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Focal Cortical Dysplasia of Taylor, Balloon Cell Subtype: MR Differentiation from Low-Grade Tumors

Richard A. Bronen, Kenneth P. Vives, Jung H. Kim, Robert K. Fulbright, Susan S. Spencer, and Dennis D. Spencer

PURPOSE: To test the hypothesis that focal cortical dysplasia of Taylor (FCDT) can be distinguished from low-grade tumors by means of clinical and MR findings. **METHODS:** We examined 10 clinical and 19 MR imaging variables in patients who underwent surgery for intractable epilepsy over an 8-year period. The 54 patients with low-grade glial neoplasms were compared with the eight patients who had balloon cell FCDT. **RESULTS:** Statistically significant differences were seen with respect to eight of the MR variables and none of the clinical variables. MR findings suggesting dysplasia rather than tumor included the presence of gray matter thickening associated with a homogeneous hyperintense signal in the subcortical white matter that tapers as it extends to the lateral ventricle. A frontal lobe location favors dysplasia, while a temporal lobe (especially medial temporal lobe) location is more suggestive of a neoplasm. **CONCLUSION:** Several MR features help distinguish balloon cell FCDT from neoplasms, especially cortical thickening and a tapered signal to the ventricle. This distinction is important for surgical planning, as the decision to operate and the extent of surgical resection often depend on the presence or absence of neoplastic tissue.

Index terms: Brain, abnormalities and anomalies; Brain neoplasms, magnetic resonance; Sclerosis, tuberous; Seizures

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In 1971 Taylor et al (1) described a constellation of findings that they thought deserved to be categorized as a unique entity: focal cortical dysplasia in patients with intractable epilepsy. Histologically, this entity, which we refer to as *focal cortical dysplasia of Taylor* (FCDT), consists of cytoarchitectural disarray of the cortex caused by large, bizarre, disoriented neurons and the presence of balloon cells in the subcortical white matter and cortex. This developmental disorder has a histologic pattern very similar to tuberous sclerosis.

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With the advent of magnetic resonance (MR) imaging, it has become clear that developmental disorders are associated with epilepsy more frequently than previously thought (2–4). Several reports have described MR imaging findings associated with FCDT, such as cortical thickening, indistinctness of the cortical-medullary junction, and macrogyria (3, 5–7). In the subgroup of FCDT associated with balloon cells, focal hyperintensity within the subcortical white matter has sometimes been noted on MR images obtained with a long repetition time (TR) (3, 5–7). This MR characteristic of focal, well-circumscribed white matter hyperintensity on long-TR images is typically associated with a neoplastic process in patients with intractable epilepsy. In fact, several articles point out the difficulty of distinguishing solitary focal cortical dysplasias (of either the FCDT or tuberous sclerosis variety) from neoplasms on MR images (8, 9). It is important to make this distinction before surgery, because the decision to operate may depend on the presence or absence of neoplastic tissue (10). Surgical planning for le-

sions in eloquent regions of brain may be altered on the basis of presumed histopathology.

The purpose of this study was to identify characteristics that differentiate FCDT associated with balloon cells (balloon cell FCDT) from low-grade neoplasms by evaluating a range of clinical and imaging findings in a consecutive group of patients with surgically treated intractable epilepsy.

Materials and Methods

Patients

The study group was derived from a consecutive series of patients who underwent surgery for medically intractable epilepsy at our institution between June 1986 and September 1993. For the purposes of this study, intractability was defined as one or more seizures per month for the 6 months preceding surgery despite a regimen of maximal medical therapy. All patients were operated on by the same surgeon. Resected tissue was examined by a neuropathologist who specializes in epilepsy.

Patients were classified into one of two groups on the basis of neuropathologic findings: those with low-grade tumors (11) and those with balloon cell FCDT. Balloon cells are defined as giant cells of uncertain lineage, containing pale eosinophilic cytoplasm with eccentric nuclei, a prominent nucleolus, and an absence of Nissl substance (12). These cells were found in both subcortical white matter and cortical gray matter. Patients without balloon cells but with other findings of FCDT (eg, presence of large, bizarre, disoriented neurons in the cortex and numerous neurons in the cortex resulting in disruption of the normal laminar cytoarchitecture) were excluded from analysis.

Patients without balloon cells were excluded for several reasons. First, non–balloon cell FCDT tends not to have increased signal in the subcortical white matter and thus is not readily confused with tumor. Second, non–balloon cell FCDT is not as clearly defined pathologically. One must be able to distinguish among various gradations of cortical dysgenesis, including those associated with destructive lesions (which may or may not have a genetic basis) (12). We found a case of dysplastic cortex due to an early ischemic event that appeared similar to non–balloon cell FCDT. Although there was cytoarchitectural lamina disarray and clusters of neurons in the cortex, the association of scar tissue with loss of neurons suggested an ischemic origin. In another case in which balloon cells were absent, it was difficult to determine whether the presence of a few large bizarre neurons in the occipital cortex represented FCDT or a normal variety of cortical neurons found in the occipital lobe, known as Meynert cells (13).

Histologic specimens were fixed in formalin for 8 hours, dehydrated through graded alcohols, embedded in paraffin, and then sectioned into 6-μm-thick slices for microscopic analysis. Routine staining was done with hematoxylin-eosin. Immunohistochemical analysis was performed using anti-GFAP (glial fibrillary acidic protein) antibody to detect cells of astrocytic lineage. Nissl stain was used to detect cells of neuronal lineage.

