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The 2021 WHO Classification for Gliomas and Implications on Imaging Diagnosis: Part 3—Summary of Imaging Findings on Glioneuronal and Neuronal Tumors

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The fifth edition of the World Health Organization classification of central nervous system tumors published in 2021 reflects the current transitional state between traditional classification system based on histopathology and the state-of-the-art molecular diagnostics. This Part 3 Review focuses on the molecular diagnostics and imaging findings of glioneuronal and neuronal tumors. Histological and molecular features in glioneuronal and neuronal tumors often overlap with pediatric-type diffuse low-grade gliomas and circumscribed astrocytic gliomas (discussed in the Part 2 Review). Due to this overlap, in several tumor types of glioneuronal and neuronal tumors the diagnosis may be inconclusive with histopathology and genetic alterations, and imaging features may be helpful to distinguish difficult cases. Thus, it is crucial for radiologists to understand the underlying molecular diagnostics as well as imaging findings for application on clinical practice.

Evidence Level: 3

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Glioneuronal and neuronal tumors encompass a heterogeneous group of neuroepithelial tumors which contain neuronal elements such as ganglion-like cells, differentiated neurocytes, or poorly differentiated neuroblastic cells. As their names suggest, glioneuronal tumors are composed of both neuronal and glial cells, while neuronal tumors are composed of pure neuronal cell tumors. These tumors were grouped as "neuronal and mixed neuronal-glial tumors" at the 2007 and 2016 World Health Organization (WHO) classifications of central nervous system (CNS) tumors.[1,2] The 2021 WHO classification on gliomas continues to group all tumors with neuronal elements and name them as "glioneuronal and neuronal tumors."[3] These tumors are less common than pure glial neoplasms discussed at the Part 1 and 2 Reviews, and account for 1.2% of primary brain tumors in a recent population-based report from the United States.[4] Furthermore, these tumors are low-grade with slow growth and a relatively favorable prognosis. Thus, they have been understudied for a long period.

A brief introduction of the history of classification as well as the discovery of new tumor types within glioneuronal and neuronal tumors helps us understand these tumors. In the first edition of WHO classification in 1979, ganglioglioma,

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anaplastic ganglioglioma (which is currently an omitted tumor type), gangliocytoma, and dysplastic cerebellar gangliocytoma (Lhermitte–Duclos disease) were the only tumor types defined by histopathology findings based on H&E staining within glioneuronal and neuronal tumors.[5] Then, the spectrum of these glioneuronal and neuronal tumors was first expanded by advances in immunohistochemical detection of neuron-specific and neuronal-associated antigens. Immunohistochemical neuronal markers such as synaptophysin, neuron-specific enolase (NSE), and neuronal nuclear antigen (NeuN) have resulted in the discovery of neuronal elements in certain brain tumors.[6] These discoveries helped refine the subsequent WHO classifications. Afterwards, within the last two decades, novel molecular diagnostics such as next-generation sequencing (NGS) and DNA methylation profiling have revolutionized the insights in these tumors and further expanded the tumor spectrum. Some of the recent insights based on molecular diagnostics have been reflected in the Consortium to Inform Molecular and Practical Approaches to CNS Tumor Taxonomy (cIMPACT-NOW) updates of glioneuronal and neuronal tumors[7,8] and in the subsequent 2021 WHO classification.[3]

In the previous Part 1 and 2 Reviews, major changes of the 2021 WHO classification on gliomas were summarized, and imaging findings on adult-type diffuse gliomas, pediatric-type diffuse high-grade gliomas, pediatric-type diffuse low-grade gliomas, and circumscribed astrocytic gliomas were illustrated.[9,10] This Part 3 Review will focus on the molecular diagnostics and imaging findings of glioneuronal and neuronal tumors. We will also briefly discuss the basic histopathological concepts as well as the treatment and prognosis of each tumor type in some tumors, because this information is less familiar to radiologists in practice.

Understanding the Neuroepithelial Origin

As stated in the Part 1 Review, the classification of tumors is broadly based on the concept of cell of origin. The concept of "neuroepithelial cells" will be briefly reviewed to enhance the understanding of glioneuronal and neuronal tumors. Neuroepithelial cells, or neural stem cells, are classically defined as cells active in development, cell turnover, or repair that are self-renewing and multipotent. These cells are able to generate progeny cells that terminally differentiate into neurons, oligodendrocytes, and astrocytes (Fig. 1). As neuroepithelial cells go through a complex and incompletely understood process of interactive differentiation, they have the potential for oncogenic transformations, leading to various types of tumors including single lineage, mixed lineage, and undifferentiated pathologic types. The origin of glioneuronal tumors is not fully elucidated, but origin from bipotent glioneuronal progenitor cells capable of divergent glioneuronal differentiation has been suggested.[11,12] On the other hand, neuronal tumors may originate preferentially from neural progenitor cells rather than glioneuronal progenitor cells.[13,14]

Understanding Neuronal and Glial Elements in Glioneuronal and Neuronal Tumors

Glioneuronal and neuronal tumors show a broad histological spectrum with varying morphologic patterns, and therefore may be difficult to diagnose, even to neuropathologists. The neuronal elements can vary from dysplastic and neoplastic neurons to almost normal and mature neurons which are difficult to distinguish from pre-existing neurons in the cortical ribbon.[15] The current lack of specific marker proteins for detecting "dysplastic" neurons remains a challenging issue in this field. The glial elements may be either an astroglial or oligodendroglia-like/clear-cell phenotype according to specific tumor types.[15] This element is suggested to represent the neoplastically transformed portion of the tumor[16]; however, in gangliocytoma, glial elements are free of atypia.

Low-Grade Developmental and Epilepsy-Associated Brain Tumors (LEAT) and Glioneuronal and Neuronal Tumors

In the Part 2 Review, we have only shortly mentioned the concept of low-grade developmental and epilepsy-associated brain tumors, so-called LEAT.[10] The full-term for LEAT has changed from "long-term epilepsy-associated tumors" to "low-grade epilepsy-associated brain tumors," and more recently to "low-grade developmental and epilepsy-associated brain tumors." The term changed firstly because advanced imaging techniques are leading to early detection and surgery before a "long-term" epilepsy-associated tumor can be recognized,[17] and secondly because the "neurodevelopmental" origin of LEAT has been proposed. Due to its pleomorphic microscopic appearance, early onset, benign clinical course, detection of glioneuronal progenitor marker CD34, and association with focal cortical dysplasia type IIIb, LEAT is postulated to be a developmental tumor.[18,19] Followed by hippocampal sclerosis, LEAT is the second most frequent category in surgical epilepsy.[20] Ganglioglioma and dysembryoplastic neuroepithelial tumors (DNT) are the most frequent LEAT.

The concept of LEAT and its studies are mainly driven by the Neuropathology Task Force of the International League against Epilepsy (ILAE), mainly by Blümcke's group.[15,17,21,22] All glioneuronal and neuronal tumors fall into this category because they can be associated with epilepsy. Several pediatric-type diffuse low-grade gliomas and circumscribed astrocytic gliomas may also fall into the LEAT category. The notion of LEAT may seem to contrast recent trends in understanding the molecular-genetic basis in each specific type of tumor in the 2021 WHO classification. This broad concept on LEAT comes from results that there is poor inter-rater agreement for a specific histopathology diagnosis

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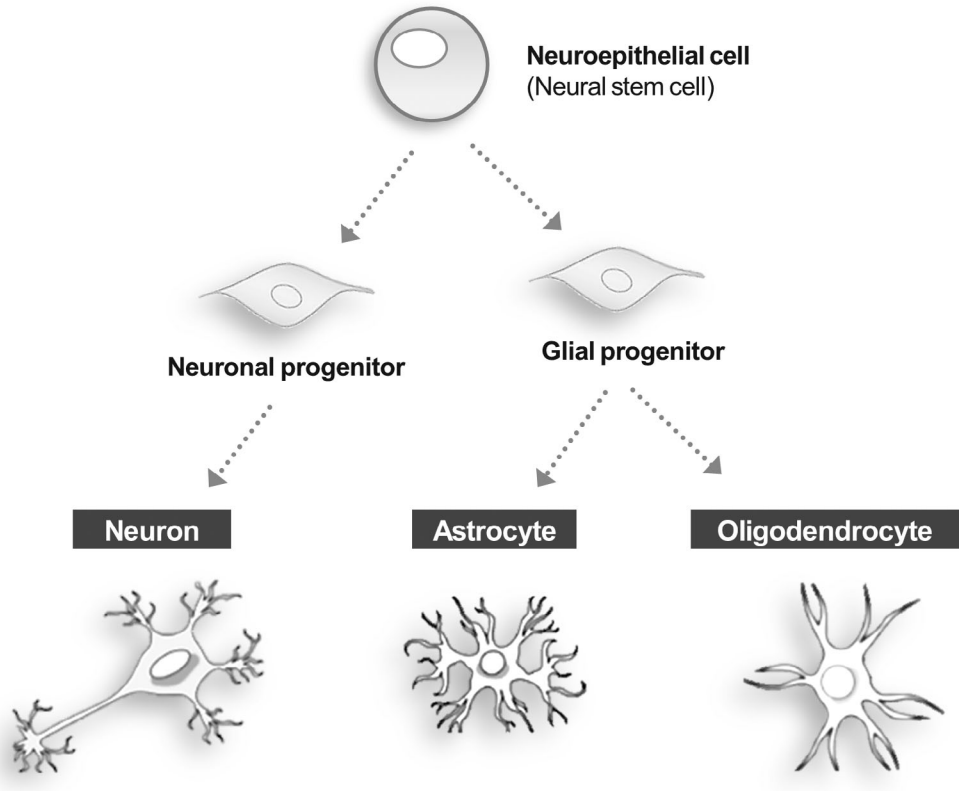

FIGURE 1: Schematic of neuroepithelial cell (neural stem cell) differentiation. Neural stem cells are able to differentiate into neurons, oligodendrocytes, and astrocytes. Glioneuronal tumors may be originated from bipotent glioneuronal progenitor cells, whereas neuronal tumors may be originated from neuronal progenitor cells.

within LEAT; the ILAE group shows that suggesting a new terminology or histopathological criteria did not satisfactorily increase the yield of histopathology agreement.[18]

There are also suggestions that the astounding number of new LEAT types introduced in the 2021 WHO classification may not be clinically meaningful and thus may be debatable[23–25]; those who are interested in this opinion may dig in further. LEAT types can be roughly divided into two groups according to their molecular pattern (Fig. 2),[15] and this approach is useful for understanding glioneuronal and neuronal tumors. The first group shows astrocyte predominance and *BRAF* mutations, and gangliolgioma is the most common tumor type in this group; the second group shows oligodendroglial-like cells predominance with *FGFR1* alterations, and DNT is the most common tumor type in this group.

Molecular Diagnostics

Molecular biomarker testing in glioneuronal and neuronal tumors is *not* in continuum with other diffuse gliomas stated in the Part 1 and 2 Reviews. A recent guideline suggests a pathological processing step in glioneuronal and neuronal tumors.[26] Tumor diagnosis in glioneuronal and neuronal tumors may still be primarily based on H&E stained sections, and the molecular workup is interactive with the results derived from the histopathology examination. The age and location along with histological findings should be considered for the molecular testing for these tumors.

