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SURGICAL NEUROLOGY INTERNATIONAL
SNI: Cerebrovascular, a supplement to Surgical Neurology International
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Editor: James I. Ausman, MD, PhD University of California, Los Angeles, CA, USA

# Long-term drug-resistant temporal lobe epilepsy associated with a mixed ganglioglioma and dysembryoplastic neuroepithelial tumor in an elderly patient

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Received: 19 November 15 Accepted: 15 February 16 Published: 01 April 16

## Abstract

**Background:** Mixed ganglioglioma and dysembryoplastic neuroepithelial tumor (DNET) is an extremely rare neuropathological diagnosis. The sparse number of patients described are children or young adults with long-term drug-resistant epilepsy.

**Case Description:** We report on a rare case of this tumor in a 61-year-old patient with an epilepsy duration of almost 60 years. This patient received an epilepsy surgery work-up with the intention to cure his drug-resistant epilepsy by performing a complete lesionectomy. The available literature on these mixed tumors is reviewed.

**Conclusion:** A contrast-enhancing mixed ganglioglioma and DNET can mimic a malignant tumor and appears not only in children and young adults, but also in the elderly patients with chronic epilepsy. A long-lasting epilepsy, in this case almost 60 years, can be completely cured by a complete lesionectomy.

**Key Words:** Dysembryoplastic neuroepithelial tumor, ganglioglioma, glioneuronal tumor, surgery, temporal lobe epilepsy

Access this article online
Website: www.surgicalneurologyint.com
DOI: 10.4103/2152-7806.179583
Quick Response Code:

## INTRODUCTION

Gangliogliomas are the prototype of composite glioneuronal tumors, first described in 1926.[7] These tumors consist of dysmorphic, well-differentiated neurons together with neoplastic glial cells, most frequently fibrillary astrocytic cells.

Dysembryoplastic neuroepithelial tumors (DNETs) were first described in 1988.[1] These tumors occur less frequently compared to gangliogliomas and are also composed of a mixture of neuronal and glial cells,[10] though these glial cells have morphological similarities with oligodendrocytes. Intracortically, the glial cells are arranged in a multinodular way with well-differentiated and occasionally dysmorphic, neurons floating in the myxoid environment between the nodules. The majority of both these tumors arise preferentially in the temporal lobe of children and young adults with a long-term drug-resistant epilepsy. Malignant de-differentiation is rare, but described for both DNETs and more frequently



**How to cite this article:** Schijns OE, Beckervordersandforth J, Wagner L, Hoogland G. Long-term drug-resistant temporal lobe epilepsy associated with a mixed ganglioglioma and dysembryoplastic neuroepithelial tumor in an elderly patient. Surg Neurol Int 2016;7:S243-6.
http://surgicalneurologyint.com/Long-term-drug-resistant-temporal-lobe-epilepsy-associated-with-a-mixed-ganglioglioma-and-dysembryoplastic-neuroepithelial-tumor-in-an-elderly-patient/

low-grade gangliogliomas.[4,13,15] After resective surgery, the oncological and epileptological prognosis is in almost all cases favorable.[1,5,14,17]

This case report describes the very rare combination of a mixed DNET-ganglioglioma in an elderly patient with a seizure duration of almost 60 years.

Since the first description of this tumor in 1997, only two patients (out of a total of 14), including this case, older than 50 years of age, have been described [Table 1].

## CASE REPORT

A 61-year-old man presented with chronic drug-resistant seizures since the age of four. After video-electroencephalogram (EEG) analysis, he was found to have complex partial seizures arising from the left temporal lobe. The seizures started with an unforced, nonversive head turning to the left, followed by a dystonic posturing of the right hand. Impairment of consciousness and apprehension together with dysphasia occurred. Postictally, the dysphasia continued and frequently there was nose wiping with the left hand. When he was considered a candidate for surgery, the patient had 1–2 seizures per month with a duration of 1 min. The seizures were treated with oxcarbazepine 1200 mg/day and valproic acid 1500 mg/day. The medical history was negative for epilepsy-associated risk factors such as febrile seizures, meningitis, and head trauma. The family history was negative with regard to epilepsy. Neurological examination demonstrated no abnormalities. A 3-Tesla magnetic resonance imaging (MRI) scan showed a cortical lesion in the medial and superior temporal gyrus of the anterior left temporal lobe, which appeared partially cystic and partially solid.

The solid part and the cyst wall enhanced after gadolinium administration. Signs of calcification or hemosiderin products were seen in the cyst wall [Figures 1 and 2]. Ictal and interictal EEG showed an epileptiform focus in the left temporal lobe, congruent with the clinical semiology and the lesion on MRI. The surgical treatment consisted of an awake craniotomy (Penfield procedure) with a maximal left-sided temporal lobectomy plus amygdalohippocampectomy and gross-total lesionectomy. The histological diagnosis was a mixed ganglioglioma-DNET, WHO Grade I. One part of the lesion [Figure 3] had a nodular myxoid, mucinous aspect with axonal bundles surrounded by oligodendrocyte-like cells. Between these bundles, an eosinophil matrix with neurons was found. The lesion stained positive with synaptophysin and S100, but was negative for glial fibrillary acidic protein (GFAP). A Ki-67-staining showed no elevated proliferative activity. This part of the lesion matched the diagnosis of a DNET, WHO Grade I. The other part of the lesion [Figure 4] had a clear neuronal and glial component and showed large and polymorph ganglion cells in a fibrillary matrix with glial cells and perivascular lymphocytic infiltrates. The neuronal part stained positive with synaptophysin and some ganglion cells were CD34 positive. Glial cells stained positive with GFAP, and Ki-67-staining was negative. Hence, this part of the lesion was compatible with a ganglioglioma.