Clinical Information

The following demographic and clinical information was collected for each patient: sex, handedness, age at surgery, age at onset of seizures, number of years of seizures, presence or absence of febrile seizures, presence of an adverse event during gestation or birth, full-scale IQ score, number of different seizure types, preoperative seizure frequency, and presence or absence of secondary generalization of seizures.

MR Imaging

MR imaging was performed on a 1.5-T magnet. In all patients, axial and coronal long TR images were obtained with the following parameters: 2000–3000/20–30,80–100/0.5–2 (TR/echo time[TE]/excitations), 20- to 24-cm field of view, 128–256 $\times$ 256 matrix, and 3- to 5-mm section thickness with a gap of 0.9 to 2.5 mm. In 45 patients, conventional T1-weighted spin-echo images were obtained with parameters of 400–600/20/4, 128 $\times$ 256 matrix, 16-cm field of view, and 5-mm-thick contiguous sections, or three-dimensional volume spoiled gradient-echo images were obtained with parameters of 25/5/2, 45° flip angle, 16-cm field of view, 256 $\times$ 192 matrix, and 3-mm-thick contiguous sections. Contrast material was used in 38 MR studies: five in patients with balloon cell FCDT and 33 in patients with neoplasms.

The following aspects of the MR study were noted to be present or absent: calvarial remodeling (ie, erosion of the calvaria or diploic space by the lesion); gray matter involvement; white matter involvement; both gray and white matter involvement; lobar location (frontal, parietal, occipital, temporal); presence in limbic lobe (hippocampus, parahippocampal gyrus, cingulate gyrus, or subcallosal area); presence in subdivisions of medial temporal or lateral temporal lobes; presence of multilobar involvement; hemispheric location (left or right); mass effect; edema; signal intensity; hyperintensity in the subcortical white matter location; gray matter thickening; and extension of abnormality to the ventricle. For coding of signal intensity, we determined whether the abnormality was homogeneously hyperintense relative to gray matter on both long-TR/short-TE and long-TR/long-TE images (a positive condition). In patients with associated gray matter thickening, we considered that finding to be independent of other signal characteristics. For example, homogeneously hyperintense lesions associated with gray matter thickening were coded as positive for both the gray matter thickening and the signal intensity variables; they were not considered to represent a heterogeneous signal lesion consisting of two components (ie, hyperintense and isointense regions relative to gray matter). Conditions for the variable

hyperintensity in the subcortical white matter location, referred to as *subcortical white matter,* included lesion location in the subcortical white matter adjacent to the cortical ribbon with a hyperintense signal on long-TR images throughout most of the lesion (some heterogeneity of signal was allowed as long as most of the lesion was hyperintense). Conditions for the variable *ventricular extension* consisted of a lesion with extension to the lateral ventricle and signal intensity of this extension being hyperintense relative to white matter on long-TR images. Conditions for MR variables were arrived at empirically and by using findings described for tuberous sclerosis. Data were insufficient to ascertain statistically the role of contrast enhancement as a variable.

In the subgroup of patients who had lesions extending to the lateral ventricle, the following aspects were additionally evaluated: tapering to the ventricle, enlargement of the ventricle, mass effect on the ventricle, and deformation of the ventricle.

Statistics

Univariate analysis was performed of the above-mentioned clinical and radiologic variables and their differences between the two groups of patients. Fisher's Exact Test (two-tailed) was used for nominal variables and Student's *t* test (two-tailed) was used for interval variables. Risk ratios were then computed for the patients on the basis of the above data. Multivariate analysis was carried out via stepwise logistic regression for the radiologic variables. The dependent variable was coded as "1" if the patient had the diagnosis of cortical dysplasia and "0" if the diagnosis was low-grade tumor. To provide stability for those cases in which a zero cell frequency was encountered, a small number (0.01) was added to the calculated frequency in each cell. At each step, the variable that had the greatest maximum likelihood value was allowed to enter the model. The likelihood ratio for the full model including the new variable compared with the reduced model excluding the variable was calculated. For the variable to enter the model, the one-tailed probability for the χ^2 test for the likelihood ratio was required to be less than 0.1. After the addition of each variable, all other variables were tested for removal by the likelihood ratio test as above. All variables with one-tailed *P* values less than .1 were allowed to remain in the model. Variables were added until no other variables met the above-mentioned criteria for entry. The odds ratio for each variable and the full versus reduced χ^2 *P* value were calculated for each variable in the final model. An additional logistic regression analysis was performed for variables listed above for those patients who were noted to have extension to the ventricle. This was carried out in the same fashion as above.

To assess the possible influence of the clinical variables, an additional stepwise logistic regression, including each clinical variable and its first-order interaction with the radiologic variables, was performed in the same manner as above.

Results

Pathologic Findings

Fifty-four patients had a histologic diagnosis of a low-grade glial tumor, consisting of either astrocytic, oligodendroglial, ganglioglial, or a mixed type. Eight patients had histologic findings consistent with balloon cell FCDT. All eight patients with balloon cell FCDT had, by definition, evidence of pale giant eosinophilic balloon cells, which have features of both neuron and glial cells (Fig 1). These cells are variably glial fibrillary acidic protein positive, have eccentric nuclei, contain prominent nucleoli, and are found in both the cortex and subcortical white matter (in the latter more frequently). One patient with balloon cells also had associated calcification, raising the possibility of tuberous sclerosis; however, there was no other evidence to suggest a possible or definite diagnosis of tuberous sclerosis, such as additional intracranial abnormalities on MR images or skin manifestations. The degree of cytoarchitectural abnormalities in this patient was greater than in the other seven and could be categorized as type III cortical dysplasia in the classification system suggested by Palmini et al (3). All eight patients had congregates of large, bizarre neurons in the cortex with abnormal morphology and orientation, resulting in disarray of the laminar cytoarchitecture of the cortex.