The diagnostic workup to glioneuronal and neuronal tumors typically starts with histological identification of the neoplastic neuronal element on pathology, followed by immunohistochemical analyses of neuronal markers such as MAP2, neurofilament, chromogranin A, NSE, and synaptophysin which highlight the neuronal element. On the other hand, NeuN expression is seen on mature neurons and may be low or absent in neoplastic neurons. CD34 is also a useful marker; although it is not a neuronal marker and its precise nature is unknown, CD34 expression is speculated to represent a form of glioneuronal progenitor cell.[27] Glial elements in glioneuronal tumors can be identified by glial markers (typically GFAP or Olig2). IDH1/2 mutation testing is not mandatory but may help exclusion of IDH-mutant gliomas within adult-type diffuse gliomas (astrocytoma, IDH-mutant and oligodendroglioma, IDH-mutant and 1p/19q-codeleted), as all glioneuronal and neuronal tumors are IDH-wildtype. In many tumor types in glioneuronal and neuronal tumors, the histological evaluation will guide further molecular testing that may be desirable or essential for diagnosis. In unresolvable cases by histopathology and targeted

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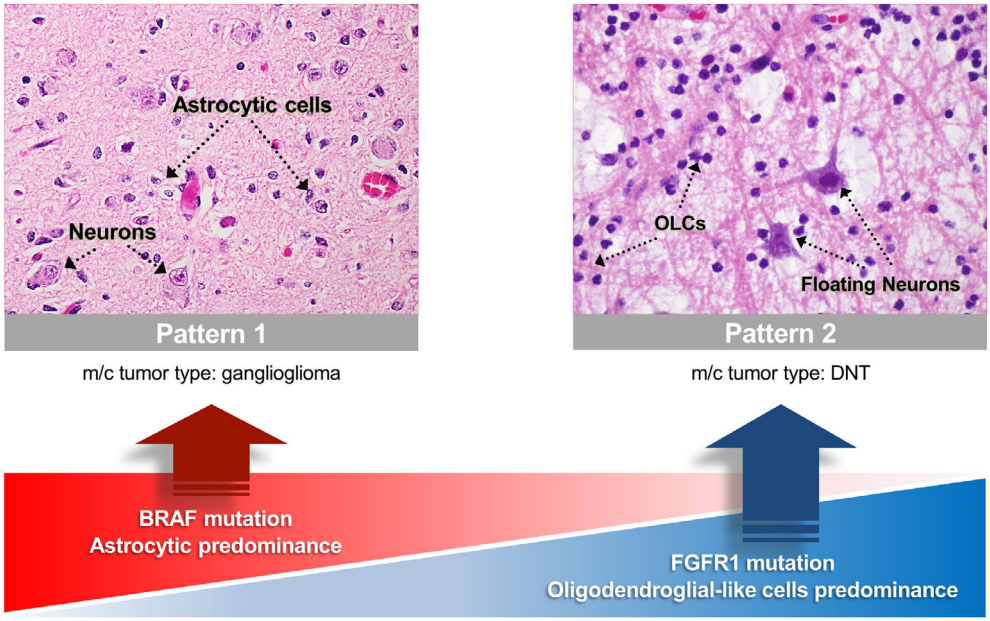

FIGURE 2: Two subgroups in glioneuronal and neuronal tumors according to their molecular characteristics. The first group shows astrocyte predominance and *BRAF* mutations, and ganglioglioma is the most common tumor type in this group. The second group shows oligodendroglial-like cells predominance with *FGFR1* alterations, and DNT is the most common tumor type in this group. This strategy is concise and easy to memorize and helps understand glioneuronal and neuronal tumors. (H&E; ×400 in both slides.) DNT = dysembryoplastic neuroepithelial tumor; OLC = oligodendroglial-like cells.

molecular testing, DNA methylation profiling may aid for the classification. However, as mentioned in Part 1 and 2 reviews, DNA methylation profiling is not reimbursed in many countries and may be unavailable. A representative case showing the pathological processing of glioneuronal and neuronal tumors from our institution is shown in Fig. 3; we have included the imaging findings to show that it may assist in final diagnosis.

The molecular alterations of glioneuronal and neuronal tumors largely overlap with pediatric-type diffuse low-grade gliomas and circumscribed astrocytic gliomas, so we advise to go over the molecular diagnostics section in Part 2 for better comprehension.[10] However, we will repeat the explanation of molecular alterations in this Part 3 Review for separate readers.

Molecular Diagnostics of Glioneuronal and Neuronal Tumors

We suggest several simple rules to understand the molecular landscape of glioneuronal and neuronal tumors. Intuitively, one would expect that a gene driver mutation such as *BRAF p.V600E* would establish a single tumor type. However, this intuition does not fit in glioneuronal and neuronal tumors (as well as pediatric-type diffuse low-grade gliomas and circumscribed astrocytic gliomas) which makes comprehension difficult at a glance.

First, similarly to pediatric-type diffuse low-grade gliomas, mitogen-activated protein kinase (MAPK) pathway alteration is the major genetic event driving the tumorigenesis in these tumors.[28–30] The upregulation of MAPK pathway alteration results in increased cell growth and differentiation.[31] Within MAPK pathway alteration, BRAF mutation (*BRAF p. V600E*, in which a valine is replaced with a glutamic acid at position 600), BRAF oncogenic fusion such as *KIAA1549::BRAF*, and FGFR alterations are the most common pathway alterations in these tumors. BRAF mutation is a gain-of-function mutation, while BRAF oncogenic fusion results in activation of its kinase domain, which eventually leads to tumorigenesis.[32] Introduction of targeted treatments in *BRAF p. V600E* mutant glioneuronal tumors such as RAF and MEK inhibitors has been a major paradigm shift.[33]

Second, outside of the canonical MAPK pathway, non-MAPK pathway alterations exist albeit the low event numbers. Papillary glioneuronal tumor with *PRKCA* fusion, myxoid glioneounal tumor with *PDGFRA* mutation, dysplastic cerebellar gangliocytoma (Lhermitte–Duclos disease) with *PTEN* mutation are within this category.

Third, several tumors currently have no specific molecular marker; gangliocytoma central neurocytoma, and cerebellar lipocytoma have no signature molecular abnormalities.

Fourth, diffuse glioneuronal tumor with oligodendroglioma-like features and nuclear clusters (DGONC) is diagnosed by epigenetic analysis with DNA methylation profile rather than molecular markers, although monosomy 14 is a characteristic finding.

Fifth, as mentioned earlier, many tumor types in pediatric diffuse low-grade gliomas, circumscribed astrocytic gliomas, and glioneuronal and neuronal tumors may have overlap in molecular information; for example, the differential

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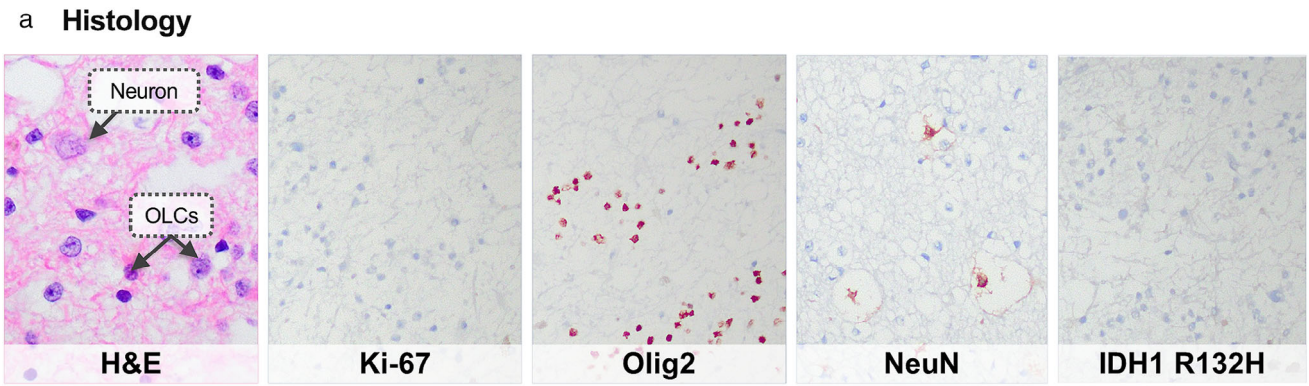

FIGURE 3: A representative case showing the pathological processing of glioneuronal and neuronal tumors from our institution. (a) Diagnostic workup begins with histological evaluation of the classic H&E slide. In this patient's case both neuronal elements (floating neurons) and glial elements (oligodendroglial-like cells) can be seen, directing the diagnosis toward glioneuronal tumor (H&E; ×200 in all slides). Immunohistochemical analysis of proliferation marker (Ki-67), glial marker (OLIG-2), neuronal marker (NeuN), and mutation specific immunohistochemistry of IDH1 R132H can further confirms the findings. This patient showed low proliferation index, and was positive for both glial and neuronal markers. This patient was negative for IDH1 mutation. IDH mutation status may help in excluding IDH-mutant tumors such as oligodendroglioma, IDH-mutant and 1p/19q-codeleted and astrocytoma, IDH-mutant. (b) FGFR1 mutation was seen in NGS results, which is seen in 40%–80% of dysembryoplastic neuroepithelial tumors (DNTs). Based on these findings, the lesion was diagnosed as DNT. In unresolvable cases by histology and targeted molecular testing, DNA methylation profiling may aid in classification. (c) MRI shows a nonenhancing T2 high expansile mass with cystic changes involving the left medial temporal cortex and subcortex, which strongly supports the pathological diagnosis of DNT and increases the reliability of final diagnosis. DNT = dysembryoplastic neuroepithelial tumor; NGS = next-generation sequencing; OLC = oligodendroglial-like cells.

diagnosis of low-grade glioma with a *BRAF p.V600E* mutation includes ganglioglioma, diffuse low-grade glioma, MAPK pathway-altered, pleomorphic xanthoastrocytoma, and pilocytic astrocytoma. An integrated diagnosis is made based on the histopathological and molecular information.

A subset of molecular findings in the 2021 WHO classification that involve the classification of glioneuronal and neuronal tumors are summarized in Fig. 4. A comprehensive schematic to the molecular findings in pediatric-type diffuse low-grade glioma, circumscribed astrocytic gliomas, and glioneuronal and neuronal tumors encompassing Part 2 and Part 3 Reviews are summarized in Fig. S1. The molecular alterations of these tumors in Part 2 and Part 3 Reviews frequently overlap.

Before Starting: Always Keep the "Big Picture' in Mind

As stated in the Part 1 and Part 2 reviews and highlighted again, we should refrain from being focused on a particular imaging finding to make a specific diagnosis. This goes on in glioneuronal and neuronal tumors. Even the most common tumor types within glioneuronal and neuronal tumors such as ganglioglioma and DNT are rare and the prevalence is not clearly established yet. The age and location should be always considered when establishing an imaging diagnosis. Except for cases with typical imaging features and appropriate clinical settings (i.e., a young adult with characteristic clustering T2 hyperintense nodular lesions in the temporal subcortex, suggesting multinodular vacuolating neuronal tumor [MVNT]), most tumors in these categories should be included in the differential diagnosis on preoperative imaging, rather than giving just one definite imaging diagnosis.

Table 1 shows a summary of key molecular alterations, WHO grade, age, location, and imaging features in each type of tumor in glioneuronal and neuronal tumors. The common locations of each type of tumors in glioneuronal and neuronal tumors are also shown in Fig. 5, temporal lobe being the most common location in most tumors.

