RadioGraphics

From the Archives of the AFIP

Pilocytic Astrocytoma: Radiologic-Pathologic Correlation[1]

CME FEATURE

See accompanying test at 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 salient demographic and clinical features of pilocytic astrocytoma.
- Identify the characteristic imaging appearances of pilocytic astrocytoma in children and adults, including the presence of dissemination.
- Discuss the direct correlation of the imaging appearances with the gross pathologic and histologic appearances in pilocytic astrocytoma.

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Pilocytic astrocytoma is the most common pediatric central nervous system glial neoplasm and the most common pediatric cerebellar tumor. This tumor has a noteworthy benign biologic behavior that translates into an extremely high survival rate—94% at 10 years—that is by far the best of any glial tumor. Most patients present in the first 2 decades, and clinical symptoms and signs are usually of several months duration and directly related to the specific location of the tumor. The cerebellum, optic nerve and chiasm, and hypothalamic region are the most common locations, but the tumor can also be found in the cerebral hemisphere, ventricles, and spinal cord. Surgical resection is the treatment of choice for all tumors, except for those involving the optic pathway and hypothalamic region, which may be treated with radiation therapy and chemotherapy. Cross-sectional imaging often demonstrates a classic appearance: a cystic mass with an enhancing mural nodule. Less common appearances are quite nonspecific. Surrounding vasogenic edema is rarely present, and this feature provides a valuable clue to the correct diagnosis. Accurate interpretation of imaging studies plays an essential role in directing treatment of these tumors, particularly when they arise in the optic pathway of patients with neurofibromatosis type 1. Disseminated disease and recurrence are extremely rare.

Abbreviations: NF1 = neurofibromatosis type 1, WHO = World Health Organization

Index terms: Astrocytoma, 10.3639 • Brain neoplasms, 10.3639 • Neoplasms, in infants and children, 10.3639

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Introduction

Originally identified in a series of 76 cases of cerebellar astrocytomas by Harvey Cushing in 1931, the pilocytic astrocytoma occupies a unique place among cerebral neoplasms (1). With its notable indolent biologic behavior, pilocytic astrocytoma carries one of the highest survival rates of any brain tumor and certainly the highest rate for any astrocytoma. Yet, as reviewed herein, there are numerous oddities about this neoplasm. It appears well circumscribed, yet occasionally it infiltrates the surrounding brain tissue, as seen at histologic examination. It enhances intensely, sometimes with a ringlike pattern that is more commonly seen in highly malignant astrocytomas, yet it is not a high-grade neoplasm. In rare cases, it can even produce widespread dissemination, which seems incongruous for a brain tumor with slow growth and fairly bland histologic characteristics. Even more fascinating, such metastatic spread can occur without associated increased mortality, in contrast to the poor prognosis so common in patients with metastatic high-grade tumors. In view of these many contradictions, pilocytic astrocytoma qualifies as "the tumor that is the exception to the rule."

In this article, we use case material from the Thompson Archives of the Department of Radiologic Pathology at the Armed Forces Institute of Pathology to illustrate the spectrum of cross-sectional imaging manifestations of this common tumor and to present a comprehensive summation of the history, pertinent clinical findings, pathologic features, histogenesis, and prognosis associated with this tumor. Salient demographic and imaging features of pilocytic astrocytoma are listed in the Table.

Epidemiologic Characteristics

Pilocytic astrocytoma is the most common pediatric cerebellar neoplasm and the most common pediatric glioma, constituting 85% of all cerebellar astrocytomas and 10% of all cerebral astrocytomas in this age group (2). Overall, it accounts for 0.6%–5.1% of all intracranial neoplasms and 1.7%–7% of all glial tumors (3).

Pilocytic astrocytoma occurs most commonly in children and young adults, with most cases (75%) manifesting in the first 2 decades of life (2,4). No gender predilection is reported (2). Most of the lesions occur in or near the midline, usually arising from the cerebellum, the optic nerve and chiasm, or the region of the hypothalamus-thalamus. Less common locations include the cerebral hemispheres, the cerebral ventricles, velum interpositum, and spinal cord (5–9). In adults, the tumor more frequently occurs in the cerebral hemisphere (8,10).

The association of pilocytic astrocytoma with neurofibromatosis type 1 (NF1) is well documented. Pilocytic astrocytoma is the most common tumor seen in this population, occurring in up to 15%–21% of all NF1 patients, and typically involves the optic nerve or chiasm (3,11–16). Because the vast majority of optic pathway gliomas are histologically regarded as pilocytic astrocytoma, it has been suggested that the most appropriate term for this entity should be "pilocytic astrocytoma of the optic pathway" (16). Nearly all optic pathway gliomas in NF1 patients manifest before the age of 6 years and females are more commonly affected by a 2:1 ratio (16,17). Of all patients with an optic pathway glioma, about one-third have NF1, and, of all tumors in this region, 40%–70% occur in NF1 patients (14,16,18).

Pilocytic astrocytomas account for 1.5%–3.5% of all orbital neoplasms and two-thirds of all neoplasms of the optic nerve (3). Most optic pathway pilocytic astrocytomas (75%) arise in children less than 12 years old; in addition, the tumor is more likely to arise in the optic nerve in children, whereas it is more commonly located in the optic chiasm in adolescents and young adults (19,20). Involvement of the chiasm and hypothalamus has been reported to occur in 25%–60% of patients (11,19,20). Optic pathway gliomas much less commonly manifest in adult patients without NF1; when they do, these tumors have a dramatically different biologic behavior and are regarded histologically as anaplastic astrocytoma or glioblastoma multiforme (21).

Clinical Features

Clinical presentation of patients with a pilocytic astrocytoma varies with its site of origin. Headache, vomiting, gait disturbance, blurred vision, diplopia, and neck pain are common symptoms in patients with a cerebellar pilocytic astrocytoma (22–24). Clinical signs usually include hydrocephalus, papilledema, truncal ataxia, appendicular dysmetria, head tilt, sixth nerve palsy, and nystagmus (22,24).

Characteristics of Pilocytic Astrocytoma

Feature	Characteristic Manifestation
Prevalence	Most common (85%) pediatric cerebellar neoplasm and most common pediatric glioma; constitutes 10% of all childhood intracranial neoplasms, 0.6%–5% of all intracranial tumors, and 1.7%–7% of all gliomas
Age	Most patients present before 20 years of age; about 25% are older than 18 years at time of presentation
Gender	No predominance
Location	Cerebellum, brainstem, optic nerve and optic chiasm, hypothalamus/thalamus most common; cerebral hemisphere, ventricles, and spinal cord less common; in adults, more common in cerebral hemisphere
Clinical symptoms and signs	Dependent on location; typically long duration; tumors in the cerebellum manifest with headache, vomiting, gait disturbance, blurred vision, papilledema, truncal ataxia
Special features	Association with neurofibromatosis type 1, especially for tumors located in the optic pathway
Histologic features	Reactive astrocytes with biphasic morphology (loose glial component and compact piloid regions), eosinophilic granular bodies ("protein droplets"), Rosenthal fibers; pilomyxoid subtype has affinity for hypothalamic region
CT appearance	Hypoattenuated cystlike component combined with isoattenuated soft-tissue mural nodule
MR imaging appearance	On T1-weighted images, intense to hypointense; on T2-weighted images, hyperintense (cystic portion), mixed signal (soft-tissue portion); mural nodule shows intense enhancement; other patterns: ringlike enhancement of cysts, solid near homogeneous enhancement, necrosis with central nonenhancing zone
Therapy	Surgical resection is treatment of choice and often curative; radiation therapy and chemotherapy reserved for tumors of the optic chiasm and hypothalamic region, recurrent tumor, and disseminated disease (rare); chemotherapy used for children younger than 5 years
Prognosis	Excellent overall with up to 79% 20-year survival; less favorable for hypothalamic location; recurrence rare, carries poorer prognosis

When a pilocytic astrocytoma arises in the brainstem, it typically extends exophytically from its dorsal margin and causes symptoms of nausea, vomiting, and ataxia, with evidence of torticollis, papilledema, nystagmus, and palsies of the sixth and seventh cranial nerves at physical examination (25–27). Long-tract signs are conspicuously absent (25,27). Pilocytic astrocytomas arising from the tectum characteristically manifest with headache, vomiting, paresis, abnormal gait, somnolence, Parinaud syndrome, and diplopia (28,29).