Clinical Aspects

There was no statistical difference between the tumor and cortical dysplasia groups for any

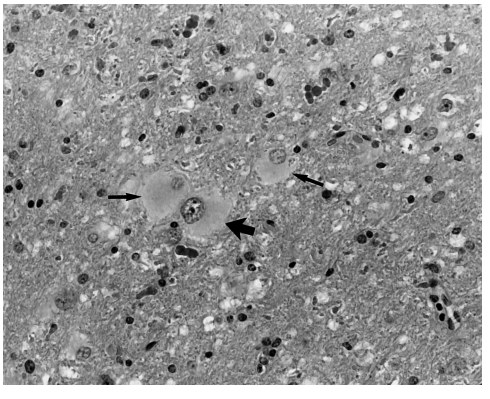


Fig 1. Three balloon cells (*arrows*) are seen in the center of this histologic specimen. Note the marked enlargement of these cells and the eccentrically located nucleus. In one balloon cell (*thick arrow*), the nucleus contains a prominent nucleolus, similar to that seen in neuronal nuclei, yet there is an absence of Nissl substance (hematoxylin-eosin, original magnification ×370).

TABLE 1: Univariate analysis of the clinical characteristics based on neuropathologic findings

Variable		Group	No. or Mean†	% or SE‡	*P*§
Sex	Male	Tumor	24	44.4	1.00
		FCDT	3	37.5	
Handedness	Right	Tumor	47	87.0	1.00
		FCDT	7	87.5	
Febrile seizures	Present	Tumor	5	9.3	0.58
		FCDT	1	12.5	
Abnormal gestation/birth	Present	Tumor	12	22.2	1.00
		FCDT	2	25.0	
Number of seizure types	More than one	Tumor	8	14.8	1.00
		FCDT	1	12.5	
Secondary generalization	Present	Tumor	24	44.4	0.46
		FCDT	5	62.5	
Age of seizure Onset*		Tumor	11	1.1	0.06
		FCDT	6	2.0	
Age at surgery, y*		Tumor	25	1.4	0.89
		FCDT	25	2.6	
No. of years of seizures*		Tumor	14	1.2	0.13
		FCDT	19	1.9	
Preoperative seizure frequency*		Tumor	46	12	0.82
		FCDT	53	11	
Preoperative full-scale IQ score*		Tumor	81	5	0.73
		FCDT	76	11	

Note.—FCDT indicates focal dysplasia of Taylor. Fifty-four patients had neoplasms and eight had balloon cell FCDT.

* Continuous or interval variable: Mean†, standard error (SE)‡, and *P* value from the two-tailed Student's *t* test†† were used for continuous or interval variables.

Number (No.)†, percentage‡, and *P* value for the two-tailed Fisher's Exact Test§ were used for nominal variables.

of the clinical variables relating to sex, seizure history, or intelligence (Table 1). There was a trend toward significance ($P = .06$) for age of seizure onset, with a mean onset at 5.8 years of age for the dysplasia group compared with 11.3 years for the neoplastic group.

MR Imaging

Significant differences between the two groups were found for eight radiologic variables by using the univariate analysis (Tables 2 and 3). MR findings suggesting balloon cell FCDT rather than tumor included the presence of associated gray matter thickening; a homogeneous hyperintense signal; location of a hyperintense signal in the subcortical white matter; a lobar location in the frontal lobes but not in the temporal lobe and especially not in the medial temporal lobe (these latter locations are more suggestive of tumor); a hyperintense signal extending to the lateral ventricles; and tapering of this signal as it extends to the ventricle (Figs 2–5).

Multivariate analysis (of the variables listed in Tables 2 and 3) using stepwise logistic regression showed a significant difference for the variable *gray matter thickening*, with a relative odds ratio of 500:1, indicating cortical dysplasia compared with tumor ($P = .0001$). There was a trend toward significance for the *homogeneous hyperintense signal intensity* variable, with a relative odds ratio of 9.5:1 ($P = .0615$). For variables assessing those patients with ventricular extension (from Table 3), only the variable *tapering to the ventricle* was significant in the multivariate analysis (relative odds ratio of 62.5:1, $P = .0001$).

Eleven of the 38 patients who had contrast-enhanced MR imaging had definite enhancement of the lesion. Of the five patients with balloon cell FCDT who had contrast-enhanced imaging, one (20%) had definite enhancement, one (20%) had questionable enhancement, and three (60%) had no enhancement. Of the 33 patients with neoplasms who had contrast-enhanced imaging, 10 (30%) had definite enhancement, seven (21%) had questionable enhancement, and 16 (48%) had no enhancement.