In the first two postoperative weeks, the patient had mixed speech disturbances most probably due to manipulation-induced edema. Three weeks after operation, these disturbances had disappeared completely. Until now (60 months after operation), the patient is seizure-free.

## DISCUSSION

Glial tumors make up approximately half of the newly diagnosed primary brain tumors, with low-grade gliomas (LGGs) accounting for 15% of all brain tumors in adults.[3] Within the LGG group, the mixed glioneuronal tumors form a distinct entity as they occur preferentially in children and young adults with long-term drug-resistant epilepsy and seem to have a very indolent tumor-biological behavior. Gangliogliomas and DNETs are classical prototypes of these tumors, have many characteristics in common, but also clear differences. For example, gangliogliomas show a cellular

**Table 1: Summary of reports of mixed dysembryoplastic neuroepithelial tumor and ganglioglioma**

| Case reports (total 5 case reports) | Author/year/number of patients (total 14 patients) | Age at surgery (range - years) | Sex | Seizure duration (range - years) | Location | Follow-up (months) |
|---|---|---|---|---|---|---|
| 1 | Schijns/2015/1 patient | 61 | 1 male | 57 years | Left temporal | 60; Engel IA |
| 2 | Prayson/2012/8 patients | 5-48 | 7 female/ 1 male | New onset-36 years | 3X left temporal<br>3X right temporal<br>1X right front<br>1X right parietal-temporal | 1-141; all Engel I |
| 3 | Hirose/1998/1 patient | 15 | Female | New onset | Right parietal-occipital | 7; Engel I |
| 4 | Shimbo/1997/1 patient | 17 | Male | 2 years | Left temporal | 25; Engel I |
| 5 | Davis/1997/3 patients | 22-58 | 3 female | 20-36 | 3X temporal (laterality not specified) | Follow-up unknown; all Engel I |

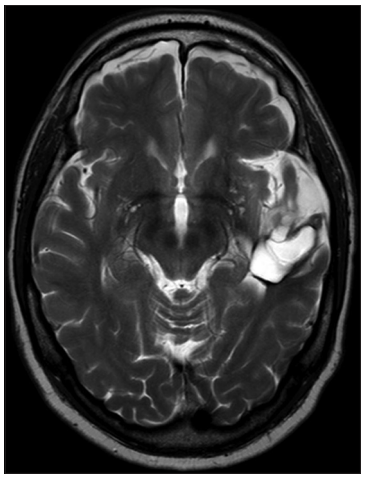

**Figure 1: T2-weighted magnetic resonance imaging (3 Tesla) with a cortical solid-cystic mass lesion in the medial and superior temporal gyrus of the anterior left temporal lobe**

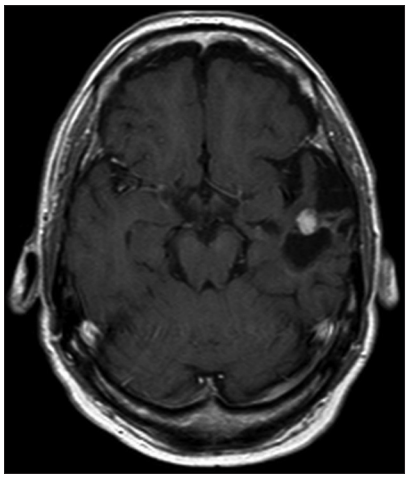

**Figure 2: T1-weighted magnetic resonance imaging + gadolinium (3 Tesla) shows a contrast-enhancing nodule in the cystic lesion together with calcification or hemosiderin products in the cyst wall**

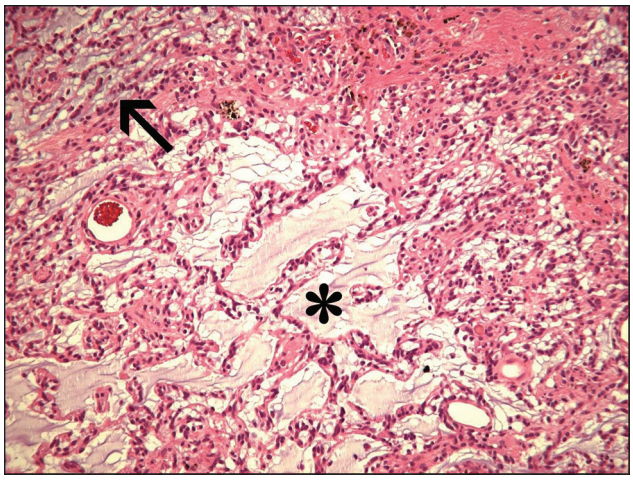

**Figure 3: The dysembryoplastic neuroepithelial tumor component is composed of myxoid (arrow) and multicystic (*) areas**