Pilocytic astrocytoma of the optic pathway frequently produces visual loss or visual-field deficit, with optic disk pallor and optic nerve atrophy in the involved eye secondary to axonal damage and ischemia (3,21,30). Proptosis may be seen with larger masses. Papilledema is common for lesions arising from the optic nerve but unusual for those originating from the optic chiasm (21). Some patients may show spasmus nutans, a nystagmus characterized by high frequency and low amplitude and associated with head nodding movements (31). Precocious puberty is commonly seen (39% of cases) in NF1 patients with an optic pathway glioma and has not been reported in its absence (16). Less specific manifestations include amblyopia (30). Smaller lesions may not be associated with any symptoms at all (2).

Pilocytic astrocytoma of the hypothalamus may produce symptoms related to obesity, diabetes insipidus, and other symptoms of hypothalamic-pituitary dysfunction (2). On occasion, these masses may produce the so-called diencephalic syndrome, which is characterized by emaciation despite a normal to slightly decreased caloric intake, alert appearance, hyperkinesis, irritability, and normal to accelerated growth (20,32,33). Although this syndrome may occur with any hypothalamic mass, the vast majority of

reported cases are secondary to a pilocytic astrocytoma, with widespread dissemination noted in some cases (32). When the tumor involves the thalamus, hydrocephalus or hemiparesis secondary to compression of the corticospinal tract within the nearby internal capsule is typical (2,34).

Headache, seizure activity, hemiparesis, ataxia, nausea, and vomiting are common clinical manifestations for pilocytic astrocytomas arising in the cerebral hemispheres (7). The occurrence of seizure activity generally indicates cortical gray matter involvement (2). Papilledema is noted in about one-third of these patients (7).

Pathologic Characteristics

Pilocytic astrocytoma has been known by many names over the years. Because of its resemblance histologically to the spongioblastic cells of the fetus, German pathologists called it "spongioblastoma polare," a term that has now been abandoned (35,36). Russell and Rubenstein (37) distinguished the tumor into adult and juvenile forms. In addition, many generic pseudonyms and euphemisms based on the geographic location of the tumor have persistently appeared in the prior pathology lexicon to describe these lesions. Hence, a variety of names—optic nerve glioma, hypothalamic glioma, cerebellar astrocytoma, microcystic astrocytoma, cystic astrocytoma, and others—have inadvertently blurred the true identity of the pilocytic astrocytoma and led to confusion (26).

Although this tumor may be found in many central nervous system locations and may account for a significant proportion of the tumors in those locations, pilocytic astrocytoma is now regarded by the latest World Health Organization (WHO) classification as a distinct clinicopathologic entity, and use of these less specific terms should be avoided if the pathologic findings warrant the diagnosis (26).

The macroscopic appearance of pilocytic astrocytoma varies with its location within the central nervous system. Tumors of the cerebellum and cerebral hemisphere are typically well-circumscribed, cystlike masses with a discrete mural nodule, whereas those arising in the hypothalamus and optic chiasm tend to be large, soft, cystlike masses. When the tumor arises within the optic nerve, it infiltrates and engulfs the nerve to produce fusiform enlargement of that structure, with peripheral extension into the surrounding leptomeninges. Brainstem pilocytic astrocytomas are usually peripheral and are attached to the brainstem surface without extensive infiltration (38).

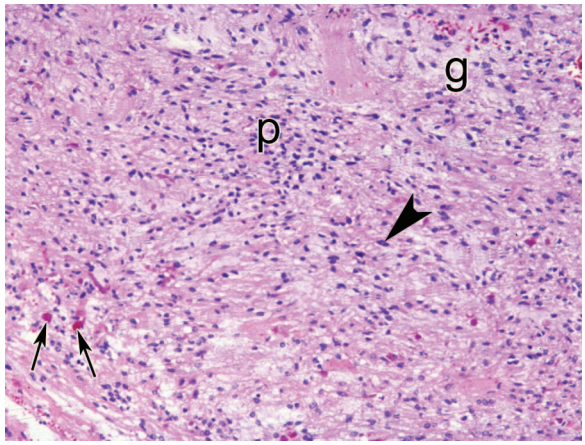


Figure 1. Pilocytic astrocytoma. Photomicrograph (original magnification, ×40; hematoxylin-eosin stain) of a classic pilocytic astrocytoma reveals a biphasic appearance with a loose glial component *(g)* with numerous microcysts and vacuoles and more compact piloid tissue *(p)* with elongated bipolar cells (arrowhead) showing fine fibrillary processes. Rosenthal fibers (arrows) are also noted.

At histologic examination, pilocytic astrocytoma classically manifests in a noteworthy biphasic pattern composed of a combination of loose glial tissue punctuated by numerous vacuoles, microcysts, occasional macrocysts, and compacted piloid tissue (Fig 1) (38). The piloid tissue component is composed of dense sheets of elongated bipolar cells that demonstrate fine fibrillary (hairlike) processes, a highly distinctive feature, and typically an abundance of Rosenthal fibers (38). In contrast, the multipolar cells of the loose glial tissue, frequently called protoplasmic astrocytes, are much less fibrillated and commonly are intermixed with degenerative products of astrocyte formation, known as eosinophilic granular bodies or "protein droplets" (2). These "classic" but nonspecific granular bodies are believed to indicate slow growth and low histologic grade and are associated with a favorable prognosis (38). Calcification is an uncommon feature, usually occurring in those tumors arising from the optic nerve or hypothalamic-thalamic region, but it can be extensive (2,38). The tumor is suspected to arise from reactive astrocytes (2).

There is considerable variability in the contribution of each pattern to the overall histologic appearance of pilocytic astrocytomas. Some tumors have a predominance of the glial component, whereas others show more of the piloid tissue. A minority of pilocytic astrocytomas demonstrates both components equally (38). More recently, a subset of pilocytic astrocytomas known as the pilomyxoid variant has been identified with

monomorphous histologic features and lack of Rosenthal fibers. The few reported cases have occurred in the chiasmatic-hypothalamic region in children less than 2 years of age; these tumors were associated with a higher rate of recurrence and cerebrospinal fluid dissemination (2,39). These tumors have some ultrastructural features that have fueled speculation that this subtype may be of tanycytic origin, leading some authorities to describe it as a "tanycytoma." However, more evidence is needed to prove this cellular lineage and justify use of this term (40).

Slow growth is the rule for most pilocytic astrocytomas (41). However, some tumors, particularly those of the optic nerve and chiasm, may show a propensity for periods of accelerated growth (19). Growth of the tumor, especially those occurring in the cerebellum, may overrun normal ganglion cells (neurons), producing the "trapped neuron" appearance (2,38). The growth pattern of optic pathway glioma (including pilocytic astrocytoma) correlates with the presence or absence of NF1 in the patient. When the tumor arises in patients with NF1, it tends to grow within the nerve, whereas a circumferential pattern is observed when it occurs in patients without NF1 (42).

