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Tumor-like lesions of the brain

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Abstract

Differentiation between tumors and tumor-like lesions of the central nervous system is essential for planning adequate treatment and for estimating outcome and future prognosis. Neuroimaging fulfills an essential role in the correct differentiation between both entities. The radiologist should be aware of all non-neoplastic pathologies and diseases that may mimic tumors. High-end anatomic and functional neuroimaging tools integrating multiple modalities and clinical correlation is mandatory. In the current review, frequent tumor-like lesions are discussed.

Keywords: *Tumor-like; brain; central nervous system; advanced magnetic resonance imaging.*

Introduction

Differentiation between tumors and tumor-like lesions of the central nervous system (CNS) is essential for planning adequate treatment and for estimating outcome and future prognosis. By definition, tumor and tumor-like lesions are lesions that look alike on ultrasound (US), computer tomography (CT) or magnetic resonance imaging (MRI) studies. Typically, tumor-like lesions are reported as: findings compatible with a tumor-like lesion, however neoplasm cannot be ruled out. Clinical correlation and follow-up examinations are recommended to rule out malignancy. In practice, a tumor (e.g. astrocytoma) is a lesion that should be treated aggressively, whereas a tumor-like lesion (e.g. multiple sclerosis (MS) plaque) can be treated more conservatively. Misinterpretation may lead to a significant delay of adequate treatment of malignant tumors or may result in over-treatment of a tumor-like, benign lesion. The essential question is how does a radiologist reliably differentiate between both entities? Typically, anatomic imaging studies such US, CT or MRI are used. A tumor is suspected when a focal density or signal alteration is seen displacing or infiltrating adjacent structures with or without a matching contrast enhancement and possibly surrounded by vasogenic edema. Unfortunately, many tumor-like lesions including tumefactive MS plaques, abscesses, resolving hematomas, vascular malformations, giant Virchow–Robin spaces, and even metabolic disorders may have similar imaging features. In addition, a frequent, difficult question is the differentiation between postsurgical changes and residual tumor after recent brain tumor surgery. The recent development of functional MRI sequences such as diffusion tensor imaging (DTI), perfusion-weighted imaging (PWI), ^{1}H magnetic resonance spectroscopy (MRS), susceptibility-weighted imaging (SWI) and pH-weighted MRI facilitates the differentiation between tumor and tumor-like lesions.

It is impossible to present a complete list of tumor-like lesions, however, this article reviews the most frequent tumor-like lesions, their so-called characteristic neuroimaging presentation and how to differentiate them from tumors.

Diagnosis and clinical presentation

Infectious tumor-like lesions

The classic tumor-like lesion is an intracranial abscess. Abscesses may occur as complications of a meningoencephalitis, from direct extension from paranasal sinus and temporal bone infections and may result from hematogenous spread (septic emboli) of an extracranial infection. In addition, abscesses may result from penetrating traumas or as a result of a neurosurgical procedure.

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Abscesses are especially frequent seen in immunocompromised patients. Most intracranial abscesses are bacterial (staphylococcus, streptococcus and pneumococcus). Intracranial abscesses may present with imaging features that are identical to high-grade neoplasms such as a glioblastoma multiforme. Differentiation has been difficult for many years. On conventional imaging abscesses are round, mass lesions with various degrees of adjacent vasogenic white matter edema and a strong peripheral contrast enhancement. The ring of enhancement is usually closed and may appear thicker towards the direction of the cortex. With the advent of diffusion-weighted imaging (DWI), the identification of restricted diffusion within the center of the abscess facilitated differentiation from necrotic high-grade malignancies significantly. The pus within the abscess typically shows a restricted diffusion, whereas necrosis in the center of malignant tumors typically shows an increased diffusion.

Several infectious diseases involving the CNS like TORCH (Toxoplasmosis, Rubella, Cytomegalovirus and Herpes simplex) infections, tuberculosis, neurocysticercosis and various other fungal and opportunistic infections including parasitic infections (echinococcus, schistosomiasis and paragonimiasis) may mimic metastatic disease from extracranial neoplasms in children. Typically the lesions are multiple, may show various degrees of calcifications, vasogenic edema and contrast enhancement. The clinical history and laboratory tests are usually sufficient to differentiate between metastatic and infectious causes. In addition, if migrational abnormalities, cerebellar hypoplasia, orbital lesions including microphtalmia and microcephaly are noted, congenital infections that interfered with the brain development should be considered.

