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Intracranial Cystic Lesions: A Review

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Abstract Cysts and cystic-appearing intracranial lesions are common findings with routine cerebral imaging examination. These lesions often represent a challenge in diagnosis. Intracranial cystic lesions have wide pathologic and imaging spectra, of which some require an aggressive and tailored treatment, whereas many others remain asymptomatic and do not require follow-up or intervention. Intracranial cysts can be divided in non-neoplastic lesions that are often of developmental origin but comprise as well infectious cysts and neoplastic lesions that include benign cysts associated with low-grade tumors and cysts as a component of higher grade neoplasms. Reviewed are the pathology, origin, radiologic appearance, differential diagnosis, and therapeutic aspects of intracranial cystic lesions.

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Introduction

Intracranial cysts are common radiographic findings with magnetic resonance (MRI) and computerized tomography (CT) brain imaging. Cyst detection may be instigated by neurologic focal signs or incidental when an imaging examination is performed for nonspecific symptoms such as chronic headaches. The pathologic spectrum of intracranial cysts is broad, and differentiation on the basis of imaging alone can be challenging. However, once observed, such an abnormality requires a determination as to the type of cyst since treatment may or may not be required and, furthermore, prognosis varies from one type of lesion to another. The current review aims to familiarize the clinician with the major types of intracranial cystic lesions based in part on the diagnostic features seen with brain imaging. Tables 1 and 2 illustrate MRI aspects of non-neoplastic and neoplastic cystic lesions, respectively, and Fig. 1 displays a classification of intracranial cysts based presumed origin.

Non-Neoplastic Cystic Lesions

Epidermoid, dermoid, arachnoid, and colloid cysts are the most common non-neoplastic cystic lesions found in brain. Other less common cystic lesions such as choroid plexus cysts, enlarged perivascular (Virchow-Robin) spaces, neurenteric cysts, Rathke cleft cysts, porencephalic cysts, ependymal cysts, neuroglial cysts, and pineal cysts are briefly discussed as well.

Table 1 MRI aspects of non-neoplastic cystic lesions

	T1-W MRI	T2-W MRI	Gd enhanced MRI	DWI	ADC	MRS	Most common location
Neurocysticercosis	Core, iso to hypo I	Core, iso to hypo I with hypo I rim	Rim CE	No rest	High	var	Convexity or basal SA spaces
Brain abscess	Core hyper I, surrounding hypo I edema	Cavity hypo I, surrounded by hyper I edema	Ring CE	Rest	Low	Lact, lip, AAs, acetate and succ peaks	Frontal and temporal lobe (MCA territory)
Tuberculoma	Core, iso to hypo I	Core, iso to hypo I with iso to hyper I rim	Rim CE, irregular outline	Rest	Low	Lip peak	Supratent any location, Infratent (children++)
Hydatid cyst	Hypo I (wall also)	Hyper I except wall (hypo I)	none	NC	NC	Lact, pyr, acetate peaks	Parietal lobe
Epidermoid cyst (white EC: inverted in T1 and T2)	Iso to slightly hyper I	Iso to slightly hypo I	none +/− minimal rim CE	Rest	Low	CSF-like Cho Ø NAA Ø Cr Ø Lact +	Cereb-pont angle cistern
Dermoid cyst	Hyper I	Heterogeneity (hypo to hyper)	none	No rest	High	NC	Sellar/parasellar/ frontonasal (midline)
Arachnoid cyst	CSF-like	CSF-like	none	No rest	High	Cho Ø NAA Ø Cr Ø Lac + (very small)	Middle cranial fossa
Colloid cyst	Hyper I	hypo I	none	No rest	High	Pseudo-NAA peak	3rd vent (foramen of Monro)
Enlarged PVS	Iso-CSF	Iso-CSF	none	No rest	High	_	Basal ganglia /midbrain
Neurenteric cyst	Iso to hyper I	Hyper I +++	None +/− rim CE	No to mild rest.	var	NAA peak	prepont
Rathke cleft cyst	Variable 50 % iso I and 50 % hypo I intracystic hyper I nodule	70 % hyper I, 30 % iso or hypo I intracyst hypo I nodule	None 50 % rim CE intracystic non-CE nodule = pathog	–	–	–	Sellar/suprasellar
Porencephalic cyst	Iso-CSF	Iso-CSF Surrounding white mater hyper I	none	–	–	Absence of Nl brain metab	Cerebral hem
Ependymal cyst	Iso-CSF	Iso-CSF	none	No rest	High	–	Lateral vent
Neuroglial cyst	Iso-CSF	Iso-CSF	none	No rest	High	–	Frontal lobe
Pineal cyst	1/3 Hypo I 2/3 hyper I	Hyper I	2/3 CE rim or nodular CE	No rest	High	–	Pineal gland

AAs aminoacids, *AC* arachnoid cyst, *ADC* apparent diffusion coefficient, *ATRT* atypical teratoid/rhabdoid tumor, *BM* brain metastases, *CC* colloid cyst, *CE* contrast-enhancement, *Cereb* cerebellar, *Cereb-pont* cerebellopontine, *CN* central neurocytoma, *CP* craniopharyngioma, *CPC* choroid plexus cyst, *CSF* cerebrospinal fluid, *DC* dermoid cyst, *DIA/G* Desmoplastic infantile astrocytoma/ganglioglioma, *DNET* dysembryoplastic neuroepithelial tumor, *DWI* diffusion-weighted imaging, *EC* epidermoid cyst, *EP*C ependymal cyst, *ETANT*R embryonal tumors with abundant neuropil and true rosettes, *ETME* embryonal tumors with multilayered rosettes, *EVN* extra-ventricular neurocytoma, *FLAI*R fluid-attenuated inversion-recovery, *GB* glioblastoma, *GC* gangliocytoma, *GG* ganglioglioma, *HB* hemangioblastoma, *Hem* hemisphere, *Heter* heterogeneous, *Homo* homogeneous, intense, *Infratent* infratentorial, *Lac* lactates, *Lip* lipids, *M*B medulloblastoma, *MCA* middle cerebral artery, *Metab* metabolic, *MRI* magnetic resonance imaging, *MRS* magnetic resonance spectroscopy, *NA* not available, *NC* noncontributive, *NEC* neurenteric cyst, *NGC* neuroglial cyst, *PA* pilocytic astrocytoma, *pathog* pathognomonic, *PC* porencephalic cyst, *PET* Positron emission tomography, *PIC* pineal cyst, *PNET* primitive neuroectodermal tumor, *pont* pontine, *prepont* prepontine, *PVS* perivascular space, *Pyr* pyruvates, *RCC* Rathke cleft cyst, *Rest* restriction, *RFGNT* Rosette-forming glioneuronal tumor of the fourth ventricle, *SA* subarachnoid spaces, *Succ* succinate, *Supratent* supratentorial, *T1-WI* T1-weighted imaging, *T2-WI* T2-weighted imaging, *Ten*t tentorial, *Var* variable, *Vent* ventricle

