

MR of CNS Tumors & Tumor Mimics

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The diagnostic evaluation of brain tumors and other mass lesions once required invasive surgery or indirect diagnostic modalities such as pneumoencephalography and angiography. Direct cross-sectional imaging capabilities now allow for superior detection, localization and characterization of CNS lesions. As imaging equipment continues to advance in sophistication, so too must the capabilities and knowledge of neuroimagers in the realm of neuroanatomy, pathology, and imaging principles.

Although neuroangiography is no longer used as a primary diagnostic tool for evaluating brain lesions, it does serve an adjunctive role for the evaluation of neoplasms, especially if embolization therapy is utilized prior to surgery. Determining the degree of tumor vascularity and the blood supply is best performed with conventional angiography. However the art of tumor localization, based on the angiographic appearance of vascular displacement, is no longer propagated with the same intensity because of the current reliance on more accurate and noninvasive imaging modalities.

Computed tomography (CT) is the initial imaging study performed in many cases of suspected intracranial pathology due to its availability and utility as a diagnostic screening tool. Direct imaging is generally accomplished in the axial or coronal plane, and the tissue contrast provided is based on tissue density. Brain morphology is well depicted on CT images, although not as elegantly as with magnetic resonance (MR) imaging. Because CT is more sensitive for the detection of calcification and bony destruction, it is often employed as an adjunct to MR for the assessment of skeletal changes and tumoral calcification.

Magnetic resonance imaging has supplanted CT as the modality of choice for imaging CNS tumors. The multiplanar capabilities of MRI provide superior localization of brain lesions. In addition, superior contrast resolution is provided via multiple sequences which exploit the various tissue characteristics of normal and pathologic structures. MR is exquisitely sensitive for the detection of both solid and cystic lesions within the brain, and it is excellent for characterizing secondary effects of tumors such as edema, necrosis, hemorrhage and infarction. Multiplanar images provide superior evaluation of mass

effect and associated anatomic distortion.

MR interpretation demands a greater understanding of the imaging principles to optimize image quality and avoid diagnostic pitfalls inherent to this powerful technique. While CT images provide a single "electron density-weighted" sequence, multiple sequences must be interpreted when performing an MR examination. While this greatly expands the capabilities of the technique to characterize tissue, it also demands a higher level of expertise from the neuroimager. Familiarity with principles such as relaxivity, susceptibility and flow phenomenon are essential for accurate MR interpretation. Several technical pitfalls, or artifacts, must be also considered when reading MR studies. Thus, a working knowledge of neuroanatomy, pathology and MR imaging principles (including artifacts) constitute the prerequisites for accurate cranial MR interpretation.

Functional imaging techniques are rapidly moving from a research tools to clinically-proven diagnostic modalities. Positron emission tomography (PET) to assess metabolism is useful for distinguishing hypermetabolic lesions such as some tumors from entities such as radiation necrosis, which may have similar CT and MR features. Functional MR allows for improved temporal resolution, and is already employed to map eloquent cortex prior to surgery on adjacent lesions.

Magnetic resonance spectroscopy allows *in vivo* detection of certain inorganic and organic molecules. Characterization of lesions based on tumor constituents can be effected by MR spectroscopic mapping. Further refinement of this technology and more clinical trials will determine the ubiquity of MR spectroscopy in neurodiagnosis.

Magnetoencephalography is another recent addition to the armamentarium of neuroimagers. Mapping functional brain topography can be utilized to plan the surgical approach in order to avoid eloquent brain such as the motor strip. Simple reliance on morphology in tumor patients is unreliable, as functional anatomy may be displaced by, or even reorganized due to, the offending mass.

In this section, we will review the clinical and imaging features of central nervous system neoplasms and lesions which mimic tumors on imaging studies. The imaging features and keys to differential diagnosis will be

reviewed.

SUPRATENTORIAL NEOPLASMS

Gliomas

Gliomas are the most common primary intracranial neoplasm, representing 40% to 45% of brain tumors. The vast majority of gliomas are derived from astrocytic cell lines. Astrocytomas have been traditionally classified by three- or four-tiered systems based on the degree of histologic malignancy. In increasing order of histologic malignancy, astrocytomas may be categorized as low-grade astrocytoma (LGA), malignant (anaplastic) astrocytoma (AA) and glioblastoma multiforme (GBM). Practical limitations of any grading system result from the usual heterogeneity tumor cell populations, sampling errors, and the possibility of subsequent malignant degeneration. These limitations are all important considerations when evaluating gliomas.

Low-grade astrocytoma

Clinicopathology

This group comprises 15-20% of gliomas. Despite a less fulminant clinical course and more organized histology of this tumor relative to high-grade astrocytomas, a fatal outcome is the rule. Patients may present with focal seizures or neurologic deficits. Symptoms often antedate the diagnosis by more than a year. The five-year survival rate is 20% to 33%. The peak incidence is in the fourth decade for hemispheric tumors, exclusive of cerebellar and brainstem gliomas.

The most common pathologic subtype is the diffuse fibrillary astrocytoma. Microscopically, these tumors consist of cells containing pleomorphic nuclei of variable shape and size. Astrocytomas tumors lack a well-defined interface with the adjacent parenchyma. Similar to oligodendrogliomas, lobar localization within the brain is proportional to the white matter volume. Thus, they are most frequently located in the frontal lobes, followed by the parietal, temporal and occipital lobes. Posterior fossa astrocytomas are uncommon in adults, whereas in children, brainstem and cerebellar astrocytomas are the most common intracranial tumor in some age groups.

Imaging

CT images of low-grade astrocytomas reveal a low density lesion. They are most often localized to the cerebral hemispheres, usually within the cortex or subcortical white matter. Perifocal edema is sparse. Enhancement is variable; a majority of low-grade astrocytomas do not enhance. In approximately 40% there is faint, patchy enhancement of at least a portion of the lesion. Calcifications are detected in 15% to 20% of lesions, and are less common in the more aggressive astrocytomas. Occasionally, the tumors are predominately cystic, a feature that is typical of childhood pilocytic astrocytomas.

