

# From the Archives of the AFIP

## Superficial Gliomas: Radiologic-Pathologic Correlation<sup>1</sup>

### CME FEATURE

See accompanying  
test at [http://  
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/education  
/rg\\_cme.html](http://www.rsna.org/education/rg_cme.html)

### LEARNING OBJECTIVES FOR TEST 6

After reading this  
article and taking  
the test, the reader  
will be able to:

- Describe the essential imaging features of superficial cerebral gliomas.
- Identify the characteristic imaging appearances of the different types of superficial cerebral gliomas so that a specific diagnosis can be favored.
- Correlate the imaging appearances of superficial cerebral gliomas with the gross pathologic appearances.

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Glial neoplasms that are peripherally located and involve the cortical gray matter are noteworthy because of their predilection to serve as a seizure locus, their amenability to surgical resection, their generally favorable prognosis, and their characteristic imaging features, which facilitate diagnosis before surgery. The smaller lesions include ganglioglioma and dysembryoplastic neuroepithelial tumor. Gangliogliomas contain both neuronal and glial components and occur most commonly in the temporal lobe. Variant forms of gangliogliomas may occur and are related to the different compositions of the underlying cellular population. Gangliocytomas lack glial cells and are located both in the cerebral hemispheres and the cerebellum. Lhermitte-Duclos disease represents a specific type of cerebellar gangliocytoma with dysplastic features and is characterized by a laminar pattern at imaging. Dysembryoplastic neuroepithelial tumors occur predominantly in children and young adults with partial seizures and most commonly arise in the temporal lobe, frequently in combination with cortical dysplasia. Surrounding vasogenic edema is conspicuously absent in both gangliogliomas and dysembryoplastic neuroepithelial tumors. The larger masses in this group include desmoplastic infantile ganglioglioma and pleomorphic xanthoastrocytoma and tend to involve the leptomeninges and cortical territory. Both invoke an intense desmoplastic reaction, which appears as an enhancing soft-tissue component at imaging.

### Introduction

Neoplasms of the central nervous system are comparatively infrequent, with an estimated prevalence of more than 17,000 new cases annually in the United States (1). Despite the progress that has been made in the treatment of systemic cancers in the past several decades, those of the central nervous system continue to defy multifac-

**Abbreviation:** WHO = World Health Organization

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**Demographic and Imaging Features of the Superficial Cerebral Gliomas**

Tumor	Patient Age	CT* Features	MR† Imaging Features	Hallmarks
Ganglioglioma	80% younger than 30 y; peak age 10–20 y	Hypoattenuating (38%), mixed attenuation (32%); calcification common; variable enhancement	Hypointense to isointense on T1-weighted images; hyperintense on T2-weighted images; variable enhancement	Most common cause of chronic temporal lobe epilepsy
Desmoplastic infantile ganglioglioma	1st year of life	Solid portion is hyperattenuating, usually along cortical margin; cystic portion is hypoattenuating; solid portion enhances	Solid portion is isointense on T1- and T2-weighted images; solid portion enhances with leptomeningeal extension	Very large heterogeneous cerebral mass; no calcification
Gangliocytoma	Children and young adults	Hyperattenuating	Hypointense on T1- and T2-weighted images	Floor of third ventricle most common location; glial cells absent
Dysplastic cerebellar gangliocytoma	Young adults	Usually hypoattenuating; calcification uncommon	Alternating bands of low and normal signal intensity (T1-weighted images) or high and normal signal intensity (T2-weighted images)	Striated cerebellum
Pleomorphic xanthoastrocytoma	Adolescents or young adults typically but wide age range	Solid portion is hyperattenuating, usually along cortical margin; cystic portion is hypoattenuating; solid portion enhances	Solid portion is isointense on T1- and T2-weighted images; solid portion enhances with leptomeningeal extension	Peripheral cystic mass with enhancing mural nodule; temporal lobe most common site
Dysembryoplastic neuroepithelial tumor	Most younger than 20 y	Hypoattenuating	Hypointense on T1-weighted images; hyperintense on T2-weighted images	Cortical location; temporal lobe (62%); neurologic deficits uncommon

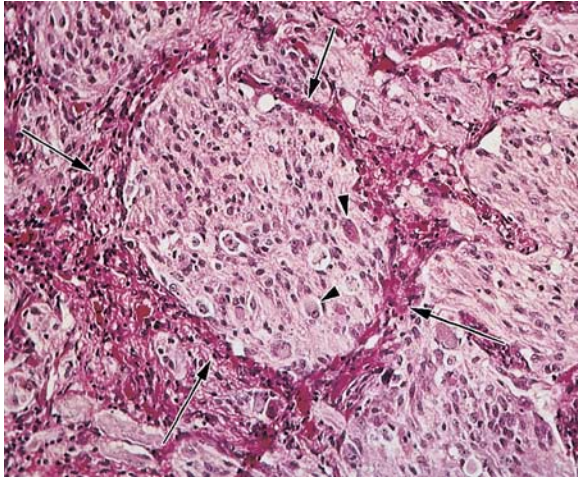
\*CT = computed tomography.

†MR = magnetic resonance.

eted therapeutic regimens. However, there are several tumors that are remarkable because of their generally favorable prognosis following surgical resection. Still more striking is their affinity for either origin in or involvement of the cortical gray matter. Many of these special cases of neuroepithelial tumors are associated with medically refractory seizures that often leave patients incapacitated, and complete resection of these tumors is usually curative. Even partial resection frequently leads to a dramatic improvement in the quality of life for the patient. Detection and correct interpretation of the imaging appearance of these lesions assume prime importance because cross-sectional imaging represents the first step in the successful treatment of these patients. On the basis of case material from the Thompson Archives

of the Department of Radiologic Pathology at the Armed Forces Institute of Pathology, this article reviews the salient features of the gray-matter gliomas: ganglioglioma, desmoplastic infantile ganglioglioma, gangliocytoma, dysplastic cerebellar gangliocytoma, pleomorphic xanthoastrocytoma, and dysembryoplastic neuroepithelial tumor.

According to the third edition of the World Health Organization (WHO) classification of brain tumors, neuroepithelial tissue is composed of glial cells, neuronal cells, neuroblastic cells, pineal parenchymal cells, and embryonal cells (2). Most intraaxial brain neoplasms are of glial origin, composed of astrocytes, oligodendrocytes, ependymal cells, and their derivatives in the choroid plexus. Such tumors account for 40%–50% of all primary neoplasms of the central nervous system. Ganglion cell tumors are composed of purely abnormal neoplastic neuronal cells or a mixture of neuronal and astrocytic elements.



**Figure 1.** Photomicrograph (original magnification,  $\times 60$ ; hematoxylin-eosin stain) of a ganglioglioma shows typical nesting and clustering of tumor cells due to delicate branching vasculature (arrows). The larger neuronal elements (arrowheads) are imbedded within a spindled glial matrix.

Ganglioglioma, gangliocytoma, ganglioneuroma, and ganglioneuroblastoma are included in this group, with the names reflecting modifications in the cellular populations. Two other variants, desmoplastic infantile ganglioglioma and desmoplastic infantile astrocytoma, are characterized by prominent desmoplasia in extremely large supratentorial masses. Pleomorphic xanthoastrocytoma typically involves both the meninges and the cortex and demonstrates prominent heterogeneity among the astrocytic population, which frequently also shows cytoplasmic lipid (xanthomatous) deposits. Dysembryoplastic neuroepithelial tumor is a recently described neuroepithelial mass featuring a characteristic glioneuronal substrate associated with multinodular cortical dysplasia. With the exception of pleomorphic xanthoastrocytoma, these lesions are included within grade I of the WHO classification. Their inclusion in this category reflects an unusually good prognosis based on their origin as malformative or hamartomatous tumefactions, in contrast to the neoplastic origin of other neuroepithelial tumors. The salient demographic and imaging features of these lesions are outlined in the Table.

### Ganglioglioma

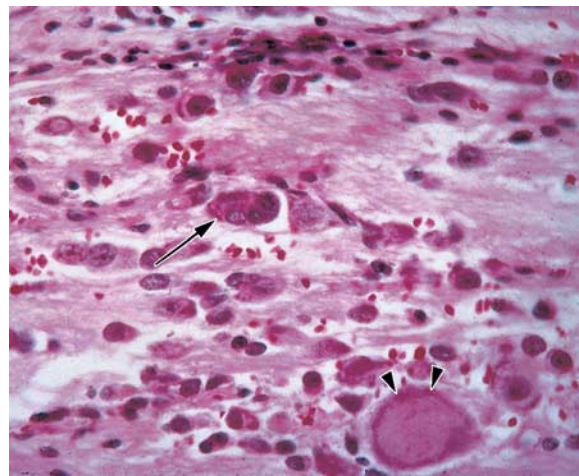
Gangliogliomas account for 0.4%–0.9% of all intracranial neoplasms and 1%–4% of all pediatric neoplasms of the central nervous system (3–5). Most (80%) occur in patients younger than 30 years with a peak age of incidence between 10 and 20 years (6). They may manifest in newborns with or without neurologic impairment and are slightly more common in males (7–9). There is a distinct predilection for the cerebral hemispheres,

especially the temporal lobe. In the largest series (99 patients) of pediatric gangliogliomas, the majority occurred in the temporal lobe (38%), followed by the parietal lobe (30%) and the frontal lobe (18%) (10). Numerous other locations have been reported, including the brainstem, cerebellum, pineal region, spinal cord, optic nerve, optic chiasm, and ventricles (11–16). Involvement of the optic nerve is especially interesting, since this structure does not normally contain neuronal cell bodies. Tumors in this location may arise from ectopic neuronal tissue (embryonal rests) or primitive neurons or by direct extension from nearby structures (eg, the floor of the third ventricle) (11). There is one report in the literature of a ganglioglioma arising within the trigeminal nerve (cranial nerve V) (17). The lack of enhancement in this case provided a clue that this lesion was unlikely to be of nerve sheath origin (eg, a schwannoma or neurofibroma) (17). Gangliogliomas of the temporal lobe are commonly associated with the clinical presentation of medically refractory seizures, particularly those of the partial complex type. These tumors are the most common cause (40%) of chronic temporal lobe epilepsy. Clinical associations include several reports in the literature of “hemifacial spasm” in combination with a cerebellar ganglioglioma occurring in infants and one case report of coexisting ganglioglioma and Rasmussen encephalitis in the same cerebral hemisphere (18,19).

Gross total resection of these tumors is recommended as the treatment of choice, resulting in resolution of seizure activity for the majority of patients (20,21). The role of radiation therapy and chemotherapy has been debated in the literature. Most authorities believe that radiation therapy and chemotherapy should be reserved for those patients with rare malignant forms of ganglioglioma (eg, anaplastic ganglioglioma), disease progression, or an unresectable ganglioglioma (eg, one located in the optic nerve, optic chiasm, or hypothalamus) (10,11,20). The deleterious side effects on the developing nervous system of children with these tumors are cited as a strong argument against the use of radiation as a primary therapeutic modality (10,20).

Originally described by Loretz (22) in 1870 with the detection of the initial case as a mass in the thoracic cavity, the term *ganglioglioma* was popularized by Perkins (23) in 1926. Courville and Anderson (24) were the first to correctly state that gangliogliomas contain both ganglion and glial elements of varying differentiation. Gangliogliomas and gangliocytomas are part of the family of tumors composed of mature ganglion cells and dysplastic neurons (Fig 1). Corresponding

**Figure 2.** Photomicrograph (original magnification,  $\times 180$ ; hematoxylin-eosin stain) of a ganglioglioma shows a continuum of neuronal elements, including a multinucleated variant (arrow), within a well-differentiated spindled glial matrix that resembles pilocytic astrocytoma. Nissl substance (arrowheads) is present in the cytoplasm of a large neuron.