Although many pilocytic astrocytomas appear well circumscribed macroscopically, they may infiltrate into the surrounding brain parenchyma for several millimeters (2). Infiltration occurs more commonly for those tumors that arise from the optic nerve and chiasm, where there is frequently no clear demarcation between the tumor and normal tissue (2). Infiltration of the adjacent leptomeninges is a signature feature of a cerebellar pilocytic astrocytoma, causing fixation of the cerebellar folia and filling of the sulci (2). This infiltration, along with perivascular space extension, may also be seen with tumors in other locations (2).

Pilocytic astrocytomas are highly vascular (2). Some long-standing tumors, such as those of the cerebellum and cerebral hemisphere, frequently have markedly hyalinized and glomeruloid vessels (2). This new vessel formation is particularly evident within the cyst wall, and it is believed that the fluid within the cyst directly supports vascular proliferation (2) The presence of these glomeruloid vessels accompanied by extensive nuclear pleomorphism may mimic some of the features of high-grade astrocytomas (2,38). The increased vascularity of pilocytic astrocytoma may explain why it may even be a target for metastatic disease, as in one case of a breast carcinoma that spread to a pilocytic astrocytoma (43).

The overwhelming majority of pilocytic astrocytomas are regarded as grade I tumors in the WHO classification (2,38). Most tumors demonstrate sufficient characteristic histologic features that a definitive diagnosis can be rendered with confidence. However, the variety of histologic patterns among pilocytic astrocytomas and the lack of specific immunohistochemical, cytogenetic, and molecular markers may occasionally make the diagnosis difficult (2). Occasional hyperchromasia and pleomorphism, especially when they are noted in a diffuse tumor, may cause pilocytic astrocytoma to be confused with a higher-grade astrocytoma (2). In rare cases, some tumors, especially those arising in patients who underwent radiation therapy, may have frankly malignant features (increased mitotic activity, hypercellularity, endothelial proliferation, and necrosis with pseudopalisading) and also demonstrate aggressive biologic behavior (38).

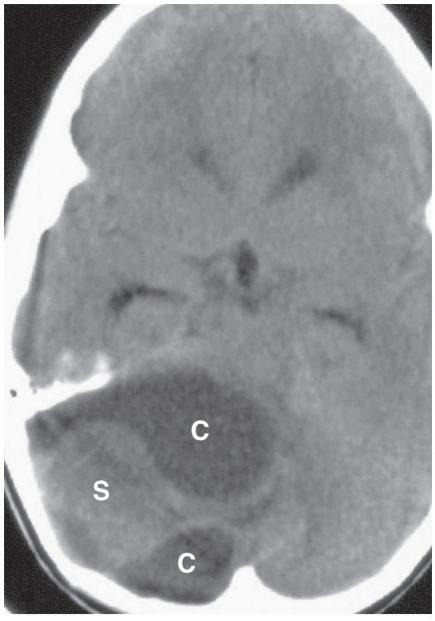
Very rarely, a pilocytic astrocytoma may undergo malignant transformation with an aggressive histologic appearance; such a tumor is called an anaplastic (malignant) pilocytic astrocytoma. Although fatal cases have been reported, this event does not necessarily carry a less favorable outcome (2,8,44–46). Many cases of malignant transformation have occurred after administration of radiation therapy, leading to speculation that irradiation is at least a contributing factor in the development of this change, which may manifest up to 52 years after initial treatment (45).

Cytogenetic studies of pilocytic astrocytomas have revealed loss of genetic material involving the long arm of chromosome 17 (17q) near the same locus for the NF1 tumor suppressor gene (47). Furthermore, lack of expression of an NF1 gene product, neurofibromin, has been documented in NF1-associated pilocytic astrocytomas (48). These findings have fueled speculation that the NF1 tumor suppressor gene is linked with the expression of pilocytic astrocytoma. Additional chromosomal mutations have been identified on chromosomes 7, 8, 11, 19, and 21 (2,49).

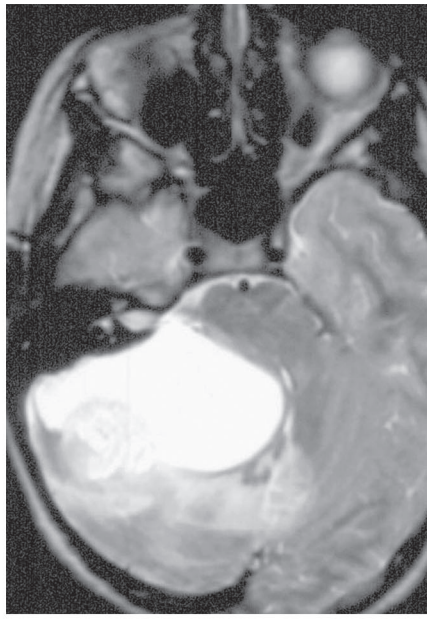
Imaging Characteristics

At computed tomography (CT), most cerebellar and cerebral pilocytic astrocytomas have a well-demarcated appearance with a round or oval shape smaller than 4 cm in size, cystlike features, smooth margins, and occasional calcifications (Figs 2–4) (8,50,51). Most tumors (82% in one series) are located near the ventricular system, and almost all (94%) enhance, typically intensely, on postcontrast images obtained after intravenous administration of contrast material (51).

Figures 2, 3. **(2)** Cerebellar pilocytic astrocytoma. **(a)** Axial CT image shows a well-marginated mass of the right cerebellar hemisphere. The mass has both cystic *(c)* and soft-tissue *(s)* components. **(b)** Axial T2-weighted image reveals predominant hyperintensity within the mass with slightly lower signal intensity of the soft-tissue component. **(c)** Contrast material–enhanced axial T1-weighted image demonstrates intense enhancement of the soft-tissue nodule and lack of enhancement of the cystic portion. **(d)** Intraoperative photograph shows the smooth margin of the cystic portion *(c)*. **(3)** Pilocytic astrocytoma with hemorrhage in an 11-year-old girl with onset of headache, nausea, and vomiting. Within 24 hours, the patient was obtunded and unresponsive. **(a)** Axial CT image shows hyperattenuation (arrow) consistent with hemorrhage within a vermian mass that effaces the fourth ventricle. **(b)** Photograph of a cut cerebellum specimen reveals a large hemorrhagic mass *(m)*. Findings from histologic analysis confirmed pilocytic astrocytoma with hemorrhage.



2a.



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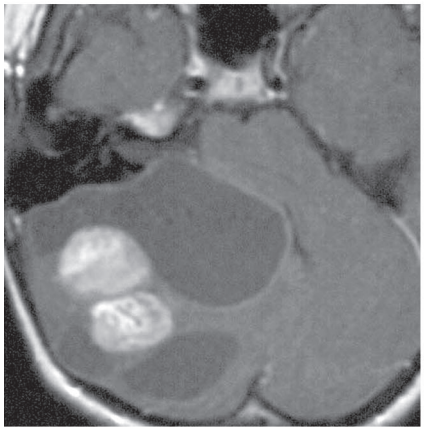
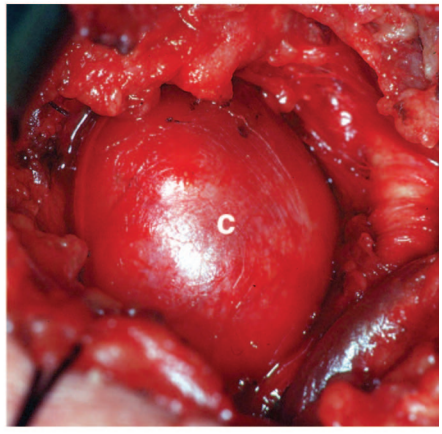


2c.