Table 2 MRI aspects of cystic neoplastic lesions

	T1-W MRI	T2-W MRI	Gd enhanced	DWI	ADC	MRS	Most common location
BM	Hypo I	Hyper I	Thick rim or nodular CE	No rest	High	Suppressed NAA and creatinine. Elevated choline and lactate	Parietal, temporal, occipital, and frontal lobes
GBM	Hypo I	Hyper I	Thick rim or nodular CE	Var	High	Suppressed NAA and creatinine. Elevated choline and lactate	Frontal > temporal > parietal > occipital
PA	Solid iso I Cyst hypo I	Solid hyper I Cyst hyper I	Homo CE +++ Cysts with a CE nodule are characteristics	Rest	High	Increased choline. Low NAA High lactate	Cerellar hem and around 3rd vent > cerebral hem
GG and GC	Iso to hypo I	Hyper I	Homo CE	Rest	High	Reduced Cho/creat and NAA/creat. Increased Cho/NAA	Temporal lobe
DIA/G	Cyst hypo I solid periphery iso I	Cyst hyper I Solid iso I or heter	CE of Solid part and cyst septations	Peripheral solid part: rest –	High (solid)	Lactate peak Low choline	Cerebral hemispheres
Neurocytoma	Heter Iso-slight hyper I	Iso to hyper I	Variable CE ++	rest	Low	Increased choline Decreased NAA Glycine +/-Ala peaks	Intra vent: lat and 3rd vent Extra vent: intraparenchymal supra and infra tentorial
RFGNT	Hypo I +/−heter	Hyper I +/− heter	Heter patchy CE	–	–	–	4th vent (hydrocephalus+++)
Astroblastoma	Hypo I	Bubbly aspect Hyper I	Var CE	Rest	Low	Increased Chol/phosphocreat/creat ratio Decreased NAA increased lactate/lipid increased myo-inositol	Supra-tentorial
MB	Iso or hypo Intense	heter	Heter CE	Restriction	Low	Decreased NAA and Cr Increased Cho and lipid/lactate	Midline or paramedian cerebellar
PNET	Hyper I	Hyper I	Heter CE	Rest	Low	Increased chol Decreased NAA	Hemispheres
ETMR	Hypo T1	Hyper T2	Heter or homo CE	–	–	–	ETANTR:supra-tentorial medulloepithelioma:peri-ventricular temporal and parietal
ATRT	Hypo I	Iso to hypo T2	Heter CE	–	–	–	Cerebellum
Malignant FH		Hypo I (tumor) Hyper I (necrosis)	Thick irregular CE	No rest	High	–	Attached to dura or intraparenchymal
HB	Iso I	Hyper I	Heter nodule with a cyst	No rest	High	High lipid peak No NAA No lactate Low creat/phosphocreat Increased choline	Cerebellar, brainstem

AAs aminoacids, *AC* arachnoid cyst, *ADC* apparent diffusion coefficient, *ATRT* atypical teratoid/rhabdoid tumor, *BM* brain metastases, *CC* colloid cyst, *CE* contrast-enhancement, *Cereb* cerebellar, *Cereb-pont* cerebellopontine, *CN* central neurocytoma, *CP* craniopharyngioma, *CPC* choroid plexus cyst, *CSF* cerebrospinal fluid, *DC* dermoid cyst, *DIA/G* Desmoplastic infantile astrocytoma/ganglioglioma, *DNET* dysembryoplastic neuroepithelial tumor, *DWI* diffusion-weighted imaging, *EC* epidermoid cyst, *EPC* ependymal cyst, *ETANTR* embryonal tumors with abundant neuropil and true rosettes, *ETME* embryonal tumors with multilayered rosettes, *EVN* extra-ventricular neurocytoma, *FLAIR* fluid-attenuated inversion-recovery, *GB* glioblastoma, *GC* gangliocytoma, *GG* ganglioglioma, *HB* hemangioblastoma, *Hem* hemisphere, *Heter* heterogeneous, *Homo* homogeneous, *I* intense, *Lac* lactates, *Lip* lipids, *MB* medulloblastoma, *MCA* middle cerebral artery, *Meta*b metabolic, *MRI* magnetic resonance imaging, *MR*S magnetic resonance spectroscopy, *NA* non available, *NC* noncontributive, *NEC* neurenteric cyst, *NGC* neuroglial cyst, *PA* pilocytic astrocytoma, *pathog* pathognomonic, *PC* porencephalic cyst, *PET* Positron emission tomography, *PIC* pineal cyst, *PNET* primitive neuroectodermal tumor, *pont* pontine, *prepont* prepontine, *PVS* perivascular space, *Pyr* pyruvates, *RCC* Rathke cleft cyst, *Rest* restriction, *RFGNT* Rosette-forming glioneuronal tumor of the fourth ventricle, *SA* subarachnoid spaces, *Succ* succinate, *T1-WI* T1-weighted imaging, *T2-WI* T2-weighted imaging, *Tent* tentorial, *Var* variable, *Vent* ventricle

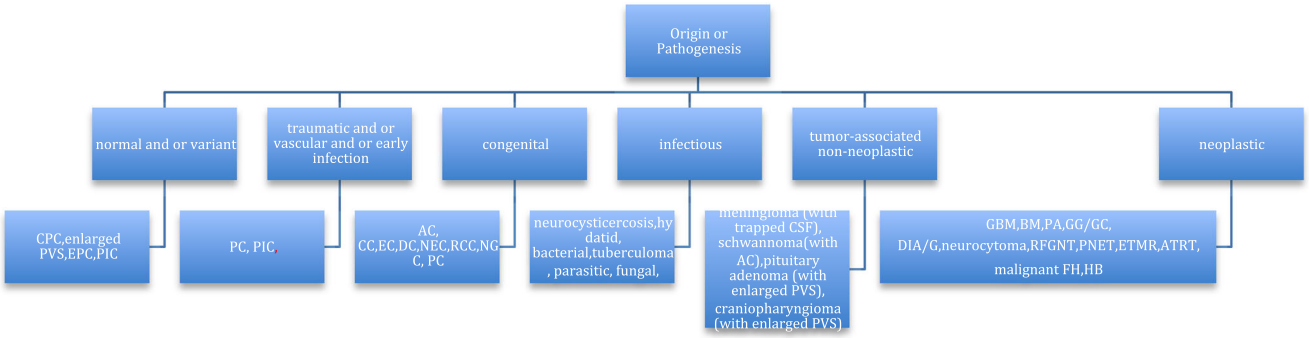

Fig. 1 Classification of intracranial cysts according to origin or pathogenesis. *AC* arachnoid cyst, *ATRT* atypical teratoid/rhabdoid tumor, *BM* brain metastases, *CC* colloid cyst, *CN* central neurocytoma, *CP* craniopharyngioma, *CPC* choroid plexus cyst, *CSF* cerebrospinal fluid, *DC* dermoid cyst, *DNET* dysembryoplastic neuroepithelial tumor, *EC* epidermoid cyst, *EPC* ependymal cyst, *ETME* embryonal tumors with multilayered rosettes, *ETANTR* embryonal tumors with abundant neuropil and true rosettes, *EVN* extra-ventricular neurocytoma, *GBM* glioblastoma, *GC* gangliocytoma, *GG* ganglioglioma, *HB* hemangioblastoma, *IDH* isocitrate dehydrogenase, *MB* medulloblastoma, *MRI* magnetic resonance imaging, *MRS* magnetic resonance spectroscopy, *NEC* neurenteric cyst, *NGC* neuroglial cyst, *PA* pilocytic astrocytoma, *PC* porencephalic cyst, *PIC* pineal cyst, *PNET* primitive neuroectodermal tumor, *PVS* perivascular space, *RCC* Rathke cleft cyst, *RFGNT* Rosette-forming glioneuronal tumor of the fourth ventricle

Epidermoid Cysts (EC)

Pathologic Findings

EC, also called primary cholesteatomas, are congenital inclusion cysts that originate from epithelial cells that are retained during closure of the neural tube. Their growth is due to an accumulation of cholesterol and keratin from desquamation of the lining epithelium that can enclose or compress nearby nerves and vasculature. EC are 4–9 times more common than dermoid cysts [1, 2]. All EC are located off the midline and most often located within the basilar cisterns. Very occasionally EC may occur within the ventricles, the sellar or parasellar region and less frequently in the cerebral parenchyma or brainstem [3]. Most are asymptomatic but may occasionally result in mass effect, cranial neuropathy(s), or seizures. Cyst leakage may result in aseptic granulomatous meningitis [4].

EC arise from ectodermal inclusion during neural tube closure [2, 5]. The cyst interior is filled with waxy or keratohyalin material [1]. The cyst lining consists of stratified squamous epithelium surrounded by an outer layer of collagenous connective tissue. Cystic contents include debris, keratin, water, and cholesterol organized in a lamellar fashion. EC by definition do not contain dermal structures.

Imaging

MRI/CT studies typically show extra-axial, noncontrast-enhancing lesions whose characteristics are similar to CSF and that encase adjacent nerves and vessels [2]. By CT, EC are well-delineated hypoattenuated nonenhancing CSF-like masses that may contain calcifications. Occasionally intracystic hemorrhage results in hyperdensity thereby, having the appearance of a meningioma.

EC are isointense or slightly hyperintense to CSF on T1- and T2-weighted MRI. EC only partially suppress on MRI FLAIR images. EC show characteristic restricted diffusion on diffusion-weighted imaging (DWI) MRI. The majority of EC do not enhance, although some rim enhancement occurs in 25 % [6].