Intracranial tumor-like hemorrhage

Intracranial hemorrhages may result from a variety of intrinsic and/or extrinsic causes[1]. Extrinsic causes include accidental head trauma as well as surgical interventions. Intrinsic causes are manifold and include hemorrhagic stroke, vascular malformations, aneurysms, hematological disorders, bleeding diathesis, anticoagulation treatment, intracranial neoplasms, dural sinus thrombosis and complications from infections (e.g. herpes encephalitis).The imaging features of intra-axial hematomas can be heterogeneous and vary over time. Factors that influence hematoma evolution include location (gray versus white matter), size (punctuate versus confluent, unifocal versus multifocal), etiology (arterial versus venous, trauma versus hypertension), temporal occurrence of hemorrhage (acute event versus multi-staged, recurrent hemorrhage) as well as many biologic factors such as the patient's general physical condition, associated systemic diseases, hematocrit level, tissue oxygenation level (pO_2), pH and protein concentration (hemoglobin (Hb)). In addition, medical treatment and interventions may influence evolution of the hematoma. Transformation of hematomas may show imaging features very similar to tumors. Especially in the subacute to chronic phase, the spontaneous clot evolution with peripheral contrast enhancement and surrounding edema may mimic a tumor. The clinical history is usually helpful; most patients present with a sudden onset of symptoms. Careful evaluation of the imaging results and the use of functional sequences, in particular SWI for identifying blood products, DWI and MRS are helpful for differentiation. If an underlying vascular malformation is suspected MR angiography (MRA) and MR venography (MRV) may reveal dilated supplying and/or draining veins. If a cavernoma is suspected, SWI is helpful to exclude additional lesions. Despite all high-end anatomic and functional sequences, a hemorrhage within a tumor remains challenging on imaging. The tumor can be hidden within the hemorrhage.

Ischemic tumor-like stroke

Similar to intracranial hemorrhages, ischemic arterial or venous strokes may mimic tumors on neuroimaging. Ischemic strokes may have a significant mass effect with irregular contrast enhancement. The clinical history with an acute onset of symptoms and a matching clinical history is usually highly suggestive of a stroke. In addition, most lesions are located within a vascular territory with simultaneous involvement of cortex and the adjacent white matter. Finally, the imaging characteristics as seen on anatomic MRI as well as functional MRI with restricted diffusion on DWI and hypoperfusion on PWI usually prevent misinterpretation. Occasionally, hemorrhagic infarctions may be challenging. Especially during the spontaneous resolution of ischemic brain tissue, various patterns of contrast enhancement due to the blood–brain barrier disruption may mimic tumors. If a focal lesion crosses arterial vascular territories, a venous infarction should be considered.

Tumefactive tumor-like demyelination

Various demyelinating diseases, including MS, acute disseminated encephalomyelitis (ADEM) and progressive multifocal leucoencephalopathy (PML) may present tumor-like, also known as tumefactive, areas of demyelination. On imaging, these lesions may show imaging features suggestive of a brain tumor or abscess displaying solitary or multiple focal areas of signal alteration with an irregular peripheral enhancement and a mild to moderate mass effect on adjacent brain structures. Differential diagnosis may also include parasitic infections. Pathologic studies report large areas of confluent demyelination with an inflammatory response, often associated with perilesional edema and mass effect. Correlation with the clinical history usually prevents misdiagnosis. However, even in patients with established diagnosis of

MS, the diagnosis of tumefactive demyelination can occasionally be difficult[2]. Patients with MS frequently receive immunosuppressive medications putting them at risk for opportunistic infections, abscesses or even neoplasm. Tumefactive demyelination should be suspected if multiple lesions are present, if multiple areas of the CNS are involved including the spinal cord, if the lesions are periventricular and if they follow the course of the intramedullary veins (Dawson fingers, named after the Scottish pathologist James Walker Dawson). In addition, the kind of enhancement may help to differentiate between tumefactive MS plaques and abscesses. Typically, MS plaques show an incomplete ring of contrast enhancement towards the cortex, whereas an abscess shows a complete ring of enhancement. In addition, DWI is helpful in differentiating both entities. Finally, a rapid response of the lesion to corticosteroid treatment is suggestive of demyelinating diseases. Tumors and abscesses do not respond quickly.