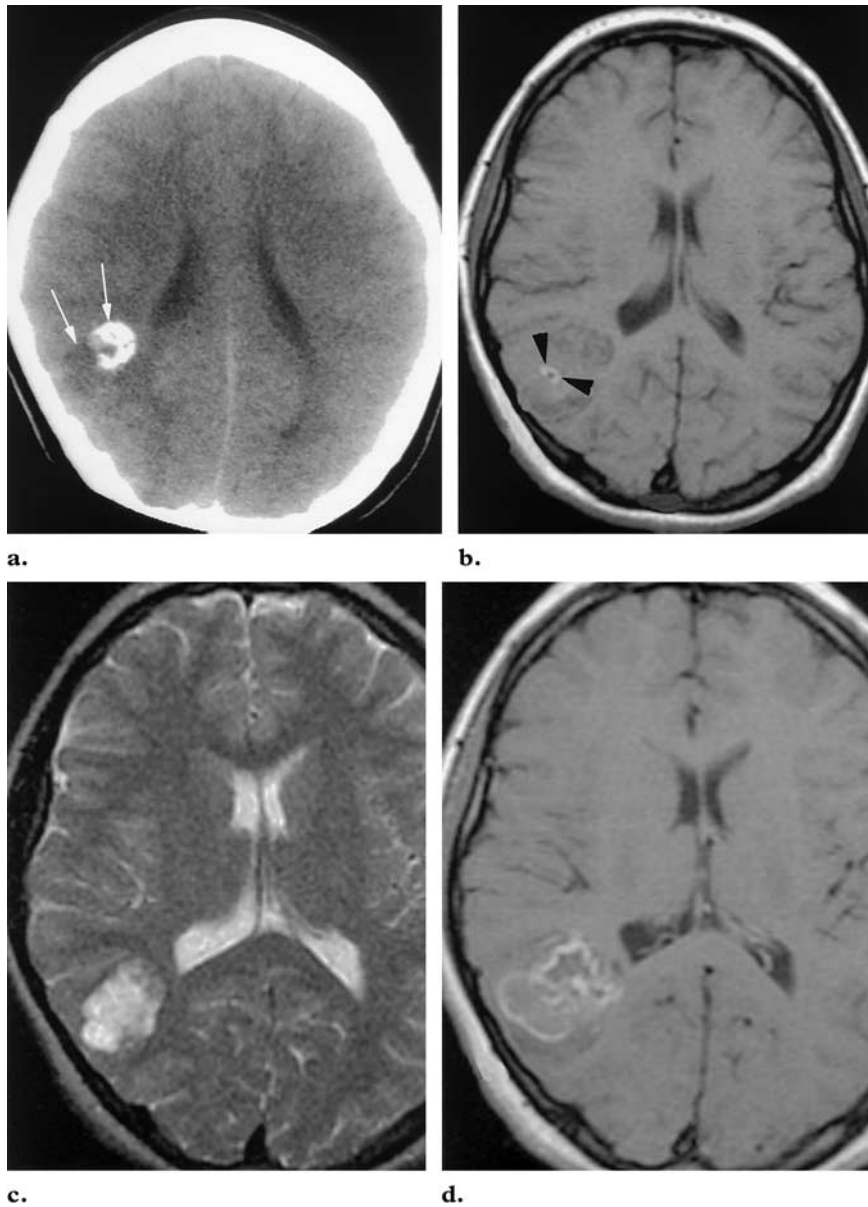
immunoreactivity for these two cellular populations is noted with appropriate immunohistochemical stains, typically glial fibrillary acidic protein for the glial cells and synaptophysin and neurofilament protein for the neuronal group (25). The glial component is absent in gangliocytomas. Only gangliogliomas contain neoplastic glial cells, typically composed of astrocytes in varying states of differentiation (Fig 1). These glial cells directly affect the biologic behavior of the tumor. Since most gangliogliomas have astrocytes with histologic features more typical of a low-grade pilocytic astrocytoma, the biologic behavior of these lesions tends to be benign and correlates with the slow growth typically seen in these lesions. In the rare instance of a biologically aggressive ganglioglioma, the astrocytic cells are less differentiated and more similar to those seen in higher-grade glial neoplasms (3,15,26). Despite the presence of aggressive histologic features, the biologic behavior of these anaplastic gangliogliomas is quite variable (21,27). Some patients with these tumors will die secondary to diffuse dissemination of their disease, whereas others may have extended survival times following surgical intervention. The location of the tumor appears to have the most effect on the eventual outcome for these patients (28).

The neuronal and ganglion cell population in gangliogliomas and gangliocytomas reflects an intrinsic component of these lesions. The cells typically contain large nuclei, prominent nucleoli, generous amounts of cytoplasm, and frequently Nissl substance (Fig 2) (20). These abnormal ganglion cells are often clumped together and

have bizarre forms with binucleation (15,20). In association with a preponderance of undifferentiated neuronal precursor cells, including primitive neuroectodermal elements, ganglion cell neoplasms may be classified as ganglioneuroblastoma or differentiating neuroblastoma. Occasional rare examples of anaplastic ganglioglioma (WHO grade III) have been described (6).

Other variants in this spectrum of mixed glioneuronal tumors include papillary glioneuronal tumor and ganglioglioneurocytoma (9). Both of these variant forms are characterized by a benign biologic behavior and a well-circumscribed cystic appearance at imaging with focal intense enhancement and occasional calcification (9,29). Unlike in ganglioglioma, a clinical history of medically refractory seizures is usually absent in the setting of these lesions (29).

Malignant degeneration of gangliogliomas is rare, with an estimated occurrence of 6% (30). Transformation of the glial component from the typical low-grade appearance to a higher-grade form (usually grade III or IV glioma) is present in almost all cases (21,31,32). Very rarely, a de novo ganglioglioma may degenerate in both glial and neuronal cell populations (33,34). There is one recent case report of malignant transformation in a ganglioglioma that was wholly secondary to degeneration of the neuronal component into a neuroblastoma (35). Some reports in the literature suggest that postoperative radiation therapy may predispose a ganglioglioma to malignant degeneration (21,36). However, other investigators have questioned whether some of these cases of "malignant degeneration" may reflect differentiation or maturation of a primitive neuroectodermal tumor (32).



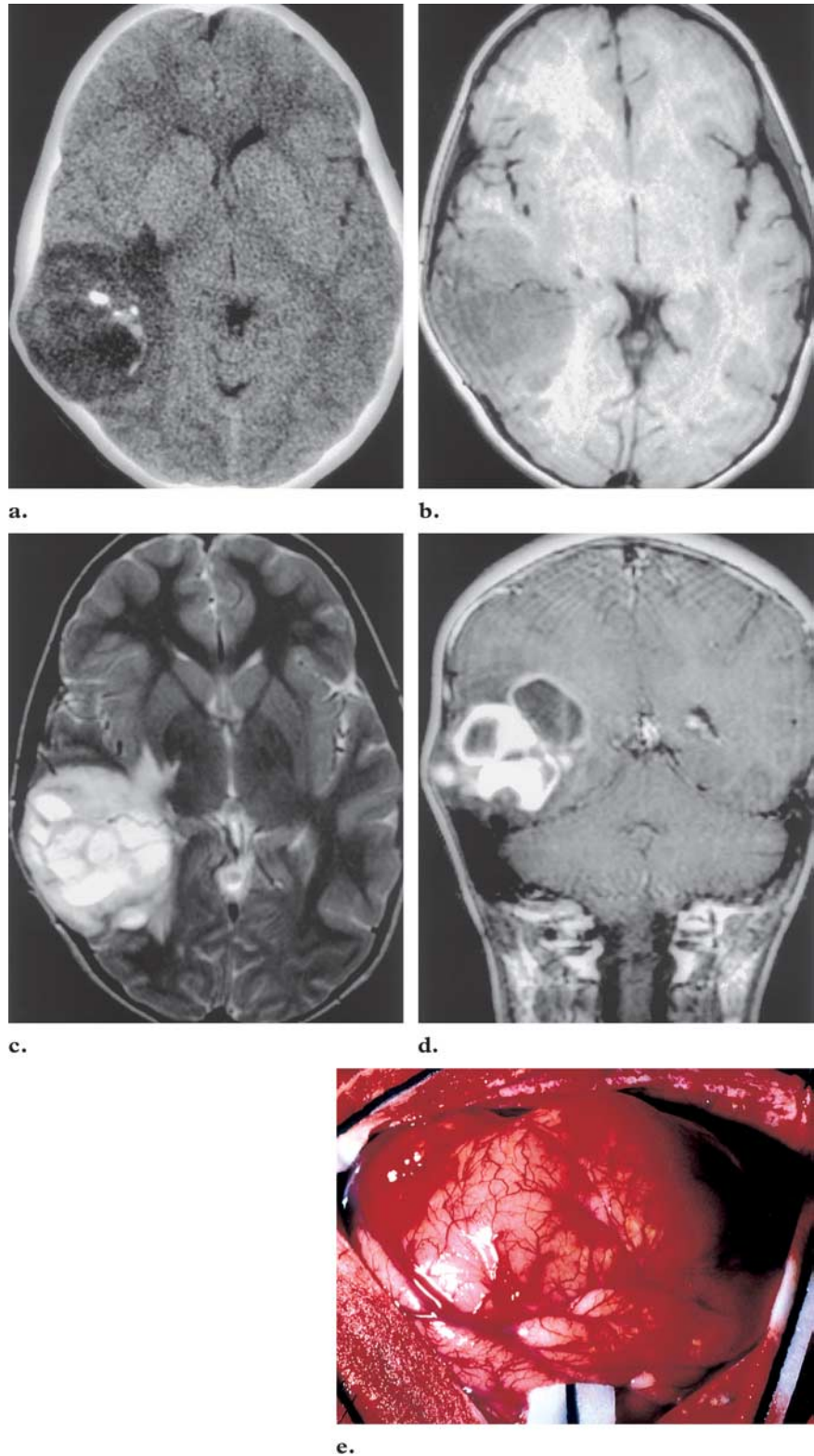
**Figure 3.** Ganglioglioma in a 15-year-old girl who experienced a generalized tonic-clonic seizure. **(a)** Axial CT image shows a heavily calcified mass (arrows) of the posterior right temporal lobe. The mass is otherwise hypoattenuating. **(b)** Axial T1-weighted MR image better shows the true size of the lesion. It is heterogeneously hypointense with a central region of ringlike high signal intensity (arrowheads), an appearance that corresponds to the calcification seen at CT. **(c)** Axial T2-weighted MR image shows high signal intensity of the mass without evidence of surrounding vasogenic edema. **(d)** Contrast material-enhanced axial T1-weighted MR image shows ringlike enhancement of the mass.

Gangliogliomas share many imaging features with other low-grade neoplasms. Cross-sectional imaging studies reveal a solid mass (43%), a cystic mass (5%), or a solid-cystic combination (52%) that is typically located in the periphery of a cerebral hemisphere (37,38). Calcification is a common finding (3,4,37). Reflecting a generally benign biologic nature, there is usually little associated mass effect or evidence of surrounding vasogenic edema. Data from a study by Provenzale et al (39) suggest that gangliogliomas that occur in children tend to have greater overall tumor volume (average: eight times larger) than those arising in adults.