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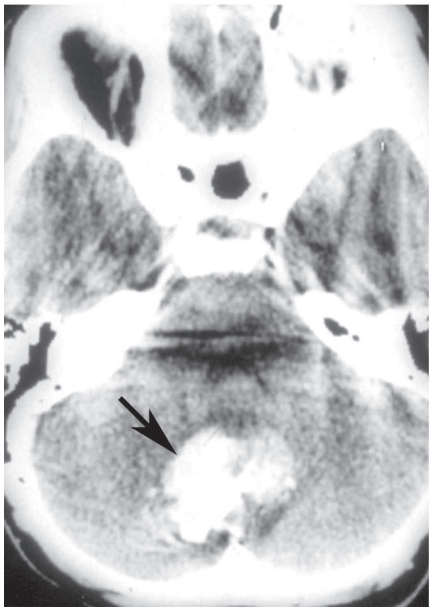
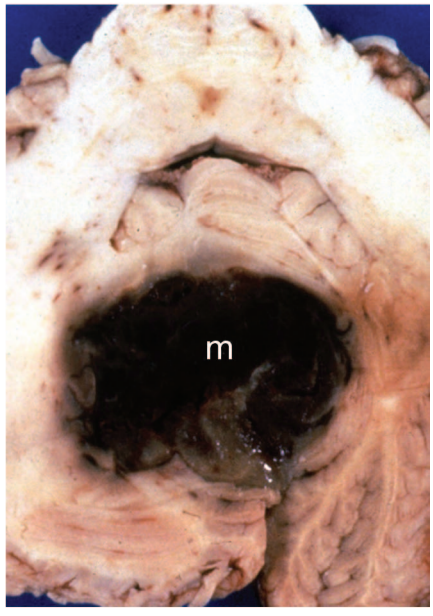


3a.



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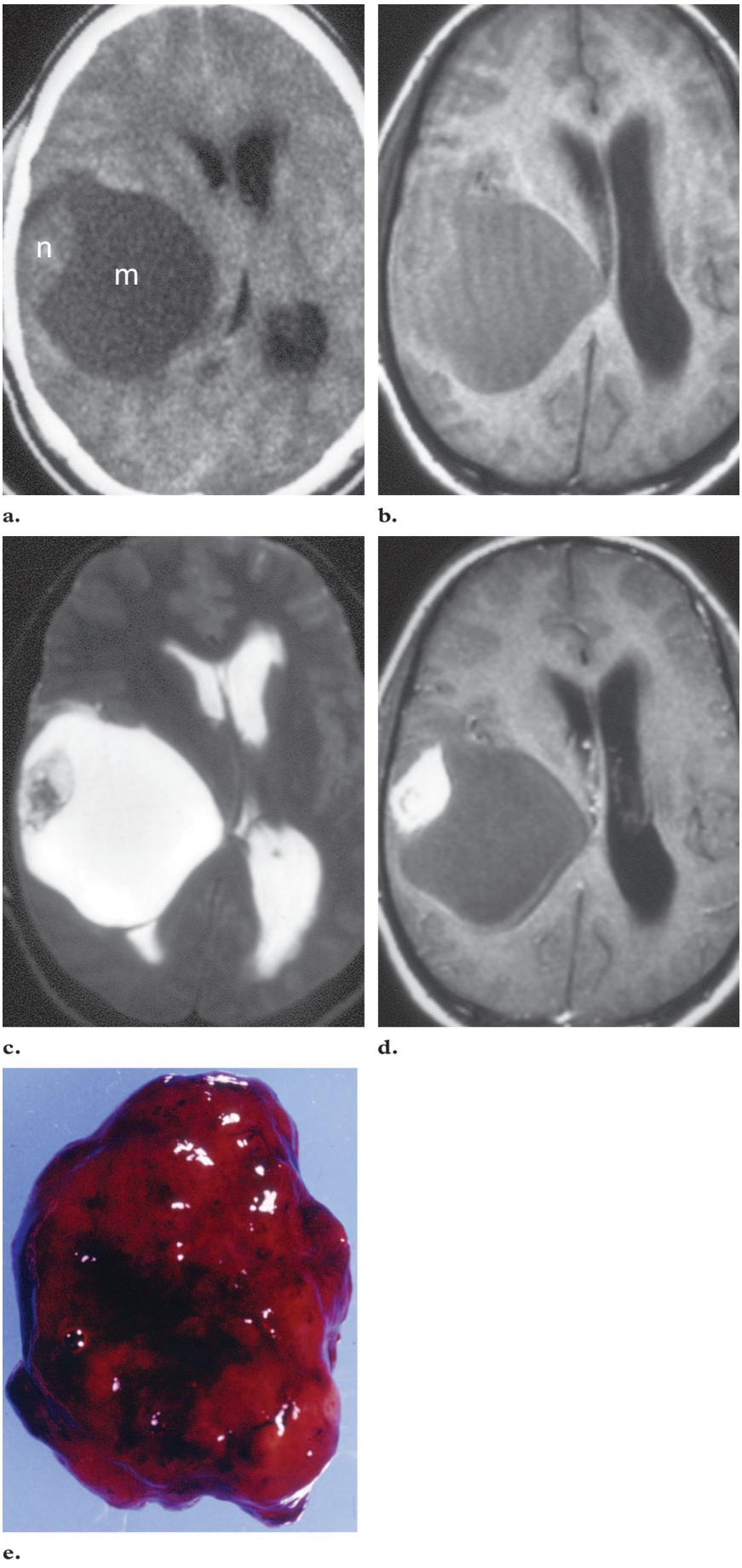
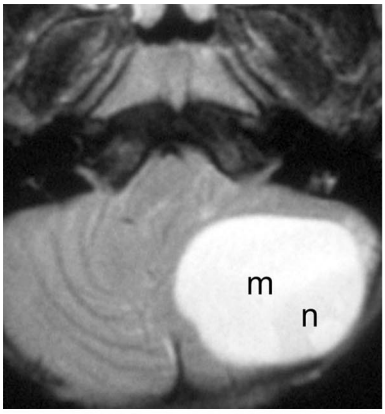


Figure 4. Supratentorial pilocytic astrocytoma of the temporal lobe. **(a)** Axial CT image shows a hypoattenuated mass *(m)* of the right temporal lobe and a soft-tissue mural nodule *(n)* along its lateral margin. **(b)** Axial T1-weighted image reveals hypointensity of the mass with slightly higher signal intensity of the mural nodule. **(c)** Axial T2-weighted image demonstrates predominant hyperintensity of the mass with lower signal intensity of the mural nodule. **(d)** Contrast-enhanced axial T1-weighted image shows intense enhancement of the mural nodule. Signal intensity of the cyst is higher than that of cerebrospinal fluid within the lateral ventricles, a finding indicative of hemorrhagic or proteinaceous content. **(e)** Photograph of the resected mural nodule reveals a hemorrhagic mass.