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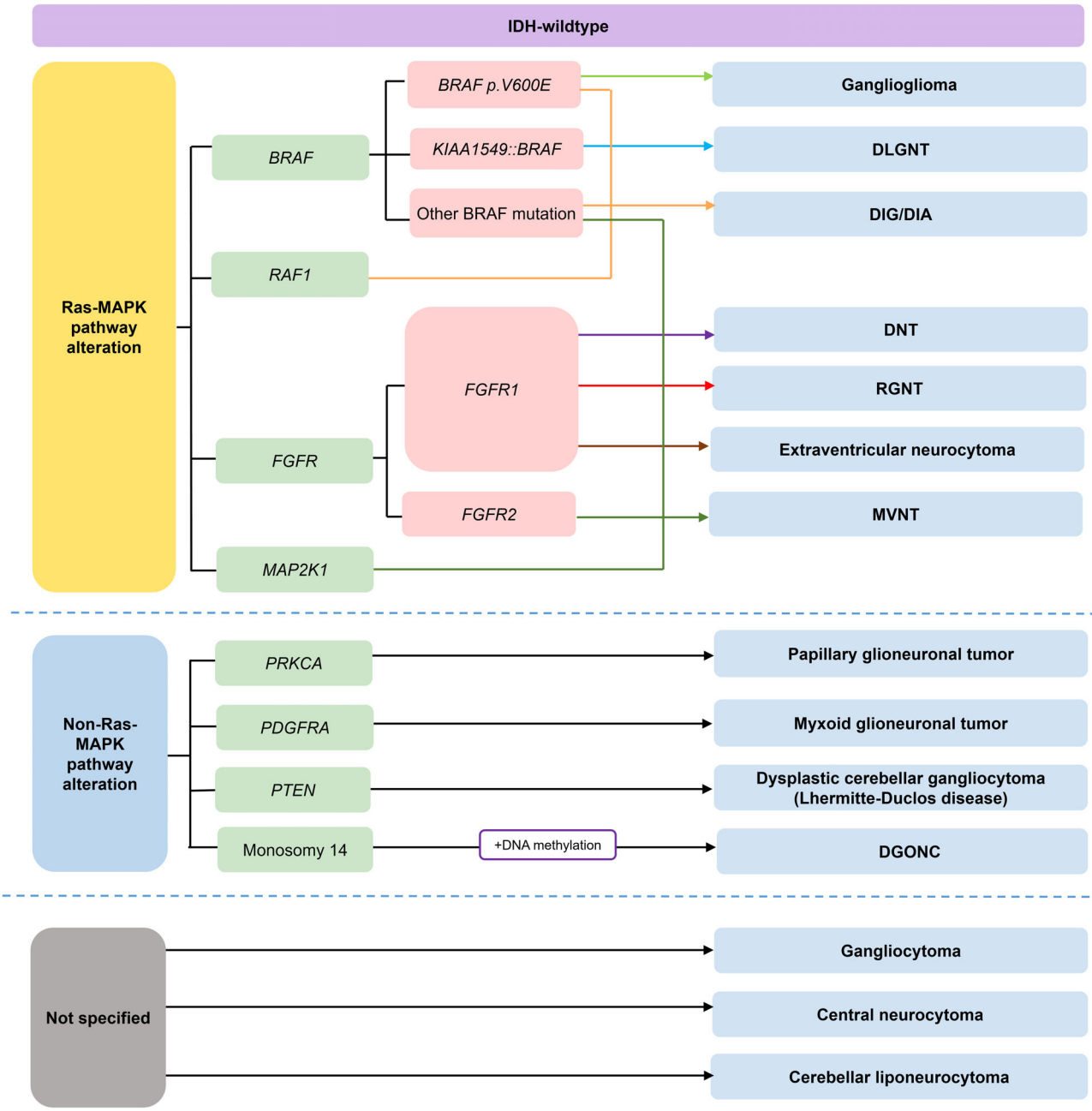

FIGURE 4: Molecular findings in the 2021 WHO classification that involve the classification of glioneuronal and neuronal tumors. Ras-MAPK pathway alteration is the major event driving the oncogenesis. Within MAPK pathway, *BRAF* alterations and *FGFR1/2* alterations are commonly seen. DNA methylation profile is essential for DGONC diagnosis. In central neurocytoma, gangliocytoma, and cerebellar lipocytoma the molecular alteration is not specified. DIA = desmoplastic infantile astrocytoma; DIG = desmoplastic infantile ganglioglioma; DGONC = diffuse glioneuronal tumor with oligodendroglioma-like features and nuclear clusters; DNT = dysembryoplastic neuroepithelial tumor; DLGNT = diffuse leptomeningeal glioneuronal tumor; MAPK = mitogen-activated protein kinase; MVNT = multinodular and vacuolating neuronal tumor; RGNT = rosette-forming glioneuronal tumor.

Diagnostic Approach of Glioneuronal and Neuronal Tumors by Imaging

As radiologists we often encounter preoperative MRIs with findings that suggest the possibility of glioneuronal and neuronal tumors; mostly the clinical scenario being a well-defined intraaxial tumor in children or young adults. Table 2 shows frequent clinical, molecular, and imaging characteristics of glioneuronal and neuronal tumors that assist in the initial diagnostic approach. The embarrassing truth is that we cannot even confidentially differentiate glioneuronal and neuronal tumors from pediatric-type diffuse low-grade gliomas or circumscribed astrocytic gliomas purely by imaging in a

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TABLE 1. Summary of Key Molecular Alterations, WHO Grade, Age, Location, and Imaging Features in Each Type of Glioneuronal and Neuronal Tumors

Tumor Type	Key Molecular Alteration	WHO Grade	Age	Location	Imaging Features
Ganglioglioma	*BRAF p.V600E* mutation	1	All ages, mostly young adults	Temporal lobe (m/c)	Cystic mass with enhancing mural nodule Frequent calcification (up to 30%–50%)
Gangliocytoma	-	1	Mostly children	Temporal lobe (m/c)	Similar appearance to ganglioglioma
DIG/DIA	BRAF or RAF1 mutation or fusion	1	Mostly infants	Cerebral hemisphere	Large cystic mass with dural-based enhancing solid portion
DNT	*FGFR1* alteration	1	Children and young adults	Temporal lobe (m/c)	Cystic or multicystic lesion, "bubbly" appearance
DGONC	- (DNA methylation)	-[a]	Children	Temporal lobe (m/c)	Well-defined lesion with little-or-no contrast enhancement
Papillary glioneuronal tumor	*PRKCA* gene fusion	1	All ages, mostly second decade	Cerebral hemisphere	Purely cystic, mixed cystic and solid, or solid Common calcification
RGNT	*FGFR1* hotspot mutation	1	Young adults	Fourth ventricle (m/c)	"Green bell pepper sign" (cystic and solid mass showing ring enhancement with central hypointensity)
Myxoid glioneuronal tumor	*PDGFRA*	1	Mostly second–third decade	Septal nuclei, septum pellucidum	Well-defined cystic lesions without contrast enhancement
Diffuse leptomeningeal glioneuronal tumor	1p deletion, *KIAA1549::BRAF*	-[a]	Mostly children and adolescents	Leptomeninges	Diffuse leptomeningeal enhancement May show small cystic or nodular T2-hyperintense lesions along the subpial surface
MVNT	*MAP2K1, BRAF, FGFR2*	1	Mostly adults	Temporal lobe (m/c)	Spares superficial cortex (juxtacortical) Subcortical clustering of T2 high nodular lesions without contrast enhancement

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TABLE 1. Continued

Tumor Type	Key Molecular Alteration	WHO Grade	Age	Location	Imaging Features
Dysplastic cerebellar gangliocytoma (Lhermitte–Duclos disease)	*PTEN*	1	Mostly third–fourth decade	Cerebellum	"Tiger-stripe" appearance (alternating T1 hypointense and T2 hyperintense stripes in the enlarged folia) No or superficial enhancement
Central neurocytoma	-	2	All ages, mostly second–third decade	Lateral ventricle	Multiloculated cystic and solid mass ("soap bubble" appearance) with heterogeneous enhancement Calcification, hemorrhage may be present
Extraventricular neurocytoma	*FGFR1::TACC1* fusions	2	Mostly third-fourth decade		Well-circumscribed, heterogeneously enhancing, cystic and solid mass with moderate edema
Cerebellar liponeurocytoma	-	2	Adults	Cerebellum	Areas of T1 hyperintensity corresponding to high lipid content

DIA = desmoplastic infantile astrocytoma; DIG = desmoplastic infantile ganglioglioma; DGONC = diffuse glioneuronal tumor with oligodendroglioma-like features and nuclear clusters; DNT = dysembryoplastic neuroepithelial tumor; DLGNT = diffuse leptomeningeal glioneuronal tumor; MAPK = mitogen-activated protein kinase; MVNT = multinodular and vacuolating neuronal tumor; RGNT = rosette-forming glioneuronal tumor.
[a]These types of tumors do not have an established CNS WHO grade yet.

majority of cases because imaging findings of these tumor categories often overlap. Then which diagnostic approach should we take in these tumors?

First, our preoperative role is to narrow down the differential diagnosis list than rather point out one correct answer in many cases. In case of a well-circumscribed mixed solid and cystic mass in a young adult at the cerebral hemisphere, the differential diagnosis may include ganglioglioma, gangliocytoma, as well as pilocytic astrocytoma, pleomorphic astrocytoma, and even adult-type diffuse glioma. Meticulous investigation of the imaging findings may help narrow down the wide range of differential diagnoses into a narrower one; you will need to study imaging features of each tumor type more intensively to do so. Do not be discouraged that you could not indicate one tumor type specifically, because these differential diagnoses do not crucially impact the surgical strategy. The surgical strategy of these tumors will all be gross total resection. The definite diagnosis is left for the pathologist to decide with the surgical tissue.

Second, there are several tumor types from glioneuronal and neuronal tumors in which imaging alone may be important and further surgery can be avoided. Thus, radiologists may be aware of these findings for correct diagnosis and suggest follow-up rather than surgery. A recent study suggests that MVNT may be a "leave me alone" lesion and does not require surgery and may be diagnosed alone by the highly characteristic imaging finding.[34] Dysplastic cerebellar gangliocytoma (Lhermitte–Duclos disease) is another tumor type that may not require surgery in asymptomatic patients and may be diagnosed preoperatively by its highly characteristic imaging findings.