TABLE 2: Univariate analysis of the radiologic characteristics based on neuropathologic findings

Variable	Group	No.	%	*P* Value
Calvarial remodeling	Tumor	19	35.2	0.09
	FCDT	0	0	
Gray matter involvement	Tumor	48	88.9	0.27
	FCDT	6	75.0	
White matter involvement	Tumor	40	74.1	0.18
	FCDT	8	100	
White and gray matter involvement	Tumor	34	63.0	0.70
	FCDT	6	75.0	
Frontal lobe involvement	Tumor	3	5.6	**0.004**
	FCDT	4	50.0	
Parietal lobe involvement	Tumor	7	13.0	0.33
	FCDT	2	25.0	
Occipital lobe involvement	Tumor	8	14.8	1.00
	FCDT	1	12.5	
Limbic lobe involvement	Tumor	26	48.2	0.12
	FCDT	1	12.5	
Temporal lobe involvement	Tumor	39	72.2	**0.002**
	FCDT	1	12.5	
Medial temporal lobe involvement	Tumor	24	44.4	**0.019**
	FCDT	0	0	
Lateral temporal lobe involvement	Tumor	15	27.8	0.67
	FCDT	1	12.5	
Multilobar involvement	Tumor	3	5.6	1.00
	FCDT	0	0	
Left-sided involvement	Tumor	24	44.4	1.00
	FCDT	4	50.0	
Mass effect	Tumor	38	70.4	0.42
	FCDT	4	50.0	
Edema	Tumor	4	7.4	1.00
	FCDT	0	0	
Homogeneous hyperintense signal	Tumor	14	26.0	**0.00147**
	FCDT	7	87.5	
Subcortical white matter hyperintensity	Tumor	24	44.4	**0.00484**
	FCDT	8	100	
Gray matter thickening	Tumor	7	13.0	**0.0000019**
	FCDT	8	100	
Venticular extension of signal	Tumor	20	37.0	**0.00985**
	FCDT	7	87.5	

Note.—FCDT indicates focal dysplasia of Taylor. The number of patients with each characteristic is followed by the percentage of patients in that group (total group numbers were 54 and eight, respectively). The *P* values are derived from a two-tailed Fisher's Exact Test. Significant differences are listed in **bold** type.

Discussion

Since the report by Taylor et al in 1971 (1), it has been recognized that developmental disorders are an important cause of focal intractable epilepsy and that these disorders may be amenable to surgical treatment. Currently, focal developmental disorders occur in 6% to 20% of surgical epilepsy series (14, 15). With the advent of MR imaging, it became clear that developmental disorders were more frequently associated with epilepsy than previously thought (2–4). While the MR imaging studies have certainly improved our understanding of developmental disorders, they have also created confusion because of the lack of universally recognized terminology for MR findings (16) (Table 4). Confusion has also developed because some authors use histologic terms to describe MR findings. The terms *dysplasia* and *cortical dysplasia* are frequently used to designate any developmental disorder of the cerebrum. Some authors use the term *focal cortical dysplasia* to refer to the histologic entity described by Taylor et al (1), while others use this term in a general sense to describe focal developmental abnormalities affecting the cortex, including the histologic correlates of polymicrogyria. We prefer the terms *cortical developmental disorder, malformations of cortical development,* or *cortical dysgenesis* for MR findings of diffuse or focal

