Dysembryoplastic Neuroepithelial Tumors: MR and CT Evaluation


PURPOSE: To evaluate dysembryoplastic neuroepithelial tumors (DNTs) on MR and CT studies and to compare DNT with other frequently encountered epileptogenic glioneuronal lesions. METHODS: We analyzed the MR images and CT scans of 16 patients who had complex partial epilepsy and DNT with respect to tumor location, size, CT density, MR signal intensity, mass effect, contrast enhancement, and heterogeneity, and compared these features with CT and MR findings in 51 cases of ganglioglioma and 33 cases of glioneuronal malformation. RESULTS: DNTs were located in the temporal lobe in 14 patients and in the frontal lobe in 2 patients. The cortex was involved in all cases and the subcortical white matter in 10 cases. Fifty percent of the tumors had poorly defined contours. On MR images, 14 DNTs had multiple cysts and 2 had single cysts. Contrast enhancement was observed in 6 DNTs, and mass effect was present in 9. CT scans disclosed moderately hypodense lesions in 7 patients and markedly hypodense cystic lesions in 6 patients. Two DNTs were calcified. Tumor hemorrhage with perifocal edema was observed in 1 case. Contrary to previous reports, slow but definite tumor growth was present during a 13-year period in 2 of 6 patients in whom serial CT or MR studies were obtained. CONCLUSION: A multicystic appearance on MR images is a characteristic feature of DNT and corresponds to its myxoid matrix and multinodular architecture. This feature is rare in gangliogliomas and glioneuronal malformations, and, as such, may help differentiate DNTs from these disorders.

Index terms: Brain neoplasms, magnetic resonance; Seizures


The term dysembryoplastic neuroepithelial tumor (DNT) was introduced by Daumas-Dupont et al in 1988 (1) and has recently been included as a mixed neuroglial tumor in the World Health Organization classification of brain tumors (2, 3). Clinically, DNT is usually associated with chronic epilepsy in adolescents and young adults. DNTs are most commonly located in the temporal lobe (1) and usually cause no neurologic deficit. Histopathologically, DNT is a benign multinodular lesion composed of glial and neuronal elements (1, 4–11). DNTs share several important features with gangliogliomas and glioneuronal malformations, such as glioneuronal hamartomas and hamartias (small glioneuronal malformations) (10). These consist of glial cells and highly differentiated ganglion cells and are frequently associated with chronic focal epilepsy.

In a series of 216 temporal lobe resections for chronic focal epilepsy, 34 gangliogliomas, 6 DNTs, and 32 glioneuronal malformations were found histopathologically (9). Therefore, presurgical criteria for the differentiation of these glioneuronal lesions are of interest. A few studies have mentioned the appearance of DNTs on magnetic resonance (MR) and computed tomographic (CT) studies (6–8, 12–19). These publications describe lesions with nonspecific low signal intensity on T1-weighted images and high signal intensity on T2-weighted images, similar to other gliomas. We present the MR (n = 16) and CT (n = 10) findings in 16 patients with DNT and discuss criteria to distinguish DNT from gangliogliomas and glioneuronal malformations.
Material and Methods

Clinical records, 10 CT scans, and 16 MR studies of 16 patients with a histopathologic diagnosis of DNT were analyzed retrospectively to determine the CT and MR characteristics of DNTs as well as their clinical presentation and postoperative course. All patients had surgery during the period from December 1988 to March 1995. Ten patients were female, 6 were male. All patients suffered from epilepsy, with a mean duration of 10.5 years (range, 0.2 to 31 years). Complex partial seizures were the only symptom except in 1 patient with insular DNT who also had a minimal motor deficit. The mean age at onset of epilepsy was 18.4 years (range, 1.5 to 60.5 years) (Table 1), and the average seizure frequency was 25 per month (range, 3 to 120 seizures per month). At surgery, the patients’ mean age was 28.9 years (range, 4.5 to 62.5 years).

Preoperative MR imaging was performed at various institutions from 1988 to 1994. The imaging studies included at least T1-weighted images obtained before and after intravenous administration of contrast material, and proton density-weighted and T2-weighted images in at least one plane. In 8 cases, preoperative CT studies were obtained before and after intravenous administration of contrast medium. Two patients had only an unenhanced CT examination. In 6 patients, two or more CT or MR studies had been obtained over a period of 1.5 to 13 years preoperatively. The following criteria were evaluated: exact location (gyrus), mass effect, edema, size, shape, sharpness of margin, homogeneity, and signal intensity on T1-weighted, proton density-weighted, and T2-weighted spin-echo images, and T1-weighted inversion recovery images. Contrast enhancement and calcifications were also noted. If solid and cystic components of the lesion could be identified, they were measured and characterized separately and their location within the whole lesion was characterized as central or excentric. Cystic components were described as monocystic or multicystic and they were categorized as small (<2 mm in diameter) or large (>2 mm in diameter). The MR and CT findings were compared with those of 51 gangliogliomas and 33 glioneuronal malformations that had been evaluated according to the same criteria (20, 21).