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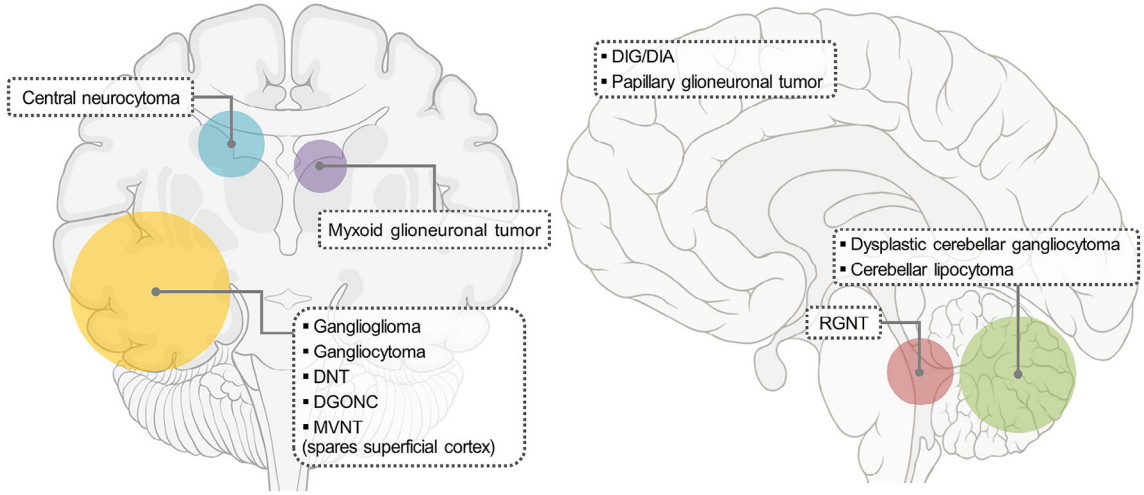

FIGURE 5: Common locations of glioneuronal and neuronal tumors. Temporal lobe is the most common location in ganglioglioma, gangliocytoma, DNT, DGONC, and MVNT. Of note, MVNT spares the superficial cortex. Central neurocytoma is usually located at the anterior portion of the lateral ventricles, usually attached to the septum pellucidum, whereas myxoid glioneuronal tumors is located at the septal nuclei or septum pellucidum. DIG/DIA and papillary glioneuronal tumor are located at the cerebral hemisphere. Three types of tumors show posterior fossa location: RGNT at the fourth ventricle, and dysplastic cerebellar gangliocytoma (Lhermitte–Duclos disease) and cerebellar lipocytoma at the cerebellum. DLGNT is located at the leptomeninges. DIA = desmoplastic infantile astrocytoma; DIG = desmoplastic infantile ganglioglioma; DGONC = diffuse glioneuronal tumor with oligodendroglioma-like features and nuclear clusters; DNT = dysembryoplastic neuroepithelial tumor; DLGNT = diffuse leptomeningeal glioneuronal tumor; MVNT = multinodular and vacuolating neuronal tumor; RGNT = rosette-forming glioneuronal tumor.

Third, imaging may assist pathological diagnosis in complicated cases. For example, distinguishing a diffuse glioma from a glial element of a ganglioglioma, pilocytic astrocytoma, or pleomorphic xanthoastrocytoma could be difficult on histopathology.[7] Also, a diffuse glioma with oligodendroglial differentiation appears identical to certain regions of DNT.[7] In these cases, references to the imaging characteristics of the tumor by the radiologist may be useful, although not conclusive.

Specific Molecular and Imaging Features

Glioneuronal and Neuronal Tumors

Three new tumor types are added in the 2021 WHO classification in the category of glioneuronal and neuronal tumors: DGONC, which is a provisional type; myxoid glioneuronal tumor, and MVNT. Except for DGONC and diffuse leptomeningeal glioneuronal tumor, which do not have an established CNS WHO grade yet, all tumor types in glioneuronal and neuronal tumors are WHO grade 1 or 2.

GANGLIOGLIOMA. Gangliogliomas were among the first tumors recognized in the first edition of WHO classification due to its distinct histopathological findings.[35] Ganglioglioma is a well-differentiated, slow-growing neoplasm composed of a combination of neoplastic ganglion and glial cells resembling astrocytoma, which is molecularly characterized by genetic alterations that cause MAPK pathway activation, most commonly *BRAF p.V600E* mutation.[36] It can be seen at any age, but is most common in young adults. Both ganglioglioma

TABLE 2. Frequent Clinical, Molecular, and Imaging Characteristics of Glioneuronal and Neuronal Tumors

Clinical	Mostly found in children or young adults
	Associated with seizures; within category of LEAT
	Favorable prognosis on gross total resection
Molecular	All IDH-wildtype
	Common MAPK pathway alterations
Imaging	Temporal lobe location is the most common
	Frequent cortical location
	Well-defined
	Little or no mass effect
	Frequent cystic changes
	Variable contrast enhancement
	Generally no diffusion restriction on ADC map
	Generally no rCBV increase on CBV map

Note that some tumor types within glioneuronal and neuronal tumors may not show these imaging findings. ADC = apparent diffusion coefficient; CBV = cerebral blood volume; IDH = isocitrate dehydrogenase; LEAT = low-grade developmental and epilepsy-associated brain tumors; MAPK = mitogen-activated protein kinase; rCBV = relative cerebral blood volume.

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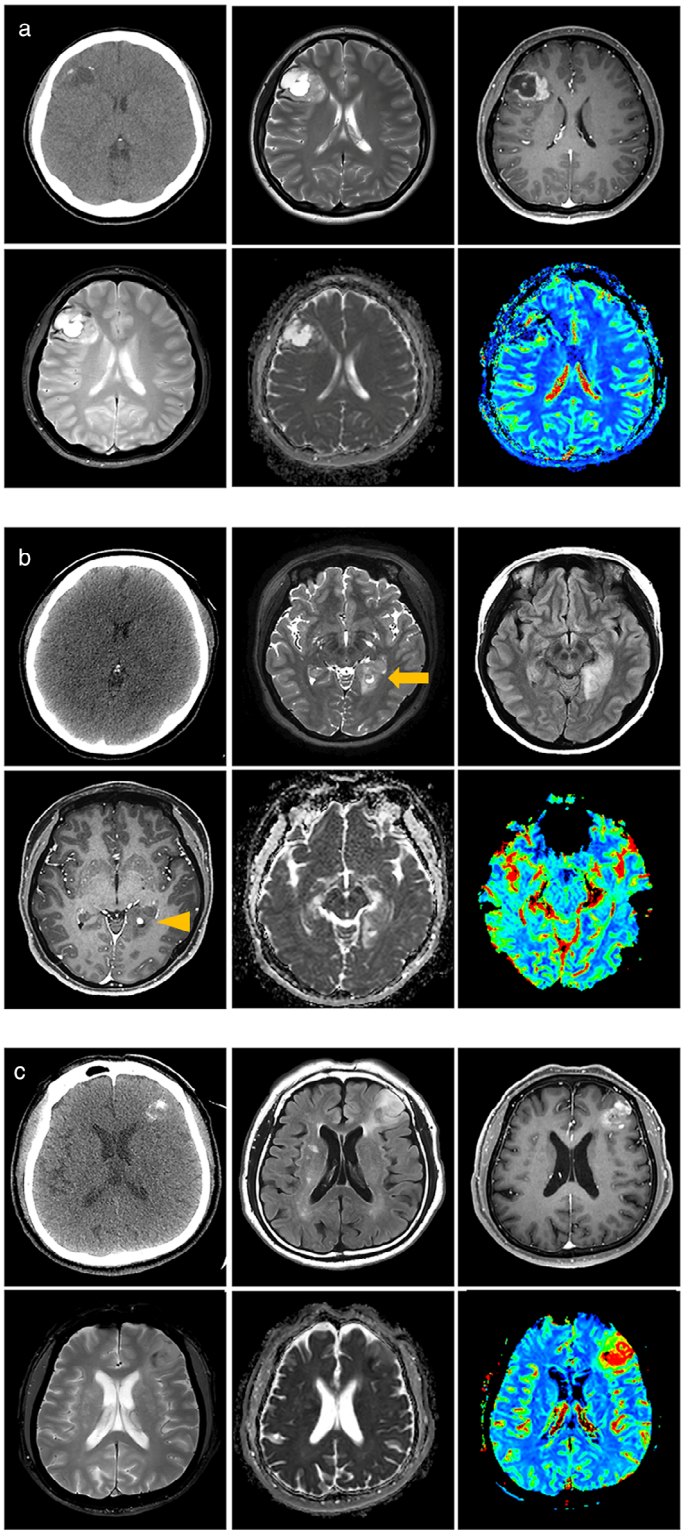

FIGURE 6: Images in three different patients with ganglioglioma. (a) Images of a 34-year-old female. A low-attenuating mass at the right frontal lobe with peripheral calcification is seen on CT. On MRI, this cystic and solid mass shows strong enhancement of solid portion, with T2 low signal rim and GRE blooming due to calcification. There is mild ADC decrease at the solid portion, and mild rCBV elevation on CBV map. (b) Images of a 25-year-old female. On CT, it is difficult to delineate the mass and there only is subtle low attenuation at the left medial temporal lobe. On MRI, there is a T2 hyperintense mass at the left medial temporal lobe, and there is a focal cystic area (arrow) with enhancing mural nodule (arrowhead) within the mass. There is focal cellularity increase at the enhancing mural nodule. There is no rCBV elevation. (c) Images in a 73-year-old male. On CT, there is a calcified mass at the left frontal lobe. On MRI, there is a T2 hyperintense mass at the left frontal lobe with cortical expansion without cystic portion. This mass shows areas of heterogeneous enhancement. There is an area of low cellularity on ADC map, while there is marked rCBV elevation.

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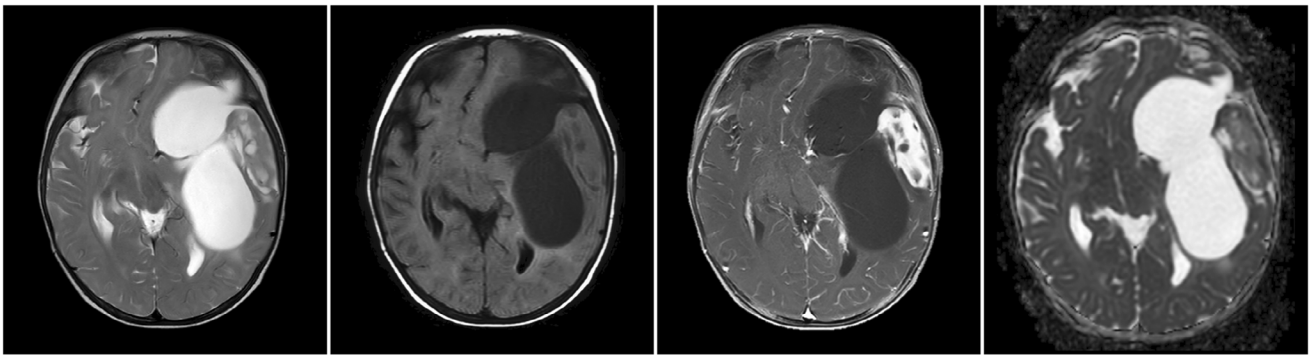

FIGURE 7: Images of a 6-year-old infant (male) with desmoplastic infantile ganglioglioma. Imaging shows a large multicystic mass with dural-based enhancing solid portion with minimal peritumoral edema at the left cerebral hemisphere. There is subtle cellularity increase on ADC map at the periphery of solid portion.

and gangliocytoma contain dysplastic neurons, but differences are that 1) ganglioglioma is a biphasic tumor composed of admixture of neuronal and glial cells, whereas gangliocytoma is mainly composed of only neuronal cells and glial elements are sparsely represented, and 2) there is neoplasia or atypia in glial elements of ganglioglioma, whereas glial elements of gangliocytoma show no atypia. However, clear-cut pathological differentiation between ganglioglioma and gangliocytoma may not always be possible. The existence of anaplastic ganglioglioma, showing features such as high mitotic activity, proliferation index, necrosis, and microvascular proliferation,[37] is controversial because prior reports lacked molecular analysis to exclude other high-grade glioma types. Thus, anaplastic ganglioglioma is currently an omitted tumor type. Gangliogliomas generally have a favorable prognosis on surgical resection.