Figures 5, 6. **(5)** Classic appearance of a cerebellar pilocytic astrocytoma. **(a)** Axial T2-weighted image shows a hyperintense mass *(m)* of the left cerebellar hemisphere with a less intense soft-tissue nodule *(n)* along its posterolateral margin. Note absence of surrounding vasogenic edema. **(b)** Contrast-enhanced coronal T1-weighted image demonstrates intense enhancement of the mural nodule. **(6)** Atypical appearance of a supratentorial pilocytic astrocytoma with prominent vasogenic edema. **(a)** Sagittal T1-weighted image shows a large supratentorial mass with a soft-tissue component *(s)* in the region of the lateral ventricle trigone and cystlike regions *(c)* located more superiorly and anteriorly. **(b)** Axial T2-weighted image demonstrates extreme hyperintensity of the cystlike portions *(c)* and more mild hyperintensity of the soft-tissue mass *(s)* within the lateral ventricle. Note vasogenic edema around the mass (arrows). Vasogenic edema is not a common feature of pilocytic astrocytomas. **(c)** Contrast-enhanced axial T1-weighted image reveals intense enhancement of the soft-tissue portion and lack of enhancement of the cystic portion.



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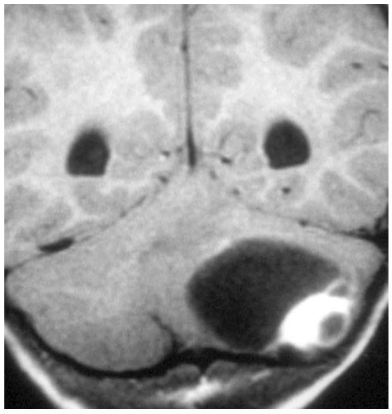

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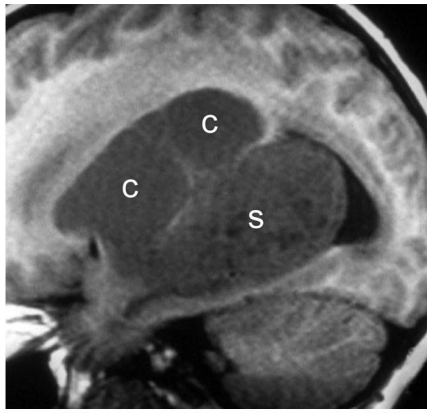

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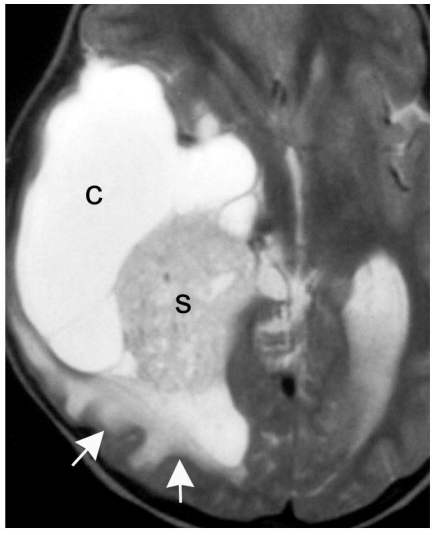

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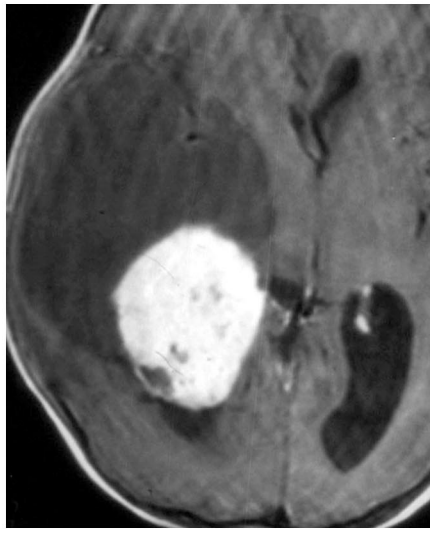
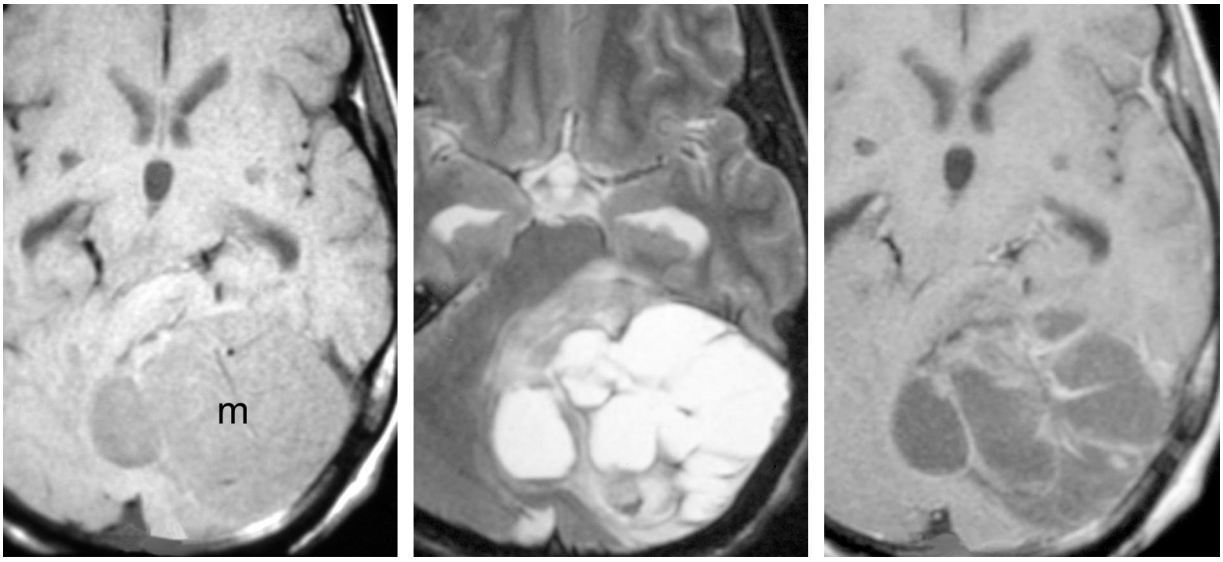


6c.

At MR imaging, pilocytic astrocytoma is typically isointense to hypointense relative to normal brain with T1-weighted pulse sequences and hyperintense compared with normal brain with T2-weighted pulse sequences (Fig 5) (50). As expected for a tumor of low biologic activity, the degree of surrounding vasogenic edema is diminished in comparison with that seen in high-grade (WHO grade III and IV) glial neoplasms (8,9). When it does occur, the area of edema is smaller in size than the diameter of the tumor (Fig 6) (51). Postcontrast imaging features are similar to those reported with CT. Because of its superiority to CT in assessing the posterior fossa and the usefulness of multiplanar imaging, MR imaging is regarded as the imaging study of choice for evaluation of pilocytic astrocytomas (24). The well-demarcated appearance of virtually all (96%) pilocytic astrocytomas is misleading, as most (64%) show infiltration into the surrounding brain parenchyma at histologic examination (51).