MR images reveal homogeneously increased signal on long-TR images and intermediate to low signal on the T1-weighted sequences. Local mass effect varies with lesion size, and perifocal edema is usually minimal. Cyst formation, hemorrhage and necrosis are not common features of low-grade astrocytomas, although hemorrhage and cystic foci are occasionally present. Enhancement is mild and irregular when present. The degree of enhancement demonstrated by a fibrillary astrocytoma correlates positively with histologic malignancy. An interval increase in the intensity and amount of enhancement within a tumor indicates a more aggressive population of cells, and may reflect progression to anaplastic astrocytoma or GBM.

The differential diagnosis for low-grade astrocytomas depends on location and imaging appearance. Other primary brain neoplasms should be considered. High grade tumors and metastases are usually distinguished by more intense enhancement, a greater tendency to be heterogeneous, and an association with more pronounced perifocal edema. In addition, magnetic susceptibility effect, best observed with gradient-echo sequences, portends a higher tumor grade of glioma. A cortical LGA may appear similar to an infarct. Cerebritis is occasionally a diagnostic consideration.

Anaplastic (Malignant) Astrocytoma

Clinicopathology

Anaplastic astrocytomas are intermediate in degree of histologic malignancy between low-grade astrocytomas and glioblastoma multiforme. They represent 30-35% of gliomas. Presentation is often similar to low-grade astrocytomas, but a shorter interval to diagnosis reflects the more aggressive nature of this lesion. Generally, AA's affect a slightly older population than their lower-

grade counterpart, with a peak incidence in the fifth decade of life. Prognosis is significantly worse, with a mean survival of approximately two years following diagnosis.

Microscopically, anaplastic astrocytomas demonstrate high cellular density and more malignant features than LGA, such as greater nuclear pleomorphism and mitotic figures. Cells with more abundant cytoplasm are occasionally present. The so called "gemistocytic" subtype is diagnosed when a significant number of these plump cells are present. The tumors lack the vascular proliferation and necrosis which characterize the more malignant glioblastoma multiforme, however. "Dedifferentiation" of these tumors to glioblastoma most likely occurs, and the spectrum of malignant features ranges from sparse mitotic figures to very aggressive lesions, which approach classification as a GBM.

Imaging

On CT images, anaplastic astrocytomas demonstrate more heterogeneity than low grade astrocytomas due to cyst formation and hemorrhage. Nonetheless, the lesions usually appear well-defined. Moderate mass effect and edema are characteristic. The lesions are generally low density relative to brain parenchyma.

T1- and T2-prolongation characterize the tumors on MR, frequently with signal characteristics indicating hemorrhage and focal cystic degeneration. Calcifications are not generally seen with anaplastic astrocytomas. It is uncertain whether those lesions which do contain calcifications arose *de novo*, or represent a calcified LGA which degenerated into an AA. Enhancement is usually focal and irregular, most likely reflecting the heterogeneity of the tumor cell population. The more malignant components show a higher propensity to enhance.

The differential diagnosis for anaplastic astrocytomas includes other primary brain neoplasms and metastatic tumors, depending largely on patient demographics. Cortical tumors occasionally have a similar appearance to infarcts. Cerebritis or early abscess formation may also have a similar appearance.

Glioblastoma multiforme

Clinicopathology

Glioblastoma multiforme (GBM) is the most malignant of glial tumors. Unfortunately, it is also the most common, comprising approximately 50% of gliomas and 20% of all intracranial neoplasms. The tumors often

present like lower grade astrocytomas, but a more rapid initial appearance of symptoms may mimic cerebrovascular disease. The peak incidence of this lesion is in the sixth decade. Prognosis is extremely poor, with a 6-month median survival a 6% five-year survival rate following diagnosis.

Pathologically, extensive necrosis is the Hallmark feature which distinguishes GBM from lower-grade astrocytomas. Vascular endothelial proliferation appears in the adjacent brain and even within the meningeal structures. Cells with bizarre nuclei and frequent mitotic figures invade the adjacent parenchyma, leptomeninges, and dura. These malignant cells may extend along white matter fiber tracts, including the corpus callosum. At biopsy, malignant cells may be found beyond the boundaries of imaging abnormalities, centrifugal to both the margin of contrast enhancement and T2-prolongation on MR. Intratumoral hemorrhage is frequent, and hemosiderin deposition may accompany subacute blood degradation products. Calcifications are not a feature glioblastoma multiforme. Rarely, sarcomatous degeneration of the adjacent vascular elements occurs, resulting in a gliosarcoma. This compound tumor is indistinguishable from a GBM based on imaging studies, but should be suspected when rare extracranial metastases occur.

Imaging

Imaging studies demonstrate extensive edema and significant mass effect associated with GBM. The heterogeneous appearance reflects the pathologic features described above, with regions of necrosis, hemorrhage, and cystic degeneration. The tumor is predominately low density on CT. Hyperdense areas within the tumor represent more recent hemorrhage, whereas low attenuation foci indicate cystic change, old hemorrhage and characteristic necrosis. The heterogeneous appearance is augmented following contrast administration. Enhancement is irregular, usually in a ring- or garland-like configuration due to the extensive central necrosis.

On MR images, tumoral necrosis and hemorrhagic residua are well-characterized, and contribute to the characteristic heterogeneous appearance. The extent of perifocal edema is better delineated than with CT, but it is important to bear in mind that even MR signal abnormalities do not reliably reflect the perimeter of tumor cells. Imaging-pathologic correlation studies have shown tumor cells well beyond the margins of signal abnormality on MR. This phenomenon may explain some cases of "multicentric" glioblastomas that are described in as many as 5% of cases.

Enhancement is intense and irregular. A thick, irregular peripheral pattern is characteristic, often described as "garland-like". Other common, albeit less characteristic, enhancement patterns include more extensive, irregular enhancement and smooth rim-enhancement.

The differential diagnosis for glioblastoma includes metastatic disease and, in the appropriate clinical setting, radiation necrosis. Distinguishing recurrent tumor from radiation necrosis can be problematic from a diagnostic and therapeutic standpoint. If the tumor has a simple rim-enhancing appearance, the differential diagnosis is more extensive.

Gliomatosis Cerebri

Clinicopathology

Gliomatosis cerebri (diffuse cerebral glioblastosis) demonstrates a variable clinical course but in general has a poor prognosis. Such patients most often present with personality changes and mental deterioration, but the presentation is variable and may include seizures, evidence of increasing intracranial pressure, or focal neurologic signs. Gliomatosis cerebri tends to be infiltrative rather than destructive in nature, thus the patient's neurologic deficits may be mild relative to the extent of parenchymal involvement at the time of diagnosis. Peak incidence for this rare neoplasm is in the third and fourth decades of life, but gliomatosis cerebri is seen in all age groups. Initial response to radiation therapy is often favorable, but the disease is usually refractory to treatment upon recurrence of symptoms.