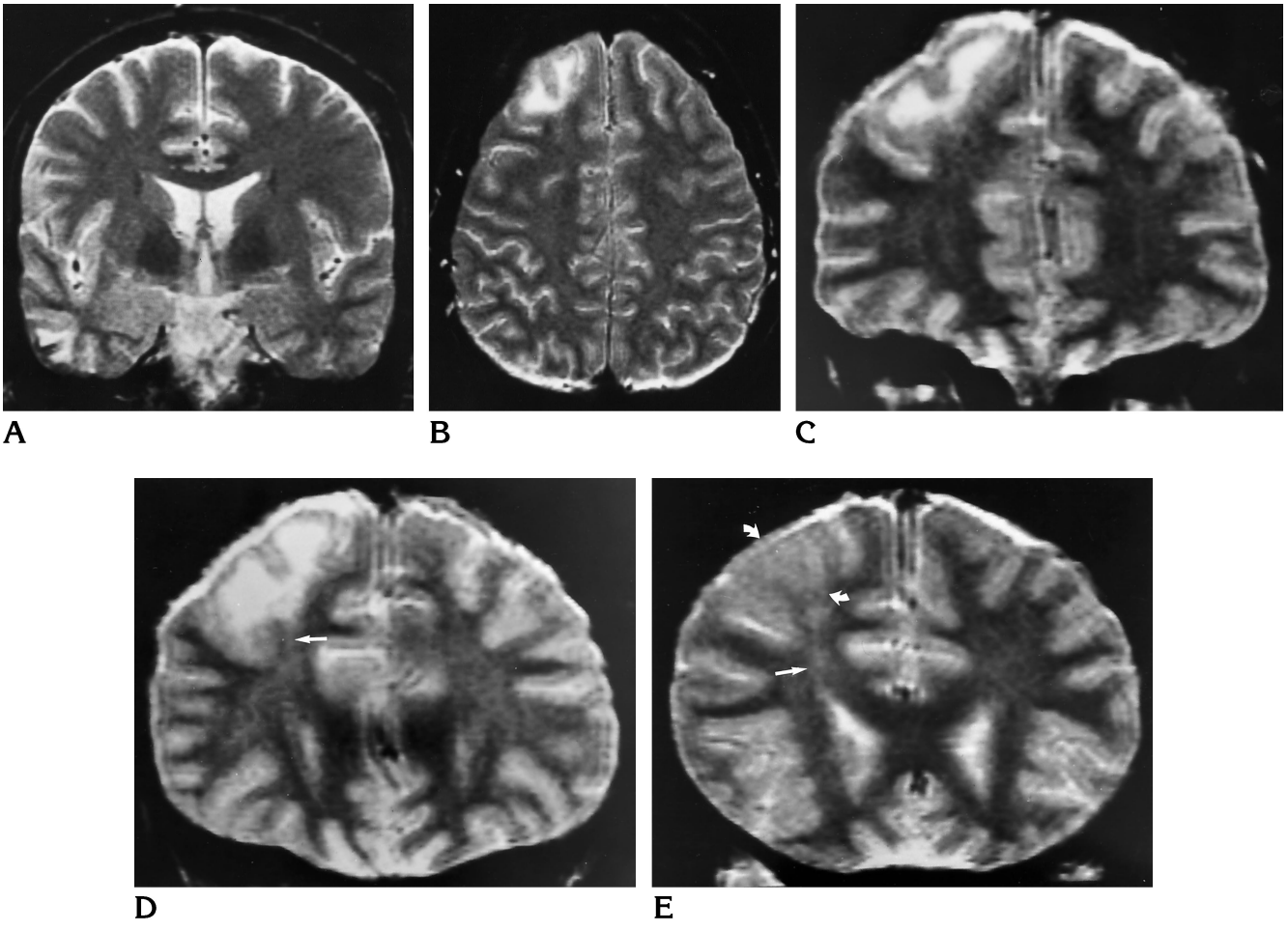


Fig 2. MR images of neoplasm (*A*) and balloon cell FCDT (*B–E*). Coronal T2-weighted image (2800/80/1) of low-grade astrocytoma (*A*) is compared with axial T2-weighted (2100/80/0.5) (*B*) and sequential coronal T2-weighted (2700/80/1) (*C–E*) images of a patient with balloon cell FCDT. This case illustrates imaging similarities and differences between certain neoplasms and balloon cell FCDT. Both the tumor and dysplasia are remarkable for their similar MR appearance with respect to the homogeneous hyperintense signal within the subcortical white matter underlying the cortical ribbon (the corresponding histologic tissue consisted of astrocytoma in the case of the tumor and dysplastic tissue in the case of dysplasia; there was no evidence of edema in either case). However, the correct diagnosis is suggested by the adjacent cortex, which is of normal thickness in the tumor but is thickened in the dysplasia. Cortical thickening is best seen in *E* (between *curved arrows*). Another finding suggesting balloon cell FCDT rather than tumor is the extension (*straight arrow* in *D* and *E*) to the lateral ventricle. The frontal location of the lesion in the case of dysplasia versus the temporal location of the lesion in the case of tumor provides further evidence of the correct diagnoses. Unlike the comparison illustrated in this example, most neoplasms can be easily distinguished from dysplasia on the basis of signal intensity and location (without evaluating for cortical thickness or signal extension to the ventricle). Only a minority of tumors have MR features of a homogeneous hyperintense signal in a subcortical location whereas these findings are seen in almost all cases of dysplasia.

cortical malformations (16, 17). To avoid confusion, we prefer the term *focal cortical dysplasia of Taylor* (FCDT) to indicate the histologic entity as opposed to *focal cortical dysplasia* (Table 4).

There is also confusion within the literature regarding histologic classification of FCDT and developmental disorders in general (16). Most reports categorize the subtype of cortical dysplasia associated with balloon cells as the most severe type of cortical dysplasia or as a completely different category of focal cortical dysplasia (3, 5, 12, 16). Balloon cells, also known as N cells, appear to have characteristics of both neurons and astrocytes, as shown by studies using electron microscopy and immunocytochemistry (Fig 1). The failure of these cells to commit to or differentiate into a specific phenotype suggests an abnormality that occurs in pluripotent brain cells (in the first trimester) (18, 19). The balloon cell subtype of FCDT was designated as severe focal cortical dysplasia type 2 by Kuzniecky et al (4, 5, 14) (Table 4). Palmini et al (3) used a three-tier classification system

TABLE 3: Univariate analysis of the radiologic characteristics assessing the relationship between lesion and ventricle based on neuropathologic findings

Variable		Group	No.	%	*P*
Tapers to the ventricle	Present	Tumor	3	10.0	0.0000696
		FCDT	7	87.5	
Enlarged ventricle	Present	Tumor	6	20.0	1.00
		FCDT	2	25.0	
Deformed ventricle	Present	Tumor	0	0	0.21
		FCDT	1	12.5	
Mass effect on ventricle	Present	Tumor	6	20.0	0.31
		FCDT	0	0	

Note.—FCDT indicates focal dysplasia of Taylor. The number of patients with each characteristic is followed by the percentage of patients in that group (total group numbers were 27 and eight, respectively). This represents a subgroup of the tumor patients whereas all the patients with cortical dysplasia are included. The *P* values are derived from a two-tailed Fisher's Exact Test. Significant differences were found between the two groups for the variable *tapers to the ventricle*.

in which balloon cells are present in both type II and III focal cortical dysplasia; these authors distinguished type II from type III by the degree of cytoarchitectural abnormalities present and formerly designated type III as forme fruste tuberous sclerosis (3, 7). We have tried to avoid confusion by categorizing any FCDT histologic lesion with balloon cells present as *balloon cell FCDT* (Table 4). This terminology is equivalent to that proposed by Barkovich et al (16). We do not subscribe to the use of the term *glioneuronal hamartoma* as a synonym for focal cortical dysplasia as described by Wolf et al (20).