The most common location for ganglioglioma is the temporal lobe (over 75%), although it can occur throughout the CNS.[38] Ganglioglioma is cortically based and often expands the cortex. The classic appearance is a partially cystic mass with enhancing mural nodule, seen in approximately 40% of cases. This "cystic mass with enhancing mural nodule" appearance overlaps with pilocytic astrocytoma and pleomorphic xanthoastrocytoma mentioned in the Part 2 review, but can sometimes be differentiated by its predominant location (cerebellum in pilocytic astrocytoma), presence of calcification (most frequent in ganglioglioma; up to 30%–50%) and presence of dural tail (present in pleomorphic xanthoastrocytoma).[39] Peritumoral edema is generally absent. The solid mass shows varying degrees of enhancement. An infiltrating, poorly-defined mass is often seen. On apparent diffusion coefficient (ADC) map, gangliogliomas have been reported to show a lower ADC value and higher relative cerebral blood volume (rCBV) on dynamic susceptibility contrast imaging than either oligodendrogliomas or pilocytic astrocytomas.[40,41] Gangliogliomas with *BRAF p.V600E* mutation are reported to have lower ADC values than gangliogliomas without *BRAF p.V600E* mutation.[42] Imaging spectrums of gangliogliomas in three different patients are shown in Fig. 6.

GANGLIOCYTOMA. The histopathology of gangliocytoma is described in conjunction with ganglioglioma at the previous paragraph. Gangliocytoma is mainly composed of neuronal cell and sparsely of glial elements. These glial cells do not have any neoplasia, but this concept is criticized to be difficult to verify microscopically and has never been scientifically proven.[18] Thus, in other words, the true existence of gangliocytoma may be questionable. No distinct genetic susceptibility factors have been reported for classic

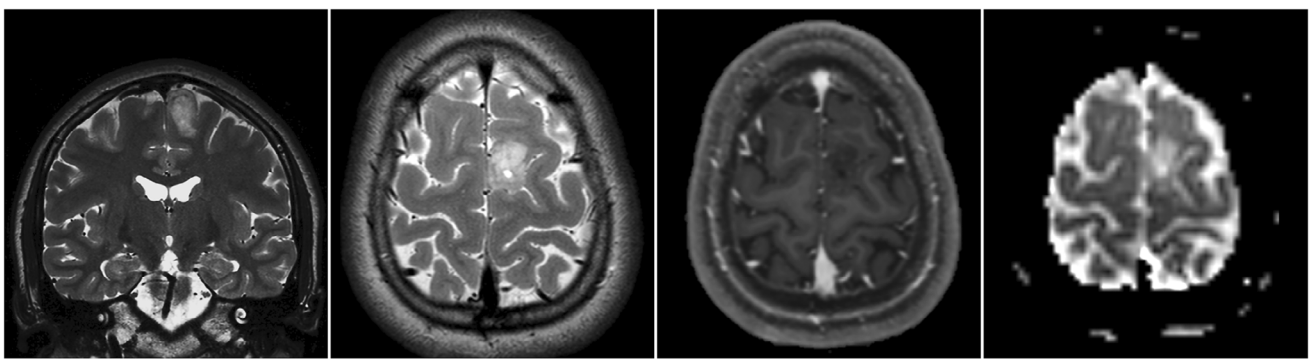

FIGURE 8: Images of a 20-year-old female with DNT. Imaging shows a T2 hyperintense nonenhancing mass with cystic change involving the left frontal cortex and subcortex. There is no cellularity increase on ADC map. DNT = dysembryoplastic neuroepithelial tumor.

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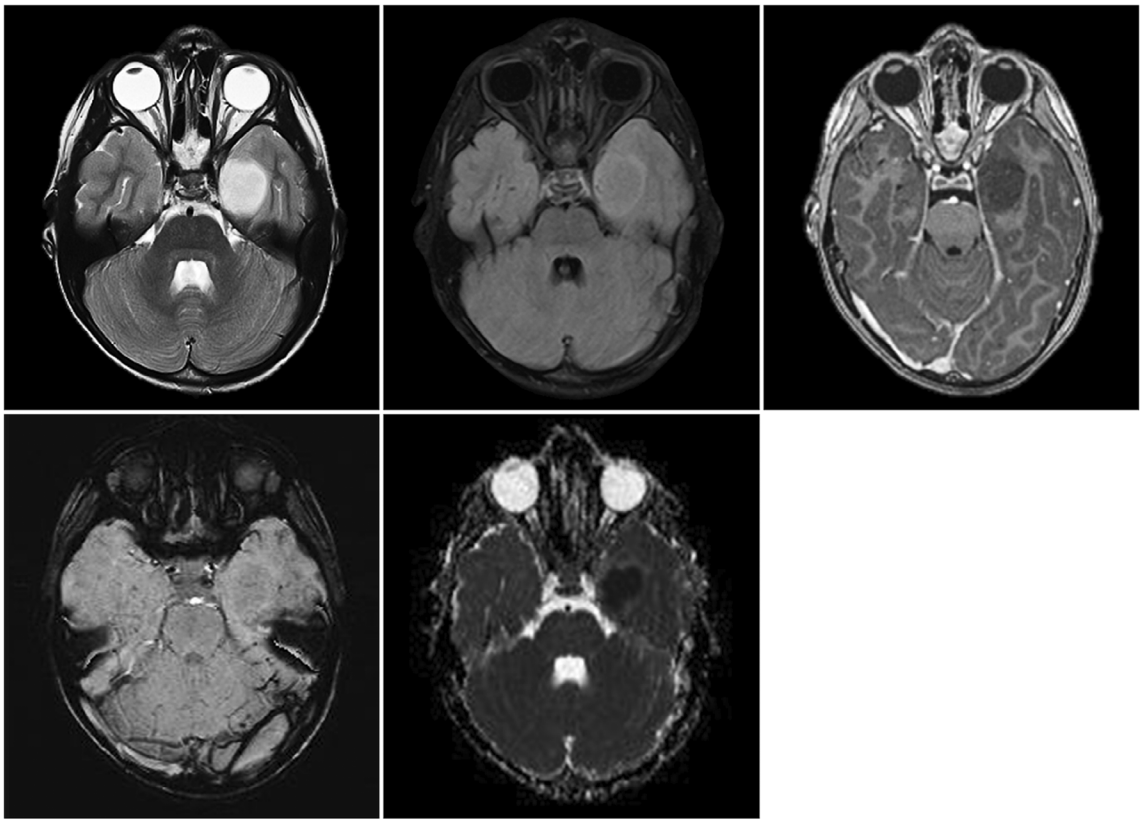

FIGURE 9: Images of a 4-year-old girl with DGONC. Imaging shows a well-defined T2 hyperintense nonenhancing mass without hemorrhage at the left medial temporal lobe. There is marked diffusion restriction on ADC map.

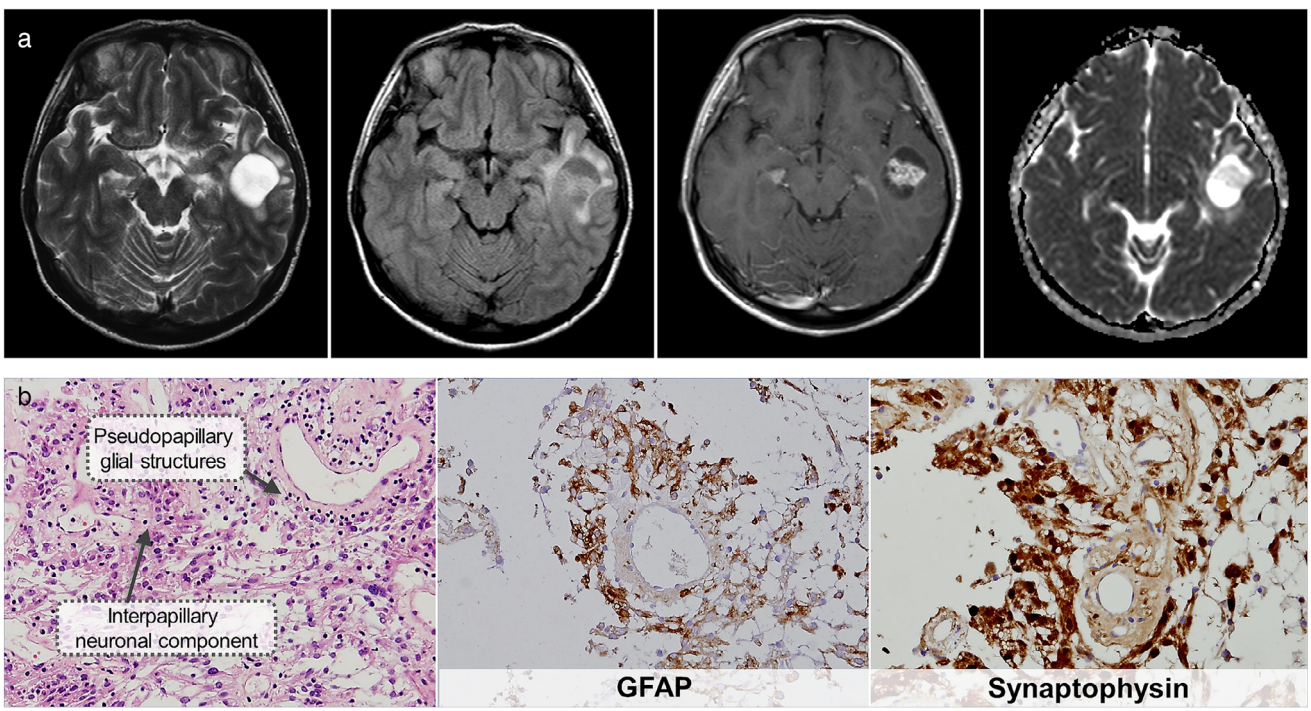

FIGURE 10: (a) Images of a 22-year-old female with papillary glioneuronal tumor. There is a well-defined cystic and solid mass with mild peritumoral edema. The solid portion shows marked enhancement. There is no cellularity increase on ADC map. (b) On histopathology, the biphasic pattern with pseudopapillary glial structures and interpapillary neuronal component is shown (H&E; ×100) (left). The GFAP-positive glial cells in pseudopapillary structures are shown (middle, ×200), while the interpapillary neuronal components show synaptophysin immunoreactivity (right, ×200).

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gangliocytoma. Gangliocytomas are rare tumors frequently occurring in children, and researches solely focused in gangliocytoma are rare.