Pathologically, gliomatosis cerebri is essentially a diffuse, confluent glioma. There is neoplastic overgrowth of glial elements which tend to infiltrate and expand the white matter over a large portion of the brain. Grossly, there may be diffuse enlargement of the cerebrum, cerebellum, white matter tracts and/or the brainstem. Commonly, there is involvement of the midline structures such as the corpus callosum, fornices, and anterior optic pathway. A diffuse array of undifferentiated astrocytes is demonstrated microscopically. There is generally preservation of the neuronal architecture, and demyelination which is proportional to the extent of involvement. At the periphery of the lesion, the tumor cells characteristically assume an elongated configuration.

Imaging

Involvement of the midline structures is characteristic, and both hemispheres are frequently involved. The lesion may be subtle

on CT, and there are several reports of occult lesions on this modality. It may manifest as ventricular effacement, decreased attenuation of the involved parenchyma or regional expansion. Thickening of the hemispheric white matter and commissural tracts, including the corpus callosum, fornices and anterior commissure, is characteristic. The septum pellucidum may also be involved. Enhancement is rarely demonstrated on CT.

MR of this rare neoplasm demonstrates ill-defined, high signal intensity on long TR images generally involving a large portion of the brain. Involvement is most pronounced in the paramedian and midline structures. The short-TR images show a corresponding decrease in signal, or isointensity with adjacent brain. Hemorrhage, calcification and enhancement are not characteristic features of this lesion, although enhancement has been reported in a patchy or leptomeningeal pattern.

Oligodendroglioma

Clinicopathology

Oligodendrogliomas constitute 5% to 7% of intracranial neoplasms. They primarily affect adults, with a peak incidence in the fourth to fifth decade. Because of the indolent nature of the tumor, there is frequently a long latent period between the onset of symptoms and diagnosis. With an average 50% to 60% five-year survival rate, many patients survive more than a decade following diagnosis.

Histologically, oligodendrogliomas are highly cellular tumors, which may result in spurious overgrading with respect to histologic malignancy. Imaging findings are thus an important adjunct to the pathological assessment. Patternless sheets of oligodendrocytes with uniformly round nuclei are often accompanied by a reticular network of small capillary structures. Focal necrosis and hemorrhage are common. Of all glial tumors, oligodendrogliomas demonstrate the greatest propensity to calcify. The calcifications associated with the tumors represent both vascular calcifications and calcospherites within the tumor and adjacent parenchyma. These unencapsulated lesions generally display a sharp interface with adjacent white matter but are highly infiltrating at the cortical or gray matter interface.

One-third to one-half of oligodendrogliomas are mixed cell forms, and may harbor astrocytic and/or ependymal elements in addition to oligodendroglial cells. A high degree of pleomorphism and other aggressive features portend a worse prognosis. The more

aggressive oligodendrogliomas tend to display a higher percentage of astrocytic attributes. Because such high-grade tumors are often reported as glioblastomas, the true incidence of malignant oligodendrogliomas is likely under-reported.

Imaging

Oligodendrogliomas occur most commonly in the frontal lobe, followed by the parietal, temporal and occipital lobes; a distribution which is proportional to the relative volume of white matter. Hemispheric lesions tend to be superficial, and these long-standing intraaxial tumors not infrequently (approximately 20%) cause calvarial erosion. Less common locations include the deep hemispheres, within the cerebellum and the spinal cord.

On CT, oligodendrogliomas are often heterogeneous, and iso- to hypodense. Calcifications are visualized in up to 90% of tumors, although most series report an incidence of 50 to 70%. Approximately 20% display focal hemorrhage, with a similar percentage displaying cystic components. There is generally a paucity of perifocal edema. Enhancement is variable, and is present in approximately 50% of cases.

MR images demonstrate a heterogeneous appearance due to the variable components cited above. T1-weighted images demonstrate a mixed hypointense signal pattern. On T2-weighted images, the lesions are primarily hyperintense. Cystic and hemorrhagic components are well characterized by these two sequences. The calvarial changes, when present, are less well seen than with CT. The solid components of the tumor may show mild to moderate enhancement, further distinguishing them from the cystic components. In the pediatric and adolescent population, the tumors demonstrate a lower frequency of enhancement, calcifications and perifocal edema.

Differential diagnosis includes other glial neoplasms: glioblastoma, astrocytoma, and ganglioglioma. When the lesion is intraventricular, central neurocytoma may be indistinguishable by light microscopy. In fact, the similar imaging and histologic appearance of these lesions is probably accounts for several cases of intraventricular oligodendrogliomas diagnosed prior to the discovery of immunohistochemical and ultrastructural differences between the two tumors. The dysembryoplastic neuroepithelial tumor is a cortical tumor which may have a similar histologic and imaging appearance. Finally, a single metastatic lesion will occasionally mimic oligodendroglioma, although there is

generally more edema and intense enhancement with metastatic disease.

Ganglioglioma

Clinicopathology

Ganglioglioma is a slow-growing tumor with an excellent clinical prognosis, although it is worse for deep or midline lesions, despite a relatively benign histology. Gangliogliomas represent approximately 1% of intracranial neoplasms and 3% to 7% of pediatric brain tumors. This tumor has a peak incidence in the second decade, and although generally considered a tumor of childhood and in young adults, up to 40% are diagnosed in patients over 30 years of age. Most of the lesions are hemispheric in location, characteristically in the temporal lobe. Gangliogliomas may also be situated at the floor of the third ventricle (suprasellar), within the cerebellum, in the brain stem and even within the spinal cord.

Pathologically, gangliogliomas are comprised of a mixture of glial cells (primarily astrocytic) and differentiated neural elements. The astrocytic elements may be fibrillary or pilocytic. When the neuronal component is predominant, the lesions are appropriately termed *ganglioneuromas*. A majority of lesions contain cystic components, and occasionally the lesions are primarily cystic, especially in the posterior fossa. Approximately one-third contain calcifications. Mineralization may occur within the wall of the tumor vessels or as organization granules within the brain parenchyma. Malignant transformation is rarely associated with these relatively benign neoplasms, but some contain less mature ganglion cells and neuroblasts. Such tumors are categorized as *ganglioneuroblastomas*.