Clinical records were reviewed with respect to the history, preoperative clinical presentation, and postoperative outcome. The latter was scored according to Engel’s classification (22) as class I (seizure free or only auras), class II (rare seizures; ie, less than two per year), class III (75% or more reduction in frequency of seizures), and class IV (unchanged; ie, less than 75% reduction).

Results

Fourteen DNTs were located in the temporal lobe, 13 medially within the lobe. In 4 patients, the hippocampus was the only affected structure. In addition to the hippocampus, 5 tumors involved the parahippocampal gyrus, 5 the uncus, 3 the amygdaloid nucleus, 2 the tempororooccipital gyrus, and 1 the temporal pole region (Table 1). Two tumors affected only the parahippocampal gyrus and amygdaloid nucleus with involvement of temporopolar tissue in 1 case. The only DNT in our series that ex-
tended to the brain surface was located in the middle temporal gyrus. No abnormality of the adjacent skull was noted in this or any other case. The frontal lobe was affected by 1 frontopolar and 1 insular DNT. Cortical involvement was present in all cases, additional involvement of the subcortical white matter was found in 10 cases. The mean tumor size was 37 mm (range, 12 to 60 mm).

MR images showed signal abnormalities in all 16 patients. DNTs appeared as space-occupying lesions with displacement of the adjacent parenchyma or cerebrospinal fluid (CSF) spaces in 9 cases. Five of these lesions had only a slight mass effect. The mass effect of a frontal tumor was caused mainly by surrounding edema. This was the only DNT with massive calcification and perifocal edema as determined by CT and MR imaging (Fig 1). The other 7 DNTs did not show any edema or tumor-related mass effect on MR images. The margins between DNT and normal tissue were sharp in 8 cases, whereas 8 lesions had poorly defined borders.

All DNTs appeared as lesions with inhomogeneous signal intensities on MR images, indicating a heterogeneous structure. The most consistent MR feature in all cases was the presence of one or multiple areas of moderately (n = 14) or markedly (n = 2) reduced T1-signal and markedly (n = 15) or moderately (n = 1) increased T2-signal, similar to CSF. This signal pattern is typical of cystic or semifluid structures. On proton density-weighted images these cysts appeared as areas of isointensity (n = 2), moderate hyperintensity (n = 10), or marked hyperintensity (n = 4). In 9 DNTs, multiple large cysts were seen, most often with a diameter of 10 to 30 mm (Fig 2). A single cyst was found in 2 cases. One tumor appeared to contain multiple small cysts. Multiple small and large cysts were found in 4 DNTs (Figs 3 and 4). In 1 temporomesial DNT (Fig 3), cysts were also found in the white matter lateral to the temporal horn of the lateral ventricle and cortically in the temporopolar region. These cysts appeared to be separate from the main tumor mass. Histopathologically, multifocal tumor involvement was found in this case.

Solid components were identified in 11 tumors. They were distinguishable from cystic areas either because of contrast enhancement (n = 6) or because of their isointense signal on T1-weighted images (n = 7). Proton density-weighted images usually (n = 8) showed moderate signal increase, whereas T2-weighted images showed moderate (n = 6) or marked (n = 5) signal increase. Their location was eccentric in relation to the tumor as a whole in 7 cases. In 3 DNTs, the solid tumor elements formed a spongiform structure in between multiple cystic areas. Multifocal nodular enhancement was identified in 2 DNTs. The enhancing areas were completely separate in 1 patient (Fig 5) and partly confluent in the other patient. One DNT showed ring enhancement of a solid component. No disruption of the blood-brain barrier could be detected in 5 solid-appearing nodules.

The CT scans of 10 patients with DNT revealed 9 lesions with sharp margins and a poorly defined margin in 1 case. The tumors appeared homogeneous in 4 cases. Inhomogeneous tumor density was present in the other 6 DNTs. In 1 patient with head trauma, an area of central hyperdensity was temporarily apparent on CT scans, whereas several MR studies over some years did not show such changes. This CT finding was consistent with hemorrhage related to the head trauma, or it may have represented a spontaneous asymptomatic intratumoral hemorrhage. Mass effect was noted by CT in 7 patients. Markedly hypodense areas resembling CSF appeared in 6 cases. Three of these cystlike lesions were associated with less markedly hypodense solid structures. In the other 3 cases, the cystlike lesions were the only visible tumor component on CT scans.