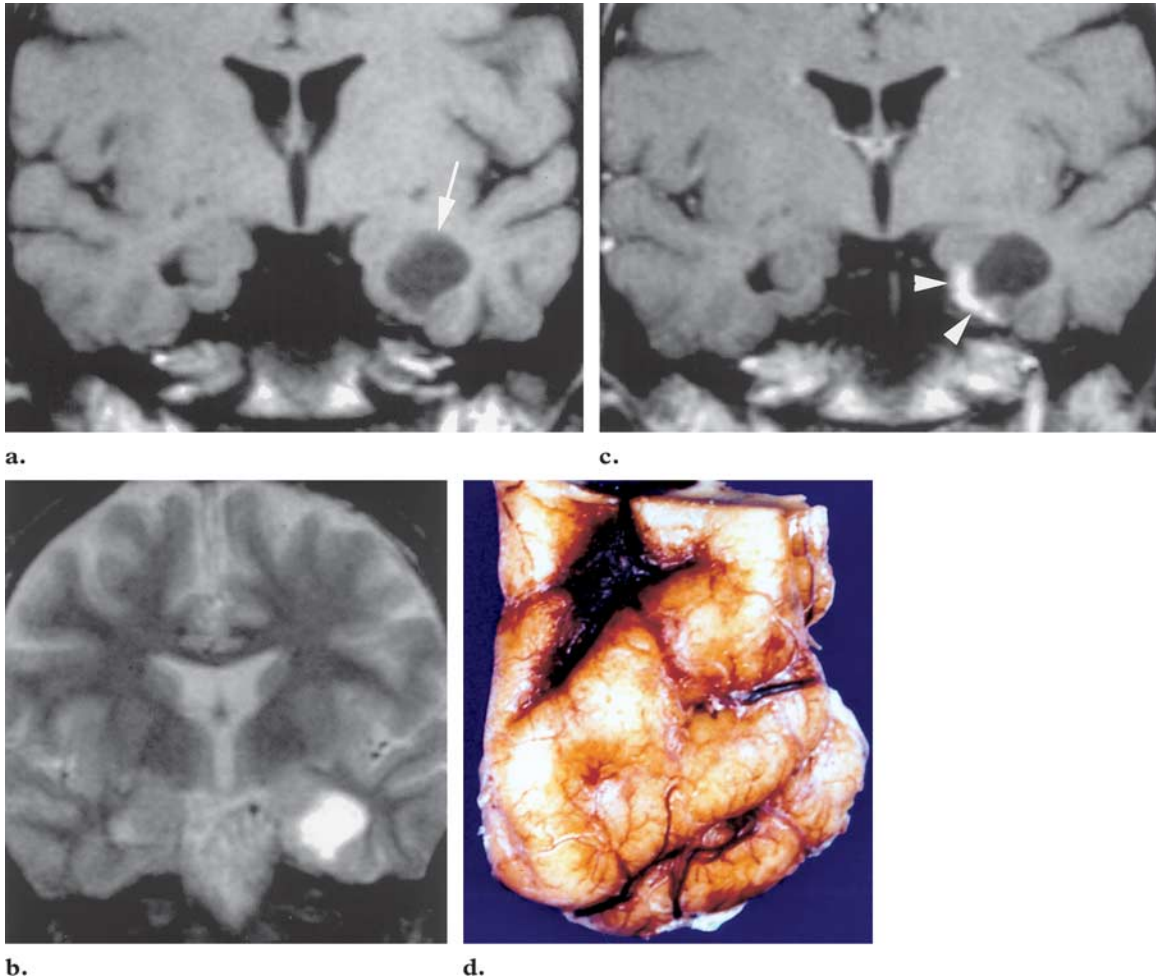
Gangliogliomas have variable manifestations at nonenhanced CT. A hypoattenuating mass is the

most frequent manifestation (38%), followed by a mixed attenuation mass (32%) and an isoattenuating mass (15%) or hyperattenuating mass (15%) (4). Calcification is less commonly seen in association with solid-appearing lesions (Figs 3, 4) (3). Remodeling of the skull may be seen if the neoplasm is located within the peripheral brain (3) (Fig 4). Occasionally, the neoplasm may be completely undetectable at CT (37,40). The frequency of enhancement following intravenous administration of iodinated contrast media is variable, occurring in 16%–80% of gangliogliomas (3,4).

**Figure 4.** Ganglioglioma in an 8-year-old girl with diplopia and headaches. **(a)** Axial CT image shows a large, heterogeneous mass of the posterior right temporal lobe. Calcification within the mass and thinning of the adjacent skull are clearly evident. **(b)** Axial T1-weighted MR image shows mild, heterogeneous low signal intensity of the mass. **(c)** Axial T2-weighted MR image shows a markedly heterogeneous appearance with apparent septa within the mass, which is hyperintense relative to the gray matter. **(d)** Contrast-enhanced coronal T1-weighted MR image shows intense enhancement in some areas and ringlike enhancement in others. **(e)** Intraoperative photograph obtained after opening of the dura shows an obviously bulging cortical surface. The mass was well-encapsulated, facilitating gross total resection. Histologic examination revealed a mixture of abnormal ganglion cells and astrocytes, with the astrocytic component appearing similar to pilocytic astrocytoma and oligodendroglioma.



**Figure 5.** Ganglioglioma in a 20-year-old woman with an 8-year history of partial complex seizures. **(a)** Coronal T1-weighted MR image shows a focal hypointense mass (arrow) of the medial left temporal lobe. **(b)** Coronal T2-weighted MR image shows high signal intensity within the mass without evidence of surrounding edema. **(c)** Contrast-enhanced coronal T1-weighted MR image shows intense focal enhancement (arrowheads) of the medial margin of the mass extending to the cortical surface. **(d)** Photograph of a specimen obtained after en bloc resection of the lateral temporal cortex shows abnormal enlargement of the gyrus. Histologic examination of this specimen showed abnormal ganglion cells combined with abnormal astrocytes and oligodendrocytes, which confirmed the diagnosis.

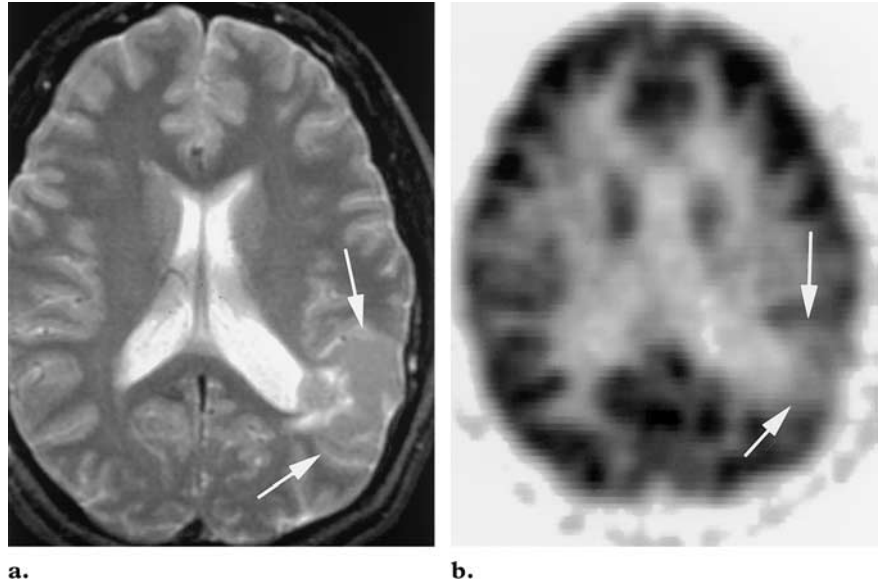


The MR imaging appearance of gangliogliomas is also variable and nonspecific. In general, the lesions are hypointense to isointense relative to gray matter on short TR images and hyperintense relative to gray matter on long TR images (Figs 3–6) (3,40). The solid-appearing components have an even more variable presentation at imaging. Some tumors may manifest as a hyperintense mass on T1-weighted images (Fig 3) (3,4,7,8). They commonly have at least some regions of high signal intensity on T2-weighted images (Figs 3–6) (3). Not all gangliogliomas are truly cystic despite a cystlike appearance, and the term *cystic* should be reserved for those that demonstrate a fluid-fluid level or pulsation artifact on MR images (38,40). Enhancement following intravenous administration of gadolinium contrast material is highly variable, ranging from nonenhancing to ringlike to intense homogeneity

(40,41). It is intriguing to speculate that patients with temporal lobe masses are more likely to have earlier clinical presentations than patients with mass lesions in other locations because of the predilection for this area as an epileptogenic locus (37).

Leptomeningeal spread of a ganglioglioma is rare (42). Gangliogliomas produce heterogeneous metabolic activity on PET images (Fig 6) (43). Kumabe et al (44) reported very high uptake on thallium-201 single photon emission CT (SPECT) images for three gangliogliomas, only one of which was histologically graded as an anaplastic ganglioglioma. All three lesions also demonstrated an increased choline-creatine ratio at hydrogen-1 MR spectroscopy, indicative of increased membrane synthesis and degradation and suggesting a malignant lesion. These apparent

**Figure 6.** Ganglioglioma in a 19-year-old man with a 12-year history of medically refractory seizures. **(a)** Axial T2-weighted MR image shows an ill-defined parietal mass of the posterior left parietotemporal lobe (arrows) that distorts the margin of the lateral ventricle. The mass is heterogeneous, with areas of high signal intensity combined with regions that are equivalent in signal intensity to the gray matter. **(b)** Axial positron emission tomographic (PET) image shows mild hypometabolic activity (arrows) in the region of the mass.



discrepancies between histologic findings and imaging findings underscore the need for further evaluation with metabolic imaging of these mixed glioneuronal neoplasms.

Rare locations for gangliogliomas include the pineal region and the ventricular system. Majos et al (12) reported a ganglioglioma attached to the septum pellucidum within the lateral ventricle with an imaging appearance virtually identical to that of a subependymoma or central neurocytoma.

### Desmoplastic Infantile Ganglioglioma

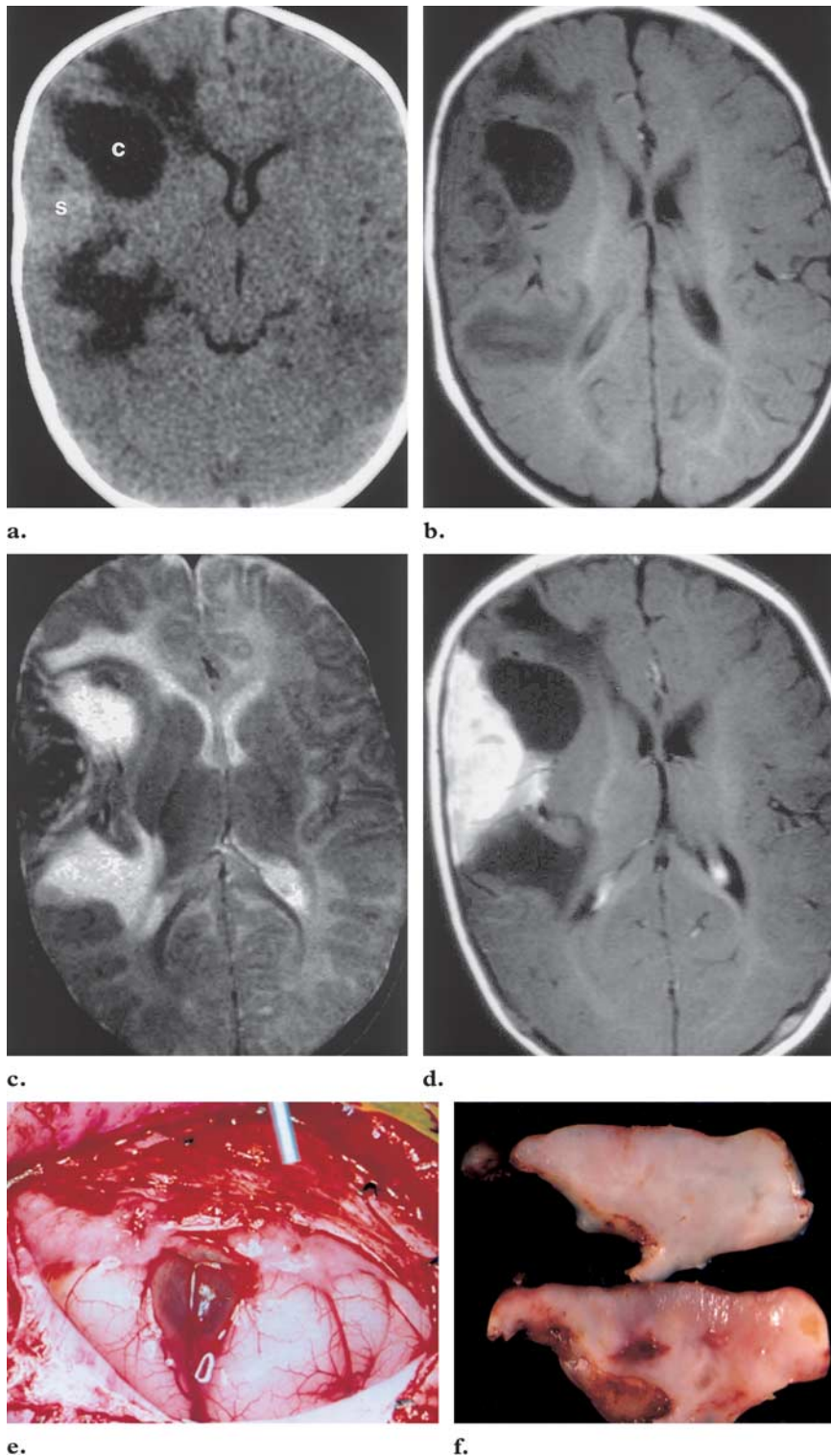
In 1987, VandenBerg et al (45) described 11 cases of a distinctly different type of ganglioglioma that manifests as a very large brain tumor in the 1st year of life. Because all of the patients were infants and the histologic features were intense desmoplasia with abnormal ganglion and glial cells, the term *desmoplastic infantile ganglioglioma* was coined (45). Just 3 years earlier, Taratuto et al (46) had reported similar tumors in infants that had an almost identical histologic appearance, except that a ganglion cell population was absent. Accordingly, this group of investigators used the diagnosis “superficial cerebral astrocytoma attached to the dura” to describe the tumors (46). Because of the considerable overlap between these two lesions, it is possible that they in fact represent a single entity (47). Hence, with the later description by VandenBerg et al (45), a pseudonym—*desmoplastic infantile astrocytoma*—was proposed.