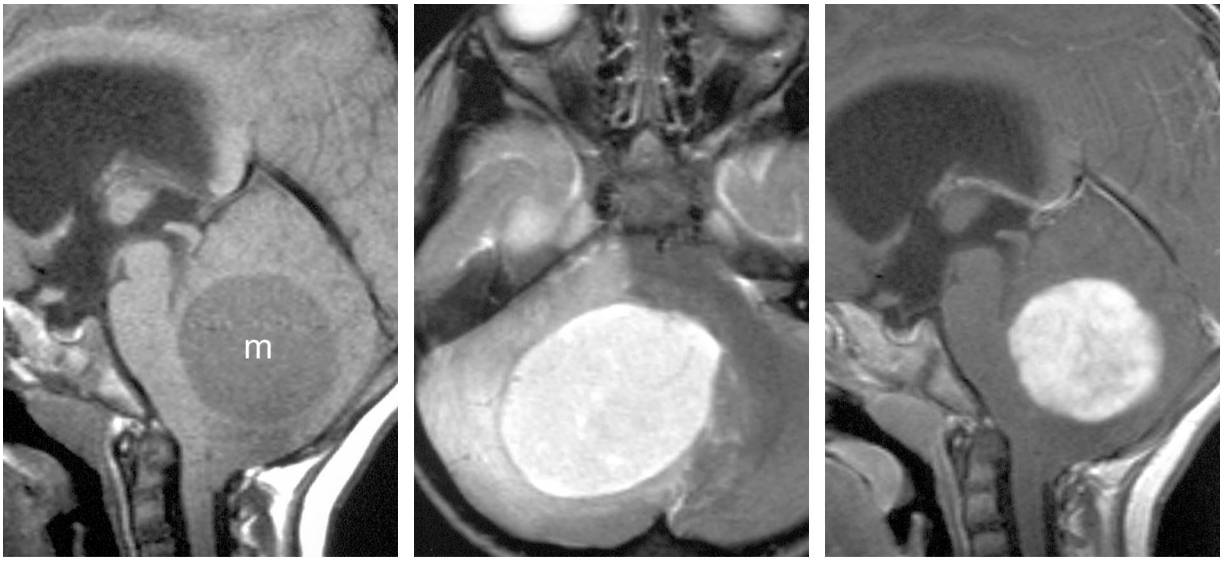
Four predominant imaging patterns of pilocytic astrocytoma have been described: *(a)* mass with a nonenhancing cyst and an intensely enhancing mural nodule (21% of cases) (Fig 5), *(b)* mass with an enhancing cyst wall and an

Figure 7. Pilocytic astrocytoma with ringlike enhancement. **(a)** Axial T1-weighted image shows a hypointense mass *(m)* of the left cerebellar hemisphere. **(b)** Axial T2-weighted image reveals hyperintensity with numerous hypointense septations within most of the mass. **(c)** Contrast-enhanced axial T1-weighted image demonstrates ringlike enhancement of multiple cystic areas within the tumor.



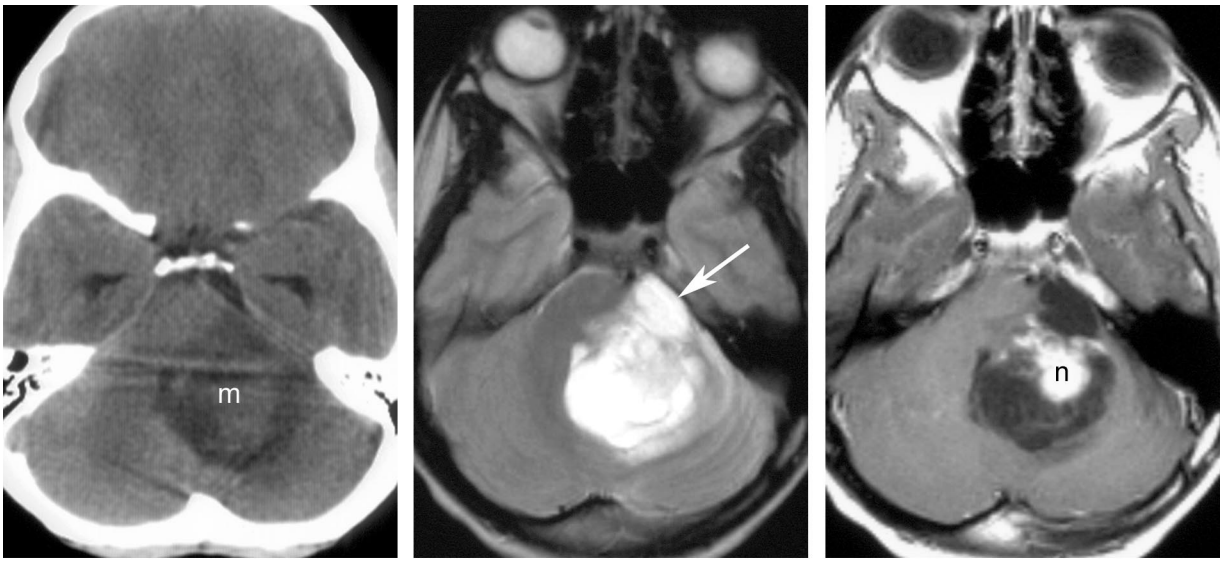
a. **b.** **c.**

Figure 8. Pilocytic astrocytoma with solid enhancement. **(a)** Sagittal T1-weighted image shows a well-circumscribed, hypointense cerebellar mass *(m)*. **(b)** Axial T2-weighted image shows the hyperintense mass of the cerebellar vermis and right cerebellar hemisphere. **(c)** Contrast-enhanced sagittal T1-weighted image demonstrates homogeneous enhancement of the mass.



a. **b.** **c.**

intensely enhancing mural nodule (46%) (Fig 7), *(c)* necrotic mass with a central nonenhancing zone (16%), and *(d)* predominantly solid mass with minimal to no cystlike component (17%) (Fig 8) (24). Hence, two-thirds of all cases demonstrate the classic imaging manifestation of a cystlike mass with an enhancing mural nodule. Although most cyst walls do not enhance, some may enhance intensely, even as much as the mural nodule (52). Although most cyst walls do not enhance, some may enhance intensely, even as much as the mural nodule; however, cyst wall enhancement is not necessarily indicative of tumor involvement (52). Beliefs vary among neurosurgeons regarding whether to resect the cyst itself in cases of pilocytic astrocytoma. Some advocate complete resection, others biopsy, and still others no resection (52). Removal of the cyst wall has not been linked with improved survival (53).



a. b. c.

Figure 9. Exophytic pilocytic astrocytoma arising from the brainstem. **(a)** Axial CT image shows a hypoattenuated mass *(m)* of the posterior margin of the mid-pons and left cerebellar hemisphere. **(b)** Axial T2-weighted image reveals heterogeneous hyperintensity of the mass, which extends into the adjacent cisternal space (arrow). **(c)** Contrast-enhanced axial T1-weighted image demonstrates intense enhancement of the soft-tissue nodule *(n)* and lack of enhancement of the cystic portion. Extension into the cerebellopontine cistern is again noted.