Moderately hypodense tumor compounds, resembling solid low-grade gliomas, were present in seven cases of DNT. Moderate contrast enhancement was noted adjacent to a cystic lesion in one solid tumor part, that was invisible because of its isodensity on the unenhanced CT scan. The three solid tumor components that were associated with cystic parts were located centrally in relation to the whole lesion. Irregular central calcification and perifocal edema was detected in one frontal DNT (Fig 1), which also showed a mass effect. A small oval area of peripheral calcification was detected in one temporomesial tumor (Fig 5).

In 6 patients, analysis of the tumor shape and size over time was possible, because two or more preoperative CT or MR studies had been obtained over a period of 1.5 to 13 years (Table 2). There was a significant change of DNT over time in two cases. In a frontal DNT (patient 6),
the comparison of CT scans obtained from 1981, 1986, and 1994 showed significant growth of a calcified tumor area with progressive mass effect. The preoperative CT and MR studies in 1994 also showed significant perilesional edema as compared with the previous CT scans (Fig 1). The mass effect was associated with a new cystic component showing discrete marginal hypointensity on T2-weighted images, which may have represented tumor hemorrhage. Histopathologically, this tumor showed intrallesional hemorrhage. A malignant transformation of this DNT was considered, but a review of the neuropathologic appearance confirmed the diagnosis of a typical DNT without signs of malignancy. In a 5-year-old girl (patient 10) with insular tumor, MR examinations were carried out over a period of 3 years. The comparison of the MR studies from 1991 and 1993 (Fig 6) showed growth of the cystic tumor parts with extension into the lower insular cortex and further into the deep white matter. Moreover, circumscribed tumor enhancement was noted for the first time in 1994. Again, histopathologic evaluation showed no signs of malignant transformation. No changes of imaging findings over time were noted in the other four patients.
Fig 1, continued.

G–L, From 1994, precontrast (G, J) and postcontrast (H, K) T1-weighted MR images and T2-weighted (I, L) MR images show a central calcification (white arrow) surrounded by multiple cysts (black arrows), enhancing tumor nodules, and perifocal edema (arrowheads).

M, Low-power photomicrograph shows the nodular growth pattern and the loose matrix of this tumor. Note the focal calcification (arrow). Many small capillaries and hemosiderin-laden macrophages are at the surface of this nodule, suggesting an organizing intratumoral hemorrhage (arrowheads) (hematoxylin-eosin; magnification ×165).

N, At high power, there are many oligodendroglia-like cells with small round nuclei (arrow) and a clear perinuclear halo. These cells are located in a neurofibrillary matrix (M) (hematoxylin-eosin; magnification ×400).
Fig 2. Right temporomesial DNT (patient 13).
A–C, Coronal T2-weighted fast spin-echo (A), heavily T1-weighted inversion-recovery (B), and axial postcontrast T1-weighted spin-echo (C) MR images show multiple large cysts (arrowheads) that appear to replace the head and body of the hippocampus without subcortical extension. There is only slight mass effect.

Fig 3. Right temporal DNT (patient 14).
A–D, Axial precontrast T2-weighted (A,C) and T1-weighted (B) MR images and postcontrast T1-weighted (D) MR images show multiple small and large cysts in the hippocampus and also in the temporal white matter (arrow) and subcortically in the temporal pole (large arrowheads) without obvious continuity with the larger medially located tumor parts. Histopathologically, there was multifocal tumor spread. A solid, enhancing tumor nodule (small arrowheads) was located eccentrically.
The postoperative outcome was evaluated with clinical follow-up examinations in 13 patients. One patient died perioperatively of an unexplained diffuse cerebral hypoxia, while in 2 patients the postoperative phase is less than 6 months so far. Nine patients are in class I (seizure free), 2 patients are in class II, and 1 patient each is in class III and IV (Table 1).

Discussion

High-resolution MR imaging has significantly contributed to the recognition of low-grade tumors and tumorlike lesions as a major cause of chronic focal epilepsy. Modern MR techniques with high resolution and high contrast permit detection of lesions measuring no more than a few millimeters in size, and because of this, MR should be routinely used to examine patients with chronic focal epilepsy. The neuroradiologic characterization of such lesions is essential for the treatment of these patients because it aids in identifying those who are likely to benefit from epilepsy surgery. Following hippocampal sclerosis, benign tumors are the second most frequent brain lesions that are associated with epilepsy (10). The high prevalence of gangliogliomas in patients with chronic focal epilepsy contrasts with the fact that they constitute only 0.4% to 1.3% of all brain tumors in general neurosurgical series (23, 24). In our epilepsy surgery series, which presently includes 469 resection specimens, there were 138 tumors, including 17 DNTs (13%), 62 gangliogliomas (45%), and 59 astrocytomas (mixed gliomas and oligodendrogliomas) (42%).