Previous reports have noted the difficulty of differentiating solitary focal cortical dysplasias from neoplasms by means of MR imaging in patients with seizures (8, 9). In patients with intractable epilepsy, it is important to be able to make this distinction before surgery (10). If imaging suggests FCDT rather than neoplasm, one could follow the patient conservatively with imaging rather than perform surgery in the case of an epileptogenic lesion located in eloquent

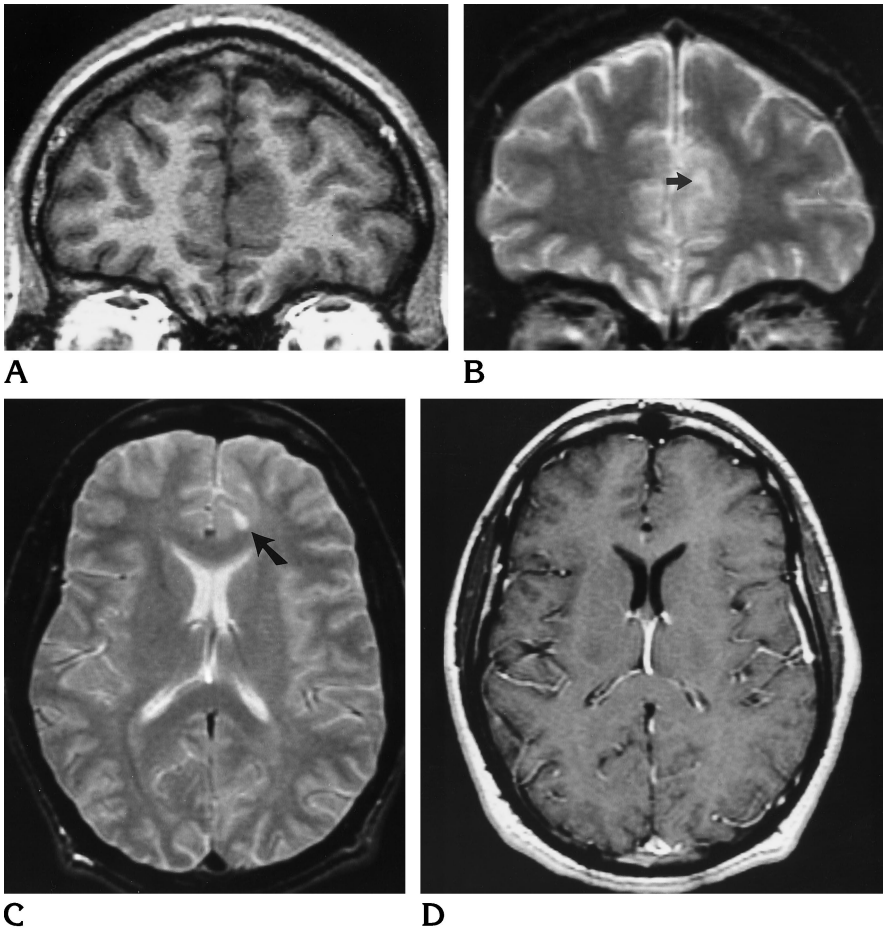
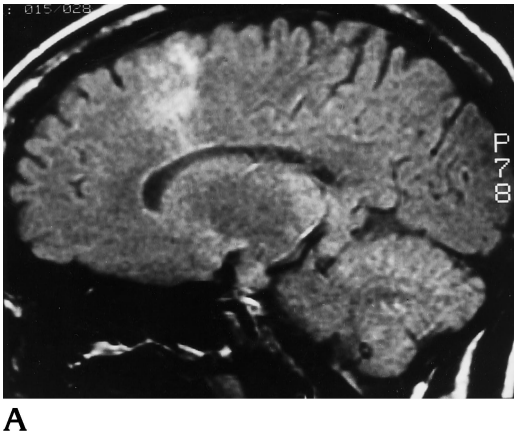
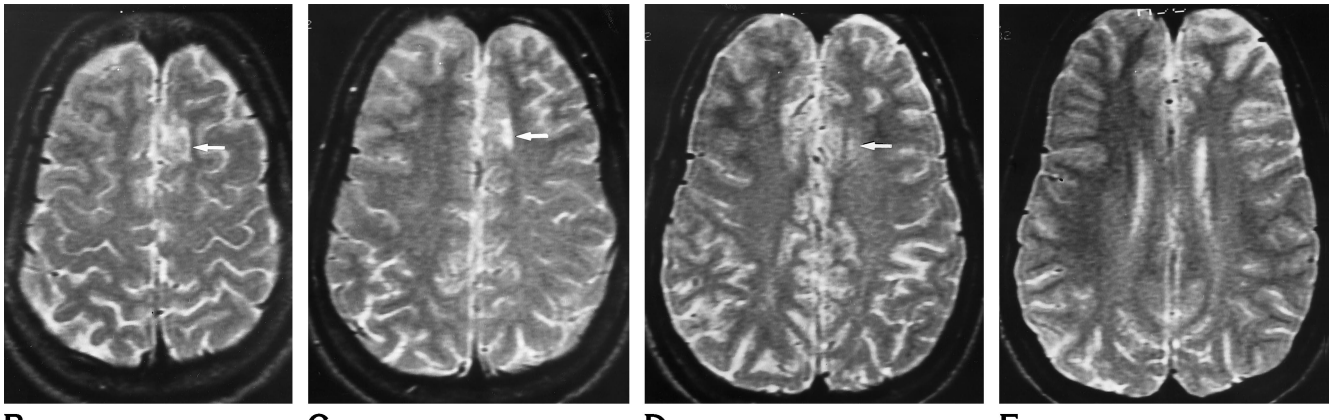


Fig 3. Cortical thickening associated with balloon cell FCDT. Coronal spoiled gradient-echo (25/5/2, 45° flip angle) (*A*) and T2-weighted (2433/80/1) (*B*) images show marked cortical thickening in the left frontal lobe. Owing to the coronal imaging plane, a region of increased signal (*arrow* in *B*) appears to be surrounded by thickened gray matter. However, the axial T2-weighted (2016/80/1) image (*C*) shows that this region of increased signal is not in the gray matter but represents a portion of hyperintense subcortical white matter. There is no abnormal enhancement on an axial contrast-enhanced T1-weighted (600/26/1) image (*D*).

