduate degree.

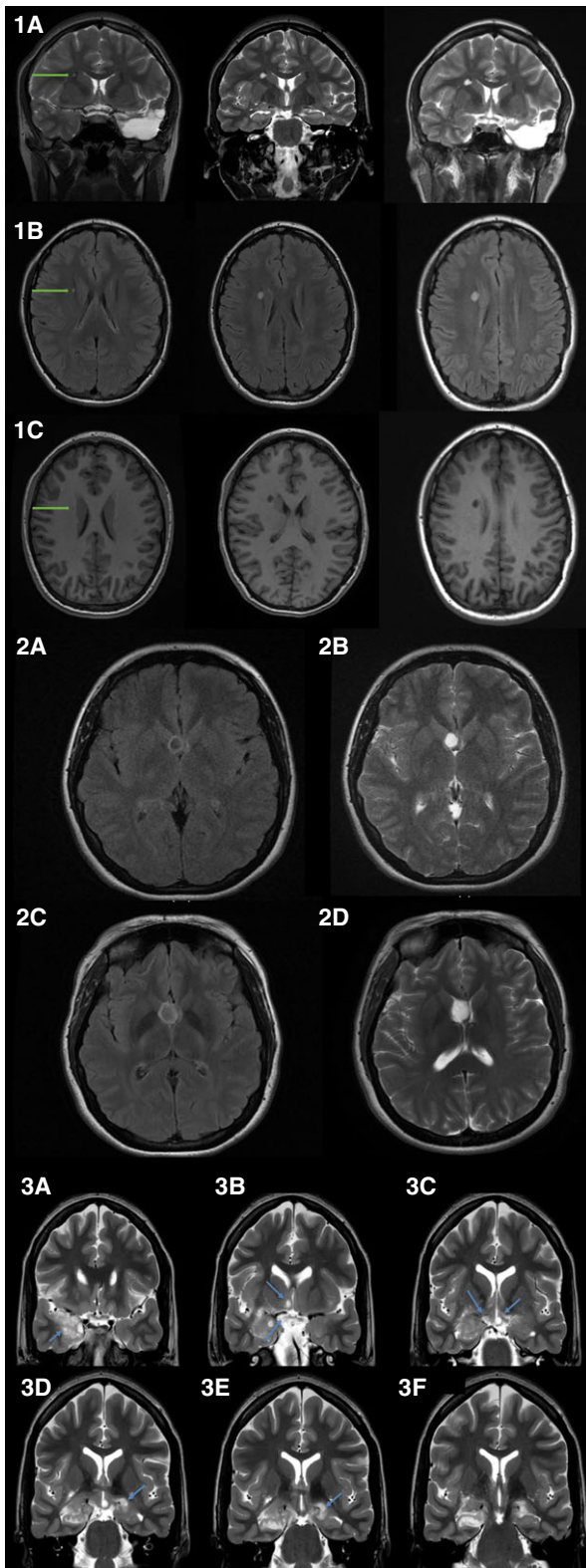
## 3 | CASE TWO

This patient was a 29-year-old female who presented with nausea, vomiting, headaches, and seizures. Her headaches originally started at the age of 21 years, and imaging at that time revealed a small right lateral intraventricular subependymal lesion. This lesion was interpreted as being a benign cysticlike lesion, and the patient was followed with serial MRIs. A few months prior to presentation to us, she started having episodes of abrupt loss of consciousness and dizziness, followed by confusion after the events. She had 4 such episodes in the month prior to intervention. Routine electroencephalographic (EEG) studies did not reveal epileptiform discharges, but given the patient's reports, these events were assumed by the consulting neurologists to represent focal impaired awareness seizures. A repeat MRI showed enlargement of the ventricular lesion (Figure 1 2.A–D). Given the progressive enlargement of the mass, and the possibility of developing obstructive hydrocephalus, a plan for resection was made without a formal inpatient video-EEG evaluation. A complete resection of

**TABLE 1** Literature review of progression in DNETs without malignant transformation

Reference	Year	Age, y	Gender	Location	Progressive primary lesion	Seizure outcome	Progression of postop residual	Seizure recurrence
Alexander <sup>4</sup>	2015	16	F	Occipital lobe	No	Continued visual seizures	Yes, 10 years postop	Na
Yamaguchi <sup>9</sup>	1998	16	M	Frontal lobe	Yes	Ns	No	Ns
Sampetean <sup>8</sup>	2006	9	M	Temporal lobe	Yes	Seizure-free	No	None at 5 years
Preuss <sup>10</sup>	2010	2.3	F	Occipital lobe	Yes	Ns	Ns	Ns
Campos <sup>11</sup>	2009	Ns	Ns	Frontal	No	Ns	Yes	Ns

This table summarizes all the published cases of DNET progression without malignant transformation. These cases were all cortical in location. DNET, dysembryoplastic neuroepithelial tumor; F, female; M, male; Na, not applicable; Ns, not specified; postop, postoperative.



