BRAIN CME

# Glioneuronal and Neuronal Tumors: Who? When? Where? An Update Based on the 2021 World Health Organization Classification

A.S. Ayres, G.A. Bandeira, S.F. Ferraciolli, J.T. Takahashi, R.A. Moreno, L.F. de Souza Godoy, Y.R. Casal, L.G.C.A. de Lima, F.P. Frasseto, and L.T. Lucato

## CME Credit

The American Society of Neuroradiology (ASNR) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. The ASNR designates this journal-based CME activity for a maximum of 1 *AMA PRA Category 1 Credit*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity. To obtain Self-Assessment CME (SA-CME) credit for this activity, an online quiz must be successfully completed and submitted. ASNR members may access this quiz at no charge by logging on to eCME at asnr.mycrowdwisdom.com. Nonmembers may pay a small fee to access the quiz and obtain credit via asnr.mycrowdwisdom.com.

## ABSTRACT

Neuronal and glioneuronal tumors usually have a benign course and may have typical imaging characteristics, allowing their diagnosis based on MR imaging findings. The most common lesions are dysembryoplastic neuroepithelial tumors and gangliogliomas, which have typical imaging characteristics. The fifth edition of the *World Health Organization Classification of Tumors of the Central Nervous System*, recently published in 2021, places greater emphasis on molecular markers to classify tumors of the CNS, leading to extensive changes in the classification of tumors, including neuronal and glioneuronal tumors. The 2021 revision included 3 new tumors types: multinodular and vacuolating neuronal tumor, diffuse glioneuronal tumor with oligodendroglioma-like features and nuclear clusters (a provisional type), and myxoid glioneuronal tumor. Following these recent changes in the World Health Organization classification, we aimed to review the main imaging features of these lesions in relation to their histopathologic and molecular features.

Learning Objectives: To list the neuronal and glioneuronal tumors; recognize the main imaging findings and histologic characteristics of neuronal and glioneuronal tumors; know the typical location of each neuronal and glioneuronal tumor; and become familiar with the main molecular alterations of neuronal and glioneuronal tumors to better understand their behavior

## INTRODUCTION

The World Health Organization (WHO) revised the brain tumor classification in 2016,[1] and it was recently updated in 2021.[2] Since 2016, the WHO suggested combining molecular and histopathologic criteria for the categorization of CNS tumors, which led to extensive changes in tumor classification. Neuronal and mixed neuronal tumors are a category of brain neoplasms. Their classification has also changed since the 2016 update and evolved across the years on the basis of the updates from the Consortium to Inform Molecular and Practical Approaches to CNS Tumor Taxonomy (cIMPACT-NOW).[3–9] Louis et

## ABBREVIATION KEY

CN = central neurocytoma
DIA = desmoplastic infantile astrocytomas
DIG = desmoplastic infantile ganglioglioma
DLGNT = diffuse leptomeningeal glioneuronal tumor
DNET = dysembryoplastic neuroepithelial tumor
EVN = extraventricular neurocytoma
GFAP = glial fibrillary acidic protein
IH = immunohistochemical
MAP = mitogen-activated protein
MGT = myxoid glial tumors
MVNT = multinodular and vacuolating neuronal tumor
NeuN = neuronal nuclei
NSE = neuron-specific enolase
PGNT = papillary glioneuronal tumors
RGNT = rosette-forming glioneuronal tumor
WHO = World Health Organization

Received October 11, 2021; accepted February 22, 2022.

From the Instituto do Câncer do Estado de São Paulo (A.S.A., J.T.T., R.A.M., L.G.C.A.d.L.), Hospital das Clínicas da Faculdade de Medicine da Universidade de São Paulo, São Paulo-SP, Brazil; Department of Radiology (G.A.B., S.F.F., L.F.d.S.G., Y.R.C., L.T.L.), Hospital das Clínicas da Faculdade de Medicine da Universidade de São Paulo, São Paulo-SP, Brazil; and Department of Anatomical Pathology (F.P.F.), Hospital das Clínicas da Faculdade de Medicine da Universidade de São Paulo, São Paulo-SP, Brazil.

Paper previously presented at the 59th Annual Meeting of the American Society of Neuroradiology, May 22–26, 2021; Virtual.

Please address correspondence to Aline Sgnolf Ayres, MD, Instituto do Câncer do Estado de São Paulo/ICESP–HC/FMUSP, Universidade de São Paulo/Hospital das Clínicas, Dr Arnaldo, 251-ICESP, Cerqueira César, São Paulo-SP, Brazil, CEP: 01246-000; email: aline.ayres@hc.fm.usp.br/alinesayres@gmail.com

http://dx.doi.org/10.3174/ng.2100047

Disclosures
L.F. de Souza Godoy—*RELATED: Stock or stock options:* United Health Group, Johnson & Johnson Co., Illumina Inc., Comments: Stock owner. F.P. Frasseto—*RELATED: All support for the present manuscript (e.g., funding, provision of study materials, medical writing, article processing charges, etc.):* Universidade de São Paulo - Hospital das Clínicas da Faculdade de Medicine.

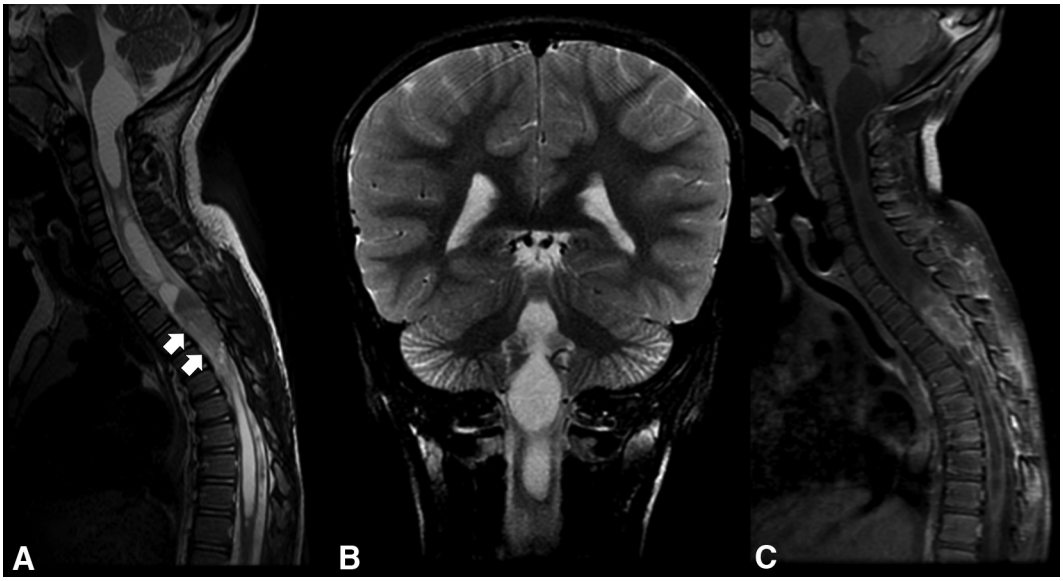


**FIG 1. Gangliocytoma. Sagittal (*A*) and coronal (*B*) T2WI and sagittal postcontrast T1WI (*C*) show a solid-cystic lesion involving the medulla and the spinal cord and presenting with hyperintensity on T2WI (*A* and *B*) and heterogeneous enhancement (*C*). Note the solid portion that is more evident in the cervicothoracic junction (*arrows*).**

al,[2] in 2021, compiled the alterations throughout the years in a résumé of the upcoming fifth edition of the WHO classification of tumors of the CNS. In their résumé, they summarized the changes in the classification of a broad spectrum of circumscribed gliomas, glioneuronal tumors, and neuronal tumors. Three new tumor types were included in the fifth edition: multinodular and vacuolating neuronal tumor (which was mentioned in the 2016 classification), diffuse glioneuronal tumor with oligodendroglioma-like features and nuclear clusters (a provisional type), and myxoid glioneuronal tumor.[2] Brain MR imaging findings are usually characteristic in patients with neuronal and glioneuronal tumors, and they are generally indicative of the diagnosis, prevent unnecessary surgical procedures, and guide the imaging follow-up. Thus, patient- and tumor-related data such as patient age, tumor location, and lesion signal pattern represent useful information that can be used to narrow the differential diagnosis.

Following the recent changes in the WHO classification, we aimed to review the main imaging features of tumor lesions in relation to their histopathologic and molecular features.

## NEURONAL TUMORS

### *Gangliocytoma*

Gangliocytomas are rare tumors accounting for 0.1% of all CNS tumors and are often associated with brain malformations and dysplasia.[10–12] The most common locations are the floor of the third ventricle, temporal lobe, parieto-occipital region, frontal lobe, cerebellum, and spinal cord.[11] Gangliocytomas occurring in the sellar region can simulate macroadenomas and lead to hormonal disorders.[13]

Gangliocytomas are WHO grade I tumors that share clinical and histopathologic characteristics with gangliogliomas, such as groups of dysmorphic neurons without neoplastic glial cells.

In imaging studies, gangliocytomas are occasionally difficult to identify. They are hyperdense lesions on CT. On MR imaging, gangliocytomas are hypointense on T1WI and isointense-to-discretely hyperintense on T2WI, with little expansive effect and no vasogenic edema in the adjacent parenchyma.[14] In some cases, cysts are observed (Fig 1).[14] The main differential diagnoses are solid ganglioglioma and cortical dysplasia, especially when occurring in the temporal lobe.