Differential Diagnosis

The major differential diagnosis is the arachnoid cyst (AC). However, AC are isointense to CSF on all MRI sequences. In addition, AC displace rather than invade structures as in EC. Finally, AC do not restrict on DWI [1]. Other diagnoses include dermoid cyst (DC), cystic neoplasm, and neurocysticercosis [2]. DC are by contrast located along the midline and resemble fat (not CSF). Cystic neoplasms usually enhance and rarely resemble CSF. Neurocysticercosis cysts often enhance and may demonstrate surrounding edema.

Treatment

Many EC may be observed with serial MRI particularly in asymptomatic patients. Surgery is the standard treatment of symptomatic EC. Surgery is often limited by anatomic constraints leading to a partial resection and may be complicated by postoperative aseptic meningitis resulting from cyst leakage that may be mitigated by the use of systemic steroids [7]. Malignant transformation into squamous cell carcinoma (SCC) rarely occurs, involving rapid clinical deterioration sometimes with CSF dissemination [8]. The prognosis of EC with transformation into a SCC is poor. There is no role for either radiotherapy (RT) or chemotherapy (CT) in the treatment of EC.

Dermoid Cysts (DC)

Pathologic Findings

DC originate from the inclusion of ectodermal cells at the time of neural tube closure [1, 4, 9]. In addition to squamous epithelium DC contain elements of retained hair, teeth, sweat, and sebaceous glands [1, 4, 9, 10].There is production of hair and oils by the dermal appendages in DC. The DC is a well-delineated lobulated mass of variable size with a thick capsule that often contains calcification. DC occur in the midline and often in the posterior fossa [1, 9, 10].

DC have heterogeneous signal intensity on T2-W MRI and vary from hypo- to hyperintense [9]. The typical appearance of a ruptured DC is fatlike droplets in the subarachnoid cisterns, sulci, and ventricles [9]. Extensive pial enhancement can be seen in instances of ruptured cysts [9, 11]. A co-associated thrombosed aneurysm with clot in different stages of organization may rarely be observed [12].

Differential Diagnosis

DC may appear like an EC, craniopharyngioma, teratoma, or lipoma. EC, however, resemble CSF (not fat), lack dermal appendages, and are located off midline. Like occasional DC, craniopharyngiomas (CP) are suprasellar, with a midline location, and often demonstrate calcification. However, most CP are hyperintense on T2-W MRI and enhance strongly. Teratomas are also midline but usually occur in the pineal region. Lipomas by MRI/CT show fat attenuation, an imaging finding not seen with DC [6].

Treatment

Surgery is the standard treatment of symptomatic DC, with a risk of recurrence in case of incomplete resection. Malignant transformation in SCC may rarely occur and is associated with a poor prognosis [8, 9]. Asymptomatic DC may like EC be followed with serial imaging. There is no role for RT or CT.

Colloid Cysts (CC)

Pathologic Findings

CC is a developmental malformation composed of an outer connective tissue layer and an inner ciliated mucin producing epithelium [13]. CC are located in the anterior third ventricle, between the fornices in the anterior third ventricle that may block the foramen of Monro and result in hydrocephalus. CC become symptomatic in the 3rd–6th decade manifesting as raised intracranial pressure with frontal or positional headaches [14, 15]. The classic combination of intermittent headaches and drop attacks occurs in only one-third of patients and sudden death may rarely occur from obstruction of the ventricles

Imaging

CT scan without contrast shows an iso- or hyperdense cystic lesion. MRI reveals a T2-W hyperintense lesion sometimes with a hypointense center that do not enhance.

Treatment

Surgical and, often, endoscopic resection is the standard treatment, which is often curative. A ventriculoperitoneal shunt may be required in instances of hydrocephalus. Stereotactic aspiration of a cyst may be useful notwithstanding a high rate of recurrence [13]. Clinical and MRI follow-up may be an option in small lesions in asymptomatic patients.

Arachnoid Cysts (AC)

Pathologic Findings

AC are common, benign, congenital, intra-arachnoidal space-occupying lesions that are filled with CSF and that do not communicate with the ventricular system [1, 16]. AC are mostly unilocular, well-delineated lesions that are shaped by surrounding brain and skull. Passive CSF diffusion into the cyst, slow distension by CSF pulsations or progressive entrapment because of a ball-valve effect has been suggested as causes of AC enlargement [17]. An embryologic pathogenesis regarding middle cranial fossa AC is the failure of temporal meninges to fuse as the sylvian fissure forms. The 2 meningeal membranes remain separate, forming a duplicate arachnoid [6]. Additionally, AC has also been attributed to trauma, mastoiditis, meningitis, and subarachnoid hemorrhage [5]. The prevalence of AC is 1 % overall with less than 5 % of lesions being symptomatic (mostly in children) [18]. AC are stable over time, although cases of sudden or progressive enlargement, have been reported [19, 20]. Most AC are filled with clear colorless fluid. The size varies, from small to a large space-occupying lesion [1, 10, 16]. Microscopically, the cyst wall is comprised of a collagenous membrane lined by arachnoid cells [1]. A significantly elevated protein level or pleocytosis suggests the possibility of cystic neoplasm rather than an AC. Most AC are found in the middle cranial fossa, anterior to the temporal lobe. Other locations include the suprasellar cistern, posterior fossa (cerebellopontine cistern), within the interhemispheric fissure; over the cerebral convexity; or in the choroidal fissure, cisterna magna, quadrigeminal cistern, or vermian fissures [1, 4, 10, 16]. Headache and seizure are the most frequent symptoms but according to the location of the lesion, obstructive hydrocephalus, visual, and

endocrine dysfunctions or brainstem-related signs may be observed. Minor head trauma may trigger an AC hemorrhage.

Imaging

Plain x-ray imaging may demonstrate thinning of adjacent bone in chronic lesions. CT or MRI shows a sharply demarcated extra-axial cyst that may displace or deform adjacent brain. The classic AC has no identifiable internal architecture, does not enhance and typically has the same signal intensity as CSF on all MRI sequences. Occasionally, however, hemorrhage, high protein content, or lack of flow within the cyst may complicate the MRI appearance [1, 10, 16].

Differential Diagnosis

The differential diagnosis includes chronic subdural hygroma, EC, and cystic neoplasms discussed below. The most challenging lesion to distinguish from the AC is an EC as both can appear nearly identical to CSF on CT. AC typically suppress completely on MRI FLAIR images whereas EC does not and AC do not restrict on DWI unlike EC. AC displace adjacent vessels and cranial nerves rather than entrap them as EC often do [1, 5, 16]. Chronic subdural hematomas also in the differential diagnosis do not show CSF signal intensity on MRI and often have an enhancing membrane.

Treatment

Clinical and MRI follow-up is adequate in the vast majority of AC that are asymptomatic. Surgery is indicated only in symptomatic lesions. Surgical options include partial or complete cystectomy, fenestration into the subarachnoid space, or cyst peritoneal shunting. Needle aspiration usually is of temporary benefit only [7].

Choroid Plexus Cysts (CPC)

Pathologic Findings

CPC are non-neoplastic epithelial-lined cysts of the choroid plexus (CP) [1, 21]. They are the most common of all intracranial neuroepithelial cysts. Most are bilateral and located in the lateral ventricles; third ventricle location is rare [21]. The majority are found incidentally. Symptomatic lesions are rare as the ventricle typically adapts itself to accommodate the cyst [1]. CPC result from lipid accumulation and degenerating or desquamating choroid epithelium in the craniopharyngioma (CP) [21]. CPC may be are cystic with or without a solid nodular component. Diameter is rarely greater than 2 centimeters. Pathology reveals microcysts containing foamy lipid-laden histiocytes, inflammatory lymphocytes, cholesterol clefts, hemosiderin, and calcification [21].

Imaging

CPC are iso- to slightly hyperattenuated, nonenhancing lesions by CT. Peripheral calcification is common. The cysts shows variable enhancement. Most CPC are iso- or hyperintense on T1-W MRI compared with CSF, show ring or nodular contrast enhancement, and are hyperintense to CSF on T2- W MRI. Most do not totally suppress on FLAIR images and remain slightly or moderately hyperintense to CSF. The majority show restriction on DWI [1, 21].

