Dysembryoplastic Neuroepithelial Tumor: A Review

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Most DNETs are benign, low-grade lesions. However, a small number appear to have the potential for malignant transformation. We report a patient with a biopsy-proven DNET with features of an oligodendroglioma and review the clinical features of DNETs and their potential for malignant transformation.

Key Words: dysembryoplastic neuroepithelial tumor, malignant transformation

In 1988 Dumas-Duport et al. first used the term dysembryoplastic neuroepithelial tumor to describe low-grade tumors found in young patients with intractable partial seizures. In 1993 the distinct pathological entity known as DNET was given a place in the WHO classification of brain tumors as a grade I tumor of neuroepithelial origin. Many studies have reported successful surgical management of this low-grade tumor in the treatment of refractory epilepsy. We report the case of a young man who experienced possible seizure activity and was found to have a biopsy-proven DNET.

Case Report

A 30-year-old man with no significant medical history experienced the sudden onset of right facial numbness, which resolved completely within hours. When questioned he stated that he had experienced occasional sensory abnormalities in his right arm and leg throughout the previous year. Computed tomographic scans showed a nonhemorrhagic hypodense lesion in the mesial temporal lobe, thalamus, and posterior limb of the internal capsule. The lesion was hyperintense on T2-weighted MR images, hypointense on T1-weighted images, and non-enhancing (Fig. 1). Based on the imaging studies, the diagnosis was unclear and we recommended that the patient undergo a needle biopsy to guide further treatment.

An intraoperative frozen specimen was interpreted as either an oligodendroglioma or a DNET. The final pathological evaluation described nodular, neoplastic, glioneuronal elements with oligoden-
droglial-like features and areas of micro
cystic change and hyalinization. On im-
mediate postoperative MR imaging, a
small hemorrhage was visible in the
tumor bed. The patient suffered no ad-
verse events and was discharged home
neurologically intact after a brief period of
observation. Interestingly, on follow-up
imaging the lesion had partially regressed.
We hypothesized that the compressive
forces of the intraoperative hemorrhage
had partially obliterated the tumor.

Discussion

In 1988 Dumas-Duport and col-
leagues first characterized DNETs when
they described neuroepithelial tumors in
39 patients with medically intractable
partial complex seizures. They noted a dis-
tinct cortical tumor with multinodular
architecture, associated cortical dysplasia,
and both neuronal and glial elements.
After resection their patients were fol-
lowed a mean of 9 years. Their outcomes
were excellent. Of the 39 patients, 30
were seizure free, 4 experienced only
rare seizures, and the number of seizures
was reduced significantly in the remain-
ing 3 patients. Two patients died. De-
spite being seizure free, one patient com-
mitted suicide 3 months after surgery.
The second patient received whole brain
radiation and polychemotherapy and was
found to have extensive radionecrosis at
autopsy.

Although the report by Dumas-Du-
port et al. is considered the first to de-
scribe these tumors and their specific his-
tology, they did credit Cavanagh of
London who published an article in
1958 called, On Certain Small Tumors En-
countered in the Temporal Lobe. The mul-
tinodular lesions that Cavanagh de-
scribed were found while he performed
temporal lobectomies for temporal lobe
epilepsy. Cavanagh described the lesions
as hamartomas but opined that areas of
“early neoplastic change” were suscep-
tible to malignant transformation into
gliomas. Dumas-Duport et al. consid-
ered the tumor to be at least partially
neoplastic and argued that these lesions
formed during embryonic development.
Dumas-Duport’s argument that
DNETs had embryonal origins was
four-fold. First, these tumors exhibited
multiple cell lineages that could arise
from multipotent cells present during
early development. Second, these tu-
mors manifest early in life. Third, there
is often an adjacent bone deformity,
which suggests that the tumors are long
standing with an early onset. Finally, the
presence of cortical dysplasia implies that
these lesions occur during cortical for-
mation and are not neoplasms that arise
within normally developed cortex. The
actual origins of these indolent tumors
and whether they are truly neoplastic are
still debated.