Imaging

CT images demonstrate most gangliogliomas to be predominantly solid. They may be hypo-, iso- or hyperdense relative to normal brain parenchyma. Approximately 50% of the lesions enhance; with an even greater percentage in some series. A majority of lesions have a partially cystic appearance. However, the actual contents of the "cystic" foci often prove to be solid at surgery. Calvarial erosion may be seen with peripheral lesions, an uncommon secondary finding described in approximately 5% of cases. There is generally a paucity of edema, and irregular enhancement is seen in approximately half of cases. Occasionally, the lesion may be occult on CT images, and this has been reported on MR as well.

On MR images gangliogliomas are

heterogeneous and generally display T1 and T2 prolongation. Occasionally, T1 shortening results in hyperintensity on the short TR images. Enhancement is usually irregular, and is demonstrated in greater than half of cases. There is usually minimal mass effect or perifocal edema. While focal calcifications are less well seen than with CT, the extent of tumor is better delineated with MR. This is important from a clinical standpoint, as total excision of the lesion is the treatment of choice; such patients can be spared radiotherapy if complete excision is accomplished and they remain free of recurrence.

Differential diagnosis includes other glial neoplasms such as low grade astrocytoma and oligodendroglioma. If the lesion appears cystic, consider juvenile pilocytic astrocytoma (which rarely calcifies) and other cystic glial neoplasms. A dysembryoplastic neuroepithelial tumor should also be considered, especially in a young patient with a history of seizures. Intracranial cysts may be confused for cystic gangliogliomas on CT, but the two are easily distinguished on MR.

Dysembryoplastic neuroepithelial tumor

Clinicopathology

Dysembryoplastic neuroepithelial tumors (DNET) are a recently described tumor which primarily affects young patients. Primarily located peripherally within the cerebral hemispheres, they most often present with a long history of partial complex seizures. Prognosis is excellent, although large series to assess survival statistics are not available.

Pathologically, the diverse cellular composition includes neuronal elements, astrocytes and oligodendrocytes within a mucinous matrix characterize the DNET. Minimal neuronal atypia may cause these to superficially resemble mixed oligodendrogliomas by light microscopy. A multinodular morphology, often with microcystic degeneration, further typifies the lesion. Cellular atypia is sparse, if present. Adjacent cortical dysplasia is characteristic.

Imaging

On CT images a hypodense cortical mass is well demarcated, and a vast majority are found within the temporal or frontal lobes. The lesion may approximate CSF attenuation. At surgery, however, the cystic-appearing component is often found to be solid. Enhancement is usually absent, but faint, irregular enhancement is reported. Like oligodendrogliomas, a small percentage of cases show adjacent calvarial erosion, reflecting the long-standing nature

of this indolent lesion.

MR images demonstrate a well-defined cortical mass with T1 and T2 prolongation. A "psuedocystic" appearance, with hyperintensity on T2-weighted images and an isointense appearance on intermediate-weighted scans, may be demonstrated. True cystic components are occasionally present. Other lesions are hyperintense on intermediate-weighted images. Faint enhancement and calcification are present in a minority of these tumors.

Other diagnostic considerations include ganglioglioma, oligodendroglioma, mixed glioma and cystic astrocytoma. This lesion should be considered in patients with imaging features described above, as such patients may be spared radiation and other aggressive therapeutic regimens.

Primary CNS Lymphoma

Clinicopathology

Primary central nervous system lymphoma now accounts for approximately 2% of intracranial neoplasms. There has been a significant increase in the number of documented cases in both immunocompetent and immunocompromised patients, with the AIDS population accounting for a significant proportion of this increase.

Clinical presentation is highly variable, depending on location of the lesion and degree of mass effect. Patients may present with manifestations of increased intracranial pressure, seizures, or focal deficits. Peak incidence of primary CNS lymphoma is in the sixth decade with males outnumbering females by at least 2:1 in the immunocompetent population. With immunocompromised patients, the age distribution is skewed to younger adults, and even children with AIDS may harbor primary CNS lymphoma. A rare case of the disease in an immunocompetent child has been reported. It is an aggressive neoplasia, with a grim prognosis. Median survival is less than 2 years following diagnosis.

Histologically, densely cellular aggregates of lymphoid cells are characteristically seen in a concentric perivascular pattern. Non-Hodgkin's lymphomas seen within the brain are histologically equivalent to the systemic lymphomas and may be classified according to the Working Formulation for the Classification of Lymphomas. Most are intermediate to high-grade B-cell lymphomas; T-cell lymphomas are rare but are being recognized with increasing frequency. Extensive central necrosis is characteristic of CNS lymphomas in AIDS patients, but is uncommon in the

immunocompetent patient. Calcification and hemorrhage prior to therapy are rare.

Criteria for the diagnosis of primary CNS lymphoma includes no evidence of disease outside the brain, spinal cord (intradural), leptomeninges or intraocular structures. Fewer than 10% of CNS lymphomas are secondary (metastatic).

Imaging

Brain lesions are multiple in approximately half of cases. There is a higher incidence of multiplicity in AIDS patients. Classically, CNS lymphoma has been described as a large, sharply demarcated tumor which is iso- to hyperdense relative to brain parenchyma. The lesions are situated in the deep or central structures, including the basal ganglia, corpus callosum and periventricular white matter. It should be noted, however, that up to half of the lesions are located within the cerebral hemispheres. The degree of mass effect and perifocal edema is variable. Other patterns include diffuse subependymal spread, infiltrating white matter lesions or a gyral distribution within the cerebral cortex. Enhancement is usually homogeneous and intense following iodinated contrast administration. In AIDS patients, there is a higher incidence of central necrosis with concomitant irregular or ring-like enhancement pattern is more characteristically seen.

On MR images, the lesions are iso- to hypointense relative to brain parenchyma on T1-weighted images. Long TR images show variable signal intensity, ranging from hypo- to hyperintense to gray matter. Because most CNS tumors demonstrate T2 prolongation, the iso- to hypointense appearance on the long TR sequences should prompt consideration of CNS lymphoma. Despite this, tissue is essential for the definitive diagnosis because treatment varies greatly for the lesions which may have a similar imaging appearance.