Differential Diagnosis

The major differential diagnosis is an EC and villous hyperplasia of the CP. EC do not enhance. Villous hyperplasia is rare and, when present, diffusely enhances.

Enlarged Perivascular Spaces (PVS)

Pathologic Findings

PVS, also called Virchow-Robin spaces, are pial-lined fluid-filled structures that accompany penetrating vessels. There is no direct communication with the subarachnoid space [22, 23]. PVS are common, incidental lesions that are frequently located in the basal ganglia, around the anterior commissure and surrounding the lenticulo-striate arteries in the anterior perforated substance [22]. Other locations include the midbrain, deep white matter, sub-insular cortex, the thalami, dentate nuclei, corpus callosum, and cingulate gyrus [22, 23]. Microscopically, PVS consist of a single or double layer of pia. No surrounding parenchymal gliosis is observed [22].

Imaging

PVS are considered a normal variant. The majority are well-delineated fluid-filled cysts, usually less than 5 millimeters in diameter, and seen in clusters within the basal ganglia or midbrain.

PVS are isointense to CSF by all MRI sequences [6]. Signal intensity of the adjacent brain parenchyma is usually normal but may sometimes be slightly increased or demonstrate a hyperintense rim. PVS do not enhance, cause mass effect, or restrict on DWI MRI. In older patients, basal ganglia PVS sometimes become prominent leading to a condition called “état criblé”, or the cribriform state.

Differential Diagnosis

Enlarged PVS are often mistaken for multiple lacunar infarcts, cystic tumors, or infectious cysts [6]. Unlike PVS, lacunar

infarcts are often adjacent to parenchymal hyperintensity (so-called état lacunaire), cystic neoplasms rarely exhibit CSF signal intensity. Neurocysticercosis cysts may have a parasite head or scolex, the cyst walls often enhance and even if multiple, are not randomly distributed in brain parenchyma [6].

Neurenteric Cysts (NEC)

Pathologic Findings

NEC are congenital benign, lesions, predominantly occurring in the spine [24]. When intracranial, NEC are usually located in the midline posterior fossa, anterior to the brainstem. They may occur in the cerebellopontine angle or clivus. Supratentorial location is rare [24].

NEC arise at the time of notochord development. The notochord and foregut fail to split resulting in endodermal cells to be integrated into the notochord. These cells ultimately become the cyst [1, 24]. Microscopic examination of the cyst wall shows an endothelium of cuboidal to columnar ciliated cells. The cysts closely imitate gastrointestinal tract mucosa [25].

Imaging

MRI shows a round or lobulated, nonenhancing hyperintense mass anterior to the medulla. The MRI signal intensity vary depending on the protein content of the cysts. Most cysts are proteinaceous and therefore, iso- to slightly hyperintense on T1-W MRI and hyperintense on FLAIR and T2-W MRI [24]. NEC may show mild restriction on DWI. NEC rarely show enhancement.

Differential Diagnosis

The differential diagnosis of a NEC includes EC, AC, and other endodermal cysts (eg, Rathke and CC) [24]. EC is most like the NEC as both are hyperintense on T1-W MRI and can be difficult to distinguish if located along the midline [24]. EC usually restrict on DWI. By contrast, AC show the same appearance as CSF on all MRI sequences. Other endodermal-derived cysts such as Rathke and CC differ from NEC in location.

Treatment

NEC are rarely symptomatic and consequently can be followed with serial imaging.

Rathke Cleft Cysts (RCC)

Pathologic Findings

RCC are congenital non-neoplastic intra- or suprasellar cysts arising from remnants of the embryonic Rathke cleft [26]. They are common incidental lesions found in up to 33 % of autopsy series [29]. Symptoms are secondary to the compression of the optic chiasm, hypothalamus, or pituitary gland. RCC arise from the failure of obliteration of the Rathke pouch, which develops as a rostral out-pouching of the primitive oral cavity during the 3rd or 4th week of embryogenesis [27]. RCC are well-marginated that vary in size (most <2 centimeters) with cyst content that varies from clear CSF-like fluid to thick mucoid material [26]. Microscopically RCC are similar to other endodermal cysts eg, neurenteric and CC. They are lined by mucin secreting ciliated epithelium [1]. The intracystic nodule consists of mucinous material at that is contains cholesterol and protein [27].

Imaging

The typical aspect on MRI is a nonenhancing noncalcified intra- or suprasellar cyst with an associated nodule [26, 27]. MRI findings are, however, variable with approximately 50 % that are hyperintense on T1-W MRI, whereas 50 % are hypointense. On T2-W MRI, 70 % are hyperintense and 30 % are iso- or hypointense [26]. An associated small nonenhancing nodule is considered a virtually pathognomonic of a RCC. The nodules are hyperintense on T1-W and hypointense on T2-W MRI. Furthermore, the nodules do not enhance although an enhancing rim of displaced pituitary gland is visible in approximately 50 % [1, 27].

Differential Diagnosis

The differential diagnosis includes craniopharyngioma (CP), cystic pituitary adenoma, or other non-neoplastic cysts [26]. Unlike RCC, CP shows calcification and most (90 %) enhance [27].

Treatment

As the great majority of RCC are asymptomatic observation only is sufficient treatment.

Porencephalic Cysts (PC)

Pathologic Findings

PC are cavities (congenital or acquired) within the cerebral hemisphere that communicate with the ventricular system [28]. The location usually corresponds to a vascular territory.

Congenital PC arise from a in or post utero destructive process that is a consequence of a vascular or infectious injury. Acquired cysts originate from trauma, surgery, infarct, or infection. PC vary in size and are CSF-filled cavities with a smooth wall surrounded by gliosis. The adjacent skull may remodel because of chronic CSF pulsations [28].

Imaging

A PC is a cystic cavity in the brain parenchyma that communicates directly with an enlarged adjacent ventricle. The cysts have the same signal as CSF at all MR sequences [28]. Adjacent white matter demonstrates hyperintensity on T2-weighted and FLAIR MRI images.

Differential Diagnosis

The differential diagnosis includes AC, schizencephaly, EC, encephalomalacia, and hydranencephaly. AC are extra-axial and displace the brain away from the overlying skull. Schizencephaly is a congenital malformation that appears as a CSF filled cavity lined with heterotopic gray matter and that extends from the ventricle to the brain surface. EC are intraventricular cysts with normal surrounding brain tissue [28].

Treatment

PC may be observed and do not require treatment.

Ependymal Cysts (EPC)

Pathologic Findings

EPC are rare, benign, ependymal-lined cysts of the lateral ventricle or juxtaventricular region mostly in the temporal, parietal, or frontal lobes [29]. Most EPC are incidental, but rare cases of symptomatic cysts have been reported with increased intracranial pressure, obstructive hydrocephalus, or seizures.

EPC arise from entrapment of developing neuroectoderm during embryogenesis. They are thin walled and filled with clear fluid secreted from lining ependymal cells. Microscopically, columnar cells, with or without cilia, line EPC [29].

Imaging

MRI typically shows a nonenhancing thin-walled CSF-containing cyst of the lateral ventricle.

Differential Diagnosis

The differential diagnosis includes CPC, AC, neurocysticercosis, and asymmetric ventricles [29]. Part or all of a ventricle may also enlarge if it is "trapped" by neoplasm or infection. CPC is dissimilar to CSF at all imaging sequences, are bilateral, and often enhance. By contrast, AC occur in the subarachnoid space. Intraventricular neurocysticercosis cysts demonstrate a hyperintense rim and scolex (parasitic head) on FLAIR MRI images.

Treatment

No treatment is required.

Neuroglial Cysts (NGC)

Pathologic Findings

NGC, also called glioependymal cysts, are uncommon, benign epithelial-lined lesions that may occur anywhere in the neuraxis with a preference in the frontal lobes. Intraparenchymal location is more common than extra-parenchymal [30]. NGC are congenital lesions, arising from embryonic neural tube elements that become. These cysts are rounded, smooth, and contain clear fluid that resembles CSF. They are lined by ependyma or choroid plexus cells [30].

Imaging

MRI shows a nonenhancing well-delineated CSF-like cyst with little or no surrounding signal intensity abnormality [30].

Differential Diagnosis

Differential diagnosis includes an enlarged PVS, infectious cyst, PC, and AC. Enlarged PVS are typically multiple and cluster within the basal ganglia. Infectious cysts, such as neurocysticercosis, are typically smaller and partially enhance. PC communicate directly with the lateral ventricle and show surrounding gliosis. AC are mostly extra-axial [30].