Classification

The original paper describing DNETs
focused on the theory that these tumors
had embryonal origins. However, it was
clear that their clinical course differed
from that of tumors classified as embry-
onal tumors of neuroepithelial origin.
Tumors listed in the WHO classification
scheme as embryonal are all considered
WHO grade IV lesions (Table 1). Thus
the term dysembryoplastic was coined to
indicate both the origin of these tumors
and the observation that they share fea-
tures with less aggressive, dysplastic le-
sions. However, the authors did not think
that the term was an entirely accurate de-
scription of these tumors, which share
some similar histologic features with neo-
plastic lesions. Nonetheless, the term dys-
embryoplastic still served to denote the
predominantly benign clinical course of
these tumors.

In 1993 DNETs were placed in the
WHO brain tumor classification scheme
as a neuronal/mixed glial-neuronal tumor
of neuroepithelial origin. They are

Figure 1. (A) Axial T2-weighted MR image shows a hyperintense lesion in the mesial temporal lobe. Axial T1-weighted MR images (B)
with and (C) without contrast show a hypointense lesion that does not enhance.
classified as Grade I tumors along with the other low-grade neuronal tumors such as gangliogliomas and gangliocytomas (Table 2). Although still debated, most contemporary neurosurgeons consider these tumors to be frankly neoplastic.

**Histology**

Three histologic forms of DNET have been described: complex, simple, and nonspecific. The complex form (Fig. 2), which is the type originally described by Dumas-Duport et al., consists of SGNE (Fig. 3), glial multinodular architecture, and associated cortical dysplasia. The nodular component of a DNET contains both glial and neuronal components and can resemble both gliomas and gangliogliomas. The neuronal component often consists of neurons “floating” in a basophilic mucinous matrix (Fig. 4). The axons are surrounded by “tumoral” oligodendrocyte-like cells. These cells exhibit oligodendrogial features, including prominent perinuclear halos (Fig. 5). The simple form, which was also described by Dumas-Duport et al., consists only of the SGNE. The nonspecific form is more controversial: It has neither the SGNE nor the multinodular architecture. It resembles a low-grade astrocytoma but has clinical and radiological features more consistent with a DNET.

**Imaging Features**

On neuroimaging DNETs are cortical lesions with little mass effect and a predilection for the temporal lobes. On computed tomography DNETs are typically well-demarcated, hypodense, cortical lesions that can be associated with deformation of the overlying skull. In a radiological study, fewer than 20% contained calcifications in contrast to gangliogliomas, which had a much higher rate. MR images often show a solid and cystic mass with the cystic portions appearing slightly more intense than cerebrospinal fluid. A cystic signal pattern is not specific to DNET; the pattern is also found in other tumors frequently associated with epilepsy such as gangliogliomas and gliomas. The solid components often appear multinodular, hypointense on T1-weighted MR images, hyperintense on T2-weighted MR images, and occasionally weakly enhancing.

**Clinical Course**

Consistent with their original description, DNETs are tumors associated with epilepsy in young adults. In 2006 Chan et al. reported the outcomes of patients who underwent surgical removal of a DNET for seizure control and reviewed the published series of DNETs. The mean long-term outcome of 18 patients with DNETs surgically resected for the treatment of epilepsy was 10.8 years. They found that 66.7% of their patients achieved Engel Class I outcomes, indicating that they were free of disabling seizures. In the reviewed series of surgical outcomes for DNETs, 52.4 to 90% of the patients achieved Engel Class I. Interestingly, the results that they had previously reported for the same group of patients at a mean of 2.7 years of follow-up were predictive of their long-term outcomes. Their results, combined with those of other studies, led them to conclude that a patient who is seizure free 3 years after resection of a DNET can be considered cured.

Nonetheless, DNETs can recur as Nolan et al. reported in 2004. Of 26 children who underwent surgical resection of their tumor for seizure control, 3 demonstrated a recurrence within 1 to 5 years. In this series, the rate of incomplete resection was high (63%), and all patients who experienced a recurrence showed some degree of residual tumor on postoperative imaging.