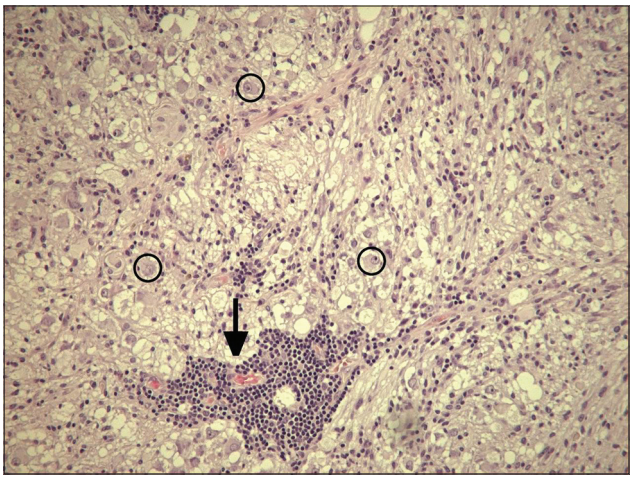

**Figure 4: Note the dysplastic neurons (circles) and perivascular lymphoid infiltrates (arrow) in the ganglioglioma component**

atypia in both the glial and neuronal components, in contrast to DNETs which display minimal, if any, atypia. Furthermore, DNETs typically reside in the cortex and have a multinodular aspect whereas gangliogliomas reside subcortically and have a unifocal aspect. The aspect of these mixed tumors on MRI is not pathognomonic. Most lesions have a low signal intensity on T1-weighted images, high signal on T2-weighted images, and have infrequent contrast enhancement. In this patient, because of the contrast-enhancing nodule, the first radiological diagnosis was that of a pleomorphic xanthoastrocytoma. A high-grade malignant tumor was included in the differential diagnosis because of two reasons. First, a small percentage of otherwise benign tumors such as a ganglioglioma, can dedifferentiate in the glial part of the tumor toward a high-grade tumor, especially in the elderly. Next to this argument, the performed MRI scan of this patient was his first scan, so earlier radiological images were not available and could not be compared with the actual MRI.

The first well-described example of a mixed ganglioglioma-DNET was the case report by Hirose *et al.* in 1998.[5] These authors described a 15-year-old girl with new-onset seizures. After an extensive neuropathological analysis, they postulate that a common neuropathobiological pathway may give origin to the formation of these composite tumors. It was postulated that pluripotent cells in the secondary germinal layer[6] may be the precursors of both the intracortical DNET as well as the ganglioglioma. In 1999 and later in 2012, Prayson *et al.*[11,12] described the same mixed tumor in a cohort of eight patients with chronic epilepsy. In five of their eight cases, neuropathological evaluation identified an area of focal cortical dysplasia (FCD) with cortical lamination disturbances (FCD Type I) in the neighborhood of the tumor. A case report of Shimbo

*et al*. described also a mixed ganglioglioma with a DNET combined with adjacent dysplasia. This led these authors to suggest a tumoral transformation of a dysplastic focus.[16] The combination of mixed glioneuronal tumors and dysplasias[8,9] could lead to the hypothesis that the dysplasia and the glioneuronal tumor are both representations of the same malformation of cortical development, which ultimately causes a drug-resistant epilepsy. Other reports suggest that this tumor behaves more like a benign neoplasm, rather than a dysplastic or hamartomatous lesion.[4,13,15] Davis *et al*.[2] describe within a group of 18 patients, 3 patients with a mixed ganglioglioma-DNET embedded in dysplastic cortical tissue and seizure-free outcome after temporal lobectomy.

This report describes the very rare case of a mixed ganglioglioma-DNET in an elderly patient; only one patient with an age above 50 was described earlier. A seizure duration of almost 60 years was not reported earlier. Most probably, the lesion was already present at the beginning of his seizures, 57 years ago. This shows once more the very indolent character of these tumors in the majority of patients and makes clear that a low-grade glioneuronal tumor always has to be included in the differential diagnosis of patients with long-term drug-resistant epilepsy, irrespective of their age. From a pragmatic, therapeutical point of view, it is important to realize that the ganglioglioma part of this mixed tumor, more frequently than the DNET component, can degenerate into an anaplastic or malignant form with a worse prognosis.

## CONCLUSION

This and the fact that in some cases a third pathology, like FCD, is present leads to the conclusion that gross-total resection is the current best advice for these tumors with an optimal epileptological and oncological control as a dual aim.

This case demonstrates that an elderly patient with a long-lasting epilepsy and its associated epileptogenic network can become seizure-free (Engel IA) after complete lesionectomy of this rare mixed lesion of DNET with ganglioglioma. Resective surgery should be offered in comparable cases.

### Financial support and sponsorship
Nil.

### Conflicts of interest
There are no conflicts of interest.

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