There are at least 25 cases of desmoplastic infantile ganglioglioma reported in the literature

(47). Although the vast majority of cases occur in children less than 1 year of age, there are reports of the disease in two noninfantile patients (48). Males are more commonly affected, by an almost 2:1 ratio (47). A rapidly increasing head circumference is the most common symptom (47). Seizure activity is actually uncommon. The duration of symptoms ranges from 5 days to 3 months and suggests rapid growth (47). Surgical resection is the therapeutic modality of choice. Unfortunately, because of the large size of these lesions and the firm attachment to the dura, complete resection is difficult. In cases of partial resection, some adjunctive chemotherapy protocols have produced a reduction in tumor volume (47). Although the number of cases reported is still small, the overall prognosis is good for most patients. Of the 25 patients reported by the Pediatric Oncology Group in 1994, six had died but some had survived for up to 10.5 years following treatment (47).

Desmoplastic infantile ganglioglioma manifests as an exceptionally large cerebral hemispheric mass composed of both cystic and solid portions (47). An intense desmoplastic reaction at the periphery of the mass with attachment to the dura and the presence of atypical or immature cellular tissue are the histologic hallmarks of desmoplastic infantile ganglioglioma and distinguish this lesion from a conventional ganglioglioma (47). Proliferative activity is very low in these tumors (49). However, mitotic activity and focal hypercellularity are common features and may lead to misdiagnosis as a high-grade neoplasm (47). Some cases had areas that were virtually indistinguishable from fibrous histiocytoma at conventional histologic examination (49). The characteristic cross-sectional imaging features may help establish the





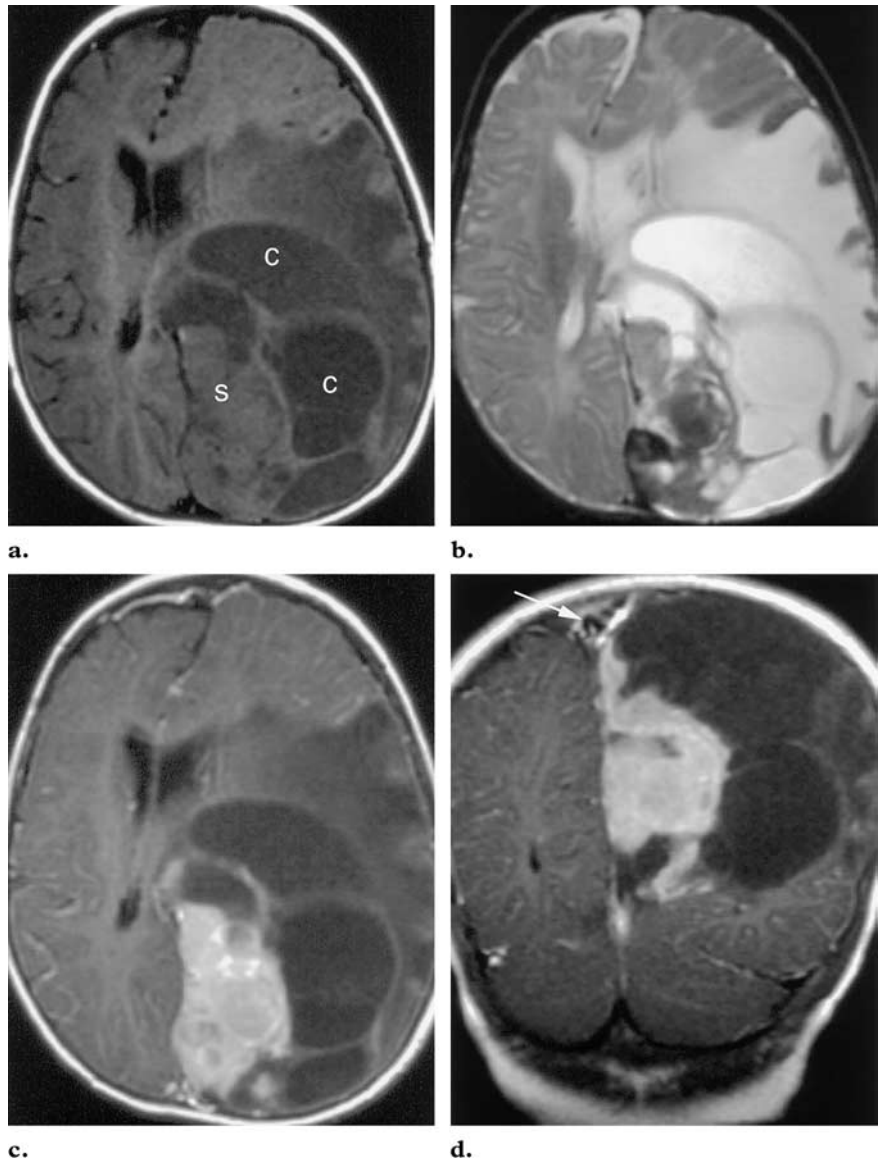
**Figure 7.** Desmoplastic infantile ganglioglioma in a 5-month-old boy with central apnea. **(a)** Axial CT image shows a large, heterogeneous mass of the right temporal region. Cystlike areas (*c*) combined with mildly hyperattenuating soft-tissue areas (*s*) are seen. **(b)** Axial T1-weighted MR image shows heterogeneity within the mass, an appearance similar to the CT appearance. The soft-tissue component appears to be extraaxial. **(c)** Axial T2-weighted MR image shows that the soft-tissue component is hypointense relative to the brain parenchyma. A mild amount of surrounding vasogenic edema is noted. **(d)** Contrast-enhanced axial T1-weighted MR image shows intense enhancement of the soft-tissue component. **(e)** Intraoperative photograph shows the extraaxial location of the mass (indicated by the silver probe). **(f)** Photograph shows resected specimens, which correlate morphologically with the extraaxial soft-tissue component seen at cross-sectional imaging.

correct diagnosis in such cases (47). To our knowledge, no cases of seeding through the cerebrospinal fluid or metastatic spread have been described (47).

A large cerebral mass with both cystlike and solid portions is the characteristic imaging appearance of desmoplastic infantile ganglioglioma at CT and MR imaging. The frontal and parietal lobes are the most common sites, with lesions of the temporal and occipital lobes reported in

smaller numbers. At CT, the solid portion (representing the region of intense desmoplasia) is slightly hyperattenuating and typically located along the cortical margin of the mass (Fig 7). It enhances intensely following intravenous administration of contrast media (47). The MR imaging appearance is similar. The solid portion is generally isointense to the brain parenchyma on T1- and T2-weighted images and enhances intensely

**Figure 8.** Desmoplastic infantile ganglioglioma in a 6-month-old boy with increasing head circumference over a 2-month period. **(a)** Axial T1-weighted MR image shows a large, heterogeneous mass of the left parietal lobe with surrounding vasogenic edema and marked midline shift. Both soft-tissue (S) and cyst-like (C) components are visible. **(b)** Axial T2-weighted MR image shows the soft-tissue areas as regions of low signal intensity compared with the high signal intensity of the cystic territories. **(c)** Contrast-enhanced axial T1-weighted MR image shows intense enhancement of the soft-tissue portions of the tumor. **(d)** Contrast-enhanced coronal T1-weighted MR image shows that the enhancing soft-tissue component contacts the dural sinus (arrow), which shows abnormal nonenhancement, suggestive of dural sinus involvement. At surgery, a portion of the mass remained tightly adherent to the dural sinus.



following administration of gadolinium contrast media. Extension of the enhancement to the leptomeningeal margin is characteristic on both CT and MR images and correlates with the firm dural attachment noted in many cases (Figs 7, 8) (47,50,51). Calcification is not a feature of desmoplastic infantile ganglioglioma and may aid in distinguishing this lesion from frequently calcified neoplasms seen in the 1st year of life, such as primitive neuroectodermal tumor and supratentorial ependymoma (50). Vasogenic edema is occasionally seen (51).

### Gangliocytoma

Gangliocytomas account for 0.1%–0.5% of all brain tumors and occur in children and young adults (52,53). They are frequently associated

with a dysplastic and malformed brain (54). The floor of the third ventricle is the most common location, followed by the temporal lobe, cerebellum, parieto-occipital region, frontal lobe, and spinal cord (52,55). There are at least 35 cases of sellar gangliocytomas with various associated endocrine abnormalities reported in the literature (56,57).

Gangliocytomas are ganglion cell tumors composed of abnormal mature ganglion cells in the absence of neoplastic glial cells and therefore do not demonstrate immunoreactivity to glial fibrillary acidic protein (53). The lack of neoplastic glial cells distinguishes this tumor from a ganglioglioma. The presence of mature ganglion cells distinguishes this tumor from a ganglioneuroblastoma, which by definition contains immature ganglion cells (55).

At CT, gangliocytoma typically appears hyperattenuating on nonenhanced images (58). There

is little mass effect associated with the lesion and no surrounding vasogenic edema (58,59). The few reports of the MR imaging appearance describe low signal intensity on T1-weighted images and mild low signal intensity on T2-weighted images (60,61). Cystlike areas occur occasionally (60).

### Dysplastic Cerebellar Gangliocytoma

In 1920, Lhermitte and Duclos (62) described a cerebellar ganglion cell tumor that manifested in a 36-year-old man with progressive neurologic deficits. The patient subsequently died of the disease. Histologic examination revealed abnormally widened cerebellar folia with abnormal ganglion cells, and they labeled the case a “diffuse ganglioneuroma” (62,63). Other cases with similar histologic features were reported over the next several decades. With refinement in histologic techniques and description, it became clear that the case reported by Lhermitte and Duclos (62) was histologically identical to other lesions, now called dysplastic gangliocytomas. Accordingly, the presence of such a mass in the cerebellum now carries the eponym *Lhermitte-Duclos disease*. Today, more than 100 cases have been reported in the literature (64). Because the lesion has conflicting clinical and histologic features, there has been considerable controversy regarding its classification. Is it a true neoplasm with the potential for malignant transformation and recurrence? Is it a hamartoma, a simple collection of normally present tissues that are abnormally configured? Or is it a congenital malformation? The answers to these questions have been elusive, although recent investigations strongly favor a hamartomatous origin (65).