Treatment

None required.

Pineal Cysts (PIC)

Pathologic Findings

PIC or cystic degeneration of the pineal gland is common and are seen in up to 10 % of cases by routine imaging and in up to 40 % of cases at autopsy [31]. Microscopically, PIC exhibit 3

distinct layers. The outer layer consists of a layer of connective tissue. The middle layer is comprised of pineal parenchyma with or without calcium. The inner layer is composed of glial tissue that often contains hemosiderin [4, 10, 31].

Imaging

MRI shows a single cavity fluid-filled cyst within the pineal gland. Signal intensity varies with cyst content. Twenty-five percent have calcium in the cyst. Enhancement is also common. On T1-W MRI, 60 % are slightly hyperintense to CSF. Most are hyperintense on FLAIR MRI, and 60 % enhance [31].

Differential Diagnosis

PIC may be mistaken for a pineocytoma, which by contrast are more likely to have solid component. Both PIC and pineocytoma grow extremely slowly, so follow-up scans are often do not distinguish between the two. Stereotactic biopsy may be needed for the evaluation and management of symptomatic cases. Other cysts in the quadrigeminal cistern that mimic PIC include AC (absent calcification) and, rarely EC [20, 31].

Treatment

Small, asymptomatic PIC do not require treatment. In case of hydrocephalus, CSF diversion alone is not recommended in the absence of histologic confirmation. Open or stereotactic cyst resection provides a cure and can obviate the need for CSF shunting [32, 33]. Clinical follow-up including repeat imaging should be performed in instances of a large cyst defined as greater than 10 millimeters. The majority of PIC can be followed with serial imaging.

Cystic Neoplastic Lesions

Uncommon brain tumors (BT) with cystic component include a wide spectrum and can be listed among the following tissue of origin categories: neuronal and neuronoglial tumors, neuroepithelial tumors, embryonal tumors including medulloblastoma, mesenchymal tumors, and tumors of the meninges eg, hemangioblastoma.

Neuronal and Neuronoglial Tumors

Among rare neoplasms characterized by a neuronal differentiation, gangliomas and gangliocytomas, dysplastic gangliocytoma of the cerebellum (Lhermitte-Duclos disease), desmoplastic infantile astrocytoma/ganglioglioma, central and extraventricular neurocytomas, and rosette-forming glioneuronal tumor of the fourth ventricle all may potentially exhibit a cystic component.

Gangliogliomas (GG) and Gangliocytomas (GC)

Pathologic Findings

GG and GC are low-grade tumors (World Health Organization [WHO] Grade 1) characterized by a neoplastic neuronal population. In GG, the neoplastic neuronal cells are accompanied by neoplastic glial cells whereas neurons are the only neoplastic component in GC. Most GG and GC are located in the temporal lobes but may occur anywhere in the neuraxis. BRAF V600E mutation is present in 60 % of GG with a mutated protein present in the neuronal cells [34, 35•]. Mutations in isocitrate dehydrogenase (IDH) may be observed in GG characterized by an older age at diagnosis, a greater risk of recurrence, and a poor prognosis [36]. GG and GC are the most common neoplastic lesional etiology of long standing epilepsy in in children and young adults.

Imaging

MRI shows hyperintense lesions on T2-W MRI with cystic component in 50 % of cases. Positron emission tomography (PET) usually shows hypometabolism, but areas of hypermetabolism compared with white matter may exist.

Treatment

The standard initial treatment is surgical. Recurrence is rare in totally resected tumors and prognosis remains good even in case of subtotal resection. Ten percent of GG become anaplastic and notwithstanding use of RT and CT are not curable. The therapeutic implications of a BRAF V600E mutation are currently under investigation [37•, 38•]. RT is not recommended for patients who have had a complete resection and its survival benefit as adjuvant therapy to subtotal resection remains to be proven. RT is usually recommended for unresectable recurrent GG and for subtotally resected GG with an anaplastic component.

Desmoplastic Infantile Astrocytoma/Ganglioglioma (DIA/G)

Pathologic and Imaging Findings

DIA/G are comprised of dual astrocytic and ganglionic differentiation with a prominent desmoplastic stroma. These tumors

usually occur in early childhood and occasionally in young adults. DIA/G are large volume lesions, typically located in cerebral hemispheres, and are characterized by solid and cystic components on MRI.

Treatment

Treatment consists of surgery, with CT in cases of incomplete resection and RT only in case of no alternatives. Prognosis is favorable.

Central (CN) and Extraventricular Neurocytoma (EVN)

Pathologic Findings

CN are well-differentiated tumors of young adults located in the ventricles whereas EVN may arise in the brain parenchyma or spinal cord. CN are neuroectodermal tumors with predominant neuronal differentiation [39]. Genetic studies identified overexpression of *MYCN*, *PTEN*, and *OR5BF1*, and underrepresentation of *BIN1*, *SNRPN*, and *HRAS*, suggesting that *MCYN* overexpression and reduced expression of the tumor suppressor *BIN1* may contribute to tumor development [40]. *IDH* mutations and MGMT promotor methylation were absent in a small series of EVN [41]. Increased intracranial pressure because of hydrocephalus, visual dysfunction, and impaired cognitive are the leading symptoms at diagnosis. Most CN present with multiple calcified cysts and are located in the lateral or third ventricle.

Imaging

CT shows a heterogeneous, hyperdense intraventricular mass, with moderate contrast enhancement. MRI shows slight hyperintensity areas on T1-WI, usually with robust contrast-enhancement. Distinction from other gliomas may be challenging.

Treatment

Complete surgical resection is the standard treatment, however, subtotal resection still provides a survival advantage since tumor regrowth is usually slow. Adjuvant RT or stereotactic radiosurgery (SRS) is an option in case of incomplete resection or atypical histology [42, 43]. Atypical CN/EVN are characterized by a growth fraction measured by the MIB-1 monoclonal antibody greater than 3 % and carry a worse prognosis. Chemotherapy may be used in instances of recurrent disease [44].

Rosette-Forming Glioneuronal Tumor of the Fourth Ventricle (RFGNT)

RFGNT of the fourth ventricle are rare, benign lesions of the young adults. This rare tumor was originally described as a variant of dysembryoplastic neuroepithelial tumor (DNET) of the cerebellum but is now classified as a distinct entity. The defining histopathologic feature is a mixed population of neurocytes organized in pseudorosettes and pilocytic astrocytes.

Imaging

Because these tumors are located in the fourth ventricle, they typically present with hydrocephalus. MRI shows a heterogeneous, cystic, or multiloculated lesion with inhomogeneous contrast-enhancement.

Treatment

Surgical resection is standard treatment in these often curable lesions.

Miscellaneous Neuroepithelial Tumors

Pathologic Findings

Astroblastoma are supratentorial mostly low-grade gliomas with solid and cystic components. These tumors are more frequent in children than in adults. They present pathologic aspects that are intermediate between astrocytoma and ependymoma with characteristic finding diffuse, perivascular, astroblastic pseudorosettes. Low-grade and high-grade variants exist.

Imaging

On MRI, the solid component has a characteristic "bubbly" appearance on T2-W MRI. Hyperintense signal on T2-W MRI is frequent with variable enhancement and calcification.

Treatment

Surgical resection is the preferred treatment. RT and CT are often added in case of high-grade tumor however, without compelling evidence of benefit.

Embryonal Neoplasms

The embryonal neoplasms mostly occur in infants and young children. The most common tumors in this group are

medulloblastomas; other tumor types include supratentorial primitive neuroectodermal tumors (PNET), ependymoblastomas, medulloepitheliomas, and atypical teratoid/rhabdoid tumors (ATRT).

Medulloblastoma (MB)

Pathologic Findings, Prognostic Factors, Classification and Prognosis

MB are the most common malignant brain tumor of childhood, rarely occur after the fourth decade of life and contain features consistent with an embryonal origin. Both molecular markers and histopathology have more recently been helpful in determining prognosis [45•, 46, 47•] and may form in the future a basis for improved pretreatment risk stratification and treatment. Integrative genomic studies suggest that MB can be divided into 4 molecular subgroups, which have divergent cell histology, genetics, clinical behavior, and patient outcome [45•, 48, 49•, 50–52]. Tumors that show activation of the Wingless (*WNT*) pathway have the best prognosis, whereas tumors with amplification of the *MYC* proto-oncogene ("group 3") have the worst prognosis. Tumors with activation of the sonic hedgehog (*SHH*) pathway and those in group 4 have an intermediate prognosis, with the exception of *SHH* tumors containing *TP53* mutations, showing a particularly poor prognosis.