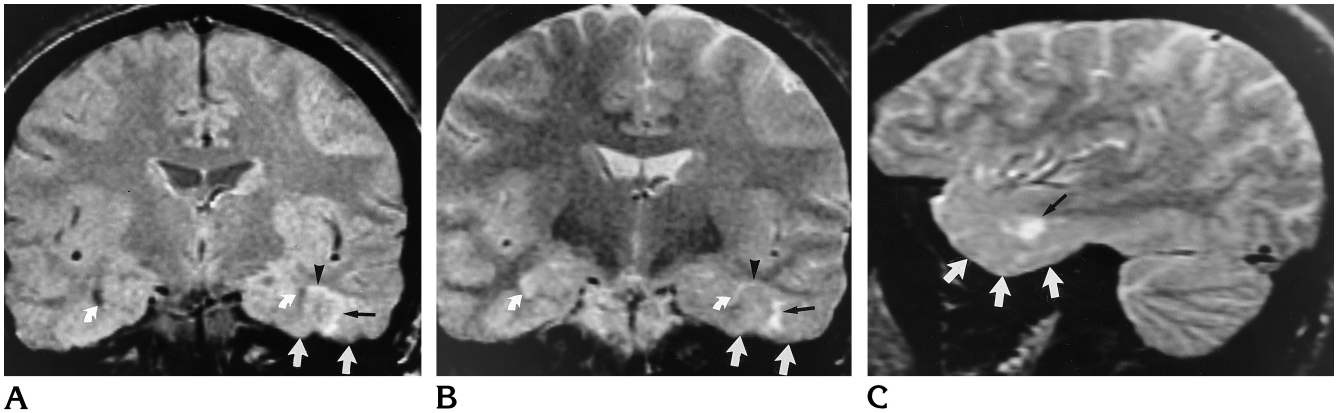


A



B C D E

Fig 4. Signal extension to the ventricle by balloon cell FCDT. Sagittal proton density–weighted image (1500/30/1) (*A*) shows a hyperintense subcortical white matter lesion with hyperintense signal extension to the ventricle. The signal tapers as it extends to the lateral ventricle. *B–E* are sequential axial T2-weighted (1700/80/2) images extending inferiorly toward the lateral ventricles of the same lesion. It is difficult to determine whether the subcortical hyperintensity (*arrows*) extends to the ventricle when viewed in planes orthogonal to the signal extension.



A B C

Fig 5. Cortical thickening and signal extension to the ventricle associated with balloon cell FCDT. Coronal proton density–weighted (2000/30/1) (*A*) and T2-weighted (2000/80/1) (*B*) images show subcortical hyperintensity (*black arrow*). Hyperintense extension (*black arrowhead*) to the ventricle is very subtle. Cortical thickening (*straight white arrows*) of the fusiform and inferior temporal gyrus is seen better on the sagittal T2-weighted (1800/80/2) image (*C*). *Curved white arrows* indicate temporal horn of the lateral ventricles.

TABLE 4: Classification of cortical dysgenesis associated with epilepsy

Classification	Synonyms, Based on Usage in the Literature	Prominent Histologic Features
Cortical dysgenesis	Cortical dysplasia Dysplasia Cortical developmental disorder Malformations of cortical dysgenesis (MCD)	Any imaging or histologic finding suggesting developmental disorder of the cortex
Focal cortical dysplasia of Taylor (FCDT)	Focal cortical dysplasia	
Non–balloon cell FCDT	Mild focal cortical dysplasia, type I (Kuzniecky [5]) Type I focal cortical dysplasia (Palmini [3])	Neuronal cytomegaly and cytoskeletal abnormalities; no balloon cells
Balloon cell FCDT	Severe focal cortical dysplasia, type II (Kuzniecky [5]) Type II focal cortical dysplasia (Palmini [3]) Forme fruste tuberous sclerosis or type III focal cortical dysplasia (Palmini [3,7]) Glioneuronal hamartoma (Wolf [20])	Balloon cells associated with neuronal cytomegaly and cytoskeletal abnormalities

Note.—See Barkovich et al (16) and Raymond et al (17) for a general classification scheme of cortical dysgenesis.

cortex or a lesion that is well controlled by medication. Surgical planning may also be altered for lesions on the basis of whether imaging findings indicate presence or absence of neoplastic tissue. The extent of surgical resection may be modified for the epileptogenic lesion situated adjacent to an eloquent region of the brain (ie, the motor or speech cortex). The surgeon may choose to limit the resection in cases of dysplasia, whereas a more extensive resection would usually be contemplated for neoplasms.

Our univariate statistical analysis comparing eight patients with balloon cell FCDT with 54 patients with low-grade neoplasms revealed significant differences for eight of the MR variables studied. MR findings suggesting balloon cell FCDT rather than tumor included the presence of gray matter thickening (Fig 3) associated with a homogeneous hyperintense signal in the subcortical white matter (Fig 2) that tapers as it extends to the lateral ventricle (Figs 2 and 4). A frontal lobe location favors balloon cell FCDT, while a temporal lobe, especially a medial temporal lobe, location is more suggestive of a neoplasm. Multivariate analysis revealed significance or a trend toward significance for only three of these variables: gray matter thickening, homogeneous hyperintense signal, and tapering of signal as it extended to the ventricle. We believe the discrepancy between the univariate and multivariate analysis is related to the small number of patients in the balloon cell FCDT group.