Histopathologically, DNT is a benign, predominantly intracortical lesion composed
mainly of a population of oligodendrocyte-like cells with admixtures of mature ganglion cells and astrocytes that are located in a myxoid or dense neurofibrillary matrix (Fig 1C and D) (1, 4–11). Involvement of the cortical gray matter and a multinodular growth pattern are typical findings. The cortex adjacent to a DNT shows a disordered architecture. On the basis of its histopathologic appearance and benign clinical course, it has been suggested that DNT may be a malformation rather than a neoplastic lesion; however, significant proliferative activity as determined by Ki-67 labeling has been reported in some DNTs (8, 11). Histopathologically, DNTs can be distinguished from gangliogliomas by their multinodular architecture, myxoid matrix, and predominant population of oligodendrocyte-like cells. In addition, DNTs lack the bizarre neurons, the abundant connective tissue stroma, and the perivascular lymphocytic infil-

TABLE 2: Preoperative MR and CT studies in six patients with dysembryoplastic neuroepithelial tumor over a period of up to 13 years

<table>
<thead>
<tr>
<th>Patient</th>
<th>Date of First Examination</th>
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<th>Last Preoperative Control</th>
<th>Date of Surgery</th>
<th>Observation Period, y</th>
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<td>MR 1/91</td>
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<td>MR 4/89</td>
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trates that are frequently encountered in gangliogliomas (1). Other epileptogenic lesions that are composed of randomly scattered glial and neuronal elements are glioneuronal malformations. Some glioneuronal malformations are large and may resemble a neoplasm grossly. These are classified as glioneuronal hamartomas. Histopathologically, glioneuronal hamartomas may show great similarity with cortical tubers of tuberous sclerosis. Other glioneuronal malformations measure only a few millimeters in size and are termed glioneuronal hamartias. Glioneuronal malformations lack the markedly increased cellularity and tumor matrix that are so characteristic of true glial and glioneuronal neoplasms. For a review of this subject, see the article by Wolf and Wiestler (10). Because of the different biological natures of these different epilepsy-associated glioneuronal lesions (tumor versus malformation), it is important to establish criteria that may help to distinguish these entities radiologically.

A large series of 39 DNTs was published by Daumas-Duport et al in 1988 (1). Other articles in peer-reviewed publications report fewer than 8 cases each (5–7, 12–16, 18). Daumas-Duport et al performed a retrospective analysis of the histopathologic features of tumors resected between 1963 and 1988 and coined the term DNT for a subset of supratentorial superficial cortical tumors that typically present with focal epilepsy before 20 years of age. The authors briefly mention MR (n = 18) and CT findings (n = 32) and report cortical hypodense lesions on CT scans.
and prolonged T1 and T2 times on MR images, findings that are seen in most brain tumors. In a recent review, Daumas-Duport (8) describes a megagyri-like appearance of DNT on MR images and mentions a possible pseudocystic appearance of DNT on CT scans. Injection of gadopentetate dimeglumine was done in only a few of these cases, so that enhancement was detected only rarely.

In our series of 16 DNTs, the lobar distribution, with a striking temporal lobe predominance (86%) similar to that found in gangliogliomas (84%) and glioneuronal malformations (85%), and the clinical presentation, with seizures in all patients, were consistent with descriptions found in the literature. The absence of neurologic deficit as found in all but one of our patients has been described previously as typical of DNT (2). Only 4 patients had their first seizure after 20 years of age, which is consistent with rare reports of cases with late seizure onset in the literature (2, 17, 25). The average duration of epilepsy before surgery was 10.5 years (range, 0.2 to 31 years). This indicates a benign clinical course. Fourteen of the 16 patients had pharmacoresistant epilepsies for more than 2 years before surgery.

Imaging findings reported so far (1, 8, 6) consistently describe well-demarcated hypodense lesions on CT scans that rarely calcify or enhance. In our analysis, CT revealed moderate hypodensity of presumably solid tumor components and marked hypodensity of cystic components of DNT. Calcification was noted in only 2 (20%) of 10 DNTs, whereas CT showed calcification in 41% of gangliogliomas (21) and in 25% of glioneuronal malformations (20). All DNTs but one were sharply demarcated; the majority had inhomogeneous density and were space-occupying, but showed no edema. Thus, CT did not provide specific features of DNT but showed the nonspecific features of a benign tumor.