Differential diagnosis depends on the location and morphology of the tumor. If the lesion is peripheral, the hyperdense appearance on CT may mimic a meningioma. Hemispheric and deep lesions may mimic metastases, primary glial neoplasms, and infarction, depending on the MR and CT characteristics. For example, metastatic small cell and germ cell tumors may also be iso- to hypointense on long-TR images. If the lesion has central necrosis and a rim-like enhancement pattern, abscess must also be considered. A frequent dilemma in AIDS patients with an intracranial mass lesion is distinguishing CNS lymphoma from toxoplasmosis, the other common enhancing brain lesion in

such patients. Imaging features which favor lymphoma include subependymal spread, hyper-attenuation on CT and iso- to hypointensity on long TR images. Such findings may warrant a needle biopsy rather than a trial of empirical toxoplasmosis therapy in these patients.

Choroid plexus papilloma

Clinicopathology

Choroid plexus papilloma it typically encountered in children, where it is generally supratentorial in location. In adults, posterior fossa locations are most common, typically within the fourth ventricle or cerebellopontine angle cistern. This rare tumor accounts for approximately 0.5% of intracranial neoplasms overall, and 3% to 6% of pediatric brain tumors. A majority of the lesions present within the first decade, less commonly in the second and third decades. Choroid plexus papillomas presenting after the third decade are very rare. In children, the most common location is within the lateral ventricles. A left-sided predominance has been described; however limited reports describe a right-sided predominance and statistical variance may account for the laterality cited in these reports. In the first decade, the lateral ventricle is most common; after the first decade, the fourth ventricle is the most common site for choroid plexus papillomas. Less commonly, they occur in the third ventricle. In children, two-thirds to 80% are seen in lateral ventricle, 16% to 20% in the fourth ventricle, and fewer than 5% in the third ventricle. Patients usually present with manifestations of hydrocephalus. In the pediatric population, this may include increasing head size, lethargy, and depressed mental status and seizures. Prognosis for the postoperative patient, if complete resection is effected, is excellent. If subarachnoid seeding or brain parenchyma involvement occurs, prognosis is negatively impacted.

Histologically, choroid plexus papillomas replicate normal choroid plexus with a frond-like pattern of growth in a single epithelial layer supported by an underlying vascular stroma. Despite the ultrastructural similarity, a tendency toward columnar epithelial cells and a more compact cellular matrix provide clues for a diagnosis of choroid plexus papilloma. The hallmark of this lesion is hydrocephalus, which is usually severe and may persist after shunting. The mechanism is generally accepted to be excessive CSF production: up to five times greater than normal. The result is prominent ventricles and extraaxial CSF spaces. The involved ventricle may be asymmetrically

enlarged relative to the remaining ventricles. Other mechanisms that have been cited as an underlying etiology for hydrocephalus include an elevated protein content due to the tumor, depressed CSF absorption by the arachnoid granulation secondary to recurrent hemorrhage, ventricular obstruction, diffuse meningeal spread of the tumor, and adhesions obstructing the outlet foramina of the fourth ventricle. Even small choroid plexus papillomas, too small to produce obstruction of the ventricle, may result in significant hydrocephalus. The diagnosis should thus be suspected when such an appearance is encountered. A fibrovascular pedicle attaches the tumor to the parent choroid plexus. This allows for motility of the tumor within the ventricles. The pliable lesion may even extend through the outlet foramina of the involved ventricles, a characteristic feature when it is encountered.

Imaging

CT images reveal a lobulated iso- to hyperdense mass within the ventricle. In children, the lesions show homogeneous attenuation as a rule. In adults, heterogeneous appearance due to central cystic degeneration is not uncommon. Such regions show low attenuation relative to the adjacent remainder of the iso- to hyperdense mass. Invasion of the adjacent brain parenchyma is uncommon but may occur as a late manifestation if resection is not performed. Following contrast administration, there is intense enhancement of the vascular lesions. Calcifications within the lesion range from finely stippled to coarse in nature. Calcifications are more common in adult tumors, but have been reported in up to 80% of pediatric series. Overall, calcifications occurred in approximately 24%. Hemorrhage is less commonly identified.

With MR imaging, choroid plexus papillomas are seen as well marginated, lobular lesions within the ventricle. The choroid plexus is engulfed by the tumor rather than displaced. T1-weighted images typically show an isointense lesion, whereas on long TR images tumors range from iso- to hyperintense. Curvilinear signal voids resulting from tumor vascularity, calcifications and/or hemorrhagic residua may also be noted. As with CT, intense enhancement is demonstrated following the administration of intravenous contrast agent. MRI is very sensitive for the demonstration of periventricular interstitial edema which frequently accompanies the pronounced hydrocephalus associated with these tumors. Cross-sectional imaging modalities allow for an early diagnosis in the appropriate clinical

setting. Diagnosis prior to brain invasion or compromise of the brain parenchyma by hydrocephalus or hemorrhage allows for favorable outcome. The lesions may recur if not entirely resected, and there is also the possibility of subarachnoid seeding prior to tumor resection. Thus, there should be a low threshold for obtaining postoperative enhanced imaging studies in such patients.

Choroid plexus carcinoma

Clinicopathology

Malignant degeneration of choroid plexus tumors may occur. Approximately 10% to 20% of choroid plexus tumors overall are malignant, are associated with a much worse prognosis. Carcinomatous degeneration is most common in the lateral ventricle and the prognosis is much worse when malignant features are present. Clinically, the hydrocephalus tends to be less severe than with choroid plexus papillomas. Histologically, an infiltrative growth pattern with a dense cellular matrix and an atypical (pseudostratified columnar) epithelial matrix is demonstrated. Aggressive features not seen in papillomas, such as mitoses, necrosis, and poor margination of the lesion, are demonstrated. Irregular growth of tumor neovascularity is also identified microscopically.

Imaging

CT and MR images demonstrate a heterogeneous lesion which invades the adjacent brain parenchyma. In children, the heterogeneity is often indicative of malignant degeneration; however in adults lack of homogeneity is frequently seen in benign choroid plexus papillomas. More pronounced cerebral edema and mass effect are demonstrated than are seen with choroid plexus papillomas.