### *Dysplastic Cerebellar Gangliocytoma (Lhermitte-Duclos Disease)*

Dysplastic cerebellar gangliocytomas of the cerebellum (Lhermitte-Duclos disease) are WHO grade I neuronal tumors[2] with approximately 300 reported cases.[15] The etiology of this tumor is still uncertain and may be related to hamartoma, neoplasia, or dysplasia. These tumors have a biphasic age distribution with the average age being 4.3 years in the pediatric group and 42.5 years in the adult group.[16,17] Dysplastic cerebellar gangliocytomas are one of the main CNS manifestations of Cowden syndrome.[15–17]

Histologically, the molecular, Purkinje, and granular layers are replaced by dysplastic ganglion cells. This process is associated with abnormal myelination of the molecular layer, white matter vacuolization, capillary calcifications, and ectatic vessels.[2,8]

Adult and pediatric patients have different genetic characteristics. Phosphatase and tensin homolog deleted on chromosome 10 (*PTEN*) mutations, either hereditary or sporadic, are present in adult-onset but not in childhood-onset cases of Lhermitte-Duclos disease (Fig 2).[15,17] On MR

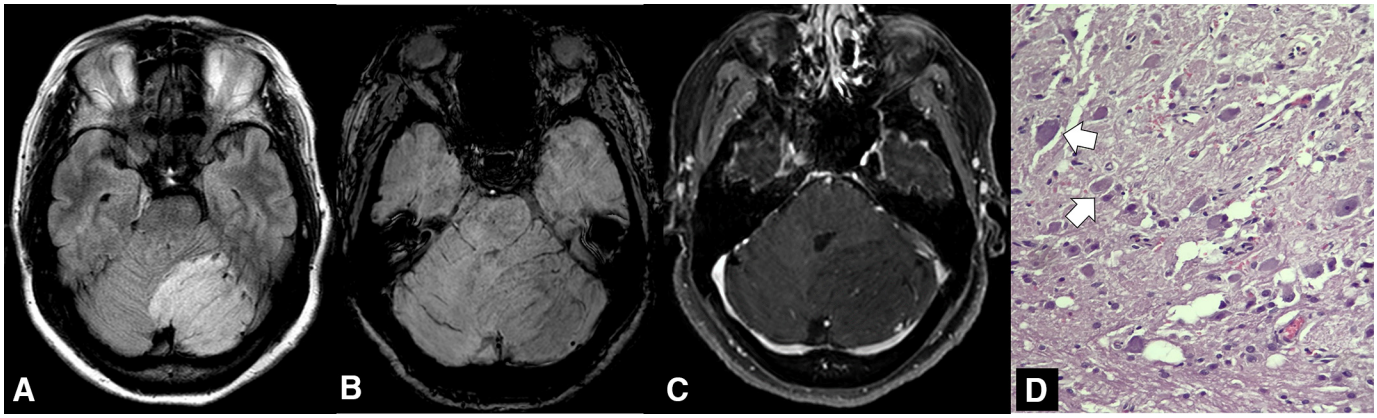


**FIG 2. Lhermitte-Duclos disease. Axial FLAIR (*A*), SWI (*B*), and T1WI gadolinium-enhanced (*C*) images show a left cerebellar lesion with hyperintensity on FLAIR (*A*), prominent vascular structures (*B*), and no substantial postcontrast enhancement (*C*). H&E, original magnification ×200 (*D*). Note increased, disorganized, and dysplastic mono- or binucleated ganglion cells with enlarged nuclei, prominent nucleoli, and abundant cytoplasm (*arrows* in *D*).**

imaging, these tumors are hypointense on T1WI, appear hyperintense on T2WI, and may show postcontrast enhancement. The distinctive tiger stripes sign is characterized by hyperintense thickening of the cerebellar folia on T2WI interspersed with linear areas of low signal intensity that may correspond to blood vessels. This sign is rarely observed in pediatric patients.[17] Some patients also show signs of hemorrhage. When MR imaging shows the typical pattern, the diagnosis can be made with some confidence (Fig 2). However, even in the presence of typical imaging characteristics, the differential diagnosis includes nonneoplastic lesions, such as stroke, especially in the adult population.

### *Central and Extraventricular Neurocytomas*

Neurocytomas are rare neoplasms of WHO grade II, comprising approximately 0.2%–0.5% of all brain tumors.[18] They are more frequent among young adults around 30 years of age.[19] A higher incidence of neurocytomas has been reported in Eastern countries, which can be attributed to genetic differences.[10] These tumors are classified as central neurocytomas (CNs) or extraventricular neurocytomas (EVNs).

Typically, neurocytomas are circumscribed lesions without entrapped neurons or axons. They are composed of neurocytic cells with clear cytoplasm, simulating oligodendrogliomas,[16,19] and contain uniform round cells with neuronal differentiation and a low proliferation rate.[10] In immunohistochemical (IH) studies, they are usually diffusely positive for synaptophysin and neuron-specific enolase (NSE), and heterogeneous expression of glial fibrillary acidic protein (GFAP) can also be observed in neurocytic cells.[10,19] *IDH1/2* mutations and 1p/19q codeletion exclude the diagnosis of CN/EVN.[16] Many types of genetic mutations have been associated with neurocytomas, in particular the overexpression of *N-MYC*, *IGF2*, *PTEN*, *PDGF-D*, and *NRG-2*.[16]

CNs usually occur in the supratentorial parenchyma, the lateral ventricles, or the third ventricle, mainly in the region of the foramen of Monro, typically attached to the septum pellucidum. When neurocytomas occur outside the ventricular system with parenchymal infiltration, they are called EVNs. They can be located along the spinal cord or in the cerebral hemispheres, brain stem, thalamus, pons, amygdala, pineal gland, retina, and cerebellum.[18,20] Clinically, they may present with obstructive hydrocephalus, signs of increased intracranial pressure, and nonspecific focal signs.

CT usually demonstrates hyperdense lesions in the lateral ventricles, and cysts and calcifications are present in up to 50% of cases.[18] On MR imaging, CNs present as intra-/periventricular lesions with heterogeneous intralesional signal, sometimes with a bubblelike appearance, mainly hyperintense on T2WI and DWI, with postcontrast enhancement.[16,18,21] They may also show low-intensity foci on SWIs, which correspond to calcifications and hemorrhages. On MR imaging, EVNs can be difficult to distinguish from aggressive gliomas, such as glioblastoma, oligodendroglioma, and anaplastic ependymoma.[21] The main differential diagnosis of CN is glioma (oligodendroglioma) and intraventricular tumors that can attach to the septum pellucidum, such as subependymoma and subependymal giant cell tumor. The topography and heterogeneous pattern are the main MR imaging features that suggest the diagnosis of neurocytoma (Figs 3 and 4).

***Cerebellar Liponeurocytoma.*** Liponeurocytomas are very rare with greater occurrence in the cerebellum, but they have also been found in the supratentorial brain parenchyma, mostly inside the lateral ventricles.[22,24,25] These tumors are classified as WHO grade II due to the possibility of recurrence after surgical resection.[22] They occur in adults 30–60 years of age, with only 42 cases reported until 2009.[23] The origin of liponeurocytoma has not yet been established.

Cerebellar liponeurocytoma has a neurocytic component accompanied by lipidized neoplastic cells that resemble mature adipocytes. In IH staining, areas of neuronal

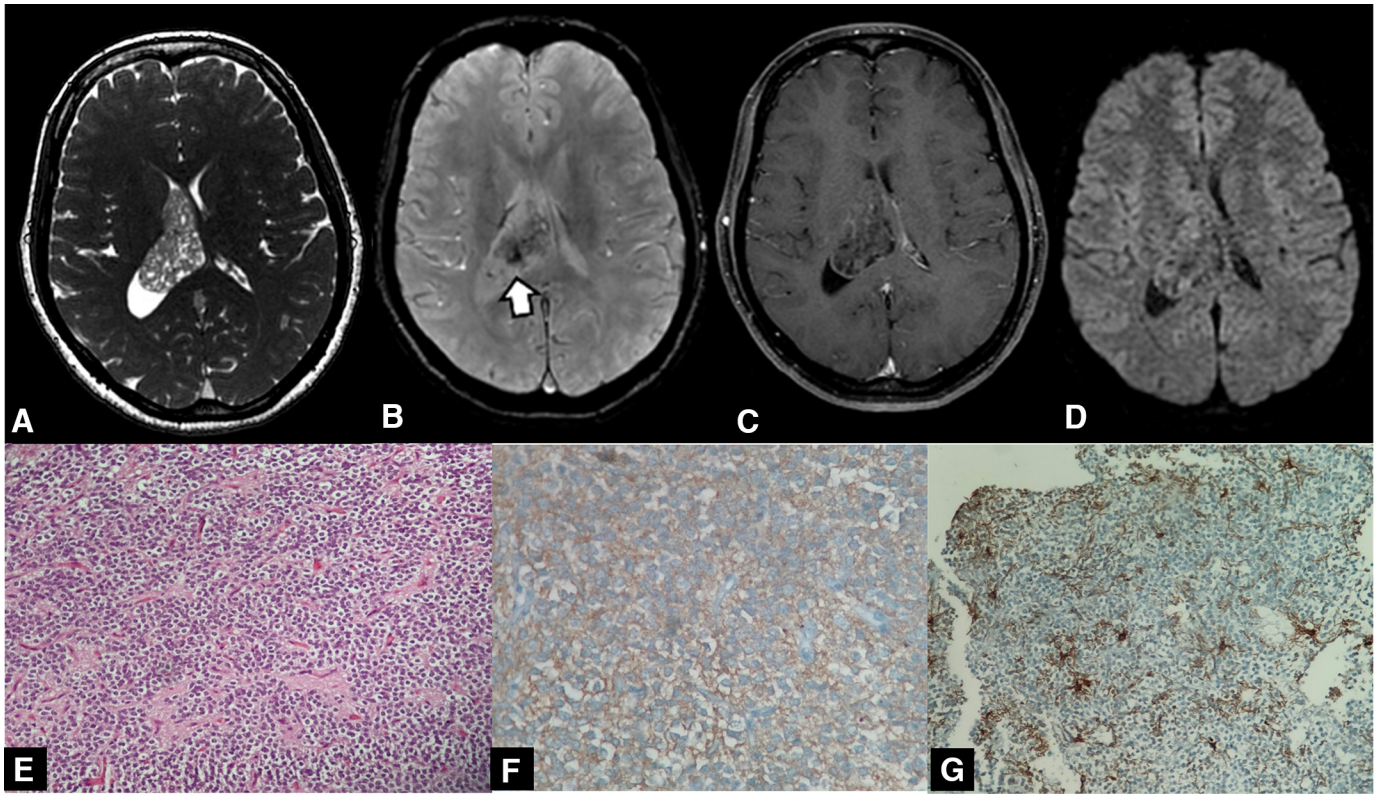


**FIG 3. Central neurocytoma. Axial T2WI (*A*), SWI (*B*), postcontrast T1WI (*C*), and DWI (*D*) show an intraventricular multicystic lesion with hyperintensity on T2WI (*A*) and intralesional hypointense foci on SWI (*arrow* in *B*), which may be caused by calcification or hemosiderin deposition, minimal contrast enhancement (*C*), and no restriction on DWI (*D*). H&E, original magnification ×200 (*E*); immunohistochemistry (IH) synaptophysin, original magnification ×400 (*F*); and IHC GFAP, original magnification ×200 (*G*). Note hypercellular neoplasm consisting of round and monotonous cells with clear cytoplasm, oval nuclei, and fine granular chromatin (*E*). Synaptophysin is diffusely positive, demonstrating the neuronlike immunophenotype (*F*); neoplastic cells are GFAP-negative, but reactive glial cells are GFAP-positive (*G*).**