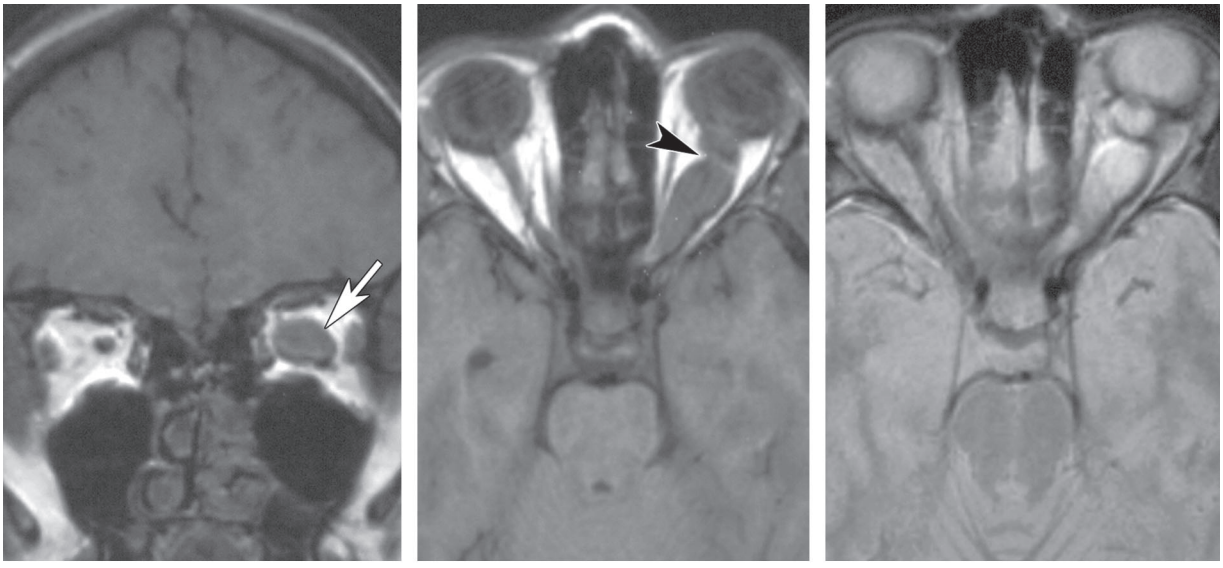
There is contradictory evidence in the literature regarding the most common location of pilocytic astrocytoma in the cerebellum. In one series of 132 patients, 16% of the tumors arose in the vermis, 53% in the cerebellar hemisphere, and 26% in both; 34% also involved the brainstem (54). However, in another review of 168 cases, 71% of the tumors were located in the vermis, whereas 29% occurred in the hemisphere (24). Those tumors arising in the cerebral hemisphere are more likely to occur in the temporal lobe (7,53). Location, enhancement, and the presence or absence of calcification seen at the time of initial presentation are not reliably predictive of the future clinical behavior of a pilocytic astrocytoma (55).

In contrast to the more biologically aggressive fibrillary astrocytoma (which is most common in the pons), pilocytic astrocytoma may be found throughout the brainstem and frequently extends in an exophytic fashion from its dorsal surface (56,57). Pilocytic astrocytoma typically demonstrates sharp delineation with cystlike regions and fourth ventricle obliteration (Fig 9) (25,27,57). The distinction between these two entities is more than an academic curiosity, since the fibrillary brainstem astrocytoma carries a dismal prognosis compared with the excellent outlook associated with the pilocytic variety (57). Because available tissue for histologic analysis from this exquisitely sensitive region of the central nervous system is generally limited, knowledge of the differences in imaging manifestations of the two diseases may help establish the correct diagnosis (26).

When pilocytic astrocytoma arises within the optic nerve, it manifests on both CT and MR images with enlargement of the optic nerve as an intraconal mass with characteristic kinking or buckling of the nerve secondary to the neoplasm itself and vascular congestion (Fig 10) (21). Isointensity on T1-weighted MR images and heterogeneous hyperintensity on T2-weighted MR images are typical, with variable enhancement following intravenous contrast material administration (21).

Differences in the imaging appearance of optic pathway gliomas in patients with NF1 versus that of tumors in patients without NF1 have been noted in one study (58). NF1-associated tumors affected the optic nerve and chiasm with nearly equal prevalence, preserved the optic nerve shape, rarely extended beyond the optic pathway, and usually were not cystic. In contrast, the majority of tumors not associated with NF1 involved the optic chiasm rather than the optic nerve, extended extraoptically, and frequently contained cystic areas. The imaging findings did not statistically correlate with the biologic behavior of the tumors (58).

Atypical imaging manifestations may be seen occasionally. Multiple cystlike masses and association with an area of gray matter heterotopia have been reported (59,60). Hemorrhage (Fig 3), either within the tumor or within the subarachnoid space, is a rare phenomenon (61–63). Pilocytic astrocytoma may masquerade as a cerebel-



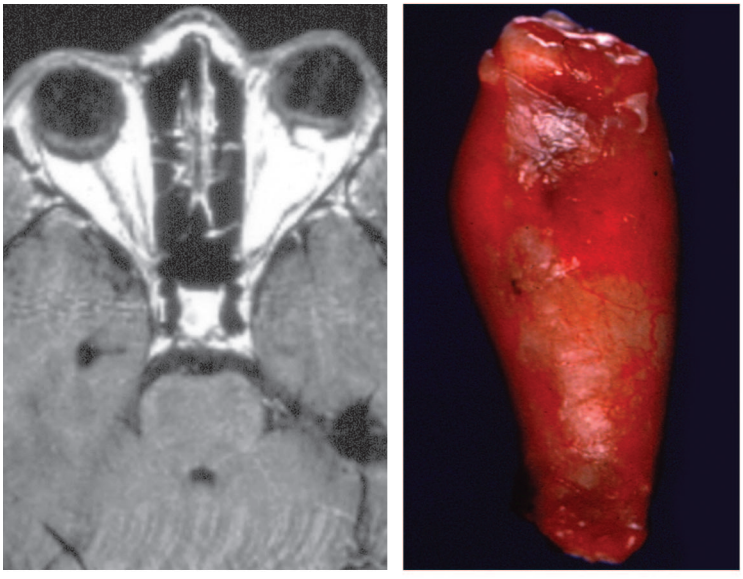


Figure 10. Pilocytic astrocytoma of the optic nerve. **(a)** Coronal T1-weighted image shows enlargement (arrow) of the left optic nerve within the intraconal compartment. **(b)** Axial T1-weighted image reveals characteristic kinking (arrowhead) of the enlarged left optic nerve. **(c)** Axial proton-density-weighted image demonstrates mild hyperintensity of the mass. **(d)** Contrast-enhanced axial T1-weighted image shows intense enhancement of the mass. **(e)** Photograph of the resected optic nerve mass reveals a well-circumscribed sausagelike appearance.

lopontine angle mass that mimics the imaging appearance of a vestibular schwannoma with widening of the internal auditory canal (64,65). When the tumor is located in or near the optic chiasm, a bilobed shape may be seen occasionally (50). The small number of pilomyxoid astrocytomas reported have occurred in the chiasmatic-hypothalamic region, with a tendency to have more intense homogeneous enhancement and homogeneous hyperintensity on T2-weighted images compared with that seen in pilocytic astrocytomas (39).

Reports of MR spectroscopy performed on the soft-tissue portions of pilocytic astrocytomas have documented elevation in the choline (Cho) to *N*-acetylaspartate (NAA) ratio, ranging from 1.80 to 3.40 (compared with 0.53–0.75 for normal cerebellum) (61,66). Elevated Cho/creatine (Cr) and lactate/Cr ratios have also been noted, whereas the NAA/Cr ratio has not been significantly elevated (61,66). There is some controversy regarding whether the Cho resonance in these tumors is truly elevated compared with that in normal tissue (67). The lipid resonance is minimally elevated, in contrast to significant elevation noted in glioblastoma multiforme and metastatic disease (61). Elevated lactate doublet resonance and diminished Cr and NAA peaks were observed in all eight patients of one study that used point-resolved spectroscopy (PRESS) (61). It is clear that this lactate elevation is not related to necrosis, which is a rare histologic feature in pilocytic astrocytomas. Instead, the lactate elevation most likely reflects alterations in mitochondrial metabolism or represents variability in glucose utilization rates among low-grade astrocytomas (61).

Follow-up surveillance imaging of cerebellar pilocytic astrocytoma is recommended at every 3 months for 2 years, followed by every 6 months for an additional 2 years, and then annually after 4 years from the time of treatment (68). A similar follow-up pattern is used to assess changes in patients with pilocytic astrocytoma of the optic pathway (16). Routine contrast-enhanced MR imaging to exclude spinal dissemination is not indicated in patients with a single primary mass and without corroborative symptoms (69). Screening imaging for this tumor in NF1 patients without symptoms is not currently recommended, because the disease rarely progresses and early detection does not currently affect the long-term outcome (17).