Differential diagnosis for choroid plexus tumors includes papillary ependymoma, which is most commonly in the fourth ventricle in children. Medulloblastomas tend to be centered within the vermis in children, with a greater tendency to involve the cerebellar hemispheres in adults. Rarely, degenerative changes in choroid plexus can mimic tumor; however hydrocephalus is not a feature when this is encountered. A rare intraventricular astrocytoma or a meningioma can also occur. The latter is generally seen in young to middle-aged adults, however. Intraventricular hematoma and colloid cysts should be distinguished by their imaging characteristics and location, respectively. Rarely, intraventricular metastases are reported, however clinical history facilitates the diagnosis.

Metastatic tumors

Clinicopathology

Secondary neoplasms involving the brain are relatively common, accounting for at least 35% of intracranial neoplasms. The reported incidence is increasing, likely due to improved survival of cancer patients as well as increased detection rates which accompany advancements in diagnostic imaging. Despite such improvements however, 10% to 15% of brain metastases develop from unknown primary tumors. Patients may be asymptomatic at the time of diagnosis, or may present with seizures, increased intracranial pressure, focal neurologic deficits, mental status changes or obtundation. Peak incidence of brain metastases parallels the peak incidence of the extra CNS tumors, which are most commonly encountered in the fifth through the seventh decades. Survival rates are unfortunately low and vary with the primary tumor site and degree of extra CNS pathology.

Microscopically, metastatic tumors often provide clues regarding the source of the neoplasm, because the metastasis generally recapitulates the histology of the primary tumor. It is not uncommon, however, for the lesion to mimic a primary glial neoplasm or to be otherwise indeterminate with respect to site of origin. Secondary tumors generally demonstrate sharper demarcation from the adjacent brain parenchyma than that seen with primary brain neoplasms.

Pulmonary neoplasms are the most common tumor to metastasize to the brain, followed by breast carcinoma and melanoma. Combined, these tumors constitute 70% to 80% of brain metastases. Eighty to ninety percent of such metastases are supratentorial. Approximately 10% of intracranial metastases result from gastrointestinal and genitourinary tract neoplasms. Almost half of these metastases occur in the posterior fossa, making the overall ratio of supra- to infratentorial metastases approximately 4:1.

Imaging

The imaging appearance of metastatic lesions is highly variable, depending upon tumor type, the presence of hemorrhage, cystic change and necrosis. Edema is usually extensive due to lack of a blood brain barrier (BBB). Hemorrhage is seen in approximately 20% of metastatic lesions, most commonly in malignant melanoma, lung, breast and renal cell carcinoma. Although multiplicity is the hallmark of metastatic disease, almost half of patients have a solitary metastases at the time of

diagnosis in some series. Most report a 60-70% incidence of multiplicity, however. Lesions occur most commonly in the middle cerebral artery distribution, concentrated in the watershed zones and at the gray/white matter junction. Although a vast majority of lesions occur in the cerebrum, posterior fossa lesions are seen in 15% to 20%, with rare occurrences in the brain stem, pineal region, and parasellar regions.

On CT images, metastatic lesions may be hypo-, iso- or hyperdense. Moderate to severe perifocal edema is present. Calcifications are rare prior to therapy. Following contrast administration, intense enhancement is noted, which may be solid or rim-like in distribution.

MR images better characterize the variable tumor constituents. Hemorrhage and other paramagnetic substances, necrosis, and other pathologic features are well delineated. Gadolinium-enhanced, T1-weighted images are the most sensitive sequence for the detection of metastases, and may be positive even prior to the appearance of abnormalities on long TR images if sufficient perifocal edema or mass effect have not yet developed. This is especially true if the lesions are subarachnoid, rather than parenchymal. Double- and triple-dose enhanced imaging (exceeding the standard 0.1 mmole/kg) shows even higher sensitivity for the detection of subtle metastatic foci. Magnetization transfer contrast imaging enhances the target-to-background ratio without the addition of additional contrast media.

PEDIATRIC INFRA-TENTORIAL NEOPLASMS

Between the second year of life and the middle of the second decade, a majority of pediatric brain tumors are located within the posterior fossa (65-75%). The most common lesions are the cerebellar astrocytoma and medulloblastoma (PNET), followed by ependymoma and brainstem glioma. During the first year or two of life, and after adolescence, supratentorial lesions are most common. In the pediatric population as a whole, intracranial tumors are equally distributed between supratentorial and posterior fossa tumors.

Cerebellar Astrocytoma

Clinicopathology

Cerebellar astrocytomas present most commonly during the first decade of life. Prognosis is excellent, with a greater than 90% 20-year survival rate. There is no

apparent gender predilection. Although these tumors are relatively indolent, late recurrence is not uncommon, sometimes several years after apparent eradication of the tumor. Pathologically, this well-circumscribed mass is usually partially cystic. Numerous microcysts, imparting a "gelatin-like" consistency, may also be encountered. The vast majority of pediatric cerebellar gliomas are juvenile pilocytic astrocytomas (JPA). A minority are infiltrating fibrillary astrocytomas, which may be low grade or anaplastic. Fibrillary astrocytomas have a less favorable prognosis and tend to present in the second decade of life. The histologic features of pilocytic and fibrillary astrocytomas readily distinguish them from the other common pediatric tumors found within the posterior fossa.

Imaging

Approximately half of cerebellar astrocytomas display the characteristic imaging appearance of a cystic lesion. The solid mural nodule shows intense enhancement, delineating it from the proteinaceous fluid within the cyst. The solid component is not as hypointense as the fluid on T1-weighted images, nor as hyperintense on long TR sequences. Some of the tumors are predominately solid, with central cavitation. Enhancement in these lesions is variable, as the solid tumor components may enhance. The areas of necrosis are appreciated as nonenhancing areas of T1- and T2-prolongation. A minority of cerebellar astrocytomas are completely solid in appearance. Most lesions are located in the midline, but up to 30% are located at least partially within the hemispheres. The juxtaventricular lesions efface the 4th ventricle, producing obstructive hydrocephalus. Calcification is seen in up to 20% of lesions, while intratumoral hemorrhage is rare.