Dysplastic cerebellar gangliocytoma manifests in young adults in the vast majority of cases (average age at presentation, 34 years), with only a few cases reported in children (66–70). There is no gender predilection. Most patients have clinical symptoms related to increased intracranial pressure and hydrocephalus. Less commonly, about 40% of patients present with a slowly progressive cerebellar syndrome (71). Megalencephaly (seen in 50% of cases) and mental retardation are other common features (69,71–74). Numerous other associations include polydactyly, partial gigantism, leontiasis ossea, and vascular malformations (73). The natural history of the disease is ill-defined. There is considerable variability in the duration of symptoms (3–29 years) in cases reported in the literature (64,75). One case of dysplastic cerebellar gangliocytoma was identified only at autopsy in an asymptomatic patient (76).

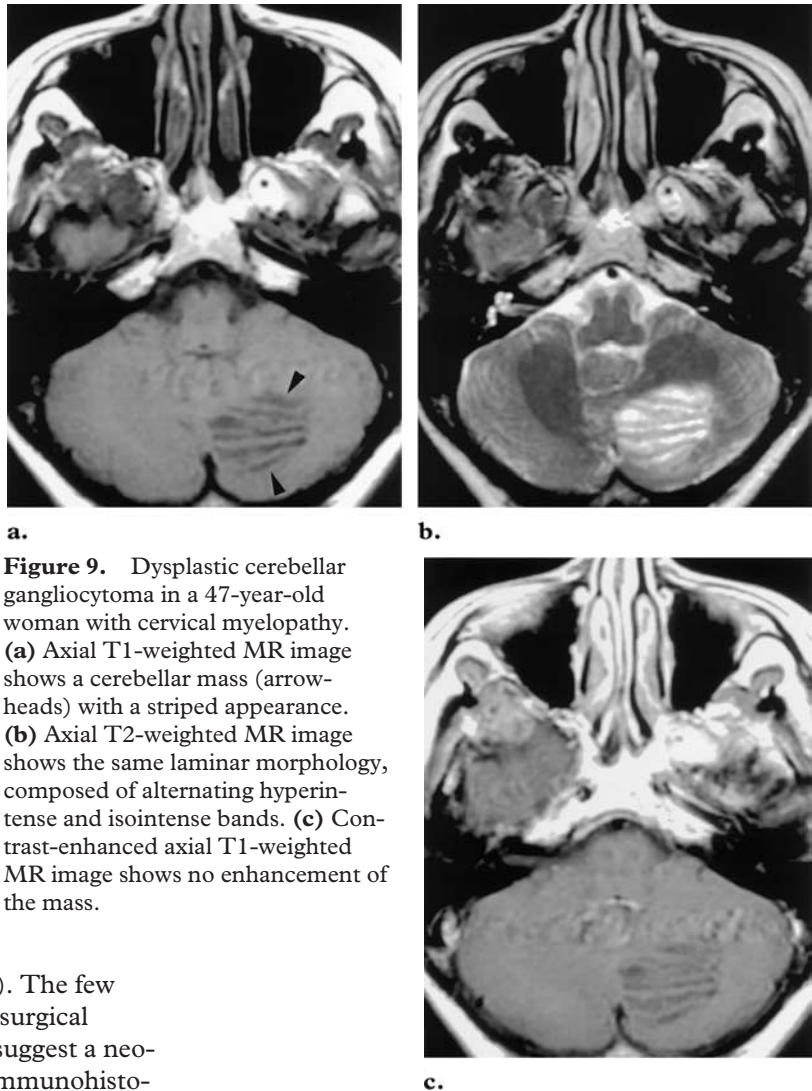
Decompression of the ventricular system is the immediate goal of therapy in virtually all symptomatic cases, with most patients undergoing

complete or partial surgical resection of the mass. The gradual change from normal cerebellar tissue to the abnormal tissue makes visualization of a tissue plane difficult and impairs a complete resection (63,69,71). Therefore, some surgeons favor an excisional biopsy of the lesion and placement of a ventricular shunt (77). The mortality rate from the disease has dropped steadily since the development of better neurosurgical techniques and monitoring equipment, so that death is now an uncommon perioperative complication (64). Although most patients do well following surgical resection, some have recurrence of their disease even after a prolonged disease-free interval (64,65,76,78–80). Accordingly, long-term follow-up is required in these patients (64).

There is a strong association of dysplastic cerebellar gangliocytoma with Cowden disease, an autosomal dominant hamartoma syndrome characterized by a variety of mucocutaneous lesions, macrocephaly, and increased frequency of hamartomas and neoplasia in the breast, thyroid, colon, genitourinary organs, and central nervous system (meningioma and glioma) (65,73,80–82). Recent investigations have established a molecular basis for Cowden disease with identification of a susceptibility gene on the long arm of chromosome 10 (10q23) (83). The combination of dysplastic cerebellar gangliocytoma and either breast cancer, thyroid cancer, or macrocephaly is one of the criteria that establish the diagnosis of Cowden disease (83). Patients with Cowden disease and family members of patients with dysplastic cerebellar gangliocytoma should be screened with brain MR imaging (64).

Histologic analysis of dysplastic cerebellar gangliocytoma reveals disruption of the normal cerebellar laminar structure, with hypertrophic ganglion cells expanding the granular and molecular layers of the cerebellar cortex and abnormally increased myelination in the molecular layer (84). A marked reduction in myelination of the central white matter of the cerebellar folia is also common (71). Mitotic activity, necrosis, and endothelial proliferation—all associated with high-grade brain neoplasms—are not characteristically seen in these lesions. To our knowledge, malignant transformation has not been observed in any cases of dysplastic cerebellar gangliocytoma to date (65).

The histogenesis of dysplastic cerebellar gangliocytoma is unclear, with evidence supporting both hamartomatous and neoplastic origins (84). Possible explanations supporting a hamartomatous lesion include hypertrophy of the granular cell layer and migrational arrest of the granular

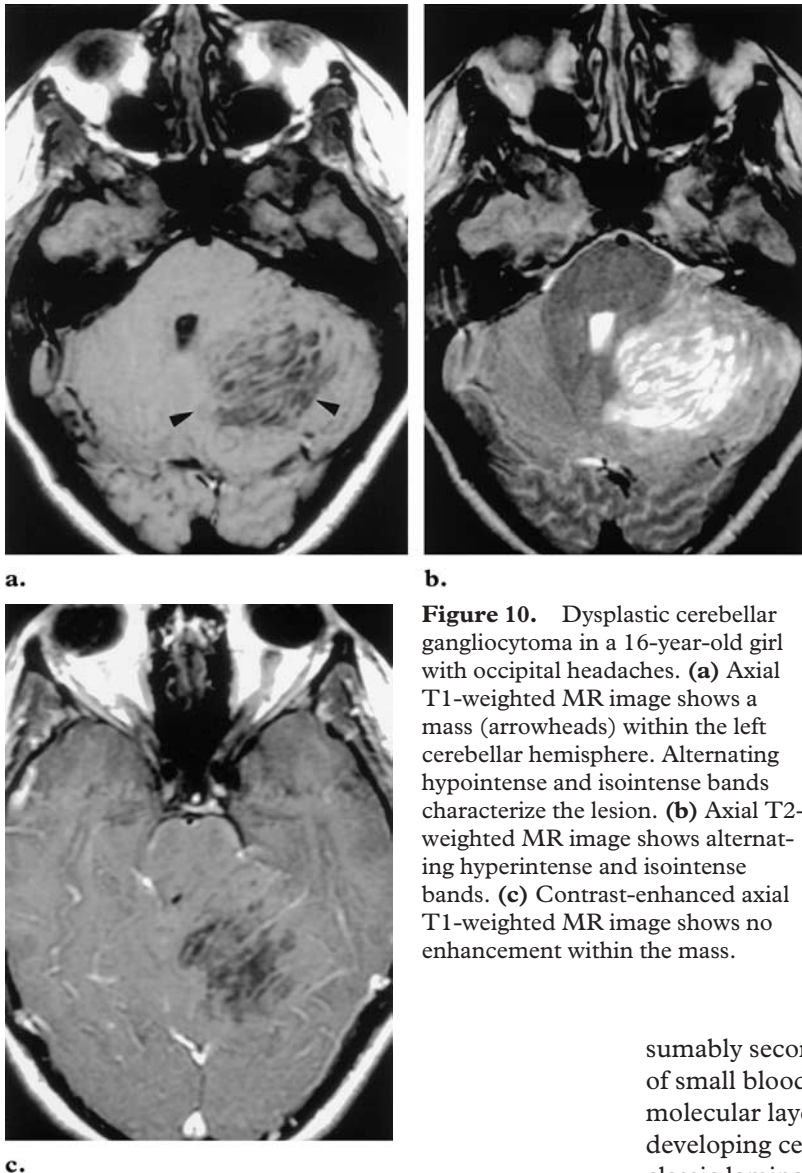


**Figure 9.** Dysplastic cerebellar gangliocytoma in a 47-year-old woman with cervical myelopathy. **(a)** Axial T1-weighted MR image shows a cerebellar mass (arrowheads) with a striped appearance. **(b)** Axial T2-weighted MR image shows the same laminar morphology, composed of alternating hyperintense and isointense bands. **(c)** Contrast-enhanced axial T1-weighted MR image shows no enhancement of the mass.

cells within the molecular layer (74). The few cases of recurrent lesions following surgical resection reported in the literature suggest a neoplastic origin (74,79,80), whereas immunohistochemical and molecular findings and the association with Cowden disease favor a hamartomatous origin (65). Consequently, myriad names have been proposed for this entity, including granular cell hypertrophy, granulomolecular hypertrophy of the cerebellum, diffuse hypertrophy of the cerebellar cortex, Purkinjeoma, hamartoma of the cerebellum, ganglioneuroma, gangliomatosis of the cerebellum, benign hypertrophy of the cerebellum, neurocystic blastoma, hamartomoblastoma, neurocytoma myelinicum, and gangliocytoma myelinicum diffusum (79,85). There is a growing body of evidence that perhaps all patients with dysplastic cerebellar gangliocytoma also have Cowden disease, with identification of Cowden disease made only after the diagnosis of dysplastic cerebellar gangliocytoma was established (65,74).

The imaging findings of dysplastic cerebellar gangliocytoma reflect the generally benign biologic behavior of these lesions. Thinning of the skull may be noted at plain radiography and at CT (71). The lesions are usually hypoattenuating at nonenhanced CT but may be isoattenuating, making detection difficult (66,71,74). Calcification may occur but is uncommon (66,69,74,76,78,79,86–88). Vertebral angiography reveals an avascular mass (71).