Phakomatoses and tumor-like malformations

Phakomatoses, also known as neurocutaneous syndromes, are disorders of histiogenesis affecting derivates of the neuroectoderm and ectoderm. The best known and most frequently diagnosed examples are neurofibromatosis type I and II, tuberous sclerosis complex, Sturge–Weber syndrome, von Hippel–Lindau syndrome and hereditary hemorrhagic teleangiectasia syndrome. The imaging features of these syndromes are well known and are frequently considered to be diagnostic in the correct, matching clinical setting. However, the diagnosis is not always suspected clinically and lesions identified on neuroimaging may mimic tumors. In neurofibromatosis type I, the so-called mass-like T2-hyperintense, non-enhancing unidentified bright objects (UBOs) also known as non-specific bright foci (NSBF) within the brainstem, basal ganglia and cerebellum and the cortical and subcortical T2-hyperintense tubers as seen in tuberous sclerosis may mimic low-grade gliomas. Correlation with the clinical findings and identification of additional characteristic lesions usually point towards the correct diagnosis.

Rarely, disorders of organogenesis, which include disorders of neuronal migration and cortical development, may present as tumor-like lesions. A cluster of heterotopic gray matter within the white matter or focal Taylor type cortical dysplasia may present as a focal mass-like lesion. The imaging characteristics on high-resolution anatomic and functional MRI and the lack of blood–brain barrier disruption will prevent misinterpretation.

Vascular malformations including arterio-venous malformations (AVM), arterio-venous fistulas (AVF), and aneurysms may present as tumor-like lesions. These vascular malformations may be especially challenging if partial thrombosis is present. The varying signal characteristics of the intravascular thrombus and related, frequently inhomogeneous contrast enhancement may mimic tumors. Vasogenic edema may be observed resulting from direct mass effect as well as from the arterial and venous hemodynamic effects of the vascular malformation. Venous edema is frequently observed in AVMs or AVFs; cytotoxic edema may result from complicating ischemia. Finally, a large spontaneous hemorrhage may compress the vascular malformation making it virtually impossible to identify the lesion on early imaging. Differentiation between a hemorrhage within a highly perfused tumor and a vascular malformation can be difficult. Follow-up imaging or an angiography may be necessary for differentiation. In uncomplicated vascular malformations, identification of dilated supplying arteries and draining vessels as well as pulsation artifacts on MRI and MRA confirm diagnosis.

Tumor-like vasculitis, angiitis

Systemic lupus erythematosus (SLE) is reported to involve the CNS in up to 70% of patients. Neurologic dysfunction may result from ischemic stroke, acute hemorrhage or transverse myelitis. Ischemic stroke results from immune complex vasculitis and thrombosis associated with antiphospholipid antibodies. Huang *et al.*[3] reported of a 14-year old boy with known SLE who was admitted in a subcomatous condition. MRI showed a large tumor-like temporal mass lesion with midline shift, brainstem compression, obstructive hydrocephalus and internal streaks of hemorrhage. Brain biopsy showed extensive perivasculitis with marked perivascular infiltration of eosinophils, macrophages and neurtrophils. No tumor was detected. Correlation of imaging findings and the clinical history suggested diagnosis.