Medulloblastoma

Clinicopathology

Medulloblastoma is the second most common posterior fossa tumor in children, representing 15% to 20% of intracranial neoplasms in the pediatric population. In some series, it is the most common pediatric infratentorial tumor. Peak incidence is in the first decade; however there is a second demographic peak early in the third decade. In fact, a full 25% to 30% of these so-called pediatric neoplasms are found in adults. Male victims outnumber females. Medulloblastomas are seen with increased frequency in patients with Turcot's syndrome, ataxia telangiectasia and basal cell nevus syndrome. This aggressive posterior fossa

neoplasm has a propensity for CNS dissemination via the subarachnoid space.

Pathologically, medulloblastomas are generally considered to arise from the pluripotential cells which originate in the germinative zone of the posterior medullary velum. In normal cerebellar development, they migrate superolaterally to form the external granular layer of the cerebellar hemispheres. Although medulloblastomas are midline tumors in the majority of cases, they may also occur lateral to the vermis within the cerebellar hemispheres. An increasing propensity to do so in older patients may relate to the temporal aspects of the tumor's pathogenesis, given the developmental sequence described above. The midline or vermian tumors may also extend secondarily into the cerebellar hemispheres. Histologically, the densely cellular tumor contains a vascular stroma.

Imaging

On imaging studies, medulloblastomas are generally well-defined, homogeneous, midline lesions. They are hyperdense on CT and show variable enhancement following contrast administration. In children, cystic foci and necrosis are uncommon. Hemorrhage and calcification are seen in a minority of cases. Tumors generally demonstrate T1 prolongation and are iso- to hypointense on T1-weighted images. On long TR images, the signal characteristics are variable. There is generally less T2 prolongation than is demonstrated by other brain tumors. Thus, the lesion may be iso-, hyper- or hypointense relative to brain parenchyma.

In young adults, the imaging features are more variable. Differences in the pathologic features such as a higher prevalence of necrosis, cystic degeneration, and desmoplastic variants provide an explanation for the variability. Lesions in adults tend to be more heterogeneous in appearance, with cystic foci accompanying the solid component of the tumor. Enhancement is less intense and tends to be more heterogeneous than those demonstrated in their pediatric counterparts. In addition, approximately half of medulloblastomas in adulthood are laterally situated within the cerebellar hemispheres. A broad-based interface with the tentorial or dural surface may even mimic an extraaxial neoplasm.

Ependymoma

Clinicopathology

Ependymomas represent approximately 5% of intracranial neoplasms overall, and 10% of pediatric intracranial tumors. The peak incidence of ependymomas occurs in the first decade, with an adult population peak in the 4th decade. Certain series of posterior fossa ependymomas in children show a peak age at 5 years of age. Two-thirds of ependymomas arise in the posterior fossa, primarily within the fourth ventricle. The second most common location is within the lateral ventricles, with a slight left-sided predominance. Adult tumors tend to be supratentorial and may be extraventricular, while the posterior fossa ependymomas occur most commonly in children. The reported prognosis for these lesions varies widely. Five-year survival rates range from 14% to 70%. An older age at diagnosis and total resection have both been statistically correlated with improved prognosis.

Histologically, approximately three-fourths of ependymomas are low-grade malignancies. Perivascular pseudorosettes are

characteristically seen. Ependymomas may be mixed tumors, and not uncommonly contain other glial elements such as astrocytic and oligodendrocytic cell lines. Various astrocytic and oligodendrocytic cell lines may be present. This histologic mélange may initially impede attempts at accurate pathologic diagnosis. Grossly, the intraventricular tumors tend to extend through into the outlet foramina, explaining their occasional appearance within the cerebellopontine angles and foramen magnum.

Imaging

CT images demonstrate a midline tumor, most commonly within an expanded fourth ventricle. Hydrocephalus is virtually always present at the time of diagnosis. The lesions tend to be solid and are often hypo- to isodense on short TR images, and hyperintense on long TR images. The tumors may be heterogeneous, which helps distinguish them from medulloblastomas. Occasionally, a hyperdense appearance will mimic a medulloblastoma. Approximately half of the lesions demonstrate calcifications, which increases the specificity of the CT appearance. Enhancement is usually intense and may be either uniform or heterogeneous in nature. Hemorrhage is a common feature of intracranial ependymomas, unlike the other posterior fossa tumors described.

MR images demonstrate an iso- to hypointense lesion with respect to white matter on T1-weighted images. On long TR images, T2 prolongation manifests as high signal intensity relative to brain parenchyma. Cystic changes, more common in the supratentorial lesions, are well depicted on MR images. Focal calcifications are not as well identified as on CT. Hemorrhage is demonstrated within ependymomas in up to 13% of lesions. The various stages of hemorrhage in evolution are well depicted on MR. The multiplanar capabilities of MR are also well suited for demonstrating the propensity of ependymomas to spread into the outlet foramina and aqueduct. Intense enhancement is seen in over 90% of lesions.

Brainstem glioma

Clinicopathology

Astrocytomas arising within the brainstem usually present during the first decade of life. The pons is the most common location, followed in frequency by the midbrain and medulla. Cranial neuropathy and long tract signs are characteristic clinical features. Although up to 60% have an exophytic component, these tumors are not resectable.

Usually responsive to radiation therapy initially, these malignancies tend to recur within a 2 year interval. Thus, prognosis is poor, with a 20% 5 year survival rate. Gliomas in the brainstem are generally fibrillary astrocytomas, with a significant minority showing histologic high grade features. Up to 20% of lesions are juvenile pilocytic astrocytomas. While the low grade fibrillary lesions demonstrate enlargement of the brainstem without a focal mass in most cases, high grade lesions show characteristic necrosis and hemorrhage.

Imaging

Brainstem gliomas display T1- and T2-prolongation, characteristic of most brain neoplasms. Enlargement of the brainstem with effacement of the adjacent cisterns and 4th ventricle are common. Ventral expansion around the basilar artery is a typical feature of this lesion. Cystic changes and hemorrhage are well depicted on MR. Enhancement is variable, and is seen in about 50% of cases. The enhancement pattern is often sparse, and may be absent in low grade fibrillary astrocytomas. A prominent exophytic component, with expansion of adjacent cisterns, may impart an extraaxial appearance to these lesions. Careful attention to signal abnormalities within the brainstem, the effect on the 4th ventricle and the MR characteristics on pre- and post-contrast images will facilitate accurate assessment of such lesions.