Because beam-hardening artifact in the posterior fossa hinders evaluation with CT, MR is considered the imaging modality of choice for dysplastic cerebellar gangliocytoma (64). MR imaging reveals a cerebellar mass typically involving one hemisphere with a highly characteristic folial pattern (also described as laminated, corduroy, lamellar, or striated), which consists of alternating



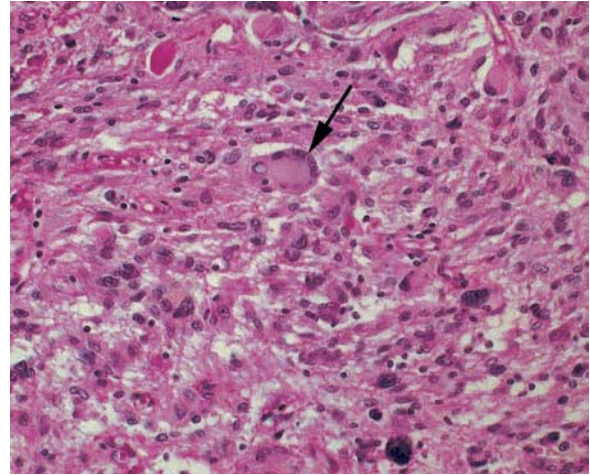
**Figure 10.** Dysplastic cerebellar gangliocytoma in a 16-year-old girl with occipital headaches. **(a)** Axial T1-weighted MR image shows a mass (arrowheads) within the left cerebellar hemisphere. Alternating hypointense and isointense bands characterize the lesion. **(b)** Axial T2-weighted MR image shows alternating hyperintense and isointense bands. **(c)** Contrast-enhanced axial T1-weighted MR image shows no enhancement within the mass.

bands of high signal intensity and normal signal intensity relative to gray matter on T2-weighted images (Figs 9, 10) (74). This signal intensity pattern may correlate with the loss of myelination seen at histologic analysis (69,74). Kulkantrakorn et al (64) confirmed that the high signal intensity seen on T2-weighted images corresponds to the inner molecular layer, granular cell layer, and loss of central white matter within the folia. The bands are isointense and hypointense on T1-weighted images (64,74,89). Kulkantrakorn et al (64) also reported one case with linear areas of high signal intensity on T1-weighted images, pre-

sumably secondary to calcification in a collection of small blood vessels seen in the pia and adjacent molecular layer at histologic analysis (64). The developing cerebellum in infants may prevent the classic laminar appearance of dysplastic cerebellar gangliocytoma seen in adults (69).

The bulk of reports in the literature involving contrast-enhanced cross-sectional imaging indicate that the overwhelming majority of these lesions do not enhance (64,65,74). When the rare enhancing dysplastic cerebellar gangliocytoma is encountered, it is believed to be secondary to vascular proliferation or the presence of anomalous veins (63,89,90). Cerebellar tonsillar displacement through the foramen magnum with or without associated syringohydromyelia has been noted in several reports (71,74,77,78,86–88,90).

**Figure 11.** Photomicrograph (original magnification,  $\times 150$ ; hematoxylin-eosin stain) of a pleomorphic xanthoastrocytoma shows densely cellular glial elements, including a large multinucleated xanthomatous cell (arrow) with foamy cytoplasm. Pleomorphism as reflected by variation in shape, size, and staining characteristics is prominent.



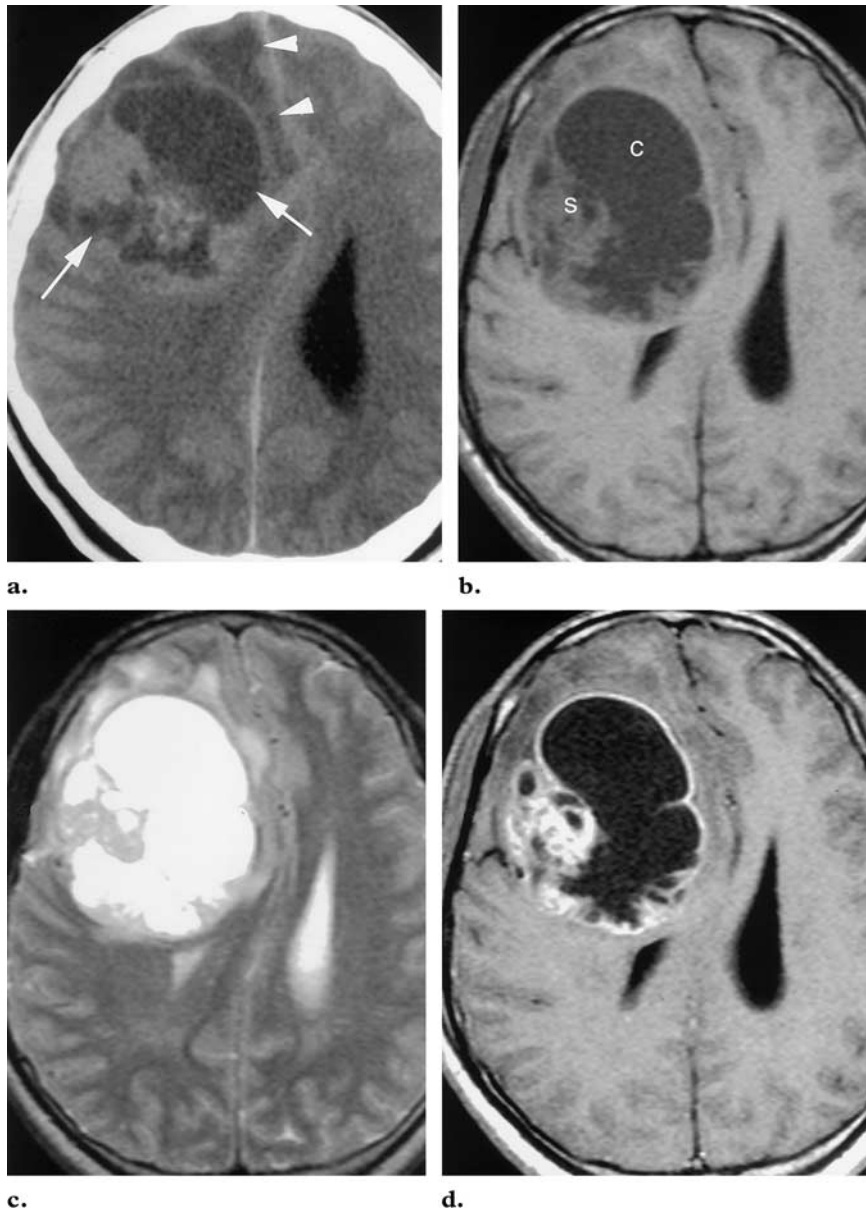
### Pleomorphic Xanthoastrocytoma

In 1979, Kepes and colleagues (91) reported 12 cases of superficially located supratentorial tumors that involved the leptomeninges. Histologic examination of these lesions consistently showed a pleomorphic appearance with a dense reticulin network and lipid (xanthomatous) deposits within the tumor cells. Accordingly, Kepes et al (91) coined the term *pleomorphic xanthoastrocytoma* to describe these new tumors. Since that time, there have been over 120 reports of this neoplasm, and it is now recognized as a distinct neuropathologic entity by the latest edition of the WHO classification of brain neoplasms (92). They are rare tumors, accounting for only about 1% of all brain neoplasms, but they are important because they have a characteristic imaging appearance and are highly amenable to surgical extirpation, which may be curative (93).

Two thorough reviews of pleomorphic xanthoastrocytomas reported in the world's literature provide the best overview of the demographic and clinical features associated with these unusual tumors (93,94). Pleomorphic xanthoastrocytomas usually occur in adolescents or young adults (average age of 26 years), although a wide age range is reported (5–82 years) (93,94). There is no gender predilection (93). A long history of seizures is very common (71%) (93). An overwhelming majority (98%) of tumors occur in the supratentorial brain, most commonly in the temporal lobe (49%) followed by the parietal lobe (17%), frontal lobe (10%), and occipital lobe (7%) (93). About 10% involve more than one lobe (93). They are rarely seen in the thalamus,

cerebellum, or spinal cord or within the globe of the orbit (92). The prognosis for these tumors following surgical resection is generally good, with an 81% survival rate at 5 years and a 70% survival rate at 10 years (93). However, the tumor is also characterized by a relatively high rate of recurrence. In addition, malignant transformation occurs in up to 20% of cases (93). These features, coupled with the degree of hypercellularity and pleomorphism seen at histologic examination, led to classification of these tumors as WHO grade II lesions (92). Surgical resection is the therapy of choice. The tumors are generally unresponsive to both chemotherapy and radiation therapy (93). Recurrent disease appears to be best treated with repeat surgery (94).

The histologic appearance is marked by pleomorphic spindled tumor cells with deposits of intracytoplasmic lipid, a dense intercellular reticulin network, giant cells (both mono- and multinucleated), and eosinophilic granular bodies (Fig 11) (93). The etiology of this tumor was hotly debated until it was shown that the xanthomatous spindly cells react to glial fibrillary acidic protein, confirming their astrocytic nature. Despite a circumscribed appearance, most pleomorphic xanthoastrocytomas demonstrate infiltration into the surrounding brain and extension into the perivascular Virchow-Robin spaces (92,93). Although the tumor is commonly attached to the meninges, invasion of the dura is rare (92). Mitotic activity is absent or low (less than 5 mitoses per high power field) in 82% of cases and is considered the best histologic correlate for the biologic behavior of these tumors by Giannini et al (93). When increased mitotic activity is noted, the rate of recurrent disease is increased and survival rates decrease (93). Giannini et al (93) concluded



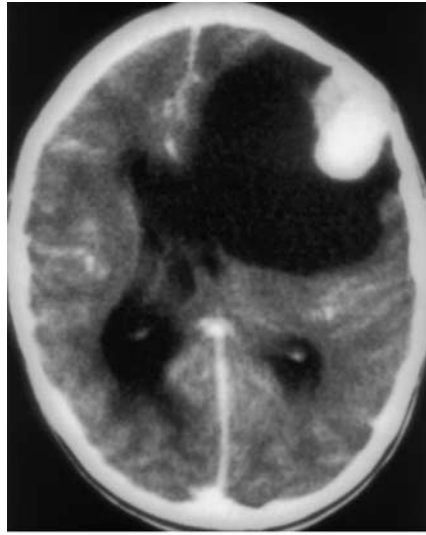
**Figure 12.** Pleomorphic xanthoastrocytoma in a 13-year-old boy with neurofibromatosis I and headaches. **(a)** Nonenhanced axial CT image shows a heterogeneous mass (arrows) of the right frontal lobe with both cystic and soft-tissue components. A mild amount of surrounding vasogenic edema (arrowheads) is present. **(b)** Axial T1-weighted MR image obtained at a slightly different level than in **a** shows that the mass does not extend to the cortical surface. Soft-tissue (S) and cystic (C) components are again noted. **(c)** Axial T2-weighted MR image shows mild low signal intensity of the soft-tissue portion of the mass, whereas the cystic portions are hyperintense. Small “fingers” of vasogenic edema surround the mass. **(d)** Contrast-enhanced axial T1-weighted MR image shows intense enhancement of the soft-tissue portion of the mass with rim enhancement of the cystic margin.

that the mitotic index and the extent of surgical resection are the two most important predictors of recurrence-free survival rates and overall survival rates (93). In contrast, Pahapill et al (94), in their review of cases reported in the literature, concluded that the presence of necrosis at histologic examination correlates with a higher death rate and a poorer prognosis.