**Potential for Malignant Transformation**

In published series the clinical course of DNETs has been stable. Only rarely does diagnostic imaging reveal a postoperative recurrence. Recent case reports, however, have shown that these
lesions may undergo malignant change. In 2000 Hammond et al. reported the first malignant transformation of a DNET that had been surgically resected.7 The patient, a 29-year-old man who suffered from partial seizures, had a nonenhancing lesion in his left frontal cortex. He first underwent surgery in 1984, when his tumor was labeled as a “fibrillary astrocytoma.” The surgeons reported subtotal resection. The patient received no radiation or chemotherapy, but 11 years later his seizures recurred. MR imaging showed a partially enhancing cystic lesion. After repeat resection the pathology was confirmed as a grade IV astrocytoma. Retrospective histological review of the initial tumor found it to be a DNET with SGNEs, glial nodules, and associated cortical dysplasia.

In 1974 Rushing et al. described a 14-year-old boy who underwent subtotal resection of a tempoparietal mass for the treatment of epilepsy.14 The pathology, which was originally diagnosed as a “mixed oligoastrocytoma,” was later shown to be a DNET. The patient received postoperative radiation therapy. One year later MR imaging showed the formation of a cyst that was drained via a craniotomy. After this procedure the patient underwent a 6-week course of chemotherapy. Three years later, his seizure activity resumed and a tumor recurrence was found. The patient underwent a third surgery, and the pathologic diagnosis of the lesion was consistent with progression to an anaplastic astrocytoma.

Three other studies also suggest the potential for transformation or progression of a DNET. Josan et al. reported a 3-year-old girl with seizures who was found to have a DNET. She was managed conservatively.9 At the age of 14 years, follow-up MR imaging showed a large cystic lesion, which was resected. The lesion was diagnosed as a pilocytic astrocytoma within a surrounding DNET. In a 9-year-old with seizures, Sampetrean et al. described a DNET with a small ring-enhancing core; the size of the lesion tripled in 3 months.15 Surgical resection confirmed the diagnosis of DNET. Five years after surgery, the patient remained seizure free without a recurrence. Jensen et al. reported a 46-year-old patient who had medically refractory seizures with a nonenhancing, low-intensity lesion in the mediotemporal lobe.8 The patient opted for conservative management until the tumor developed contrast enhancement after 15 years. Surgical pathology revealed a DNET without atypical changes. These findings suggest that on imaging these tumors can show progression that does not necessarily imply malignant transformation.

Because DNETs have only been discovered within the last 20 years, their natural history is not yet completely defined. The literature, however, suggests that these lesions hold the potential for malignant change. It is possible that the discovery of a higher-grade lesion within a histologically proven DNET is simply coincidental. Given that some DNETs display high mitotic activity based on the Ki-67 proliferation labeling index, it seems likely that these tumors arise from neoplastic cells within the DNET itself.2 These findings support the argument that a DNET is at least partially a neoplastic lesion, although its nature is still debated. Although some of these tumors progress, most are stable and rarely recur after surgery. Possibly, a subset of these tumors yet to be identified has the propensity...
for malignant transformation. When the natural history of these tumors is better defined with longer follow-up, we also may find that a greater percentage progress to more aggressive lesions than previously thought. For now these reports demonstrate the importance of regular follow-up, both clinical and radiographic, for patients who harbor DNETs.

**Conclusion**

Since their discovery in 1988, much has been learned about the characteristics and clinical course of DNETs. It is widely accepted that patients with seizures attributable to these lesions are excellent surgical candidates who achieve good outcomes and low recurrence rates without the use of adjunct therapies. Although most DNETs are benign, low-grade lesions, it is becoming increasingly apparent that a small number will progress to more aggressive lesions. Consequently, we recommend that these patients have regular follow-up examinations to identify progression at its early stages. As the natural history of DNETs is better defined, it should become increasingly possible to tailor treatments and follow-up regimens to individual patients.

**References**


**Figure 4.** Low-power view of oligodendrocyte-like cells with prominent perinuclear halos embedded in a background of abundant basophilic mucin (hematoxylin and eosin, original magnification x200).

**Figure 5.** High-power view of a floating neuron (hematoxylin and eosin, original magnification x400).