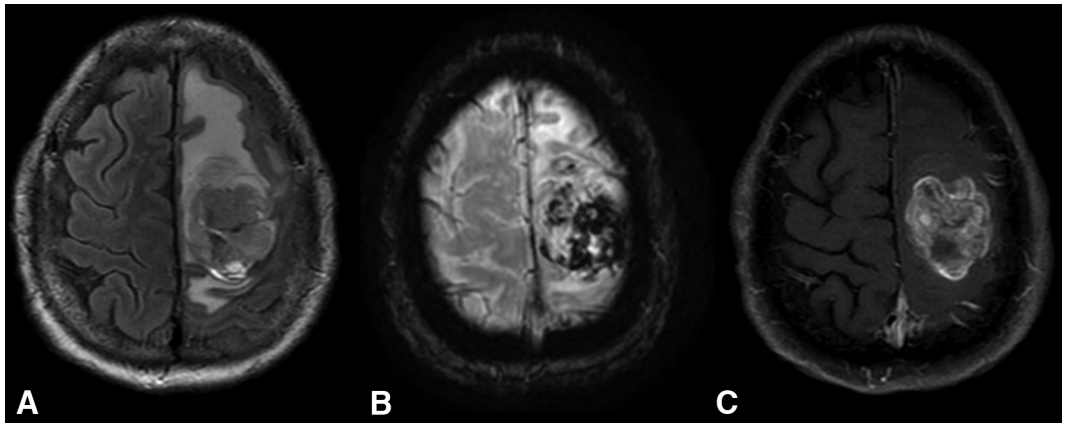


**FIG 4. Extraventricular neurocytoma. Axial FLAIR (*A*), SWI (*B*), and postcontrast T1WI (*C*) show a heterogeneous lesion, presenting as hyperintensity on FLAIR (*A*) and intralesional hypointense areas on SWI (*B*), which may be due to hemorrhage, and heterogeneous enhancement (*C*). Vasogenic edema can be seen in the surrounding brain parenchyma.**

differentiation are positive for markers such as synaptophysin and MAP-2. GFAP reactivity is usually present but focal.[22,24] In general, mitosis, necrosis, or vascular hyperplasia is not observed. The Ki-67 index is frequently low (<5%); however, there are cases with a relatively high proliferation rate and cytopathologic atypia that portend a higher risk of recurrence.[22,24]

On MR imaging, lesions are heterogeneous, predominantly isointense/hypointense on T1WI and isointense/hyperintense T2WI with intervening cysts and calcifications, which appear as hypointensities on SWIs. The accumulation of fat inside the lesion is a typical finding, though not always present, and can suggest the preoperative diagnosis of these tumors on both CT and MR imaging.[25]

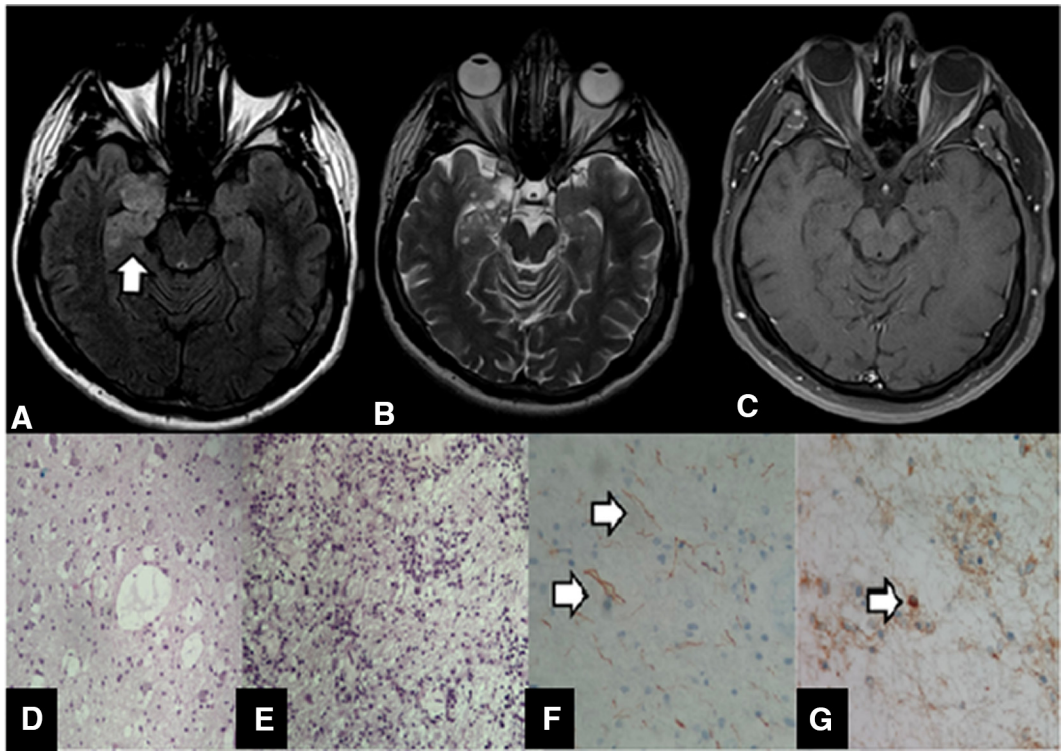


**FIG 5. DNET. Axial FLAIR (*A*), T2WI (*B*), and postcontrast T1WI (*C*) show a multicystic cortical lesion that involves the right medial temporal region and amygdala. The lesion has a bubblelike appearance, is hyperintense on T2WI (*B*), and is partially suppressed on FLAIR images (*arrow* in *A*). There is no contrast enhancement (*C*) or edema in the surrounding parenchyma. H&E, original magnification ×200 (*D* and *E*); immunohistochemistry neurofilament, original magnification ×400 (*F*), and synaptophysin, original magnification ×400 (*G*). Note microcysts associated with the classic presentation of ganglion cells in mucin lakes ("floating neurons") (*D*) and specific glioneuronal elements (columns formed by axons lined by cells similar to uniform and lined oligodendroglioma cells) (*E*). Neurofilament staining highlights mainly the cellular extensions (*F*), and synaptophysin highlights mainly the neuronal body (*G*).**

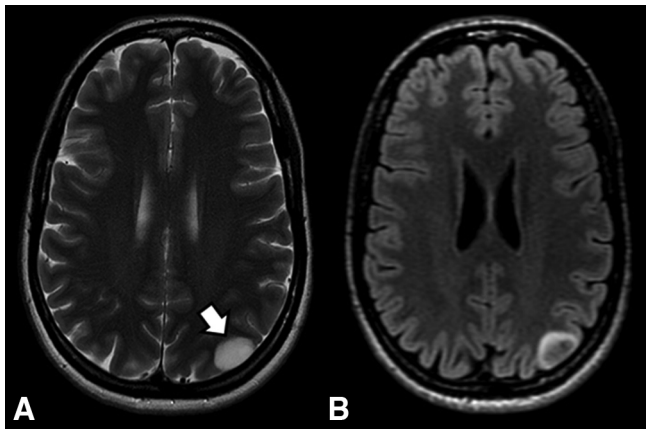


**FIG 6. DNET. Axial T2WI (*A*) and FLAIR imaging (*B*) show an extratemporal DNET presenting with the so-called mismatch sign. The lesion is hyperintense on T2WI (*arrow* in *A*) with central hypointensity on FLAIR imaging (*B*).**

## GLIONEURONAL TUMORS

### *Dysembryoplastic Neuroepithelial Tumor*

Dysembryoplastic neuroepithelial tumors (DNETs) are glioneuronal tumors that are typically located in the temporal lobes of children or young adults. DNETs correspond to 1.2% of neuroepithelial tumors diagnosed in patients younger than 20 years of age and 0.2% in patients older than 20 years of age.[1]

On imaging, these tumors are characteristically located in the cortex, especially in the temporal lobe, involve mesial structures, and present as wedge-shaped lesions with internal septations. DNETs do not generally show postcontrast enhancement; however, about 20% of these tumors are characterized by gadolinium enhancement, often in multiple rings and nodular shapes, which may also occur in a previously nonenhancing tumor.[26] Calcifications may be present, and the absence of mass effect or peritumoral edema is also a typical finding.[26] The hyperintense ring sign on FLAIR imaging and high ADC values (mean, 2.54 [SD, 0.13] $\times 10^{-3}$ $mm^2/s$) are radiologic findings that may help differentiate DNETs from other entities such as gangliogliomas and low-grade gliomas.[27] Extratemporal DNETs can present with the mismatch sign, ie, hyperintensity on T2WI and lower signal intensity on FLAIR images (Figs 5 and 6).[28]

Morphologically, DNETs are characterized by a specific glioneuronal element with intracortical multinodularity and an association with focal cortical dysplasia. They can be further divided into simple and complex tumors, with the simple form consisting of only specific glioneuronal elements, whereas complex types are characterized by specific glioneuronal elements associated with glial nodules. Nonspecific and diffuse types of DNETs lack the multinodular