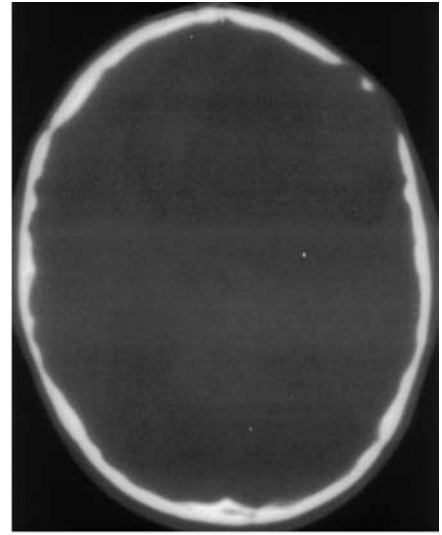
A cystic supratentorial mass containing a mural nodule that is adjacent to the peripheral leptomeninges is the classic although nonspecific imaging appearance of a pleomorphic xanthoastrocytoma. However, slightly more than half (52%) of the lesions reported in the literature occurred in

the absence of cystic change (91,93,95,96). The tumor manifests as a hypo- or isoattenuating mass at nonenhanced CT (Fig 12). Calcification is rare (94). Lesions may be well-circumscribed or ill-defined (96). Evidence of skull erosion or lytic change is uncommon (97,98). At MR imaging, pleomorphic xanthoastrocytomas are usually hypo- to isointense relative to gray matter on T1-weighted images and hyper- to isointense relative to gray matter on T2-weighted images (Figs 12, 13) (96). Involvement of the leptomeninges is

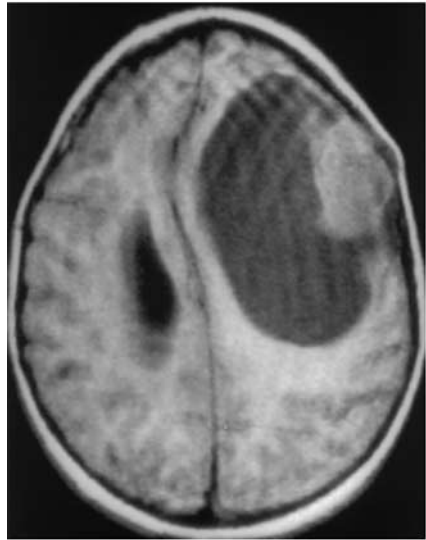
**Figure 13.** Pleomorphic xanthoastrocytoma in an 8-year-old boy with a history of vomiting, headaches, and decreased coordination for several months. **(a)** Contrast-enhanced axial CT image shows a heterogeneous mass of the left frontal region with both cystlike and soft-tissue components. **(b)** Axial CT image obtained with bone windows shows lytic change in the adjacent calvaria. **(c)** Axial T1-weighted MR image shows that the mass is cystlike with a peripheral soft-tissue component. **(d)** Axial T2-weighted MR image shows high signal intensity of the cystlike area and relative low signal intensity of the soft-tissue component. **(e)** Contrast-enhanced coronal T1-weighted MR image shows intense enhancement of the soft-tissue portion of the mass.



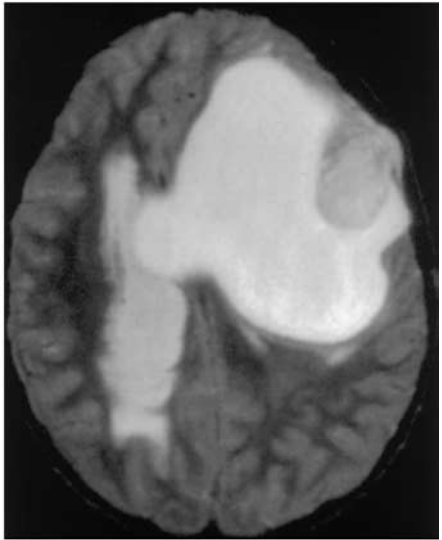
a.



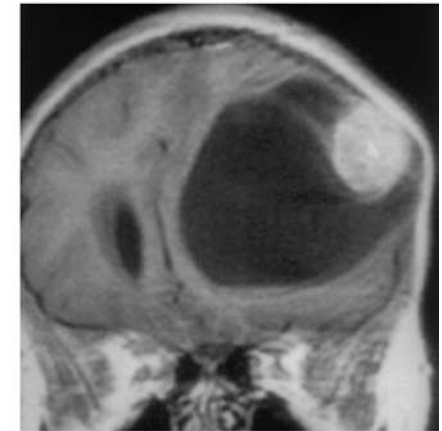
b.



c.



d.



e.



highly characteristic, seen in 71% of cases in one series (96). Peritumoral edema may be seen but is uncommon (95,96). The solid portions of the tumor enhance intensely following intravenous administration of contrast material (95,96). Pleomorphic xanthoastrocytomas are almost always avascular at cerebral angiography. When a vascular blush is seen, it may indicate a necrotic pleomorphic xanthoastrocytoma (94).

Despite some variance in the imaging appearance reported in the literature, the peripheral location of these tumors is the single most consistent imaging feature (94). At least one pleomorphic xanthoastrocytoma reported in the literature manifested with massive intracranial parenchymal and subarachnoid hemorrhage (99). There are several reports of combined ganglioglioma–pleomorphic xanthoastrocytoma tumors in both cerebral and cerebellar locations (100–103). The presence of a pleomorphic xanthoastrocytoma with dural attachment can produce an appearance that may mimic a meningioma on CT and MR images (96,104,105). The differential diagnosis is broad. Besides the tumors discussed in this article, other considerations include glioblastoma multiforme, oligodendroglioma, metastatic disease, and infectious entities.

### **Dysembryoplastic Neuroepithelial Tumor**

Dysembryoplastic neuroepithelial tumor is a benign tumor of neuroepithelial origin arising from the cortical or deep gray matter. Since the description of 39 cases in 1988 by investigators from Paris and the Mayo Clinic, there are now more than 300 cases on record (106,107). These tumors virtually always manifest in patients with medically refractory partial seizures. The vast majority of patients are younger than 20 years, and males are more commonly affected (108). In contrast to other brain neoplasms, neurologic deficits are not common with dysembryoplastic neuroepithelial tumors unless they occur in the presence of

complex congenital abnormalities (108). The temporal lobe is the most common site (62%), followed by the frontal lobe (31%) (108). Although the vast majority of dysembryoplastic neuroepithelial tumors are confined to the cortical gray matter, they may also arise within the caudate nucleus, cerebellum, or pons (109,110). Patients with cerebellar dysembryoplastic neuroepithelial tumors present with symptoms (eg, ataxia, vertigo, gait problems) related to this location rather than seizure activity (107). The locations of these tumors support the hypothesis that these lesions are derived from secondary germinal layers (106).

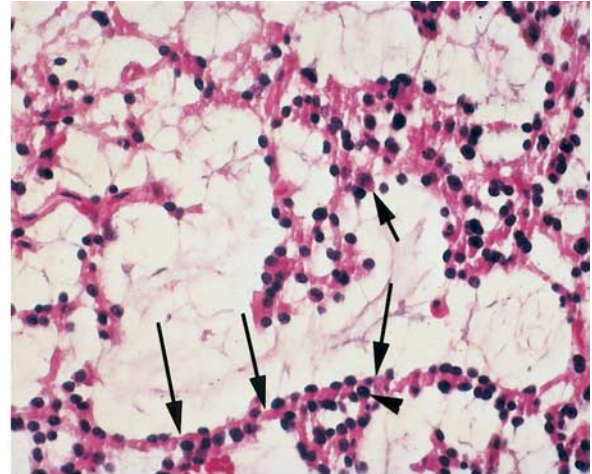
Dysembryoplastic neuroepithelial tumors appear to be remarkably stable in terms of biologic behavior. Despite only partial resection of many of these lesions, complete cessation of all seizure activity is a common result following neurosurgical intervention (106). Recurrence is also very rare (108). However, there is one recent report in the literature of malignant transformation of a dysembryoplastic neuroepithelial tumor that showed a higher degree of mitotic activity than is commonly seen in these tumors (111). The tumor in this case recurred 11 years after the initial surgical resection (111). This case emphasizes the need for long-term follow-up of patients with atypical dysembryoplastic neuroepithelial tumors.

The original description of 39 dysembryoplastic neuroepithelial tumors in 1988 resulted from a retrospective review of nearly 300 tumors initially diagnosed as low-grade astrocytomas in patients with medically refractory seizures (106). These 39 specimens shared common histologic features: a multinodular architecture, a “specific glioneuronal element” in a columnar pattern oriented perpendicular to the cortical surface, and focal areas

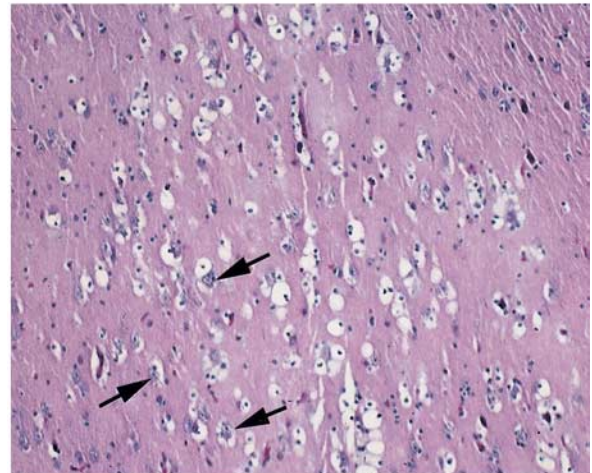
**Figures 14–16.** (14) Photograph of a resected intracortical dysembryoplastic neuroepithelial tumor shows multiple semicystic nodules (arrows) along the cortical boundary. (15) Photomicrograph (original magnification,  $\times 160$ ; hematoxylin-eosin stain) of a dysembryoplastic neuroepithelial tumor with cystic degeneration shows a trabecular pattern (long arrows) of glial elements, including astrocytes and oligodendrocytes. Oligodendroglial cells (arrowhead) contain small dark nuclei, whereas the astrocytic cells (short arrow) are somewhat larger with pink cytoplasm. (16) Photomicrograph (original magnification,  $\times 120$ ; hematoxylin-eosin stain) of a dysembryoplastic neuroepithelial tumor shows neuronal elements surrounded by prominent vacuoles, which represent so-called floating neurons (arrows).



14.



15.

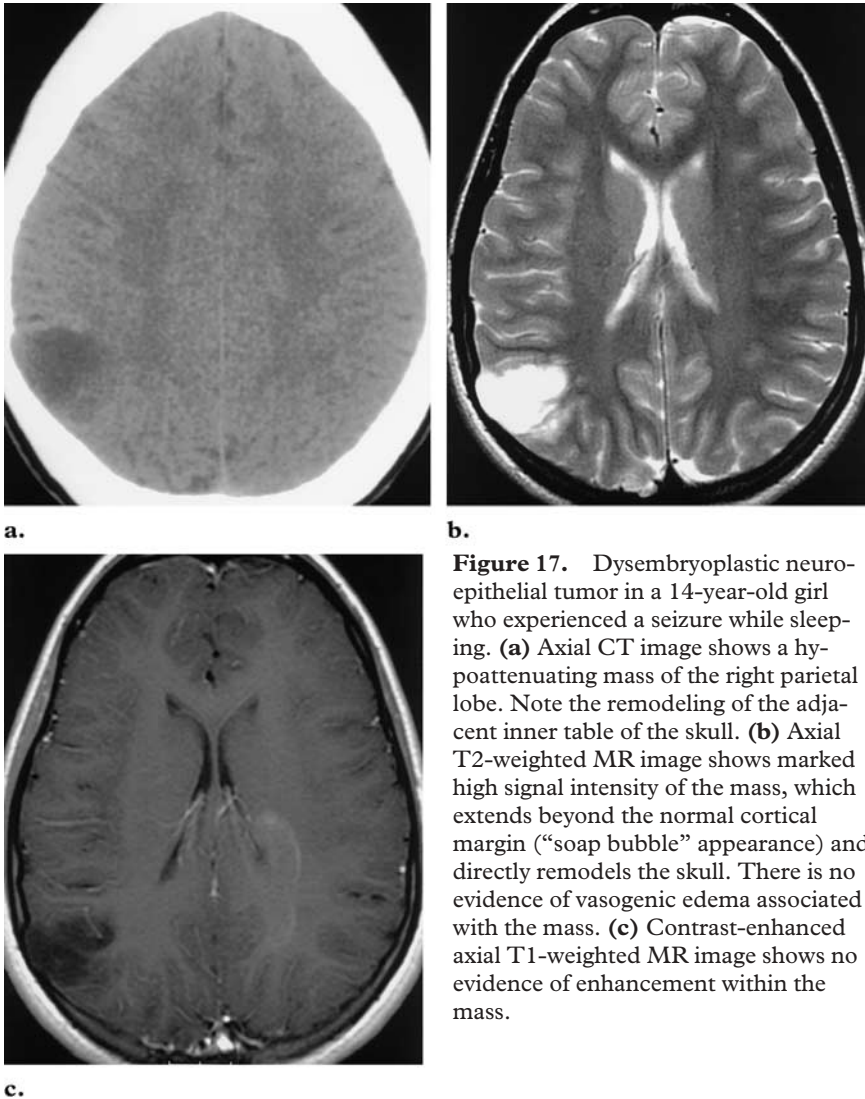


16.

of cortical dysplasia (Figs 14, 15) (106). Since that initial description, neuropathologists have noted that these three characteristics may not always be present. This observation has led to the latest classification scheme, which divides these tumors into a “simple form” (without a nodular architecture) and a “complex form” (with a multinodular appearance) (108). They are characterized by an admixture of astrocytes and oligodendroglial elements, in association with “floating neurons” and mucinous degeneration (Fig 16). The tumors generally have a low growth potential as measured by certain metabolic indexes (108). There are several reports of composite neoplasms with both ganglioglioma and dysembryoplastic neuroepithelial tumor components. Since cortical

dysplasia is commonly seen with both of these tumors, perhaps they represent the tumoral form of cortical dysplasia or neoplastic transformation of a dysplastic area (112).