MR studies allow a much more detailed evaluation of the different tumor components. Although previous studies (2, 3) have reported cystic changes only in a minority of the cases, all lesions in our study contained cystic components, which often exhibited shorter T1 than CSF and appeared hypointense, isointense, or hyperintense on proton density–weighted images (Figs 3–5). This signal pattern reflects the abundant myxoid interstitial matrix that is typical of DNT. The high protein content of the myxoid matrix explains signal differences on T1-weighted and proton density–weighted images as compared with CSF. The cystic, in most cases even multicystic, appearance on MR images is a typical feature of DNT despite the absence of true cysts intraoperatively or on microscopic examination.

A cystic signal pattern is also found in other lesions that are frequently associated with chronic epilepsy, such as gangliogliomas, glioneuronal malformations, and other gliomas. In recently published series of 51 gangliogliomas (21) and 33 glioneuronal malformations (20), 2 gangliogliomas (4%) appeared completely cystic, 21 (41%) had both solid and cystic components, and 28 gangliogliomas (55%) were purely solid on MR images. A multicystic appearance was present in only 5 (10%) of 51 gangliogliomas. Glioneuronal malformations were associated with other lesions, mainly gangliogliomas in 16 cases. Isolated glioneuronal malformations were purely solid in 62% and had solid and cystic components in 38% of cases. Only 1 glioneuronal malformation was multicystic on MR images. Thus, although the multicystic appearance on MR images is not entirely specific for DNT, it is a typical and frequent finding, which helps to distinguish DNT from gangliogliomas and glioneuronal malformations.

The signal pattern of solid DNT components on MR images is similar to that of solid gangliogliomas, which appeared isointense on T1-weighted images in 32 (73%) of 44 cases in one study (21). Approximately half of the solid DNT elements show contrast enhancement, a finding that is observed in 44% of gangliogliomas (21), whereas enhancement is never observed in solid parts of glioneuronal malformations (20). Multifocal nodular enhancement was found in only 2 DNTs, but in none of the gangliogliomas of World Health Organization grade I. In contrast to the previously reported CT findings, MR images showed poorly defined tumor contours in 8 DNTs. Calcification, which is best detected by CT, is less frequent in DNTs (2 [14%] of 14) than in gangliogliomas (7 [41%] of 17) and in glioneuronal malformations (2 [25%] of 8). In contrast to DNTs, gangliogliomas may occur infratentorially and may be malignant both histopathologically and clinically (26).

Changes in the shape or size of DNTs over time were documented in two of our cases. In one case (Fig 1) the appearance of an addi-
tional cystic formation with perifocal edema could be explained by tumor hemorrhage and may not necessarily be the result of tumor growth. CT also showed significant growth of a large solid calcified tumor component. Histopathologically, the lesion contained abundant capillaries and hemosiderin-laden macrophages, indicative of previous hemorrhage. To date, there is no evidence of recurrence 1 year after surgery in this patient.

The observation of a growing cystic tumor with mild mass effect and enhancement over time in another case (Fig 6) is unusual. It raises the possibility of a malignant transformation; however, review of the histopathologic findings showed no evidence of malignancy. The patient is seizure free 1 year after surgery, although complete tumor removal could not be achieved. In all other cases, the imaging studies yielded no evidence of growth or edema. However, our study includes some cases with approximately 20-year-old CT scans and first-generation MR images, which make the evaluation of possible changes in tumor size and demarcation difficult.

Deformities of the calvaria adjacent to superficially located DNTs were described in 11 of 12 cases by Daumas-Duput (8). In our series, only 1 DNT extended to the cortical surface. This tumor was not associated with a deformity of the calvaria. The other 15 tumors were located temporomaterially or deeply in the insula, so that remodeling of the skull would be unlikely.

Ten of 16 DNTs extended into the subcortical white matter. In some cases, such tumor extension was observed without mass effect, suggesting replacement of brain tissue by DNT. This evolution was graphically documented in a case of insular DNT with 3 years of imaging follow-up (Fig 6). The observation of a patient who had two cysts that were clearly separate from the main tumor mass in a temporomalesal DNT (Fig 3) may also raise the question of a multifocal tumor origin in such cases.

In conclusion, our analysis of the MR findings with special attention to signs of multinodularity and multicystic appearance closely reflects the well-documented histopathologic growth pattern of DNT. Together with the typical clinical presentation and the history of chronic focal epilepsy, MR findings may strongly suggest the preoperative diagnosis of DNT and may help to avoid inadequate therapy, such as radiation instead of surgical removal, which is the therapy of choice.

Acknowledgments

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References