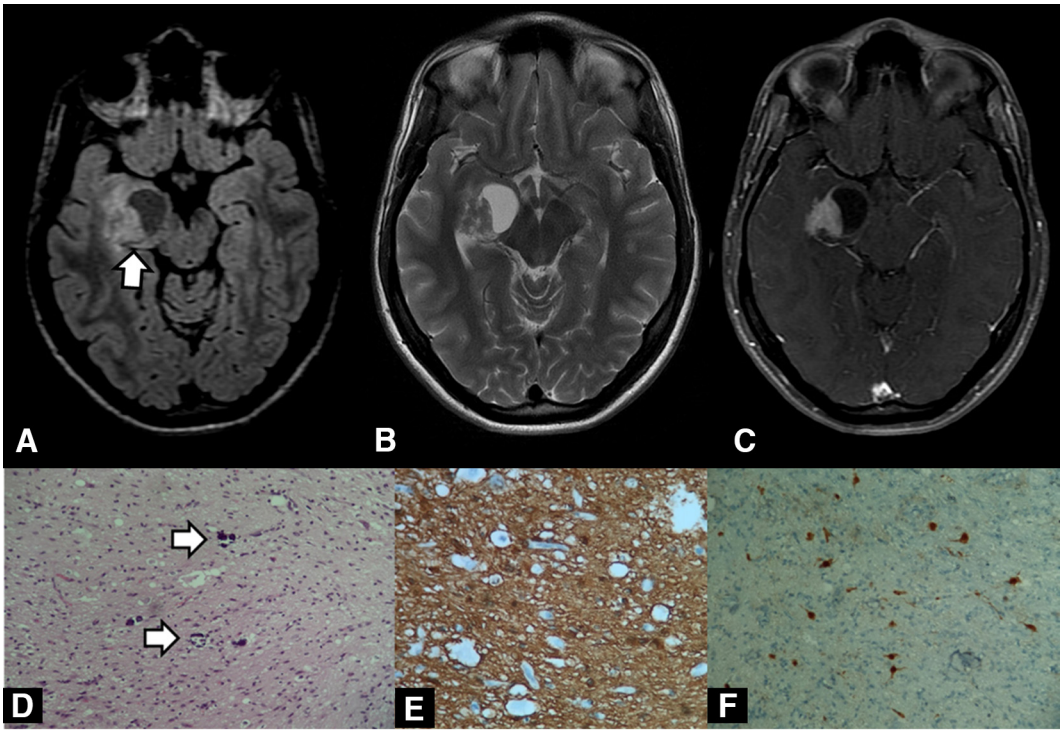


**FIG 7. Ganglioglioma. Axial FLAIR (*A*), T2WI (*B*), and postcontrast T1WI (*C*). Note a solid-cystic mass in the right anterior mesial temporal lobe that is hyperintense on FLAIR imaging (*arrow* in *A*) and T2WI (*B*). Nodular and rim contrast enhancement can be observed (*C*). H&E, original magnification ×200 (*D*), immunohistochemistry GFAP, original magnification ×400 (*E*); and NeuN, original magnification ×400 (*F*). Note a proliferative lesion composed of glial and ganglion cells arranged with irregular and disorganized spacing, with variations in cellularity and distribution, as well as multiple calcification foci (*arrows*, *D*). GFAP staining highlights the glial component (*E*), whereas synaptophysin (not shown) and NeuN (weak staining) highlight parts of the dysplastic ganglion-like cells (*F*).**

architecture and specific glioneuronal elements but show histologic findings similar to those seen in glial nodules of complex DNETs.[29,30] The existence of nonspecific DNETs has been controversial because the histology of these tumors is indistinguishable from that of conventional gliomas. They also lack the specific glioneuronal element or intracortical multinodularity typically found in DNETs.[29,30]

Despite their typical morphology, the histologic diagnosis of DNETs can be difficult. Gangliogliomas and diffuse low-grade gliomas are the main pathologic confounders. In this context, molecular evaluation can be helpful because DNETs typically do not have *IDH1* mutations or 1p/19q codeletion. The BRAF V600E mutation and *FGFR* alterations are the most recently described genetic aberrations present in DNETs.[31]

### *Ganglioglioma*

Gangliogliomas are well-differentiated, typically slow-growing glioneuronal neoplasms composed of dysplastic ganglion cells in combination with neoplastic glial cells.[1,32] Patient age at diagnosis is usually from 8.5 to 25 years, and these tumors account for only 0.5% of all CNS tumors, with a higher incidence rate in the pediatric population (1.5% of all pediatric tumors).[12] They may affect the entire neuraxis, but their most frequent and typical location is the supratentorial temporal region, occurring in approximately 70% of cases.[1] They may have atypical features and are, therefore, classified as anaplastic with a higher risk of recurrence after surgical resection.

On imaging, gangliogliomas may present as solid or solid-cystic lesions with hyperintensity on T2WI, mild mass effect, and edema.[11] Calcifications may be present, and postcontrast enhancement is highly variable, ranging from nonenhancing to ringlike or intense homogeneous gadolinium enhancement (Fig 7).[11] DNETs and low-grade gliomas are the main differential diagnoses.

Recent studies have revealed that most gangliogliomas are genetically characterized by alterations that activate the mitogen-activated protein (MAP) kinase signaling pathway, either via the BRAF V600E mutation or a spectrum of other genetic alterations, including alternative *BRAF* mutations/fusions, *RAF1* fusion, *KRAS* mutation, neurofibromin 1 (*NF1*) mutation, or *FGFR* mutations/fusions. In most cases, the genetic alteration within the MAP kinase pathway was the solitary genetic alteration identified, with few (if any) changes in the chromosomal copy number, indicating that most gangliogliomas are genetically simple tumors.[32] Thus, gangliogliomas are genetically similar to pilocytic astrocytomas, DNETs, rosette-forming glioneuronal tumors (RGNTs), polymorphous low-grade neuroepithelial tumors of the young, and multinodular and vacuolating neuronal tumors (MVNTs).[32]

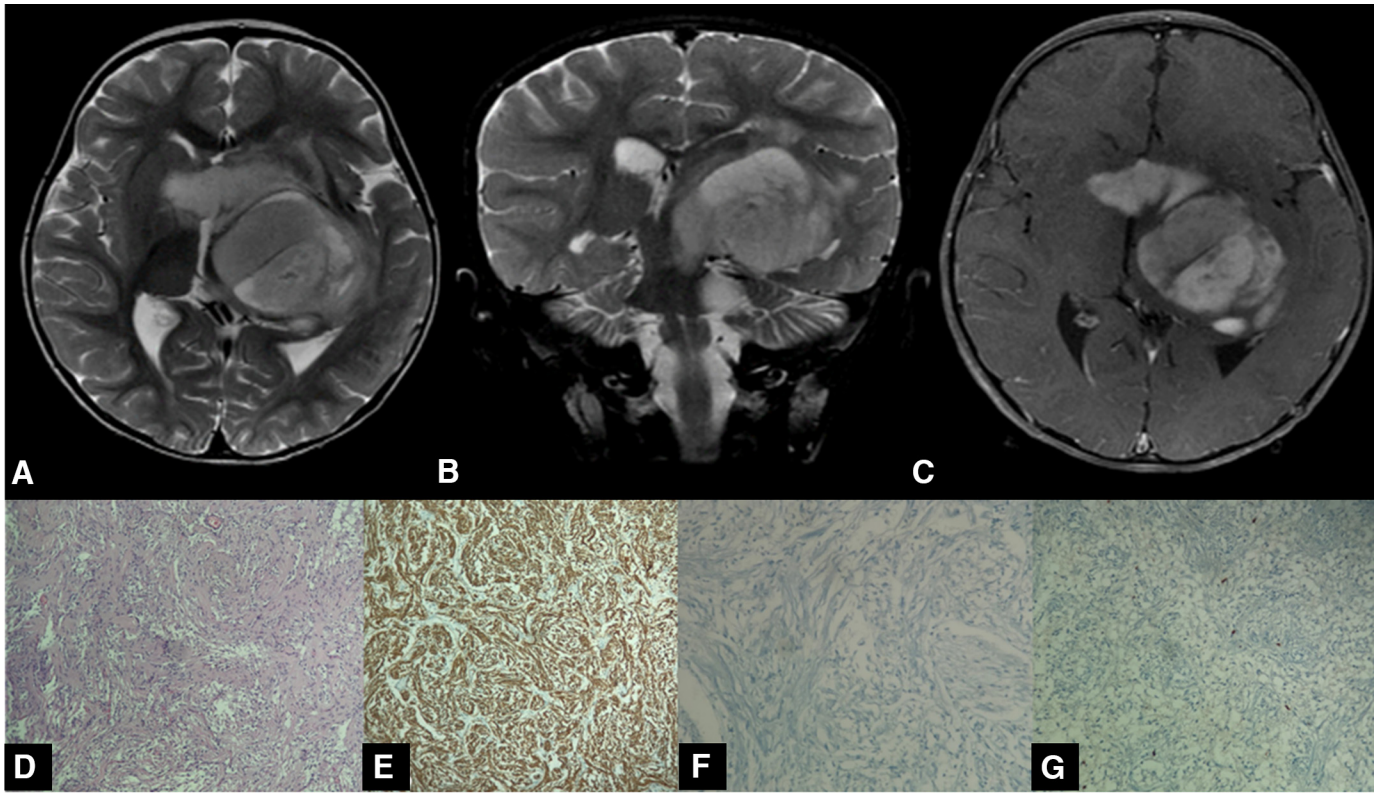


**FIG 8. DIA and DIG. Axial T2WI (*A*), coronal T2WI (*B*), and axial postcontrast T1WI (*C*) show a large lesion within the left thalamus that extends to the bilateral striatum. The tumor shows heterogeneous signal on T2WI (*A* and *B*) with cystic components, and the solid part of the lesion has avid contrast enhancement (*C*). H&E, original magnification ×200 (*D*); immunohistochemistry GFAP, original magnification ×200 (*E*); NeuN, original magnification ×200 (*F*); and Ki-67, original magnification ×200 (*G*). Note atypical and proliferative neuroepithelial cells in the desmoplastic stroma, arranged in fascicular patterns with deposition of dense pericellular stroma (mesenchymal appearance) (*D*). GFAP staining confirms the glial differentiation (*E*), and the immunonegativity for NeuN highlights the absence of a neoplastic neuronlike component (*F*). Ki-67 index < 1% (low proliferative index) (*G*).**

### *Desmoplastic Infantile Astrocytoma and Ganglioglioma*

Desmoplastic infantile astrocytomas (DIA) and gangliogliomas (DIGs) are rare glioneuronal tumors in early childhood and usually affect the age group from 1 to 24 months,[1] with an incidence rate of 0.5% of pediatric brain tumors.[33] They are superficial lesions, frequently adhere to the dura mater, appear mainly in the supratentorial compartment, and usually affect >1 brain lobe.[1,34]

Typical imaging findings consist of large solid-cystic lesions, predominantly with a peripheral solid component and central cystic component, with mild or no edema in the adjacent parenchyma.[34] Calcifications may be present.[1,34] Characteristically, these tumors show postcontrast enhancement in the solid portion, and meningeal enhancement adjacent to the tumor may also occur.[34] Remodeling of the adjacent skull is a frequent finding in these tumors.[34] Glioblastomas are the main differential diagnosis.[35]