Imaging features are similar to those of ganglioglioma. The most common location is temporal lobe, with mixed cystic and solid lesions, variable

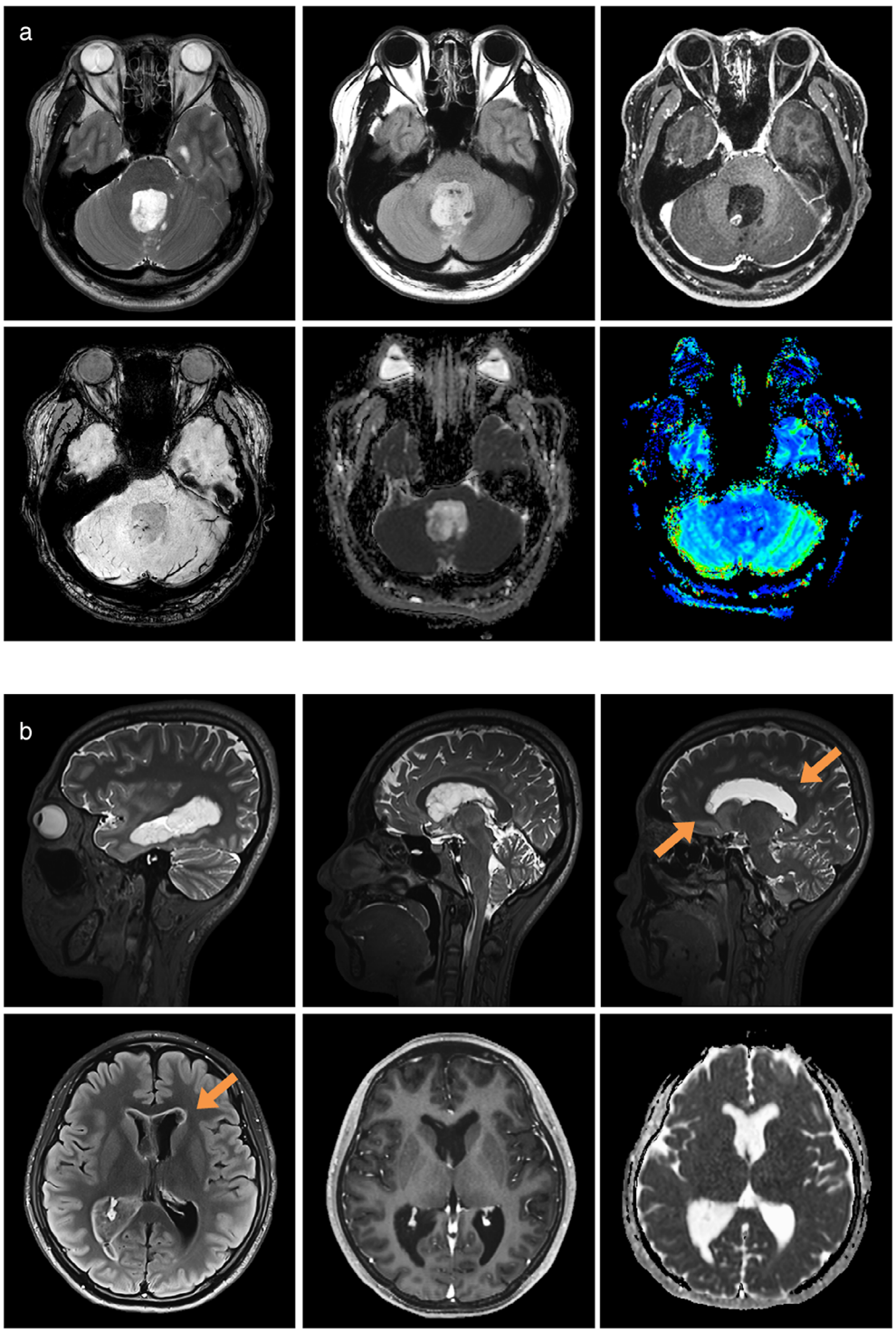

FIGURE 11: Images of two different patients with rosette-forming glioneuronal tumor with representative histopathology. (a) Images in a 36-year-old male show a T2 hyperintense mass with multiple cystic changes at the fourth ventricle and cerebellar vermis. There is a focal ring enhancement at the solid portion. Susceptibility-weighted imaging shows areas of hemorrhage. There is no cellularity increase on ADC map, and no or minimal rCBV increase. (b) Images in a 16-year-old female show a T2 hyperintense expansile mass involving the entire right lateral ventricle. Leptomeningeal metastases are manifested with cystic nodular lesions along the ependymal lining (arrows). There is no enhancement of the tumor. There is no cellularity increase on ADC map. (c) On histopathology, rosette-forming glioneuronal tumor consists of two components: neurocytic (left) and astrocytic (right) (H&E; ×40).

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enhancement, and common calcification (approximately 1/3 of cases).

DESMOPLASTIC INFANTILE GANGLIOGLIOMA/ DESMOPLASTIC INFANTILE ASTROCYTOMA. Desmoplastic infantile ganglioglioma (DIG) and desmoplastic infantile astrocytoma (DIA) are benign glioneuronal or glial tumors that are composed of a mixed astrocytic and neuronal component (DIG) or an astrocytic component only (DIA) embedded in an extensive desmoplastic stroma, often containing foci of undifferentiated embryonal-like tumor cells. The massive leptomeningeal desmoplasia (growth of connective tissue) is characteristic of DIG/DIA and has been reflected in their terminology.[43] DIG/DIA are characterized by MAPK pathway alterations, most commonly *BRAF* (including *BRAF p.V600E* mutation) or *RAF1* alterations.[44] As their terminology suggests, DIG/DIA mostly occurs in infants before the age of 24 months. Unlike other intracranial neoplasms that present in infants, the prognosis of DIG/DIA is favorable on total removal.

DIG/DIA are located in the cerebral hemispheres commonly in the frontal and parietal lobes, involving the superficial cortex. They appear as a large cystic mass with dural-based enhancing solid portion showing "dural-tail" sign. The solid mass shows strong and heterogeneous enhancement. Reported cases show variable diffusion restriction and slightly elevated rCBV.[45] A representative case is shown in Fig. 7.

DYSEMBRYOPLASTIC NEUROEPITHELIAL TUMOR. DNT is a neoplasm in the cerebral cortex of children or young adults, characterized by the pathognomonic glioneuronal element (the presence of columns oriented perpendicularly to the cortical surface, formed by bundles of axons lined by small oligodendroglia-like cells), multinodular intracortical growth, and *FGFR1* alterations. Dysplastic ganglionic cells are absent. DNTs were thought to be originated from the embryonic brain; hence comes the name "dysembryoplastic."[46] DNTs are considered benign lesions and have a favorable prognosis on surgical resection.

DNTs are located in the supratentorial cortex, most commonly temporal lobes (approximately 70%). They show well-defined T2 hyperintense cystic or multicystic lesions with "bubbly" appearance and little or no edema.[47,48] They commonly show hyperintense rim on FLAIR. Calcifications and hemorrhage are rare, while rim-like enhancement is seen in approximately 30% of patients.[49] DNTs show a lower ADC value and lower rCBV value than normal brain

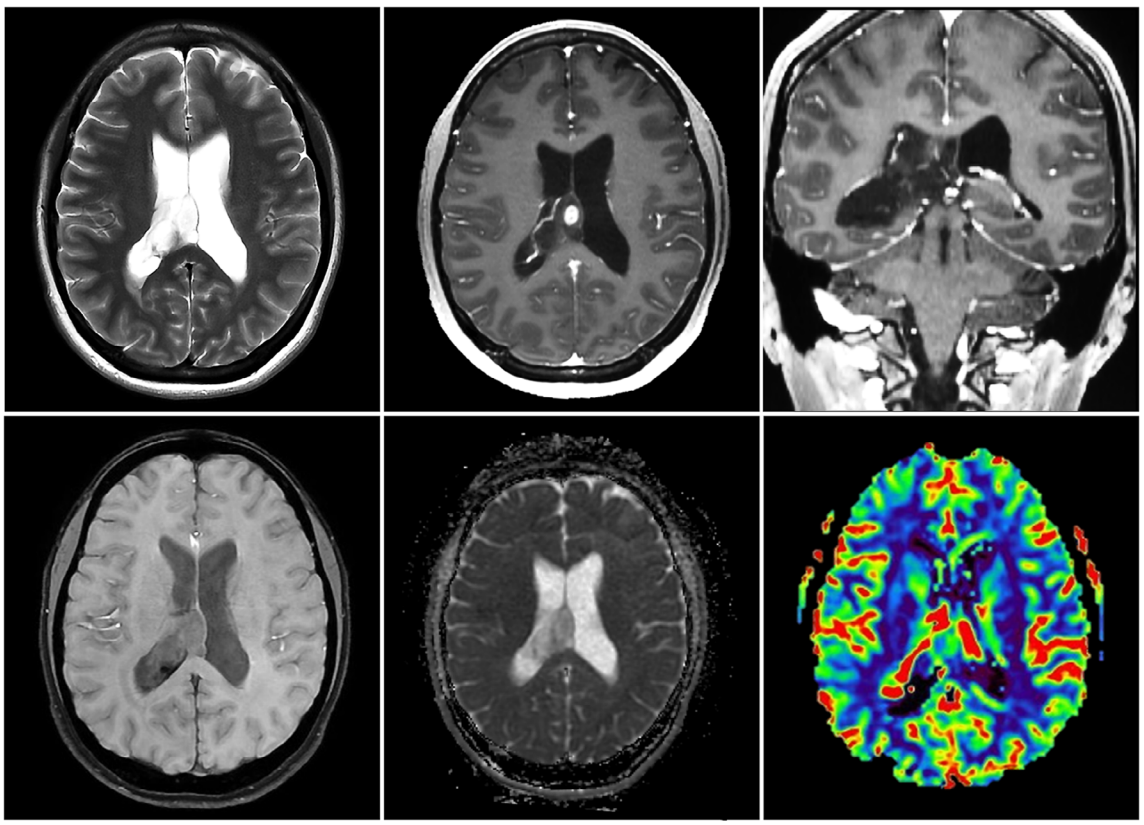

FIGURE 12: Images of a 32-year-old female with myxoid glioneuronal tumor. There is a well-defined T2 hyperintense multicystic tumor involving the right lateral ventricle and septum pellucidum. There is focal strong enhancement within the tumor. Minimal hemorrhage is noted on susceptibility-weighted imaging. There is no diffusion restriction or rCBV increase. This patient lacked *FGFR1* mutation that is typical of DNT, and was diagnosed as myxoid glioneuronal tumor after DNA methylation profiling.

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parenchyma, reflecting their benign nature.[50] A representative case is shown in Fig. 8.

DIFFUSE GLIONEURONAL TUMOR WITH OLIGODENDROGLIOMA-LIKE FEATURES AND NUCLEAR CLUSTERS. Diffuse glioneuronal tumor with oligodendroglioma-like features and nuclear clusters (DGONC) is a provisional tumor type in the fifth edition of WHO classification, which does not have an established CNS WHO grade yet. This rare tumor (31 patients in >25,000 CNS tumors)[51] requires a specific DNA methylation profile in addition to cells exhibiting oligodendroglioma-like morphology, strong expression of both Olig2 and synaptophysin, and absence of widespread GFAP expression. Monosomy of chromosome 14 is a frequent finding.[51] DGONC is mainly seen in pediatric patients, with a favorable prognosis.[51]

The most common location for DGONC is the temporal lobe.[51–53] DGONCs are well-defined with little mass effect, with little enhancement, small areas of cystic change, with possible calcification Diffusion characteristics are various, and may show inhomogeneous or restricted diffusion on the ADC map.[52,53] Representative imaging and pathology cases are shown in Fig. 9.

PAPILLARY GLIONEURONAL TUMOR. Papillary glioneuronal tumor exhibits a biphasic pattern with 1) variable representation of pseudopapillary glial structures and 2) interpapillary neuronal components. PRKCA gene fusion, mainly *SLC44A1::PRKCA* is the molecular hallmark.[54] DNA methylation profiling may help in unresolved lesions. Papillary glioneuronal tumor is a rare tumor usually occurring in adults at the second decade, with a favorable prognosis on surgical resection.

Papillary glioneuronal tumor commonly locates at the supratentorium, with close proximity to lateral ventricles, suggesting a possible origin from the germinal zone of subependymal plate.[54–56] There is no specific predilection for lobes.[54] The tumor is well-defined, with imaging findings ranging from purely cystic to mixed cystic and solid and solid.[55,57] Calcification is common. There is minimal or no edema, and contrast enhancement is variable. Several reported cases usually showed no diffusion restriction on ADC map. There is usually no rCBV increase, but there is a case report of rCBV increase in the solid portion.[58,59] A representative case is shown in Fig. 10.