The imaging appearance of dysembryoplastic neuroepithelial tumor is similar to those of other low-grade glial tumors, and in some cases it may

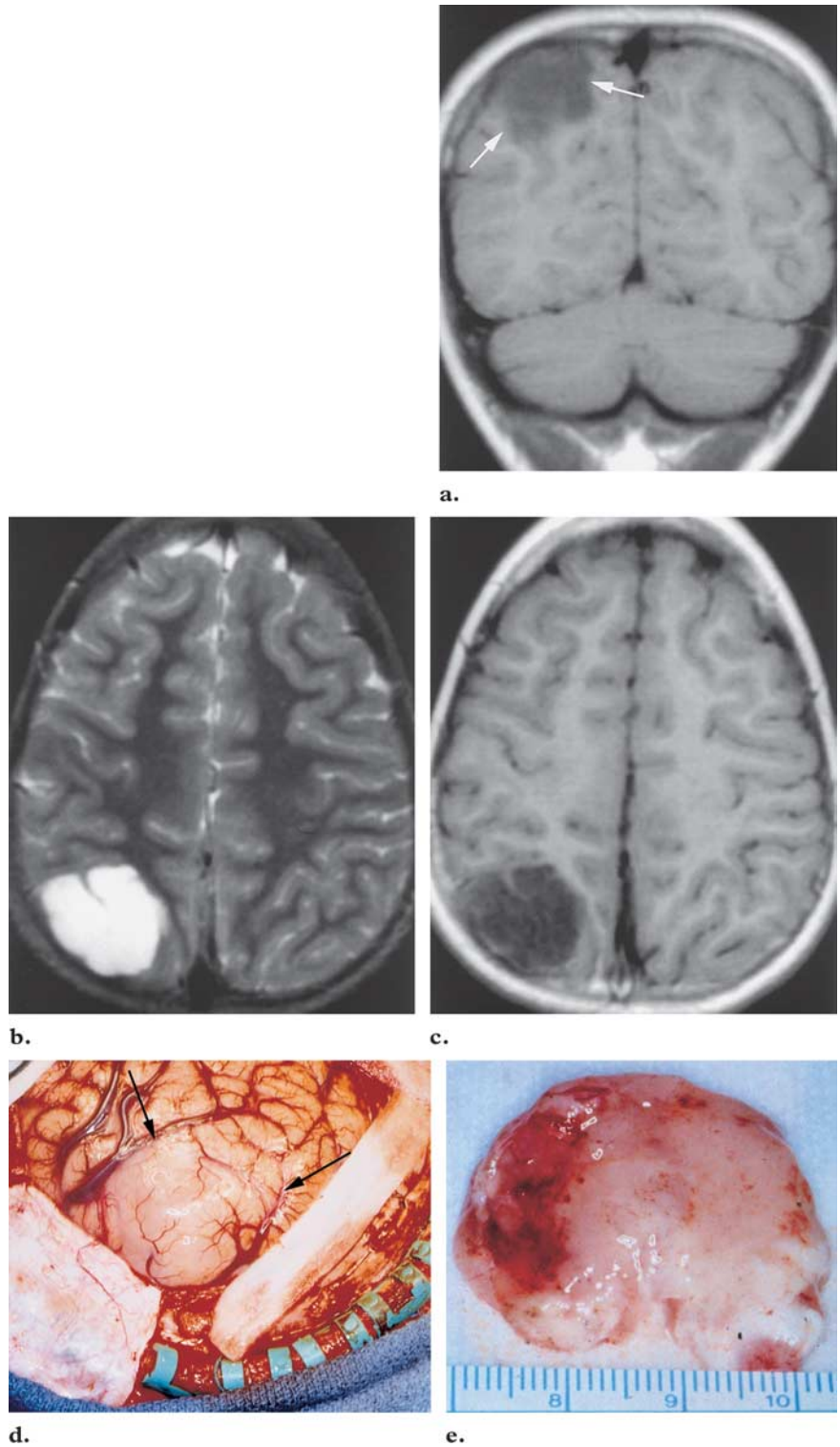


**Figure 17.** Dysembryoplastic neuroepithelial tumor in a 14-year-old girl who experienced a seizure while sleeping. **(a)** Axial CT image shows a hypoattenuating mass of the right parietal lobe. Note the remodeling of the adjacent inner table of the skull. **(b)** Axial T2-weighted MR image shows marked high signal intensity of the mass, which extends beyond the normal cortical margin (“soap bubble” appearance) and directly remodels the skull. There is no evidence of vasogenic edema associated with the mass. **(c)** Contrast-enhanced axial T1-weighted MR image shows no evidence of enhancement within the mass.

be impossible to distinguish this tumor from diffuse astrocytoma, ganglioglioma, oligodendroglioma, or other low-grade neoplasms (113). At CT, the tumor manifests as a hypoattenuating mass that may occasionally have areas of calcification. Remodeling of the adjacent inner table of the skull may also be seen (Fig 17) (113). At MR imaging, dysembryoplastic neuroepithelial tumors most commonly manifest as cortical masses that are hypointense on T1-weighted images and hyperintense on T2-weighted images without surrounding vasogenic edema (Figs 17–19). Some lesions may appear as an enlarged gyrus, producing a soap bubble appearance at the cortical mar-

gin (114). Ostertun et al (115) noted that dysembryoplastic neuroepithelial tumors show a multicystic appearance more commonly than do gangliogliomas. About one-third of dysembryoplastic neuroepithelial tumors enhance following intravenous administration of contrast material (113–115). The few lesions reported in the literature that were evaluated with SPECT demonstrated hypoperfusion on iodine-123 *N*-isopropyl-*p*-iodamphetamine (IMP) or technetium-99m hexamethyl-propyleneamine oxime (HMPAO) images and no abnormal uptake on thallium-201 images (116).

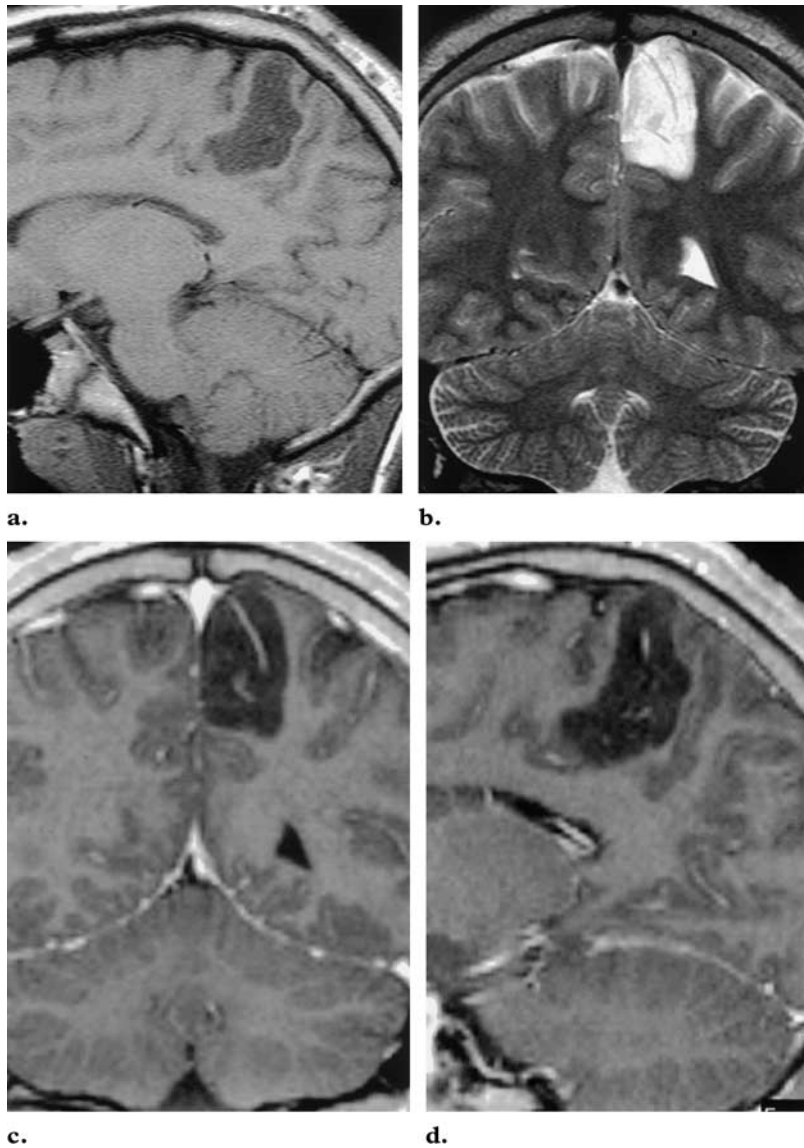
**Figure 18.** Dysembryoplastic neuroepithelial tumor in an 8-year-old boy with a 5-year history of seizures. **(a)** Coronal T1-weighted MR image shows a hypointense mass (arrows) extending to the cortical surface and remodeling the adjacent inner table of the skull. **(b)** Axial T2-weighted MR image shows high signal intensity within the mass, which has gently lobulated margins. **(c)** Contrast-enhanced axial T1-weighted MR image shows lack of enhancement within the mass. **(d)** Intraoperative photograph obtained after opening of the dura shows the mass as enlargement of the cortical surface (arrows). **(e)** Photograph of the resected specimen shows a mildly lobulated mass measuring  $3.5 \times 2.5 \times 1.2$  cm, an appearance that correlates with the imaging findings.



### Summary

As a group, the superficial cerebral gliomas are noteworthy because of several features. First, they tend to manifest in younger patients with refractory seizures. Second, resection of these tumors is often curative. Third, with the exception of pleomorphic xanthoastrocytoma, which is considered a WHO grade II lesion, they are all classified as

WHO grade I tumors. Fourth, they possess characteristic imaging features that include involvement of the cortical gray matter, soft-tissue and cystic components, and enhancement of the soft-tissue portion of the mass. Gangliogliomas are variable in size and frequently contain calcification. The striated cerebellum sign characterizes dysplastic cerebellar gangliocytoma. Desmoplastic infantile ganglioglioma and pleomorphic xanthoastrocytoma typically manifest as very large



**Figure 19.** Dysembryoplastic neuroepithelial tumor in a 15-year-old boy with long-standing progressive seizures. **(a)** Sagittal T1-weighted MR image shows a well-circumscribed hypointense mass of the parietal lobe. The mass extends to the cortical margin and produces a “megagyruus” appearance. **(b)** Coronal T2-weighted MR image shows high signal intensity within the mass. Linear areas of mild low signal intensity suggest septa or vessels within the mass. **(c)** Contrast-enhanced coronal T1-weighted MR image shows linear enhancement, which correlates with the findings in **b**. **(d)** Contrast-enhanced sagittal T1-weighted MR image shows similar linear enhancement within the substance of the mass.

supratentorial masses. Dysembryoplastic neuroepithelial tumor almost always involves the cortex and frequently extends beyond the cortical margin.

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