Therapy

Just as its clinical manifestations vary according to its different locations, treatment of pilocytic astrocytoma can also vary, depending on where it arises. Surgical resection of cerebellar and cerebral pilocytic astrocytomas is considered the treatment of choice and is generally regarded as curative when a gross total resection is attained (4,6,22,24,54,68,70–72). For lesions in less favorable locations (eg, basal ganglia), stereotactic resection may be used (34). Radiation therapy is strictly avoided, given its risk of causing significant morbidity in children younger than 5 years of age and the absence of clinical proof that it prevents recurrence (71,72).

Resection of the mural nodule, when present, is the key surgical objective, since the surrounding cyst occurs as a simple reactive change in most cases (4). However, neoplastic changes in the cyst wall, even in the absence of findings at gross inspection or at imaging studies, have been documented; these observations have led to considerable debate among neurosurgeons regarding the optimal surgical management of this structure (24). No statistical difference in survival has been noted in patients who have undergone resection of the cyst wall compared with those in which the cyst is left alone (53). Direct neurosurgical evaluation of the extent of resection is surprisingly unreliable, and postoperative contrast-enhanced cross-sectional imaging, preferably MR imaging, is essential for definitive assessment (4,68,73,74).

Patients with optic pathway gliomas and stable symptoms are managed conservatively with clinical and imaging follow-up (15,16,20). In contrast, patients who have progressive symptoms or evidence of hydrocephalus may be treated with surgical resection or radiation therapy, with the former recommended for those whose tumor is located in the optic nerve and the latter for those with an optic chiasm tumor (75,76). Large cystic masses of the chiasm may be amenable to surgical resection, thus allowing radiation therapy to be delayed (15). To avoid the deleterious effects of radiation therapy on the developing brain, chemotherapy is recommended for children younger than 5 years of age (15). Intraarterial delivery of chemotherapy to treat recurrent disease has also been reported (77).

Prognosis, Recurrence, and Dissemination

Overall, the prognosis for patients with a pilocytic astrocytoma is excellent, with a 10-year survival rate of up to 94% and a 20-year survival rate of 79%, which is in marked contrast to the more guarded prognosis seen with the diffuse (WHO grade II) astrocytoma (4,54,78,79). Other factors besides the native biologic behavior of the tumor influence this favorable outcome. The increase in 10-year survival rate (about 90% after 1970, compared with about 70% before 1970) has been attributed to improvements in neurosurgical techniques and equipment (80).

The location of the pilocytic astrocytoma directly affects the prognosis for the patient. For patients with non–optic pathway pilocytic astrocytomas, the most important factors for improved survival appear to be good neurologic status at the time of diagnosis and gross total surgical resection (6,54). Pilocytic astrocytomas arising in the optic pathway or hypothalamus have the least favorable prognosis (75). For patients whose tumor was confined to the optic pathway, the 17-year survival rate was 85%, compared with only 44% who survived 19 years when the tumor extended into the hypothalamus (81). It is believed that many, if not all, of the tumors in this latter group may represent the pilomyxoid subtype (82).

Pilocytic astrocytoma appears to have a more benign biologic behavior when it occurs in patients with NF1 (20). Only a small number of patients with NF1 and an isolated intraorbital glioma showed progression of the tumor 10 years after the time of diagnosis (16). For patients with an optic pathway tumor and NF1, the interval between primary diagnosis and first recurrence tends to be longer, compared with that for patients who do not have NF1 (11,19,76).

In contrast to the generally poor outcome (a 5-year survival of usually only 30%) for patients with an infiltrating brainstem glioma (WHO grade II), those with a dorsally exophytic brainstem pilocytic astrocytoma enjoy a much brighter outlook, with stable neurologic status and long-term survival likely (25,27). Subtotal resection and cerebrospinal fluid diversion are the recom-

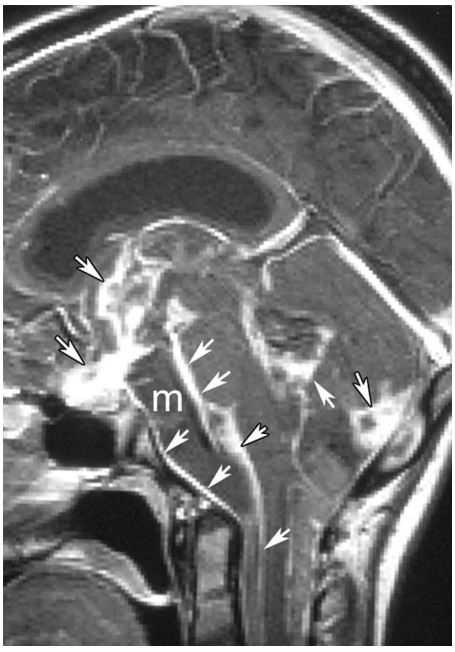


Figure 11. Dissemination from a pilocytic astrocytoma following resection. Contrast-enhanced sagittal T1-weighted image of the brain shows diffuse enhancement (arrows) of the basilar cisternal spaces, with extension into the upper cervical spine. A cystlike mass *(m)* is seen anterior to the brainstem.

mended treatment for these tumors. Recurrence may be treated with a second surgical intervention (25,27).

Although recurrence rates are low if gross total resection has been attained, they are substantially increased when only partial resection is achieved (24). Most recurrences are noted within 4 years of the initial surgery, although recurrent disease has been documented as late as 36 years after initial removal (71,83). Survival rates among patients with partial resection, compared with those for patients with gross total resection, are not statistically different (22,24,68).

Distant dissemination from pilocytic astrocytoma is rare, with a reported prevalence of 2%–12% (Fig 11) (72). The occurrence of distant dissemination appears increased in three settings: *(a)* for those tumors located in the hypothalamus (presumably because of their proximity to the ventricular system or because of the tendency of the pilomyxoid subtype to occur in this region); *(b)* for tumors that have been partially resected; and *(c)* for tumors occurring in patients less than 4 years of age at initial diagnosis (35,36,72). Dissemination in reported cases tends to manifest within 3 years of initial diagnosis (72). Dissemination from a pilocytic astrocytoma, unlike virtually all other glial neoplasms, does not necessarily correlate with a poorer prognosis, and many patients are asymptomatic with long-term survival (36,72,84–86). Reoperation for recurrent disease is preferred, whereas radiation therapy or chemotherapy is recommended for the treatment of multicentric or surgically inaccessible dissemination (24,72).

There are numerous reports of spontaneous regression of pilocytic astrocytomas arising in the optic pathway, diencephalon, and tectal region (75,87–92). Most of these cases have occurred in children with NF1, but spontaneous regression of the tumor may also occur in patients without that phakomatosis and in adults (18,75,91,93). Numerous theories have been proposed for this finding and include postsurgical apoptosis (programmed cell death), host immune reaction, thrombosis or infarction of tumor vessels, alteration of growth kinetics, removal of the offending carcinogen, genetic programming, and hormonal factors (89,94–98).

Summary

The pilocytic astrocytoma has exceptionally slow growth and a usually indolent biologic behavior that directly effects an extraordinarily promising prognosis for patients with the disease. Characterized by its classic "cystic mass with enhancing mural nodule" imaging appearance, the tumor is easily recognizable in most circumstances. MR imaging is essential in facilitating appropriate therapeutic management.

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