DIAs and DIGs are composed of neoplastic astrocytic cells with or without an associated ganglionic component, with an exuberant desmoplastic stroma composed of fibroblastic and neuroepithelial elements.[1,36] Both tumor forms may contain a population of poorly differentiated neuroepithelial cells with small, round, deeply basophilic nuclei and minimal surrounding cytoplasm.[1] In the desmoplastic leptomeningeal component, fibroblast-like cells express vimentin, with frequent GFAP and less frequent $\alpha$-smooth muscle actin expression.[1] Antibodies against collagen IV react in a reticulin-like pattern around the tumor cells. The expression of neuronal markers, such as synaptophysin, neurofilament heavy polypeptide, and class III $\beta$ tubulin, is observed in neoplastic neuronal cells, mainly in ganglion cells, but also in cells lacking neuronal differentiation on routine stains.[1] *BRAF* alterations, primarily the V600E mutation and rarely the V600D mutation, as well as *FXR1-BRAF* fusion, have been described in DIGs and DIAs (Fig 8).[33,37–39]

### *Papillary Glioneuronal Tumor*

Papillary glioneuronal tumors (PGNTs) are rare WHO grade I glioneuronal neoplasms with an unknown incidence. They are characterized by the presence of small GFAP-positive flat or cuboidal cells lining hyalinized vascular pseudopapillae.[40] Interpapillary neuronal elements are positive for GFAP and synaptophysin on IH staining.[16,20,40]

Generally, PGNTs are supratentorial tumors with a preferential frontal or temporal location, sometimes adjacent to the ventricles, suggesting a possible origin in the subependymal germinal matrix. They may have a more superficial extension to the white matter and cortex.[20,40,41] In general, PGNTs are solid-cystic lesions with well-defined margins and postcontrast enhancement, but they may also present as

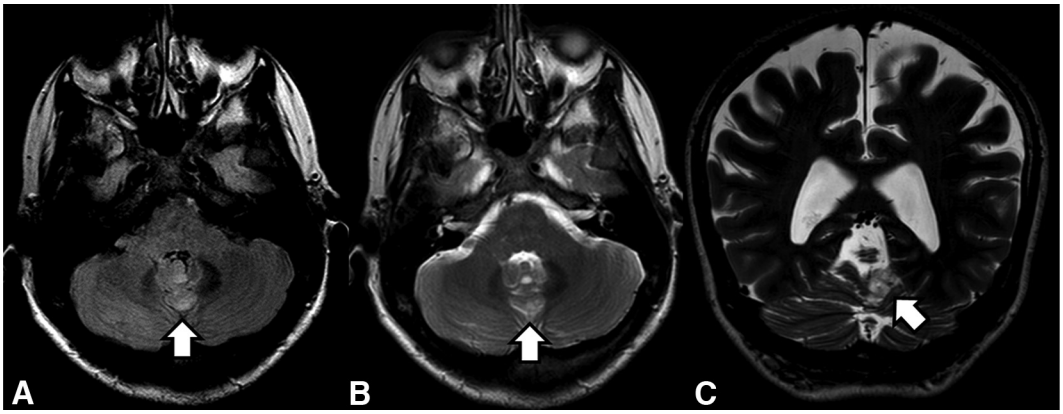


**FIG 9. RGNT. Axial FLAIR (*A*), axial T2WI (*B*), and coronal T2WI (*C*) show a solid tumor in the cerebellar vermis/floor of the fourth ventricle with hyperintensity on FLAIR imaging (*arrow* in *A*) and T2WI (*arrows* in *B* and *C*), as well as no significant enhancement (not shown).**

purely solid or cystic lesions.[40,41] On MR imaging, the solid components are hyperintense on T2WI and may show postcontrast enhancement.[20,41] Calcifications, hemorrhage, and edema are also characteristic.[41] The imaging diagnosis can be difficult because they have characteristics shared with other, more common brain neoplasms, such as aggressive glioma and extraventricular neurocytoma. However, PGNTs should be considered in cases of solid-cystic or cystic periventricular lesions.

### *Rosette-Forming Glioneuronal Tumor*

RGNTs are usually slow-growing tumors (WHO grade I), can be typically found in the midline of the posterior fossa, and commonly relate to the fourth ventricle, which may be occupied by the lesion. The characteristics of these rare tumors remain to be elucidated, and their epidemiology is unknown.[42] There are reports of their occurrence in rare locations such as the cerebellar hemispheres, thalamus, pineal region, optic chiasm, and spinal cord,[10,20] and they may display aggressive behavior, especially if they occur outside the fourth ventricle.[42] Because they are usually located in the posterior fossa, they can manifest symptoms of obstructive hydrocephalus, headache, and ataxia.[43] RGNTs occur preferentially in young adults, with case reports in children.[10,43]

The characteristic histopathologic appearance is biphasic, with the formation of neurocytic rosettes or perivascular pseudorosettes and glial elements that resemble pilocytic astrocytoma.[16,20] Neurocytic cells are NSE-positive. The center of the rosettes and the neuropil of the pseudorosettes are positive for synaptophysin.[16]

RGNTs are low-grade tumors without atypia, low Ki-67 index, and without signs of necrosis or mitosis.[18] Few molecular studies have analyzed RGNTs, revealing only 2 recurrent genetic alterations, *PIK3CA* or *FGFR1* mutations, in some cases combined with *NF1* mutations.[31] *IDH1/2* mutations and the 1p/19q codeletion are absent.[10,31]

RGNTs are usually well-defined solid-cystic tumors, but they can appear solely solid or cystic on MR imaging, sometimes with peripheral heterogeneous postcontrast enhancement(Fig 9).[10,20] They should be considered when assessing young patients with well-defined tumors located inside or next to the fourth ventricle, while considering the main differential diagnoses of pilocytic astrocytoma, ependymoma, and medulloblastoma.

### *Multinodular and Vacuolating Neuronal Tumor*

As recently described,[1,44] MVNTs were included in the neuronal/glioneuronal tumor group in the 5th edition of the WHO tumor classification.[2] They are rare tumors with an unknown incidence rate and only a few reported cases.[45] MVNTs are neuroepithelial tumors composed of discrete monomorphic neuronal elements and coalescing nodules, with vacuolar alterations in the matrix and tumor cells.[2]

MVNTs are clinically benign.[46] They occur in adults and are usually asymptomatic or associated with epilepsy, headaches, or other nonspecific symptoms. The tumors are usually superficial, most commonly involving the temporal and frontal lobes in adults.[45] Rarely, they can be found in the posterior fossa or in the cerebellar vermis or hemispheres.[47]

Tumor nodules often occupy deeper cortical layers and the subcortical white matter, though they may have a diffuse distribution of neuronal elements. In IH staining, the neuronal components are negative for GFAP and CD34. They express both HuC/antigen associated with HuD and oligodendrocyte-2 (*OLIG2*)[46] and often exhibit cytoplasmic synaptophysin; however, this last finding is usually weak in intensity.[48] Ki-67 indices are frequently low (<1%).[45]

MVNTs have typical MR imaging findings, which often suggest their diagnosis. They are nodular lesions, usually subcortical and superficial, that follow the gyral contour.[45,46] They are hyperintense on T2WI with no signal drop in the FLAIR sequence and usually do not have a mass effect.[45,46] MVNTs usually do not exhibit postcontrast enhancement or restricted diffusion.[45] The same imaging patterns can be observed when MVNTs are located in the posterior fossa, with a T2-FLAIR hypointense central dot signal being typical.[47] These imaging characteristics may suggest an MVNT diagnosis and make a biopsy unnecessary if stable on follow-up MR imaging (Fig 10).[45] Differential

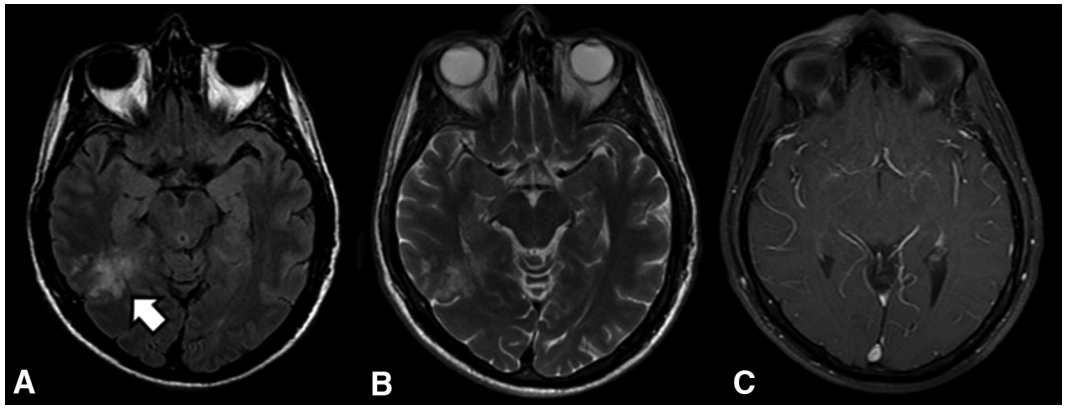


**FIG 10. MVNT. Axial FLAIR (*A*), T2WI (*B*), and postcontrast T1WI (*C*) show confluent small nodular lesions located predominantly in the subcortical white matter of the right temporal region. There is hyperintensity on FLAIR imaging (*arrow* in *A*) and T2WI (*B*) with no significant enhancement (*C*) or mass effect. The subcortical white matter adjacent to the small nodules is also slightly hyperintense on FLAIR and T2WI.**

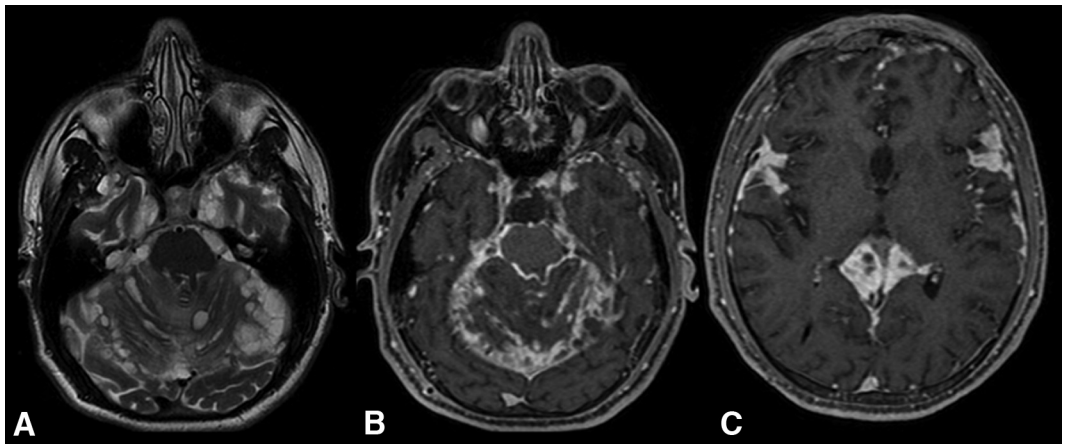


**FIG 11. DLGNT. Axial T2WI (*A*) and postcontrast T1WI (*B* and *C*) show plaque-like subarachnoid diffuse lesions with contrast enhancement (*B* and *C*) associated with cystic lesions (*A*) along the basal cisterns, posterior fossa sulci, and Sylvian fissures, without obvious intraparenchymal component.**

diagnoses include perivascular spaces, solid DNETs, nodular heterotopia, and cortical dysplasia.