Imaging

MB consists of a contrast-enhancing midline or paramedian cerebellar tumor, which often compresses the 4rth ventricle. Most tumors are iso- or hypointense on T1-W and heterogeneous on T2-W MRI. Gadolinium enhancement is usually heterogeneous, and there may be area of necrosis, hemorrhage, or cystic changes. Leptomeningeal dissemination may be seen either in the brain or in spinal cord as approximately one-third of MB disseminate throughout the CNS following cerebral spinal fluid (CSF) pathways.

Differential Diagnosis

The differential diagnosis of a cystic posterior fossa mass in a child includes other tumors with a predilection for the cerebellum, the most common of which are pilocytic astrocytoma (PA) and ATRT. PA are often cystic with a mural nodule or centrally necrotic with a thick rim of enhancing tissue. If cysts are present in MB, they are typically small and multiple rather than solitary. ATRT are much rarer than MB but can have a similar appearance on MRI. Compared with MB, ATRT are more likely to involve the lateral hemispheres or cerebellopontine angle and contain intratumoral hemorrhage. Decreased ADC values, a marker of high cellularity, are characteristic of MB and ATRT but not PA [53, 54]. In an adult with a posterior fossa mass lesion, the differential diagnosis also includes brain metastases, which are rare in childhood.

Treatment

Treatment consists of a combined modality approach that includes surgery, RT and chemotherapy in most patients. Specific inhibition of molecular targets, such as the sonic hedgehog pathway, that are involved in the pathogenesis of MB, are an area of active investigation, but acquired resistance and early relapse with monotherapy have been observed [55•, 56•].

Supratentorial Primitive Neuroectodermal Tumors (PNET)

Pathologic Findings

Central PNET are poorly differentiated (WHO Grade IV), fast growing, neuroepithelial tumors that originate from the germinal matrix of the primitive neural tube. Most frequent in pediatric population, molecular analysis of PNET occurring in adults suggests a different disease [57].

Imaging

CT imaging usually shows a well-limited hemispheric mass, with calcifications, necrotic areas and sometimes intratumoral hemorrhage. MRI shows heterogeneous enhancement with hypointense areas correlating to hemosiderin or calcification; T1 hyperintense regions correspond to hemorrhage and T2 bright regions reflect cystic components.

Treatment

Therapeutic management includes aggressive surgical resection followed immediately by RT to the neuraxis [58, 59]. Adjuvant CT may further improve survival, but the optimal regimen is not known. Management of children younger than 3 years is challenging since craniospinal irradiation put them at high risk for severe neurologic complications. To postpone RT, multi-agent CT regimens have been assessed but resulted in disappointing 5-year median survival [60–62]. High-dose CT regimens appear more promising [62]. Despite aggressive combined modality treatment, recurrence is

common [63, 64]. Children younger than 3 years and patients with pineal PNET have a worse prognosis. Treatment in adults consists of a combination of surgery, craniospinal irradiation (CSI), and adjuvant CT, based upon the approach in older children.

Embryonal tumors with Multilayered Rosettes (ETMR)

Pathologic Findings

Among the 3 histologic variants of highly malignant pediatric ETMR: embryonal tumor with abundant neuropil and true rosettes (ETANTR) and medulloepithelioma may contain a cystic component. Although histologically different, uniform molecular signatures indicate that they comprise 1 biological entity characterized by *LIN28A* positivity, amplification of C19*MC* miRNA cluster at 19q13.42, and frequent trisomy 2 [65]. ETANTR are most often supratentorial. Medulloepitheliomas are located in the periventricular regions, most commonly in the temporal and parietal lobes. Tumor growth is rapid leading to frequent inaugural signs related to increased intracranial pressure and intra-CSF dissemination is not uncommon.

Imaging

CT shows a hypodense or isodense, heterogeneous contrast-enhancing lesion that are sometimes calcified and may contain cystic components. MRI shows T1 hypointense and T2 hyperintense areas with contrast-enhancement that can be heterogeneous or homogeneous.

Treatment

Despite combined surgery, RT, and CT the prognosis is extremely poor [62].

Atypical Teratoid/Rhabdoid Tumors (ATRT)

Pathologic Findings

CNS ATRT are highly malignant tumors primarily occurring in young children less than 3 years old [66]. Histologically, ATRT are characterized by rhabdoid cells and are similar to other small round blue cell tumors; up to 70 % also contain elements typical of a PNET/medulloblastoma. Necrosis and a high rate of mitotic activity are common. Germ cell markers are negative. Over 90 % of tumors show loss of *INI1* nuclear staining, indicative of biallelic inactivation of *SMARCB1* on chromosome 22, and approximately one-third of patients harbor germline mutations in *SMARCB1* [67–70].

Imaging

The majority of ATRT occur in the cerebellum. Cysts or hemorrhages are frequent finding by imaging. MRI shows a hypointense lesion in T1-WI with iso- to hypointense signal in T2 and heterogeneous contrast- enhancement.

Treatment

Aggressive CT and RT are used but the prognosis is poor [71–75].

Mesenchymal Tumors

Pathologic Findings

Among mesenchymal tumors, malignant fibrous histiocytomas (FH) are large masses that sometimes include a cystic component representing previous hemorrhage or liquefied necrosis. FH are composed of atypical fibroblasts and histiocytes and may be either benign or malignant [76, 77]. They may be attached to the dura or be located inside the brain parenchyma.

Imaging

MRI shows a heterogeneous extra-axial mass with thick irregular contrast enhancement and hyperintense areas of liquefied necrosis on T2, whereas hypointense T2 areas represent tumor matrix.

Treatment

Treatment of malignant FH consists of surgery and adjuvant RT and chemotherapy, but provides limited efficacy [78].

Hemangioblastoma (HB)

Pathologic Findings

HB are uncommon, slow-growing, pericyte derived tumors, which most commonly occur in the cerebellum, brainstem, or spinal cord. HB may occur sporadically (approximately 75 %) or as a part of von Hippel-Lindau (VHL) disease, along with retinal angiomas, renal cell carcinoma, pheochromocytomas, pancreatic cysts, and neuroendocrine tumors. Sporadic and VHL-related HB differ significantly in their presentation. When associated with VHL, the mean age of HB diagnosis

is 29 years, 1 to 2 decades younger than in sporadic cases [79]. Distribution in the CNS varies also, with mostly isolated cerebellar lesions in sporadic cases whereas in VHL 50 % of tumors are in the spinal cord, 40 % in the cerebellum, and 10 % in the brainstem [79, 80]. As some supposedly sporadic HB may represent occult cases of VHL, the presence of multiple tumors within the neuraxis and an early age of diagnosis should raise suspicion for VHL.VHL can be detected if patients are appropriately screened for germline VHL mutations. HB can cause local symptoms by compression of neural structures, bleeding, or paraneoplastic complications. Symptoms arising from direct compression depend upon tumor location. Acute hemorrhage can be life-threatening in cerebellar location. Paraneoplastic erythrocytosis has also been reported as a result of excessive erythropoietin production by the HB [81, 82]. HB are well-delineated, highly vascular red nodules that are often located within the walls of large cysts. Microscopically, the 2 main components are an extensive vascular network and the neoplastic "stromal cells. Neoplastic stromal cells, embedded among the vascular channels, have abundant cytoplasm packed with lipid vacuoles [83]. The numerous lipid-containing vacuoles result in the typical "clear cell" morphology. These cells also have large nuclei that are often pleomorphic and hyperchromatic [84]. The mitotic rate is typically low. Many of the clear-cell morphologic features of HB overlap with those of renal cell carcinomas (RCC) but unlike RCC, HB do not have an epithelial origin and so do not express cytokeratins or epithelial membrane antigen (EMA). HB display immunoreactivity to neuron specific enolase (NSE) unlike RCC [85]. Inactivation of the VHL tumor suppressor gene, located on chromosome 3p, is involved in the pathogenesis of both sporadic as well as VHL-associated HB. Somatic mutations of the VHL gene or allelic deletion of the VHL gene may be present in as many as 50 % of sporadic HB [86, 87]. The genetic changes are found in the stromal elements but not in the vasculature, suggesting that abnormal blood vessel formation might be caused by external factors such as erythropoietin and vascular endothelial growth factor (VEGF) that are upregulated in the stromal cells of HB and may be involved in the pathogenesis of this disease [88].