We did not perform a statistical analysis to compare the use of contrast-enhanced imaging in the neoplastic and dysplasia groups because of the paucity of data available. One might suspect that a contrast-enhanced study would be helpful because of the supposition that a developmental lesion would be less likely to enhance than a tumor. However, our results show that enhancement occurs in both entities in only a minority of patients: one in five (20%) in the balloon cell FCDT group and 10 of 33 (30%) in the group with low-grade neoplasms. Other reports also indicate that enhancement occurs in a small but substantial number of developmental lesions and low-grade tumors. Developmental lesions, such as tuberous sclerosis, show enhancement in 3% of cortical tubers and in 31% of subependymal tubers (21). Latchaw et al (22) noted that low-grade astrocytomas show enhancement in up to 40% of cases. Unfortunately, we did not have a large enough sample to determine whether the enhancement that occurred in the single patient with FCDT was indicative of a sizable minority of cases or simply an aberration.

MR studies with histologic evidence of balloon cell FCDT are limited. Most of these articles use the term *focal cortical dysplasia* to refer to cortical dysgenesis or do not describe the histologic appearance in detail (23) (Table 4). However, Kuzniecky et al (5) described 10 patients with FCDT, five without balloon cells (mild dysplasia, type I) and five with either neuronal clustering or associated balloon cells (severe dysplasia, type II), in whom MR abnormalities were seen in two of the five with mild dysplasia and in all five with severe dysplasia.

MR findings consisted of focal gyral thickening, abnormal demarcation of the gray–white matter junction, and/or increased signal on long-TR images. In a recent review article, Kuzniecky (4) stated that T2-weighted abnormalities in the underlying white matter correlate with balloon cells typical of the severe type II FCDT. Palmini et al (7) reported MR imaging correlates in three patients with FCDT and two with forme fruste tuberous sclerosis (which they later classify as type III focal cortical dysplasia). MR imaging showed focal macrogyria characterized by large, thickened gyri, shallow sulci, and an abnormal gray matter transition. There was increased signal in the subcortical white matter on long-TR images in three of these patients. In a later publication, Palmini et al (3) reported that increased signal within the subcortical white matter on long-TR images occurs in 20% to 50% of patients and that the most abnormal type of MR abnormalities correlate with their type III histologic pattern. These lesions were most frequently found near the central sulcus and frontal lobes. Another report correlating MR imaging with a solitary cortical tuber in two patients without clinical stigmata of tuberous sclerosis describes subcortical signal changes without associated radial white matter bands (9). Our findings correlate well with these previous reports. Extension of MR signal to the ventricle was not mentioned in these previous reports, although a review of Figure 1C in the 1991 article by Palmini et al (7) shows an unresected lesion with signal extending and tapering to the lateral ventricle. We did not attempt to evaluate indistinctness of the gray–white matter junctions because this demarcation is obscured by signal changes in both the balloon cell FCDT and the neoplastic groups (since epileptogenic tumors occur at the brain periphery in most cases) (8).

An interesting observation regarding balloon cell FCDT is its resemblance to tuberous sclerosis in terms of their histologic and imaging features (24). In the absence of systemic or cutaneous lesions, it is difficult to distinguish FCDT from forme fruste tuberous sclerosis by histologic or immunohistochemical studies (12, 19, 24–27). Many authors believe these disorders may represent different spectra of the same entity. MR imaging characteristics of FCDT in our study are also reminiscent of those of systemic tuberous sclerosis, such as the subcortical white matter hyperintensity, frontal lobe location, and white matter extensions to the ventricle (21, 28). These MR findings lend support to the histologic evidence that FCDT and tuberous sclerosis may indeed be two spectra of the same entity or that FCDT is simply the solitary form of tuberous sclerosis.

Conclusion

Balloon cell FCDT is a developmental disorder associated with medically intractable epilepsy. There are no clinical characteristics that differentiate balloon cell FCDT from neoplasms. The MR imaging findings can easily be confused with a neoplastic lesion: a solitary lesion with signal abnormality that may have mass effect. However, our study shows that a number of imaging findings are significantly associated with balloon cell FCDT rather than neoplasm, including gray matter thickening, homogeneous hyperintense signal in the subcortical white matter, hyperintense signal extension to the lateral ventricle, tapering of this signal as it extends to the ventricle, and a frontal lobe not a temporal lobe (especially not a medial temporal lobe) location. This distinction is important for surgical planning, since the decision to operate and the extent of surgical resection often depend on the presence or absence of neoplastic tissue. While we did not formally evaluate which pulse sequence is optimal for providing this distinction, it is logical that a sequence with good gray–white matter differentiation (such as inversion recovery or spoiled gradient-echo imaging) would provide the best method for detecting subtle gray matter thickening. To detect the subcortical hyperintensity and extension to the ventricle, the optimal sequence would be a high-resolution or high-contrast long-TR sequence, such as a fast spin-echo or FLAIR (fluid-attenuated inversion-recovery) sequence, although we were able to detect these changes with conventional spin-echo sequences. Based on the findings in our limited series, we do not think that contrast-enhanced imaging would be helpful for distinguishing between tumor and dysplasia.

It is interesting to draw parallels between balloon cell FCDT and tuberous sclerosis because they have many similarities with respect to histologic and imaging findings. Clinically, both entities are usually associated with seizures; however, balloon cell FCDT is a cerebral solitary lesion that is not associated with cutaneous

or systemic manifestations known to be part of the tuberous sclerosis syndrome.

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