ROSETTE-FORMING GLIONEURONAL TUMOR. Rosette-forming glioneuronal tumor (RGNT) is a rare biphasic tumor composed of 1) uniform neurocytes forming rosettes and/or perivascular pseudorosettes and 2) glial elements with piloid and oligodendroglia-like cells, resembling pilocytic astrocytoma. In the 2007 WHO classification, RGNT was named as "rosette-forming glioneuronal tumor of the fourth ventricle," however, subsequent reports have shown that RGNT can also affect sites other than the fourth ventricle. Thus, the extension of "of the fourth ventricle" was abandoned in the 2016 and 2021 WHO classifications. For cases affecting the fourth ventricle, a subependymal origin has been suggested because they display both glial and neurocytic features.[60] RGNT is characterized by *FGFR1* hotspot mutation in combination with either *PIK3CA* or *PIK3R1* mutation and/or *NF1* mutation.[61] Usually seen in young adults, RGNTs mostly show favorable prognosis. However, tumor recurrence or progression has been described.[62,63]

RGNT typically arises in the midline, most commonly in the fourth ventricle, and can involve the adjacent brainstem, cerebral aqueduct, cerebellar vermis, pineal gland, or thalamus. Cases involving tectal, pineal, spinal cord, and diencephalic region has been also described. The tumor is well-defined, with imaging findings ranging from purely multicystic to mixed cystic and solid and solid. Peripheral or heterogeneous enhancement is frequently seen, and hemorrhage and calcification may be common.[64,65] The "green bell pepper sign," which refers to the cystic and solid mass showing ring enhancement with central hypointensity, surrounded

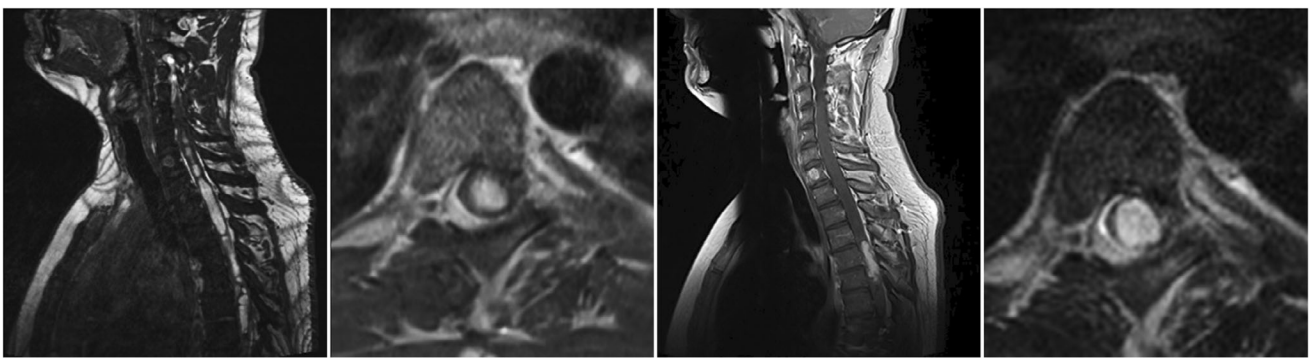

FIGURE 13: Images of a 26-year-old male with an atypical imaging presentation of diffuse leptomeningeal glioneuronal tumor. There is a T2 hyperintense multicystic and solid tumor involving the multiple cervical and thoracic spinal segments, with enhancement at the solid portion at the T4 to T5 spinal cord. There is no leptomeningeal enhancement. This patient showed 1p deletion and *KIAA1549::BRAF* fusion on NGS, fulfilling diagnostic criteria for diffuse leptomeningeal glioneuronal tumor.

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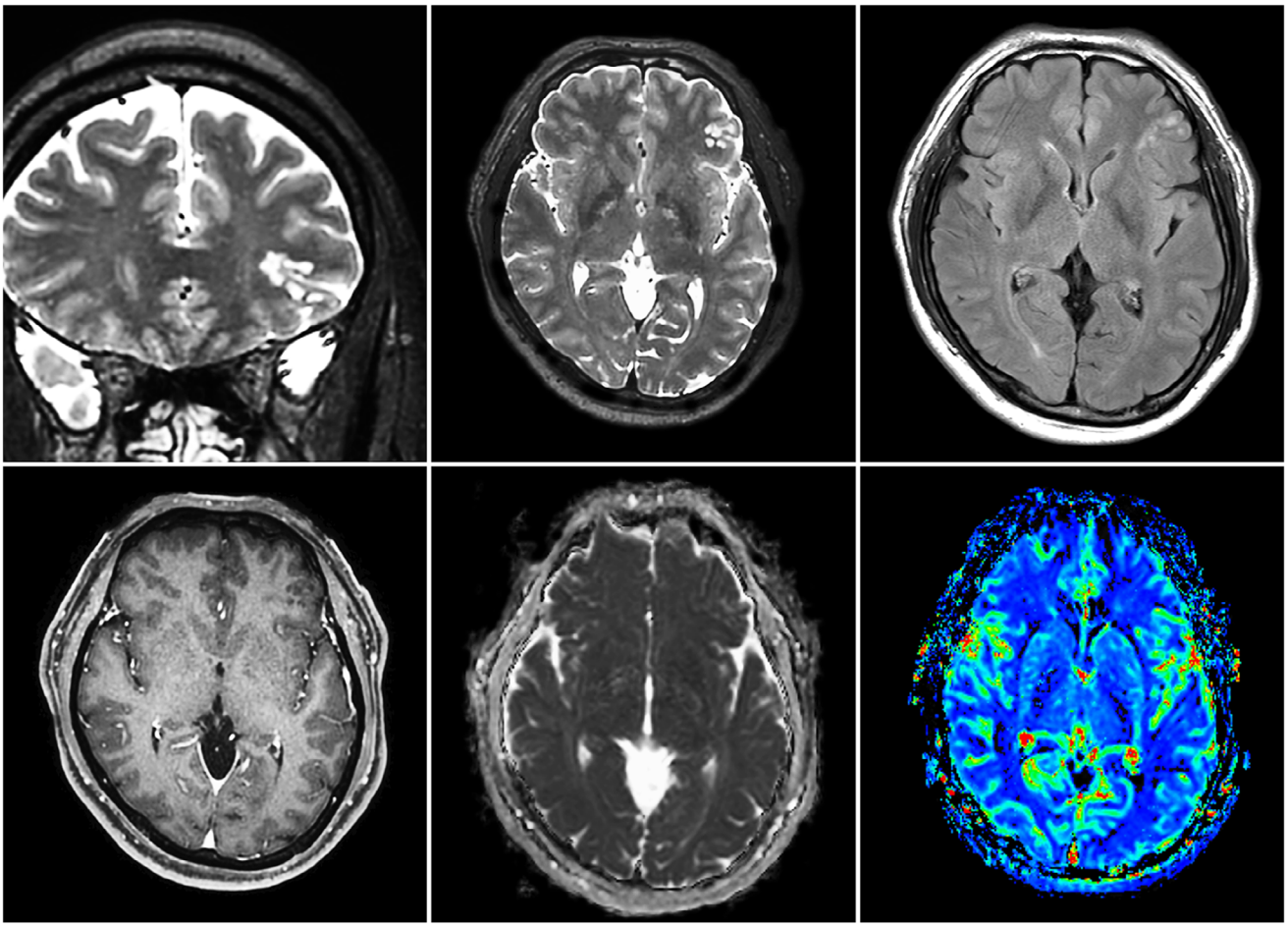

FIGURE 14: Images in a 53-year-old male with multinodular vacuolating neuronal tumor. Imaging shows well-defined nonenhancing T2 hyperintense nodular lesions at the left frontal lobe subcortex and deep cortex, without involvement of the superficial cortex. There is no diffusion restriction on ADC map and no increase of rCBV.

by thin or no enhancement, may be useful for diagnosis.[66] There is no generally diffusion restriction on ADC map.[64,66,67] A case report showed no rCBV increase.[68] Imaging spectrums of RGNT in two different patients and a representative pathology finding are shown in Fig. 11.

MYXOID GLIONEURONAL TUMOR. Myxoid glioneuronal tumor is a rare tumor characterized by a proliferation of oligodendrocyte-like tumor cells embedded in a prominent myxoid stroma, often including admixed floating neurons, neurocytic rosettes, and/or perivascular neuropil. Due to the similar histologic morphology with DNT, before the cIMPACT-NOW and subsequent 2021 WHO classification this tumor was initially considered as DNT in the septum pellucidum. However, myxoid glioneuronal tumors do not contain multiple mucin-containing nodules or *FRFR1* mutation that are typical of DNT.[8] Myxoid glioneuronal tumor is molecularly characterized by *PDGFRA* gene mutation.[69,70] It occurs in children and young adults and shows a favorable prognosis. A subset of tumors may show local recurrence or dissemination, but continues to show indolent behavior.[69,71]

Myxoid glioneuronal tumor arises in the septal nuclei, septum pellucidum, corpus callosum, or periventricular white matter. They are well-defined cystic lesions without edema showing low T1 signal and high T2/FLAIR signal probably due to the mucinous contents, and demonstrate no contrast enhancement. T2-FLAIR mismatch sign, which is usually seen in astrocytoma, IDH-mutant, has been reported in myxoid glioneuronal tumors.[72] On susceptibility weighted-imaging, tumors may show "blooming" due to previous hemorrhage. Calcification is absent. Reported cases show no diffusion restriction on ADC map[69,72] and no rCBV increase.[72] A representative case is shown in Fig. 12.

DIFFUSE LEPTOMENINGEAL GLIONEURONAL TUMOR. Diffuse leptomeningeal glioneuronal tumor (DLGNT) is a rare neoplasm that commonly shows diffuse leptomeningeal dissemination, composed of oligodendrocyte-like cells. This tumor was first recognized in the 2016 WHO classification.