ADULT INFRATENTORIAL NEOPLASMS

The most common posterior fossa neoplasms in adults are secondary (metastatic) tumors, which are described in the previous section. The following discussion includes the most common primary infratentorial tumor in adults, and some uncommon lesions found in this compartment. Occasionally, the pediatric posterior fossa tumors described above present in young adults, thus these lesions must be considered in the appropriate clinical setting as well.

Hemangioblastoma

Clinicopathology

Hemangioblastoma is the most common primary posterior fossa neoplasm in the adult. Only metastases are more common overall in the adult population. This tumor is an important component of the autosomal dominant phakomatosis, von Hippel-Lindau disease. Thus, when a hemangioblastoma is encountered, other manifestations of this neuroepithelial disorder should be excluded.

Hemangioblastomas comprise 1% of intracranial neoplasms, and 7% of posterior fossa neoplasms in the adult population. Forty percent of patients with hemangioblastomas have retinal hemangioblastoma or other manifestations of von Hippel-Lindau's disease. Approximately 15% of von Hippel-Lindau patients have hemangioblastomas. Peak incidence of this lesion is in the fifth to sixth decade, but it presents earlier in patients with von Hippel-Lindau's disease. There is a male predominance.

Pathologically, this highly vascular tumor is well demarcated but lacks a true tumor capsule. The lesion is most commonly found in the cerebellar hemispheres. Lesions in other locations such as the vermis, brainstem and cervical cord are rare, and are usually associated with von Hippel-Lindau disease. Approximately two-thirds of the lesions are cystic. The cystic tumors tend to be larger than solid lesions and usually contain a well vascularized peripheral tumor nodule. This vascular nodule abuts the pial surface and is comprised of a fine meshwork of blood channels and capillaries with an intervening stroma. The gelatinous cyst contents may contain hemorrhage. Associated polycythemia is occasionally present and is thought to be the result of tumoral erythropoietin production. One-third of the lesions are solid. The solid tumors have a higher frequency in the brain stem and supratentorial compartments.

Imaging

Angiographically, the mural nodule or solid tumor reveals its vascular nature with intense contrast accumulation via the prominent, serpiginous vessels which supply it. The cyst is hypodense relative to brain on CT images, whereas the solid components are isodense. The enhanced study displays the feeding vessels in a majority of cases with intense enhancement of solid tumors and mural nodules within cystic lesions.

On MR imaging, T1 and T2 prolongation results in a hyperintense appearance on long TR images and hypointensity on T1-weighted images. The margins and extent of tumor are better depicted than with CT. Lesion detection, especially with the solid tumors, is also more sensitive utilizing this modality. Differential diagnosis based on imaging appearance includes pilocytic astrocytoma, especially if the lesion is partially cystic. In adults, solid lesions must be distinguished from metastases. Peripheral supratentorial lesions may have a similar appearance to angioblastic meningioma.

Subependymomas

Clinicopathology

Subependymomas are often considered a subcategory of ependymomas. The lesions were described in 1945 by Scheinker and are often incidental lesions which are discovered during imaging studies or at autopsy, with peak incidence in the sixth decade. These indolent tumors affect an older population than ependymomas and are usually found along the ventricular surface, most commonly adjacent to the septum pellucidum or floor of the fourth ventricle.

Histologically, subependymomas resemble normal periventricular glial tissue. They are comprised primarily of astrocytes and ependymal tubules. Three-fourths of the lesions occur within the fourth ventricular margins.

Imaging

Imaging studies show such lesions to be indistinguishable from ependymomas. The lesions tend to be homogeneous; thus gross cystic changes favor a diagnosis of ependymoma, as does a younger age at presentation. Calcifications are common. The lesions tend to be isodense to the adjacent brain parenchyma on CT images. Isointensity on T1-weighted MR images is also the rule. T2 prolongation and/or calcification make the lesions easy to recognize. Differential considerations include ependymoma, subependymal hamartoma, giant-cell astrocytoma, and in certain cases, heterotopic gray matter.

Dysplastic cerebellar gangliocytoma

Clinicopathology

This rare entity was described in 1920 by Lhermitte and Duclos and may represent a dysplasia rather than a true neoplasm. Differentiation and migration anomalies of the granule cell precursors underlie this interesting disease. There is a female preponderance with peak incidence in the third and fourth decades if a familial tendency has been implicated.

Pathologically, there is a thickened molecular layer within the cerebellum with hypermyelination and an abnormal granular layer. Absence of Purkinje cells completes the histologic constellation. The gross specimen demonstrates flat, broad folia with hypertrophy of the involved cerebellar hemisphere. Surgically, the margins of the abnormality may be difficult to distinguish from normal adjacent cerebellum.

Imaging

CT images demonstrate low-density mass lesions without enhancement. Cystic changes, hemorrhage and calcifications are not features of the cerebellar gangliocytoma. Erosion of the adjacent calvarium may be present. Obstructive hydrocephalus may result from fourth ventricular compromise.

MR images demonstrate an inhomogeneous mass with a disorganized, serpiginous pattern of low signal structures having the appearance of folia. On long TR images, the tumor has well defined margins and displays relatively homogeneous hyperintensity. Mass effect is well demonstrated on multiplanar MR images.

Although low-grade astrocytic neoplasms and other posterior fossa tumors such as lateral medulloblastoma may be considered in the differential diagnosis, the MR features including lack of enhancement generally allow for a specific diagnosis to be suggested when this rare tumor is encountered.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for intracranial neoplasms includes cerebral abscess, which may solitary or multiple. Radiation injury may also produce mass lesion(s) which are difficult to distinguish from primary and secondary tumors within the brain. Occasionally, demyelinating disease may produce rim-enhancing lesions. The imaging appearance of these conditions are discussed in detail in another section. Vascular lesions and hematomas can also cause intracranial masses. Cavernous malformations can be recognized on the basis of blood degradation products within and bordering the lesion. Hematoma formation may follow trauma or be spontaneous in such conditions as amyloid angiopathy. The task of the imager is to exclude an underlying lesion in addition to the heme products. A bland or hemorrhagic infarction may also be mass-like in appearance. The location of the lesion, its configuration, and enhancement pattern may provide morphologic clues to its identity. Advanced techniques such as diffusion imaging or spectroscopy provide the means to assess the physiological and biochemical properties of various forms of pathology, and will be used with increasing frequency as they mature.

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