Imaging

MRI shows an enhancing nodule associated with a cyst. Smaller HB (<10 mm) may be isointense on T1-weighted images and hyperintense on T2-weighted images, with homogeneous contrast enhancement.

Treatment

For patients with VHL disease, the frequent development of multiple lesions requires that therapy should avoid treatment-related morbidity by minimizing the frequency of surgical interventions. Small asymptomatic lesions can be followed with careful surveillance. Although surgery can usually and successfully remove lesions in the spinal cord, brainstem, and cerebellum, intervention is reserved until lesions become symptomatic [87, 88]. HB are at risk for tumor growth during pregnancy and should be closely monitored [89]. Both surgical resection and RT have a role in the management of appropriately selected patients. Surgical resection offers histologic diagnosis and definitive therapy for sporadic, isolated accessible HB. In these highly vascular lesions and especially in large volume lesions, a preoperative angiogram is often needed to identify feeding arteries and allow tumor vasculature embolization [90, 91].

Increasing data support the role of RT, particularly for patients with multiple tumors, those with surgically inaccessible lesions or when the risk of postoperative neurologic deficits is high. RT appears also to be an option for recurrent or residual disease if the risk of reoperation is high. Most of the contemporary data come from series using SRS, although external beam RT or proton beam RT may be useful in selected cases [92, 93]. Local control, 5 years progression-free survival and 5 years overall survival rates are 90 %, 90 %, and 70 %, respectively. Inhibitors of angiogenesis may offer a potential therapeutic option when lesions cannot be treated surgically or with radiation, since the role of VEGF in HB genesis has been established.

Tumor-Associated Non-Neoplastic (Benign) Cysts

Pathologic Findings

Extra-axial tumors such as meningioma, schwannoma, craniopharyngioma, and pituitary macroadenoma may be associated with large non-neoplastic cysts that may appear to contain CSF [6]. Most peritumoral cysts trap CSF within the cleft between the expanding tumor and the adjacent brain. Craniopharyngioma and pituitary macroadenoma may obstruct and enlarge adjacent PVS.

Imaging

Most peritumoral cysts demonstrate a CSF-like MRI signal pattern. If protein content is elevated within the trapped CSF, the arachnoid cysts may appear slightly hyperintense to normal CSF on MR images.

Differential Diagnosis

True AC associated with neoplasm may be impossible to distinguish from enlarged PVS with trapped interstitial fluid unless biopsy is performed.

Gliomas and Brain Metastases

Pilocytic Astrocytoma (PA)

Pathologic Findings

PA formerly referred to as juvenile pilocytic astrocytomas, are WHO grade I tumors. They are slow growing, usually well delineated, and frequently cystic tumors. They are distinguished from diffuse astrocytoma and oligodendroglial glioma because of their well-defined character, earlier age of onset, lack of invasiveness, and mostly favorable outcome.

PA are frequently located in the cerebellar hemispheres and around the third ventricle, but may also be observed in the cerebral hemispheres [94]. PA occur predominantly in children and young adults.

Microscopically, when compared with fibrillary astrocytoma, there is scarce intercellular fibrillary matrix notwithstanding glial fibrillary acidic protein (GFAP)-positive fibrils are observed in the cell cytoplasm. Tumor cells distant from blood vessels have a rarefied and sparsely cellular appearance and may undergo microcystic degeneration. Rosenthal fibers are frequent and are a useful pathologic hallmark in differentiating PA from other low-grade gliomas (LGG). Molecular profile may also be helpful in discriminating PA from other LGG. A tandem duplication of chromosome 7q34, which is associated with a BRAF-KIAA fusion gene is frequent [95]. This fusion gene has been reported in 60 %–80 % of cases PA seen in conjunction with neurofibromatosis type 1, however, these tumors lack this fusion gene.

Imaging

PA are almost always well-delineated and intensely enhance on CT and MRI. Cysts with a contrast enhancing nodule are characteristic of PA, however, solid contrast enhancing tumors and cystic tumors are seen as radiographic variants as well.

Treatment

Because of their circumscribed nature, a complete surgical resection is often accomplished resulting in frequent cures and a much better prognosis than diffuse infiltrative gliomas. Rare transformation of a PA sometimes with multicentric spread, have been reported [96]. Malignant transformation occurs in 5 %–10 % of cases and can be associated with rapid evolution [97]. Surgical resection is the standard initial approach, and RT or CT is generally withheld until a tumor growth is proved, even in case of incomplete resection. Surgery should ideally be complete in order to cure PA. RT at the time of diagnosis may be required when surgery is not feasible. When RT is recommended, an involved field fractionated course to 54 Gy is usually used. Prolonged survival is observed even in case of incomplete tumor resection with 10-and 20-year overall survival rates above 80 % [94, 96]. The combination of bevacizumab and irinotecan showed some evidence of activity in case of malignant transformation in small prospective pediatric series [98].Targeting the BRAF-KIAA fusion gene may be a therapeutic option in the near future.

Glioblastoma (GB) and Brain Metastases (BM)

Pathologic Findings

Cystic GB or BM are defined by a cyst's size $\geq$50 % of tumor volume [99–101]. Large cystic components combined with peritumoral edema add to the morbid effects of GB/BM by way of increased mass effect and intracranial pressure. Although different mechanisms have been suggested as to the pathogenesis of tumor-associated cysts, it is still unclear why these cysts appear in a limited number of GB/BM [102]. Analysis of brain tumor cyst content has invalidated the concept of cyst formation being the result of tumor necrosis. A common mechanism for both vasogenic peritumoral brain edema and cyst formation, ie, blood-brain barrier (BBB) disruption, has been suggested.

Imaging

MRI of BM shows a solid enhancing mass with well-defined margins and extensive edema. Multiple lesions are frequent (80 %). Occasionally, central necrosis produces a ring enhancing mass. Lesions are isointense to mildly hypointense on T1-W MRI, hyperintense on T2-W, or FLAIR MRI. Surrounding edema is relatively hypointense on FLAIR and T1-weighted images and hyperintense on T2-weighted images.

Differential Diagnosis

As in other cystic multiple lesions, there exists a wide differential diagnosis and only biopsy or resection can confirm the diagnosis of BM. FLAIR MRI improves the distinction between intracranial cysts with a free water-like content vs those filled with a non-free water-like substance and, consequently, aids in the identification of these lesions as either neoplastic/inflammatory or developmental/porencephalic.

FLAIR has the added advantage of demonstrating a higher signal intensity difference between cystic intracranial lesions and CSF. MRS and DWI are useful for differentiating brain abscess from brain tumor, but the latter requires less time and is more accurate than is MRS [103]. Demonstration of restricted diffusion on DWI with reduced ADC is highly suggestive of brain abscess; however, in the absence of restriction, MRS is mandatory to distinguish brain abscesses from

cystic tumors [104]. The vast majority of GB do not exhibit restricted diffusion by DWI, but some display homogeneous or heterogeneous high signal intensity and decrease of ADC values. DWI alone is not helpful in the differentiation of malignant tumor from abscesses with low ADC values and similar conventional MRI findings [104].

Treatment

The treatment of GB and BM with cysts is not materially different than these tumors without cysts. BM are treated with surgery if large or solitary. GB when possible is resected maximally. Both BM and GB are treated with RT (either SRS or conventional RT in BM) and combined with chemotherapy in GB (chemoradiotherapy). On occasion cysts are problematic are managed with surgical aspiration or placement of an intra-cyst catheter and reservoir to permit aspiration and instillation of intra-cyst chemotherapy or colloidal radiotherapy [105–108].