**FIGURE 1** Magnetic resonance imaging (MRI) scans in Case 1. 1.A, T2-weighted oblique coronal MRI sequences from 2011, 2014, and 2015 (left to right) revealing a circumscribed, enlarging lesion in the right anterior limb of the internal capsule that is hyperintense on T2-weighted sequences. Left anterior temporal lobectomy changes are shown. 1.B, T2 fluid-attenuated inversion recovery (FLAIR) MRI sequences showing the right internal capsule lesion more clearly. There is no associated edema or mass effect. 1.C, T1-contrasted sequences with nonenhancing T1 hypointense lesion. 2, MRI scans in Case 2: T2 FLAIR (left images) and T2-weighted (right images). 2.A, B, MRI scan from 2006 of a right intraventricular subependymal lesion that was T2 hyperintense with suppression of T2 signal centrally and rim of hyperintense signal on FLAIR sequences. 2.C,D, MRI from 2013 revealing interval enlargement of the lesion. 3, MRI scans in Case 3: T2 coronal oblique sequence. 3.A, Right medial temporal lesion. 3.B, Lesion in right septal region and optic chiasm. 3.C, Lesion in right optic tract and left mammillary body. 3.D-F, Lesion in the left temporal stem

negative for p53. The MIB-1 labeling index was very low. In the 4 years since surgery, the patient has had only 1 seizure, which was during her pregnancy when her medication levels were not therapeutic. She therefore has an Engel outcome of Ib and an International League Against Epilepsy (ILAE) score of 2.

#### 4 | CASE THREE

This patient was a 27-year-old female who presented with a 6-year history of seizures with no known precipitating event. The patient was on multiple medications but continued to have breakthrough events. Seizures were preceded by an aura of déjà vu, and were focal impaired awareness seizures with mouth automatisms, nonresponsiveness, and nonsensical vocalization. Seizures were followed by a postictal period of nonresponsiveness for several minutes. They occurred 2-3 times a week and more frequently during menses. Imaging revealed a mixed density, multicystic lesion centered in the right mesial temporal lobe, but with distinct and separable involvement of the septal nuclei on the right, the optic tract on the right, the optic chiasm bilaterally, the left mammillary body, and the left temporal stem (Figure 1 3.A-F). She underwent a video-EEG evaluation, which revealed seizures originating in the right temporal lobe. She underwent a right anterior temporal lobectomy with an amygdalohippocampectomy and resection of tumor. Pathology revealed a DNET. She is now 6 months postoperative and seizure-free on medications with an Engel outcome of Ia and ILAE score of 1. The remaining DNET tissue located in the contralateral temporal stem, mammillary body, and ipsilateral optic apparatus will be monitored with serial MRI scans at 6 months then annually for

the mass was performed via an interhemispheric transcalscal-transventricular approach.

Pathology revealed a dysembryoplastic neuroepithelial tumor: small cells with round nuclei, perinuclear halos in a mucinous background, and floating neurons. The neoplastic cells were positive for synaptophysin and GFAP and

growth. She will be followed clinically for seizure recurrence due to the contralateral temporal stem DNET. If growth or seizures occur, laser interstitial thermal therapy to the tissue will be implemented.

## 5 | DISCUSSION

DNETs are classified as grade 1 mixed neuronal and glial tumors.<sup>1</sup> The typical presentation occurs in children and young adults with intractable seizures. Lesions are characteristically in supratentorial cortical locations, most commonly the temporal lobe, with multinodular structure demonstrating a bubbly appearance on MRI,<sup>3</sup> and no peritumoral edema or mass effect. All 3 of these cases did not show typical imaging findings, particularly in regard to their subcortical location. The histopathology displayed characteristic foci of cortical dysplasia, with small round oligodendrogliallike cells of glial-neuronal origin in a mucinous background.<sup>12</sup> DNETs are typically benign tumors, although malignant transformation has been reported rarely.<sup>13</sup> There have only been a few cases ever reported of growth in nonmalignant DNETs, and in these previously reported cases, the pathology was atypical, suggesting a more aggressive histologic subtype of these lesions<sup>8–10</sup> (see Table 1). In our cases, the pathology showed typical DNETs with no particular histological feature that might explain their growth.

Given the variations in location and imaging reported here and by others,<sup>4,9,10</sup> DNET should be considered in the differential diagnosis of young adults or children who present with intractable seizures with a T2 hyperintense mass on imaging, even if the lesion is not in a classical cortical or mesial temporal location. A complete surgical resection of these lesions should be the goal, as it will likely result in seizure freedom. In most of these cases, the epileptogenic zone (defined as the minimum amount of tissue that must be resected to resolve seizure activity<sup>14</sup>) is confined to the lesion itself, and a lesionectomy is generally curative. The general principle that excellent seizure-free outcomes can be achieved with aggressive tumor resection for most all tumors presenting with epilepsy can especially be applied here.<sup>15</sup>

## DISCLOSURE

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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