### *Diffuse Leptomeningeal Glioneuronal Tumor*

Diffuse leptomeningeal glioneuronal tumors (DLGNTs) were included in the mixed neuronal/glioneuronal tumor group in the 2016 update of the WHO tumor classification.[1] This rare tumor with an unknown incidence is more common in male children. Only a few reports in adults exist.[49] DLGNTs are characterized by generalized leptomeningeal growth. Their cytology is similar to that of oligodendrogliomas but with elements of neuronal differentiation.[10,50] They present with a characteristic dissemination along the perivascular subpial (Virchow-Robin) spaces with limited parenchymal infiltration.[16]

Histologically, DLGNTs are composed of monotonous, rounded, glial cell sheets, similar to oligodendrogliomas, with a neuronal component. This morphology is commonly combined with *BRAF* fusions and deletion of chromosome 1p alone or in combination with 19q.[50] In contrast to oligodendrogliomas, these tumors do not have *IDH* mutations.[10,20,50] IH staining can be positive for GFAP, *OLIG2*, S-100, and synaptophysin.[49] CSF samples usually show high protein levels with negative oncotic cytology, which may complicate the diagnostic investigation.[10] The cellular origin of DLGNTs is unclear; because they do not cause lesions in the brain parenchyma, they may originate from neuroepithelial cells remaining in the meninges.[10]

On imaging, they are extra-axial subarachnoid tumors that grow along the surface of the spinal cord in the basal cisterns and interhemispheric fissure without a clear parenchymal component, which may be present due to secondary infiltration.[20] Characteristically, DLGNTs cause nodular leptomeningeal thickening.[49] They can have a very typical imaging appearance with cystic subarachnoid lesions and, commonly, with peripheral contrast enhancement, which may allow their diagnosis on MR imaging (Fig 11).[49] Their imaging characteristics are quite different from those of other tumors in their group, and the differential diagnosis includes chronic inflammatory/infectious processes of the meninges, especially tuberculosis, as well as meningeal neoplastic dissemination.[49]

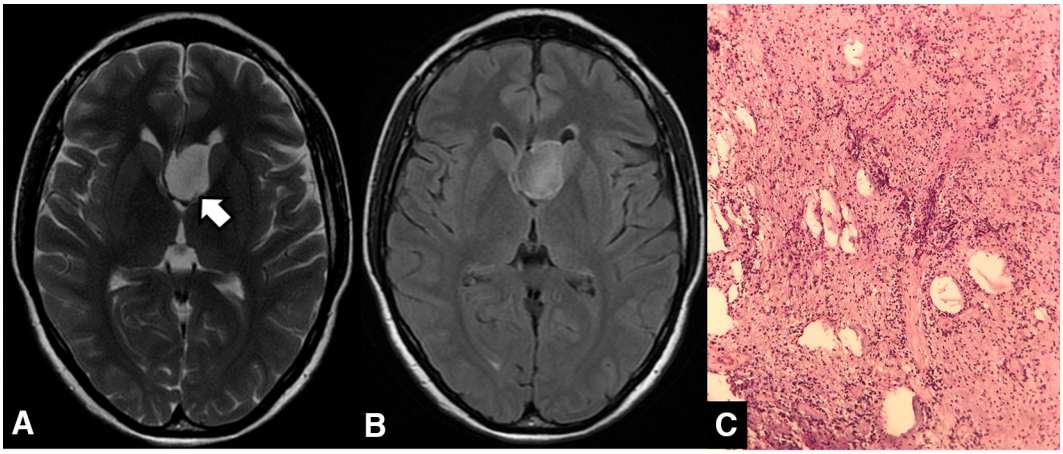


**FIG 12. MGT. Axial T2WI (*A*) and FLAIR imaging (*B*) show a periventricular nodular lesion attached to the septum pellucidum with hyperintensity on T2WI (*arrow* in *A*) and some signal suppression on FLAIR imaging (mismatch sign). H&E, original magnification ×200 (*C*). Note monomorphic proliferation of oval cells (oligodendrocyte-like) of low cytologic grade in myxoid stroma with microcystic degeneration and a branched capillary network, sometimes with cellular densification around it and some mature neuronal elements with a focal floating appearance (*C*).**

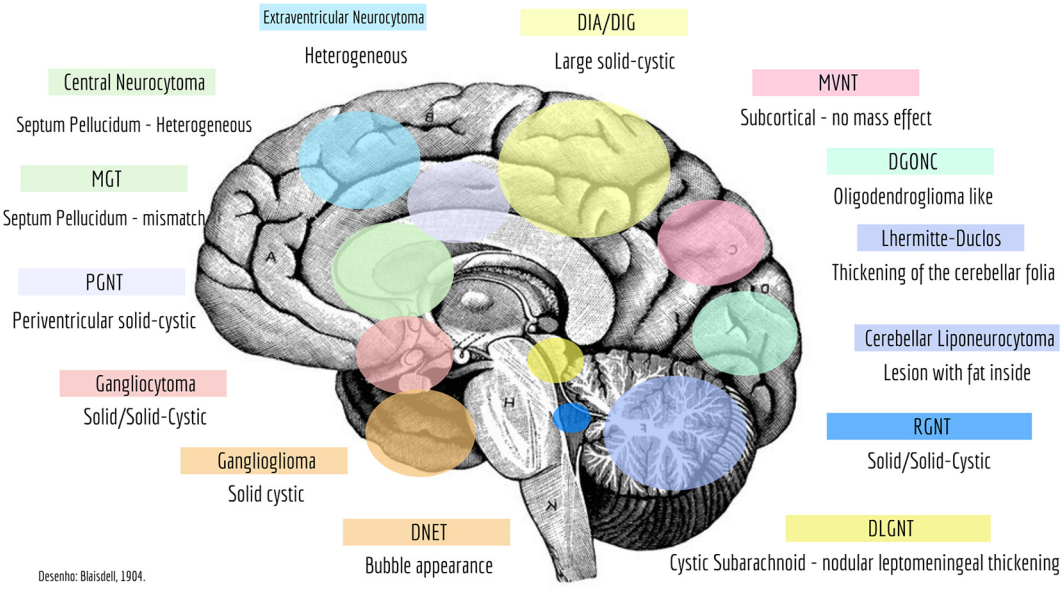


**FIG 13. Typical locations of glioneuronal and neural tumors. Schematic image shows locations and main imaging findings of each tumor. DGONC indicates diffuse glioneuronal tumour with oligodendroglioma-like features and nuclear clusters; A, B, C and D: brain hemispheres; F: cerebellum; H,K: brainstem.**

Despite being histologically low-grade and benign tumors, DLGNTs may display locally aggressive behavior due to their tendency of leptomeningeal dissemination. Furthermore, because they often occupy the cisterns around the brainstem, their surgical resection can be difficult.[20]

### *Diffuse Glioneuronal Tumor with Oligodendroglioma-like Features and Nuclear Clusters*

Recently described[51] and added as a provisional type to the group of neuronal tumors in the WHO 2021 edition,[2] diffuse glioneuronal tumors with oligodendroglioma-like features and nuclear clusters constitute a little-known entity with an unknown incidence that may occur in children.[52]

Histologically, these tumors resemble oligodendrogliomas, composed of round cells with perinuclear halos. They have nuclear clusters, some of which are multinucleated cells. Calcification, ganglion cells, apoptosis, and foam cells are commonly observed. They may be characterized by vascular proliferation, moderate cellularity, and a Ki-67 index as high as 30%. Tumor cells are positive for neuronal markers such as synaptophysin and neuronal nuclei (NeuN), as well as *OLIG2*, but they do not express GFAP.[52] In the cases described by Deng et al,[51] the recurrent monosomy of chromosome 14 (97%) was the most important genetic finding.

There are still few descriptions of MR imaging findings in these tumors. Usually, high signal intensities on T2WI and low signal intensities on T1WI without postcontrast enhancement are found. The lesions may have cystic components and associated calcifications, with no perilesional edema. ADC