Cystic Lesions of Infectious Origin

Neurocysticercosis

Pathologic Findings

Cysticercosis is the most common and widely disseminated parasitic infection of the nervous system [109–111]. Neurocysticercosis occurs in 60 %–90 % of all cases of systemic cysticercosis. The majority of neurocysticercosis cysts are found in the subarachnoid spaces and typically in the basal cisterns. Other common locations include the hemispheric parenchyma at the gray/white matter interface and in the ventricles [109, 110]. Seizures are the most common manifestation of neurocysticercosis [109, 111].

Imaging

Imaging findings in neurocysticercosis vary with the stage of cyst development.

The early vesicular stage is characterized by a smooth thin-walled cyst that is CSF-like by CT and MRI. Edema and enhancement are rare in this stage. A mural nodule may be seen that represents the larval scolex or parasite head giving an imaging pattern described as a "cyst with a dot" appearance [109, 110]. A cystic brain lesion(s) with an associated scolex is pathognomonic of neurocysticercosis.

With cyst degeneration (the so called colloidal-vesicular stage), a host inflammatory response is seen resulting in pericystic edema and cyst wall enhancement. Cyst fluid is hyperintense relative to CSF by MRI during this stage [110]. In the healing, or granular nodular stage, nonenhanced CT scans show an isodense cyst with a calcified scolex. Surrounding edema is still present, and enhancement following contrast material administration persists.

The residual cyst is isointense to the parenchyma on T1-W MRI and it is iso- to hypointense on T2-W MRI. Enhancement is common at this stage, suggesting a granuloma. A "target" or "bull's eye" appearance may be seen with the calcified scolex in the center of the mass [110]. In the quiescent or residual stage, small calcified nodules without mass effect or enhancement are seen [109, 110]. Multifocal lesions and lesions in different stages of development are common.

Differential Diagnosis

The differential diagnosis for neurocysticercosis includes abscess, tuberculosis ie, a tuberculoma, neoplasm (primary or metastatic), enlarged PVS, and other parasitic infections. Abscesses have a T2-hypointense rim by MRI, whereas neurocysticercosis cysts are typically isointense. Tuberculomas often occur with meningitis, are rarely cystic, and are usually hypointense on T2-weighted MRI. Enlarged PVS have the same appearance as CSF on all MR sequences and do not enhance. None of the above cystic lesions has the characteristic "cyst with dot" appearance [109].

Treatment

Antiepileptic therapy (AET) is administered for patients who present with seizures. Calcified lesions can also cause seizures but are not generally considered an indication for primary prophylactic AET. Optimal treatment duration is uncertain, indefinite therapy may be appropriate for calcified lesions, especially in those with recurrent seizures [112]. Most experts recommend 6 to 12 months after MRI resolution of active infection.

Antiparasitic therapy (APT) accelerates resolution of active cysts, decreases risk for seizures, and for development of hydrocephalus [113•]. Corticosteroids (CS) may provide better seizure control and faster radiologic resolution. The potential risk of APT is worsening of neurologic symptoms because of increased inflammation around the degenerating cyst, particularly in patients with multiple lesions. For this reason, CS are often administered concomitantly with APT. Patients with diffuse cerebral edema and multiple inflammatory cysticerci should be treated with CS alone. APT are not helpful in case of calcified cysts only since there is no viable lesions in that case.

Subarachnoid cysts should be treated with APT and CS. Intraventricular cysts complicated by hydrocephalus should undergo endoscopic resection when accessible [114]. If this is not the case, APT, CS, or surgical intervention should be proposed. APT should not be given prior to surgery since they

can weaken the cyst membrane, causing friability and/or adherence to the ventricular wall. APT and CS are not necessary in most cases after cyst removal unless there is a coexisting parenchymal disease. If APT is administered, albendazole is preferred over praziquantel given its favorable pharmacokinetic profile [113•]. Therapy recommended duration is variable depending on the clinical presentation, 7 days for a single enhancing lesion, 10-14 days for multiple lesions, at least 28 days for subarachnoid disease. Prior to the initiation of ATP and CS, screening for latent tuberculosis infection, strongyloidiasis, and ocular cysticercosis should be pursued. A radiological follow-up should be provided in order to confirm resolution of the cysticerci and development of calcification in patients with intraparenchymal or subarachnoid locations.

Hydatid Cyst (HC)

Pathologic Findings

Intracranial hydatid cysts (HC) are parasitic infections caused by the larval stage of

Echinococcus granulosus [110]. Cerebral hydatid HC are rare. The most common location for is within the brain parenchyma and in the territory of the middle cerebral artery [110, 115]. The subarachnoid spaces are another common site of involvement. HC are usually solitary and comprised of a single cavity. They grow slowly and are typically large (4–10 centimeter in diameter) when discovered. The cysts contain clear fluid and may also contain daughter cysts within the mother cyst. Parasitic components (protoscolices) within the cyst may form a granular deposit known as hydatid sand [115].

Imaging

MRI demonstrates a single, large, thin-walled, nonenhancing CSF-like cyst lacking perilesional edema. Imaging components characteristic of a HC are the cyst and the pericyst wherein the pericyst is defined as the capsule of the fluid filled cyst and is best observed on MRI.

Differential Diagnosis

The differential diagnosis for includes AC, EC, and neurocysticercosis [see discussion above] [110].

Treatment

The goals of surgical therapy consist of evacuating the cyst and obliterating the residual cavity. Removal of the intact cyst is preferred, if feasible. Alternatively, the cyst can be opened and sterilized with protoscolicidal agents, followed by evacuation of cyst contents and removal of the pericystic tissue. Every effort should be made to avoid fluid spillage, which can lead to secondary seeding of infection and/or anaphylaxis.

Other Bacterial, Fungal, and Parasitic Cysts

Pathologic Findings

Many infectious agents occasionally infect the central nervous system and may appear at least partially cystic. They can be divided into bacterial, fungal, and parasitic agents. The most frequent bacterial agents are causing pyogenic and tuberculous abscesses but listeria and other mycobacteria may be involved. Amongst fungal infections, nocardiosis, actinomycosis, aspergillosis, cryptococcosis and histoplasmosis are most frequent. Parasitic infections are many, including toxoplasmosis, amebiasis, paragonimiasis, schistosomiasis, and sparganosis, and can cause both uniocular and complex intraparenchymal cysts with or without associated meningoencephalitis. Perilesional edema and petechial hemorrhage are common.

Imaging

Complex multicompartmental cysts with enhancing rims and adjacent edema are common.

Differential Diagnosis

Complex parasitic cysts of any origin may mimic primary or metastatic brain tumor. A history of travel and diet as well as serologic findings are key to the diagnosis these lesions.

Treatment

Treatment is dependent upon the isolated organism and often mandates the assistance of an infectious disease expert.

Conclusions

A broad spectrum of diseases can cause intracranial cysts that may result in a diagnostic challenge. The combination of location and specific imaging findings often permits the differential diagnosis in these challenging situations to be narrowed considerably [6].

Many intracranial cysts occur in characteristic locations. Some locations are virtually pathognomonic for certain lesions (eg, colloid cyst in the third ventricle), whereas others are suggestive of but not specific for a particular diagnosis

(eg, middle cranial fossa and arachnoid cyst). Osborn et al have proposed a useful diagnostic algorithm based on a series of imaging questions that may assist clinicians with this diagnostic challenge [6].These questions, paraphrased and posed in the following order are: (a) Is the cyst in or outside of brain parenchyma (intra- or extra-axial)? (b) Is the cyst in the cerebral hemisphere or posterior fossa (supra- or infratentorial)? (c) Is the cyst extra-axial midline or off midline? (d) Is the cyst intra-axial, intraparenchymal, or intraventricular? (e) If the cyst is intraventricular, in what location and which ventricle? (f) How closely dose the cyst resemble CSF on CT/MRI? (g) Are there any distinguishing features such as calcification, contrast enhancement, or diffusion restriction?

Nevertheless, in unclear cases, or in some life-threatening conditions treatment may be required as with a bacterial brain abscess for which biopsy or surgery and subsequent microbiology/pathology analyses can establish the diagnosis.

Compliance with Ethics Guidelines

Conflict of Interest Marc C. Chamberlain declares that he has no conflict of interest. Sophie Taillibert has received board membership payments from Roche and consultancy fees and paid travel accommodations from Roche and Mundipharma. Emilie Le Rhun has received consultancy fees and paid travel accommodations from Roche and Mundipharma.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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