Tumor-like mass lesions have also been reported in patients with a primary angiitis of the CNS (PACNS). Vasculitis of the CNS usually occur secondary to systemic vasculitis or as part of other systemic inflammatory disorders. PACNS is defined as a solitary affection of the CNS. Several subgroups have been identified based on clinical, laboratory, angiographic and pathologic findings. Granulomatous angiitis is the most severe form; a less severe form is known as benign angiopathy of the CNS. Molloy *et al.*[4] described a subset of PACNS who presented on imaging with solitary tumor-like mass lesions (ML-PACNS). The 38 patients they studied presented with non-specific clinical features including headache (74%), focal neurologic deficits (64%), diffuse neurologic deficit (50%), seizures (47%), nausea and vomiting (21%) and constitutional symptoms (12%). MRI showed focal, tumor-like mass lesions with various degrees of edema, contrast enhancement and hemorrhage within the hemispheric white matter. The imaging features did not allow a reliable differentiation from neoplastic lesions. If patients fail to respond to aggressive immunosuppressive therapy, diagnosis of PACNS should

be re-evaluated. Biopsy may be necessary to exclude malignancy or infection.

Tumor-like metabolic disorders

Metabolic disorders and inborn errors of metabolism like the various leukodystrophies usually present with the typical clinical history of a delayed/arrested development or with developmental regression characterized by a progressive loss of previously mastered developmental milestones. Many different diseases can be diagnosed by identifying the pattern of de- and dysmyelination on MRI (pattern recognition) especially when analyzed in combination with ^{1}H MRS. Typical examples include Canavan disease, Alexander disease, van der Knaap disease and the various adrenoleukodystrophies. However, in several metabolic diseases, mass-like lesions may be observed that mimic tumors. The typical example is the contrast enhancing enlargement of the optic chiasm and forniceal columns in Alexander disease. To avoid misinterpretation, the radiologist should be aware of the full extent of lesions that may be observed in the various inborn error of metabolism.

The radiologist may be confronted with many other less or more frequent tumor-like lesions including true intra-axial lesions, such as primary and secondary giant tumefactive perivascular Virchow–Robin spaces, inflammatory pseudotumors, Behcet-like disease, as well as extra-axial lesions that may mimic intra-axial lesions such as tumors originating from the leptomeninges and adjacent skull that displace or invade the adjacent brain. Large osteosarcomas from the skull may mimic intra-axial malignant, partially calcified tumors. Another challenging issue is the differentiation between post-operative changes and residual/recurrent tumor after brain tumor surgery versus post-radiation changes. Frequently, only follow-up imaging may answer these questions. With the continuing advances in the development of functional sequences (DWI, DTI, ^{1}H MRS, spectroscopic imaging, PWI, SWI, pH-weighted MRI) and the multimodality approach combining data from CT, MRI, PET-CT and molecular imaging, a reliable differentiation may become possible in the near future.

Conclusions

Correct differentiation between tumor and tumor-like lesions is essential for decisions related to treatment and estimation of future prognosis and outcome. The so-called quintessential feature of a brain tumor is identification of a mass lesion within the brain. However many non-neoplastic pathologies and diseases may present as a mass lesion. The referring physician and radiologist should work together as a team to avoid misinterpretation. Frequently, the clinical findings are suggestive of the true cause of a tumor-like brain lesion. If the clinical findings are non-supporting, the radiologist should be aware of the extensive differential diagnosis of tumors and tumor-like lesions. In addition, the radiologist should use all the anatomic and functional imaging tools that are currently available to differentiate between both entities.

References

[1] Lee J, Rusin J, Perkins E, Roach ES. Intracranial hemorrhage in children. Arch Neurol 2008; 65: 1629–33.

[2] MacAdam LC, Blaser SI, Banwell BL. Pediatric tumefactive demyelination: case series and review of the literature. Pediatr Neurol 2002; 26: 18–25. doi:10.1016/S0887-8994(01)00322-8. PMid:11814730.

[3] Huang C-H, Hung C-H, Chu Y-T, Hua Y-M. Tumor-like cerebral perivasculitis in a pediatric patient with systemic lupus erythematosus. J Med Sci 2008; 24: 218–21.

[4] Molloy ES, Singhal AB, Calabrese LH. Tumour-like mass lesion: an under-recognised presentation of primary angiitis of the central nervous system. Ann Rheum Dis 2008; 67: 1732–5. doi:10.1136/ard.2008.096800. PMid:18625623.