**Table: Neuronal and glioneuronal tumors**

| Tumor | Clinical | Pathologic | Imaging |
|---|---|---|---|
| Gangliocytoma | Asymptomatic/seizure | Dysmorphic neurons without neoplastic glial cells | CT: hyperdense; MR imaging: hypointense on T1WI, isointense to discretely hyperintense on T2WI; no vasogenic edema or expansive effect |
| Dysplastic cerebellar gangliocytoma | Biphasic age distribution: children 4.3 and adult 42.5 years; Cowden syndrome | Dysplastic ganglion cells, abnormal myelination of the molecular layer, white matter vacuolization, and capillary calcifications and ectatic vessels; *PTEN* mutations are present in adult-onset | MR imaging: hypointense on T1WI, hyperintense on T2WI, and may have post-contrast enhancement; tiger stripes sign |
| Central/extraventricular neurocytoma | Young adults; obstructive hydrocephalus and signs of increased intracranial pressure | Neurocytic cells with clear cytoplasm, uniform round cells with neuronal differentiation; IH: diffusely positive for synaptophysin and NSE; overexpression of N-MYC, *IGF2*, *PTEN*, *PDGF-D,* and *NRG-2* | CT: hyperdense lesion in the lateral ventricles, which may present with cysts and calcification; MR imaging: intra-/periventricular lesions with a heterogeneous signal, enhancement, calcifications, and hemorrhage |
| Cerebellar liponeurocytoma | Very rare; adults 30–60 years of age | Neurocytic component accompanied by lipidized neoplastic cells; IH: positive for synaptophysin and *MAP-2* | MR imaging: iso-/hypointense on T1WI and hyperintense on T2WI, with cysts and calcifications; the characterization of fat is a typical finding |
| DNET | Children/young adults; seizure | Specific GN element, with intracortical multinodularity and focal cortical dysplasia; it can be further divided into simple and complex (simple: only specific GN elements. complex: specific GN elements and glial nodules); BRAF V600E mutation and *FGFR* alteration | MR imaging: cortical location, more often involving the mesial structures of temporal lobe with internal septations; may have gadolinium enhacement and calcifications; no mass effect or peritumoral edema; FLAIR hyperintense ring sign and high ADC values; extratemporal DNET could be present; the mismatch sign |
| Ganglioglioma | Children/young adults (8–25 years of age); seizure | Dysplastic ganglion cells in combination with neoplastic glial cells; MAP kinase signaling pathway via BRAF V600E mutation or a spectrum of other genetic alterations, including alternative *BRAF* mutations/fusions, *RAF1* fusion, *KRAS* mutation, *NF1* mutation, or *FGFR* mutations/fusions | MR imaging: Solid or solid-cystic lesions, hyperintense on T2WI, mild mass effect and edema; calcifications and post-contrast enhancement may be present |
| DIA/DIG | Early childhood (1–24 mo) | Neoplastic astrocytic cells with a ganglionic component, with an exuberant desmoplastic stroma composed of fibroblastic and neuroepithelial elements; poorly differentiated neuroepithelial cells, with small, round, deeply basophilic nuclei and minimal surrounding cytoplasm; *BRAF* alterations have been described | MR imaging: large solid-cystic lesion, predominantly with a peripheral solid component and a central cystic component, with mild or no edema; calcifications may be present; post-contrast enhancement in the solid portion and meningeal enhancement adjacent to the tumor; remodeling of the adjacent skull |
| Papillary glioneuronal tumor | Rare | Small GFAP-positive flat or cuboidal cells lining hyalinized vascular pseudopapillae; IH: interpapillary neuronal elements are positive for GFAP and synaptophysin | MR imaging: supratentorial tumors, with preferential frontal or temporal location, adjacent to the ventricles; usually solid-cystic lesions with well-defined margins; the solid components are hyperintense on T2WI and may have post-contrast enhancement, calcifications, hemorrhage, and edema |
| Rosette-forming glioneuronal tumor | Rare; young adults | Biphasic appearance, with formation of neurocytic rosettes and/or perivascular pseudorosettes and glial elements; IH: neurocytic cells are NSE-positive and the center of rosettes and the neuropil of pseudorosettes are positive for synaptophysin | MR imaging: well-defined solid/solid-cystic tumors located inside or next to the fourth ventricle; may present with peripheral heterogeneous post-contrast enhancement |

(Continued)

**Table: Continued**

| Tumor | Clinical | Pathologic | Imaging |
|---|---|---|---|
| Multinodular and vacuolating neuronal tumor | Rare; adults, usually asymptomatic | Tumor nodules in the deeper cortical layers and the subcortical white matter; IH: neuronal components are negative for GFAP and CD34; they express the Hu-C/antigen associated with HuD and *OLIG2* | MR imaging: nodular lesions, usually subcortical and superficial, following the gyral contour, hyperintense on T2WI, with no signal drop in the FLAIR sequence; no mass effect |
| Diffuse leptomeningeal glioneuronal tumor | Rare; more common in male children | Monotonous rounded glial cell sheets with a neuronal component; *BRAF* fusions and deletion of the chromosome 1p, alone or in combination with 19q. *IDH* wild type; IH: positive for GFAP, *OLIG2*, S100, and synaptophysin | MR imaging: cystic subarachnoid lesions, most of them with peripheral contrast enhancement, growing along the surface of the spinal cord, in the basal cisterns, and interhemispheric fissure |
| Diffuse glioneuronal tumor with oligodendroglioma-like features and nuclear clusters | Rare; pediatric group | Round cells with perinuclear halos, nuclear clusters, some of them with multinucleated cells; calcification, ganglion cells, apoptosis, and foam cells are commonly seen; IH: positive for neuronal markers such as synaptophysin, NeuN, and *OLIG2*; do not express GFAP; recurrent monosomy of chromosome 14 | MR imaging: hyperintense on T2WI and hypointense on T1WI, with no postcontrast enhancement; may have cystic components and associated calcifications, with no perilesional edema; ADC values can be low |
| Myxoid glioneuronal tumor | Rare; young adults | Oligodendrocyte-like cells with columnar arrangement and ganglion cells floating in the mucin stroma; IH: positivity for GFAP and *OLIG2*, with floating neurons and neurocytic rosettes being positive for synaptophysin | MR imaging: lesion attached to the septum pellucidum, near lateral ventricles, hyperintense on T2WI, with no post-contrast enhancement; mismatch sign; no edema |

**Note:**—GN indicates Glioneuronal.

values can be low.[52] The images of the reported cases are similar to those of oligodendrogliomas, the main differential diagnosis.

### *Myxoid Glioneuronal Tumor*

Myxoid glial tumors (MGTs), rare tumors with an unknown incidence rate, were recently added to the group of neuronal tumors in the WHO 2021 edition.[2] They are mixed neuronal focal tumors that present with glioneuronal characteristics of low-grade tumors, with morphologic similarities to those of DNETs and RGNTs.[53,54] MGTs may originate from the septum pellucidum, septal nuclei, subcallosal area, corpus callosum, and lateral ventricles.[53,54] They often occur in young adults.[55]

Histologically, they may present with oligodendrocyte-like cells with columnar arrangement, and ganglion cells "floating" in the mucin stroma are also observed.[53,55] Some cases demonstrate the presence of neurocytic rosettes. Rosenthal fibers, mitotic activity, remarkable nuclear pleomorphism, necrosis, and microvascular proliferation are not observed. In IH staining, MGTs are positive for GFAP and *OLIG2*, with floating neurons and neurocytic rosettes positive for synaptophysin.[53,55] The Ki-67 index is frequently low (<5%).[53]

On MR imaging, MGTs present with high signal intensities on T2WI with no postcontrast enhancement. The FLAIR sequence may be essential for the diagnosis because the tumor may show partial signal suppression in its center while maintaining hyperintense borders,[54] a finding similar to the mismatch sign described in astrocytomas with *IDH* mutations.[56] MGTs have high ADC values compared with normal brain parenchyma due to their low cellularity.[54] No edema is observed in the adjacent parenchyma (Fig 12).

Their main differential diagnoses are neoplastic lesions that typically occur in this topography, such as central neurocytoma and subependymoma.[54]

## CONCLUSIONS

Neuronal and glioneuronal tumors usually have a benign course and may present with typical imaging characteristics, allowing their diagnosis based on MR imaging findings. It is important for radiologists to know these tumors and comprehend their histopathologic and molecular characteristics to better understand their behavior and evolution (Table). This knowledge may have a positive impact on the diagnosis and treatment of patients affected by brain tumors (Fig 13).


## Acknowledgments

Authors would like to thank Laura Polsin for her help with figure creation.


## REFERENCES


1. Louis DN, Perry A, Reifenberger G, et al. **The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary**. *Acta Neuropathol* 2016;131:803–20. 10.1007/s00401-016-1545-1
2. Louis DN, Perry A, Wesseling P, et al. **The 2021 WHO Classification of Tumors of the Central Nervous System: a summary**. *Neuro Oncol* 2021;23:1231–51. 10.1093/neuonc/noab106

3. Louis DN, Wesseling P, Paulus W, et al. **cIMPACT-NOW update 1: not otherwise specified (NOS) and not elsewhere classified (NEC).** *Acta Neuropathol* 2018;135:481–84. 10.1007/s00401-018-1808-0
4. Louis DN, Giannini C, Capper D, et al. **cIMPACT-NOW update 2: diagnostic clarifications for diffuse midline glioma, H3 K27M-mutant and diffuse astrocytoma/anaplastic astrocytoma, IDH-mutant.** *Acta Neuropathol* 2018;135:639–42. 10.1007/s00401-018-1826-y
5. Brat DJ, Aldape K, Colman H, et al. **cIMPACT-NOW update 3: recommended diagnostic criteria for "Diffuse astrocytic glioma, IDH-wildtype, with molecular features of glioblastoma, WHO grade IV."** *Acta Neuropathol* 2018;136:805–10. 10.1007/s00401-018-1913-0
6. Ellison DW, Hawkins C, Jones DTW, et al. **cIMPACT-NOW update 4: diffuse gliomas characterized by MYB, MYBL1, or FGFR1 alterations or BRAF V600E mutation.** *Acta Neuropathol* 2019;137:683–87. 10.1007/s00401-019-01987-0
7. Brat DJ, Aldape K, Colman H, et al. **cIMPACT-NOW update 5: recommended grading criteria and terminologies for IDH-mutant astrocytomas.** *Acta Neuropathol* 2020;139:603–08. 10.1007/s00401-020-02127-9
8. Louis DN, Wesseling P, Aldape K, et al. **cIMPACT-NOW update 6: new entity and diagnostic principle recommendations of the cIMPACT-Utrecht meeting on future CNS tumor classification and grading.** *Brain Pathol* 2020;30:844–56. 10.1111/bpa.12832
9. Ellison DW, Aldape KD, Capper D, et al. **cIMPACT-NOW update 7: advancing the molecular classification of ependymal tumors.** *Brain Pathol* 2020;30:863–66. 10.1111/bpa.12866
10. Gatto L, Franceschi E, Di Nunno V, et al. **Glioneuronal tumors: clinicopathological findings and treatment options.** *Future Neurology* 2020;15:No. 3.
11. Koeller KK, Henry JM. **From the archives of the AFIP superficial gliomas: radiologic-pathologic correlation.** *Radiographics* 2001;21:1533–56. 10.1148/radiographics.21.6.g01nv051533
12. Dudley RW, Torok MR, Gallegos DR, et al. **Pediatric low grade ganglioglioma/gangliocytoma: epidemiology, treatments, and outcome analysis on 348 children from the SEER database.** *Neurosurgery* 2015;76:313–20. 10.1227/NEU.0000000000000619
13. Sakata K, Fujimori K, Komaki S, et al. **Pituitary gangliocytoma producing TSH and TRH: a review of "gangliocytomas of the sellar region."** *J Clin Endocrinol Metab* 2020;105:3109–21. 10.1210/clinem/dgaa474
14. Altman NR. **MR and CT characteristics of gangliocytoma: a rare cause of epilepsy in children.** *AJNR Am J Neuroradiol* 1988;9:917–21. [3140636]
15. Li Y, Guo J, Wei H, et al. **The surgical resection of dysplastic cerebellar gangliocytoma assisted by intraoperative sonography: illustrative case.** *J Neurosurg Case Lessons* 2021;2:12–18. 10.3171/case21451
16. Tan C, McLendon R. **Histological approach to neuronal and mixed neuronal-glial tumors of the central nervous system.** *Glioma* 2018;1:89.
17. Ma J, Jia G, Chen S, et al. **Clinical perspective on dysplastic gangliocytoma of the cerebellum (Lhermitte-Duclos disease).** *World Neurosurg* 2019;122:16–23. 10.1016/j.wneu.2018.10.085
18. Smith AB, Smirniotopoulos JG, Horkanyne-Szakaly I. **From the radiologic pathology archives: Intraventricular neoplasms: radiologic-pathologic correlation.** *Radiographics* 2013;33:21–43. 10.1148/rg.331125192
19. Lee SJ, Bui TT, Chen CHJ, et al. **Central neurocytoma: a review of clinical management and histopathologic features.** *Brain Tumor Res Treat* 2016;4:49–57. 10.14791/btrt.2016.4.2.49
20. Demir MK, Yapıcıer O, Yılmaz B, et al. **Magnetic resonance imaging findings of mixed neuronal-glial tumors with pathologic correlation: a review.** *Acta Neurol Belg* 2018;118:379–86. 10.1007/s13760-018-0981-1
21. Yang GF, Wu SY, Zhang LJ, et al. **Imaging findings of extraventricular neurocytoma: report of 3 cases and review of the literature.** *AJNR Am J Neuroradiol* 2009;30:581–85. 10.3174/ajnr.A1279
22. Wolf A, Alghefari H, Krivosheya D, et al. **Cerebellar liponeurocytoma: a rare intracranial tumor with possible familial predisposition—case report.** *J Neurosurg* 2016;125:57–61. 10.3171/2015.6.JNS142965
23. Patel N, Fallah A, Provias J, Jha NK. **Cerebellar liponeurocytoma.** *Can J Surg* 2009;52(4):E117–E119
24. Cai J, Li W, Du J, et al. **Supratentorial intracerebral cerebellar liponeurocytoma: a case report and literature review.** *Medicine (Baltimore)* 2018;97:e9556. 10.1097/MD.0000000000009556
25. Elia G, Lorenzo U, Annarita G, et al. **Cerebellar liponeurocytoma presenting with fatal tumor hemorrhage.** *Neurosurgery Cases and Reviews* 2019;210.23937/2643-4474/1710026
26. Campos AR, Clusmann H, Von Lehe M, et al. **Simple and complex dysembryoplastic neuroepithelial tumors (DNT) variants: clinical profile, MRI, and histopathology.** *Neuroradiology* 2009;51:433–43. 10.1007/s00234-009-0511-1
27. Raz E, Kapilamoorthy TR, Gupta AK, et al. **Case 186: dysembrioplastic neuroepithelial tumor.** *Radiology* 2012;265:317–20. 10.1148/radiol.12100118
28. Onishi S, Amatya VJ, Kolakshyapati M, et al. **T2-FLAIR mismatch sign in dysembryoplasticneuroepithelial tumor.** *Eur J Radiol* 2020;126:108924. 10.1016/j.ejrad.2020.108924
29. Suh YL. **Dysembryoplastic neuroepithelial tumors.** *J Pathol Transl Med* 2015;49:438–49. 10.4132/jptm.2015.10.05
30. Daumas-Duport C. **Dysembryoplastic neuroepithelial tumours.** *Brain Pathol* 1993;3:283–95. 10.1111/j.1750-3639.1993.tb00755.x
31. Lucas CH, Gupta R, Doo P, et al. **Correction to: comprehensive analysis of diverse low-grade neuroepithelial tumors with FGFR1 alterations reveals a distinct molecular signature of rosette-forming glioneuronal tumor.** *Acta Neuropathol Commun* 2020;8:1–17. 10.1186/s40478-019-0875-3
32. Pekmezci M, Villanueva-Meyer JE, Goode B, et al. **The genetic landscape of ganglioglioma.** *Acta Neuropathol Commun* 2018;6:47. 10.1186/s40478-018-0551-z
33. Gessi M, Mühlen A, Zur Hammes J, et al. **Genome-wide DNA copy number analysis of desmoplastic infantile astrocytomas and desmoplastic infantile gangliogliomas.** *J Neuropathol Exp Neurol* 2013;72:807–15. 10.1097/NEN.0b013e3182a033a0
34. Trehan G, Bruge H, Vinchon M, et al. **MR imaging in the diagnosis of desmoplastic infantile tumor: retrospective study of six cases.** *AJNR Am J Neuroradiol* 2004;25:1028–33.
35. Bader A, Heran M, Dunham C, et al. **Radiological features of infantile glioblastoma and desmoplastic infantile tumors: British Columbia's Children's Hospital experience.** *J Neurosurg Pediatr* 2015;16:119–25. 10.3171/2014.10.PEDS13634
36. Wang AC, Jones DTW, Abecassis IJ, et al. **Desmoplastic infantile ganglioglioma/astrocytoma (DIG/DIA) are distinct entities with frequent BRAFV600 mutations.** *Mol Cancer Res* 2018;16:1491–98. 10.1158/1541-7786.MCR-17-0507

37. Blessing MM, Blackburn PR, Balcom JR, et al. **Novel BRAF alteration in desmoplastic infantile ganglioglioma with response to targeted therapy.** *Acta Neuropathol Commun* 2018;6:118. 10.1186/s40478-018-0622-1
38. Dougherty MJ, Santi M, Brose MS, et al. **Activating mutations in BRAF characterize a spectrum of pediatric low-grade gliomas.** *Neuro Oncol* 2010;12:621–30. 10.1093/neuonc/noq007
39. Prabowo AS, Iyer AM, Veersema TJ, et al. **BRAF V600E mutation is associated with mTOR signaling activation in glioneuronal tumors.** *Brain Pathol* 2014;24:52–66. 10.1111/bpa.12081
40. Myung JK, Byeon SJ, Kim B, et al. **Papillary glioneuronal tumors: a review of clinicopathologic and molecular genetic studies.** *Am J Surg Pathol* 2011;35:1794–805. 10.1097/PAS.0b013e31823456e6
41. Yadav N, Rao S, Saini J, et al. **Papillary glioneuronal tumors: a radiopathologic correlation.** *Eur J Radiol* 2017;97:44–52. 10.1016/j.ejrad.2017.10.004
42. Wilson CP, Chakraborty AR, Pelargos PE, et al. **Rosette-forming glioneuronal tumor: an illustrative case and a systematic review.** *Neurooncology Adv* 2020;2:vda116. 10.1093/noajnl/vdaa116
43. Shah MN, Leonard JR, Perry A. **Rosette-forming glioneuronal tumors of the posterior fossa: report of 6 cases.** *J Neurosurg Pediatr* 2010;5:98–103. 10.3171/2009.7.PEDS09113
44. Pekmezci M, Stevers M, Phillips JJ, et al. **Multinodular and vacuolating neuronal tumor of the cerebrum is a clonal neoplasm defined by genetic alterations that activate the MAP kinase signaling pathway.** *Acta Neuropathol* 2018;135:485–88. 10.1007/s00401-018-1820-4
45. Nunes RH, Hsu CC, Da Rocha AJ, et al. **Multinodular and vacuolating neuronal tumor of the cerebrum: a new "leave me alone" lesion with a characteristic imaging pattern.** *AJNR Am J Neuroradiol* 2017;38:1899–904. 10.3174/ajnr.A5281
46. Huse JT, Edgar M, Halliday J, et al. **Multinodular and vacuolating neuronal tumors of the cerebrum: 10 cases of a distinctive seizure-associated lesion.** *Brain Pathol* 2013;23:515–24. 10.1111/bpa.12035
47. Lecler A, Bailleux J, Carsin B, et al; ENIGMA Investigation Group (EuropeaN Interdisciplinary Group for MVNT Analysis). **Multinodular and vacuolating posterior fossa lesions of unknown significance.** *AJNR Am J Neuroradiol* 2019;40:1689–94. 10.3174/ajnr.A6223
48. Bodi I, Curran O, Selway R, et al. **Two cases of multinodular and vacuolating neuronal tumour.** *Acta Neuropathol Commun* 2014;2:1–10. 10.1186/2051-5960-2-1
49. Lakhani DA, Mankad K, Chhabda S, et al. **Diffuse leptomeningeal glioneuronal tumor of childhood.** *AJNR Am J Neuroradiol* 2020;41:2155–59. 10.3174/ajnr.A6737
50. Deng MY, Sill M, Chiang J, et al. **Molecularly defined diffuse leptomeningeal glioneuronal tumor (DLGNT) comprises two subgroups with distinct clinical and genetic features.** *Acta Neuropathol* 2018;136:239–53. 10.1007/s00401-018-1865-4
51. Deng MY, Sill M, Sturm D, et al. **Diffuse glioneuronal tumour with oligodendroglioma-like features and nuclear clusters (DGONC): a molecularly defined glioneuronal CNS tumour class displaying recurrent monosomy 14.** *Neuropathol Appl Neurobiol* 2020;46:422–30. 10.1111/nan.12590
52. Pickles JC, Mankad K, Aizpurua M, et al. **A case series of diffuse glioneuronal tumours with oligodendroglioma-like features and nuclear clusters (DGONC).** *Neuropathol Appl Neurobiol* 2021;47:464–67. 10.1111/nan.12680
53. Solomon DA, Korshunov A, Sill M, et al. **Myxoid glioneuronal tumor of the septum pellucidum and lateral ventricle is defined by a recurrent PDGFRA p.K385 mutation and DNT-like methylation profile.** *Acta Neuropathol* 2018;136:339–43. 10.1007/s00401-018-1883-2
54. Narvaez E de O, Inada BS, de Almeida PR, et al. **Myxoid glioneuronal tumour: report of three cases of a new tumour in a typical location and review of literature.** *BJR Case Rep* 2021;7:20200139. 10.1259/bjrcr.20200139
55. Lucas CH, Villanueva-Meyer JE, Whipple N, et al. **Myxoid glioneuronal tumor, PDGFRA p.K385-mutant: clinical, radiologic, and histopathologic features.** *Brain Pathol* 2020;30:479–94. 10.1111/bpa.12797
56. Broen MP, Smits M, Wijnenga MM, et al. **The T2-FLAIR mismatch sign as an imaging marker for non-enhancing IDH-mutant, 1p/19q-intact lower-grade glioma: a validation study.** *Neuro Oncol* 2018;20:1393–99. 10.1093/neuonc/noy048