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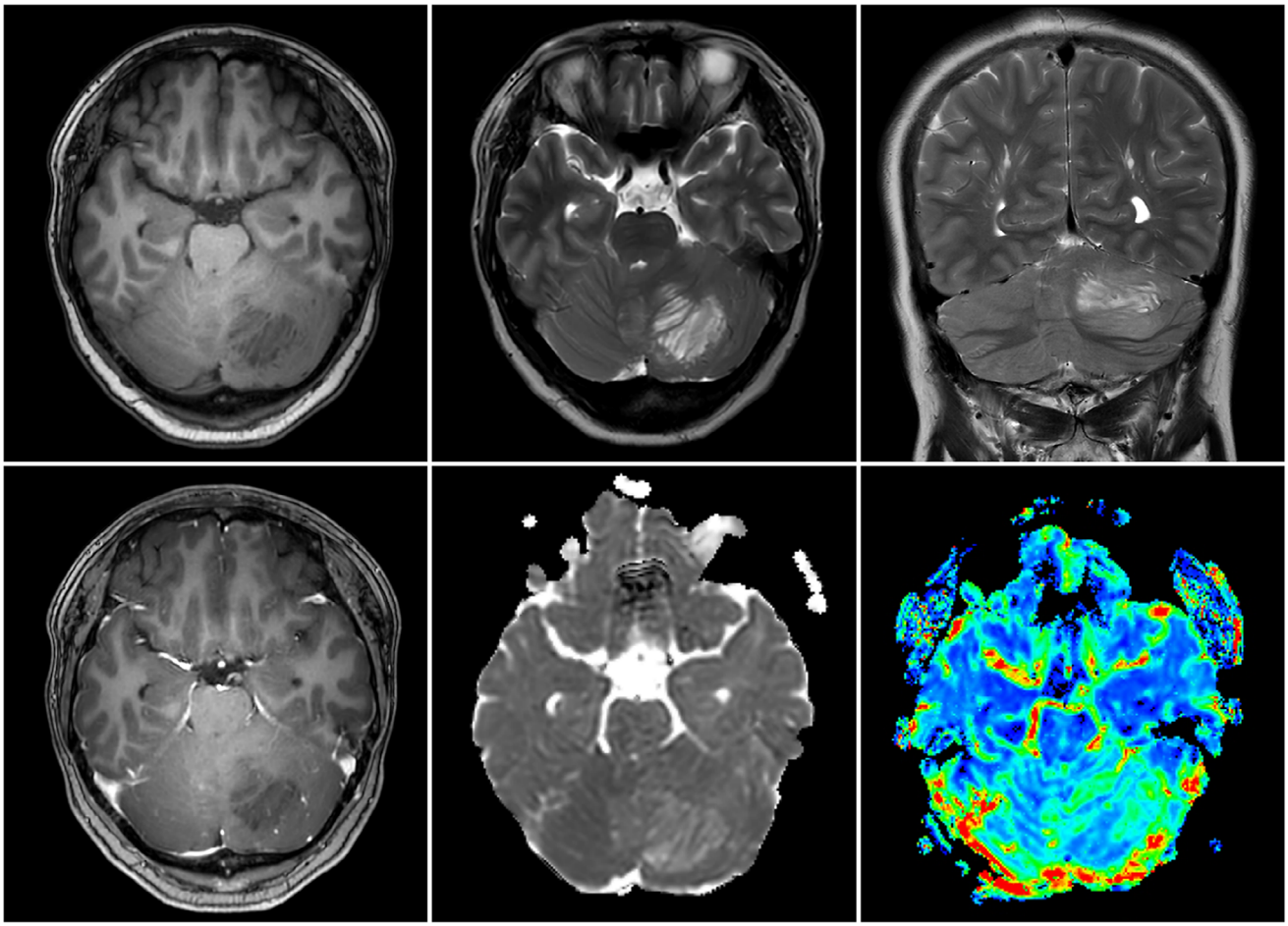

FIGURE 15: Images in a 32-year-old female with dysplastic cerebellar gangliocytoma (Lhermitte–Duclos disease). On imaging a left cerebellar mass is noted. This mass shows widened cerebellar folia with T2 hyperintense and T1 hypointense "tiger-stripe" appearance. Minimal superficial enhancement is seen due to vascular proliferation. There is no increased cellularity on ADC map. CBV map shows mild increase of rCBV, which may reflect the enlarged interfolial veins.

Due to its consistent immuoreactivity for synaptophysin in oligodendrocyte-like cells and occasional occurrence of neuronal cells, DLGNT is placed among glioneuronal and neuronal tumors. Because the pathological features of DLGNT are not specific, differential diagnoses include pilocytic astrocytoma or oligodendroglioma as well as ganglioglioma. A small subset of tumors contains overt neuronal differentiation, in the form of neurocytic rosettes, delicate perivascular pseudorosettes, neuropil-like islands, and/or ganglion cells. Molecular characteristics of chromosome arm 1p deletion or 1p/19q codeletion and a MAPK pathway gene alteration, most commonly *KIAA1549::BRAF* fusion, aids in diagnosis. The partial overlap in genetic features with oligodendroglioma (1p/19q codeletion) and pilocytic astrocytoma (*KIAA1549::BRAF* fusion) could suggest a precursor origin just upstream of this lineage segregation.[73] DNA methylation profiling may also be useful. DLGNT is most commonly found in children and adolescents. Due to its low incidence and variability of clinical outcome, DLGNT has not yet been assigned a WHO grade.

These tumors predominantly involve the spinal and intracranial leptomeninges. There are rare cases that show parenchymal involvement without leptomeningeal involvement,[74,75] most often located in the spinal cord but occasionally also in the cerebral hemispheres. Diffuse leptomeningeal enhancement and thickening along the spinal cord is most common, often extending intracranially to the posterior fossa. Small cystic or nodular T2-hyperintense lesions along the subpial surface of the spinal cord or brain are frequent. A representative case is shown in Fig. 13.

MULTINODULAR AND VACUOLATING NEURONAL TUMOR. Multinodular and vacuolating neuronal tumor (MVNT) was first recognized as a "multinodular and vacuolating pattern" in the 2016 WHO classification and incorporated as a tumor type in the 2021 WHO classification. This is a monomorphic tumor composed of neuronal elements distributed in discrete and coalescent nodules, with vacuolar changes in tumor cells and their matrix. MVNTs commonly show MAPK pathway-activating abnormalities

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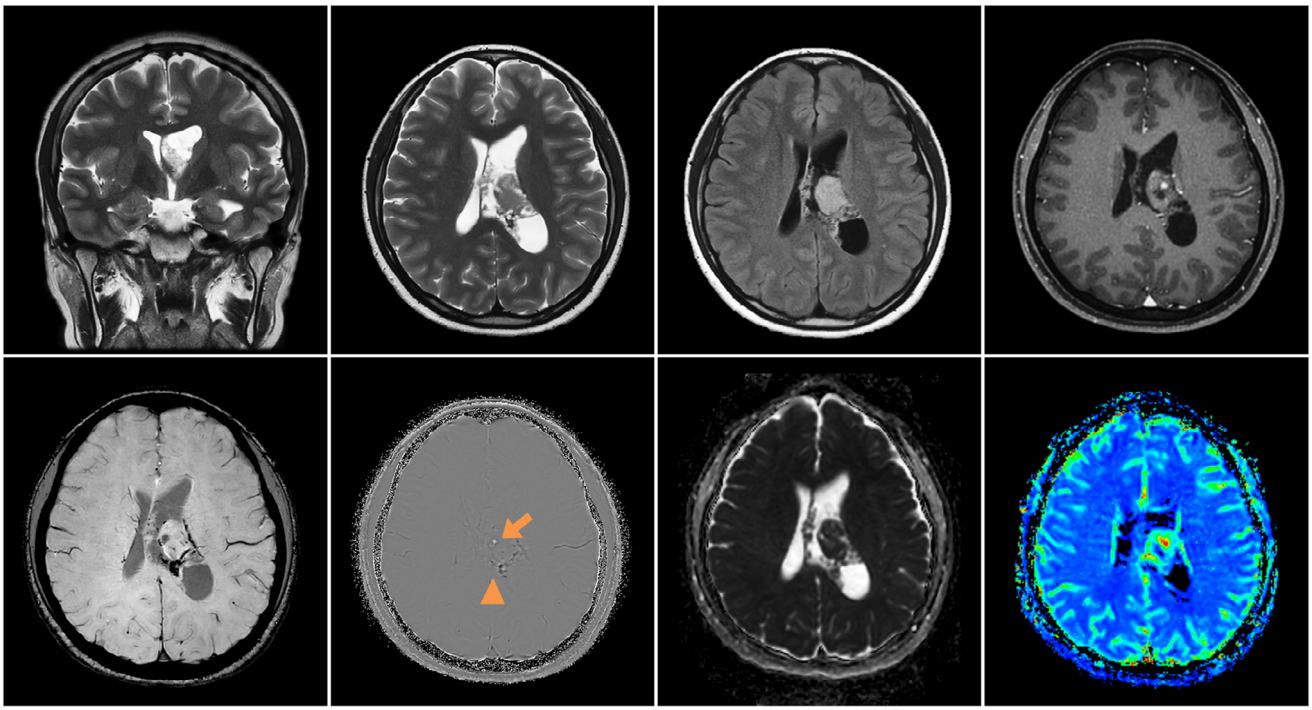

FIGURE 16: Images in a 29-year-old female with central neurocytoma. Imaging shows a well-defined multicystic tumor ("soap-bubble" appearance) tumor at the left lateral ventricle attached to the septum pellucidum near the foramen of Monro causing obstructive hydrocephalus. Heterogeneous enhancement is seen. On the post-processed susceptibility-weighted imaging there are multiple blooming areas, and the filtered phase images differentiate areas of calcification (arrow) and hemorrhage (arrowhead). There is increased cellularity on ADC map and CBV map shows increase of rCBV, which may resemble high-grade gliomas.

such as *MAP2K1* mutations, *BRAF* mutations (excluding the common *BRAF p.V600E* mutation), and *FGFR2* fusions.[76,77] The median age for MVNT is 41 years (range 8–63 years), with slight female predominance. MVNTs are benign, without progression on surgery, and some even question the necessity of surgery itself.[34,78]

In the past, MVNTs were radiologically diagnosed as enlarged perivascular spaces, focal cortical dysplasia, or DNT.[34] In highly characteristic imaging cases imaging alone may be sufficient for diagnosis, thus it is crucial for radiologists to acknowledge the hallmark imaging findings. Located in the supratentorium and predominantly the temporal lobe, MVNT involves the deep cortex and superficial white matter, without involvement of the superficial cortex. Subcortical clustering of T2 hyperintense nodular lesions without edema or contrast enhancement in the inner surface of an otherwise normal-appearing cortex is the imaging hallmark.[34] There is no diffusion restriction on ADC map and no rCBV increase.[79] Recently, remarkably similar imaging findings have been reported in the posterior fossa, but as tissue confirmation was not performed in these patients, caution should be taken in diagnosing patients as MVNT in the posterior fossa.[80] A representative case is shown in Fig. 14.

DYSPLASTIC CEREBELLAR GANGLIOCYTOMA (Lhermitte–Duclos DISEASE). Dysplastic cerebellar gangliocytoma (Lhermitte–Duclos disease) is a rare cerebellar tumor composed of dysplastic ganglion cells that conform to the existing cortical architecture and thicken the cerebellar folia. Although the molecular and internal granular layers of the cerebellum are enlarged, the cerebellar architecture is relatively preserved. Due to its discovery in 1920 by Lhermitte and Duclos, it is also called Lhermitte–Duclos disease. It may be sporadic (60% of cases) or related to Cowden syndrome (an autosomal-dominant disorders characterized by multiple hamartomas and *PTEN* mutations). Currently it remains unclear whether dysplastic cerebellar gangliocytoma is hamartomatous or neoplastic in nature. Most patients are cured by surgery, and in asymptomatic cases follow-up without surgery may be performed.

Dysplastic cerebellar gangliocytoma is usually located in the unilateral cerebellum. The highly characteristic imaging finding of "tiger-stripe" appearance, which is composed of alternating T1 hypointense and T2 hyperintense stripes in the enlarged folia, is pathognomonic for diagnosis. Enhancement is rare, and in cases of enhancement, enhancement is superficial possibly due to vascular proliferation.[81] Calcifications may be sometimes seen. There is T2 shine-through effect either with or without true diffusion restriction on ADC map.[81] Increased rCBV is noted, reflecting the prominent enlarged interfolial veins.[82] A representative case is shown in Fig. 15.

CENTRAL NEUROCYTOMA. Central neurocytoma is a WHO grade 2 intraventricular tumor composed of uniform round cells with a rounded nucleus and an expanded lateral

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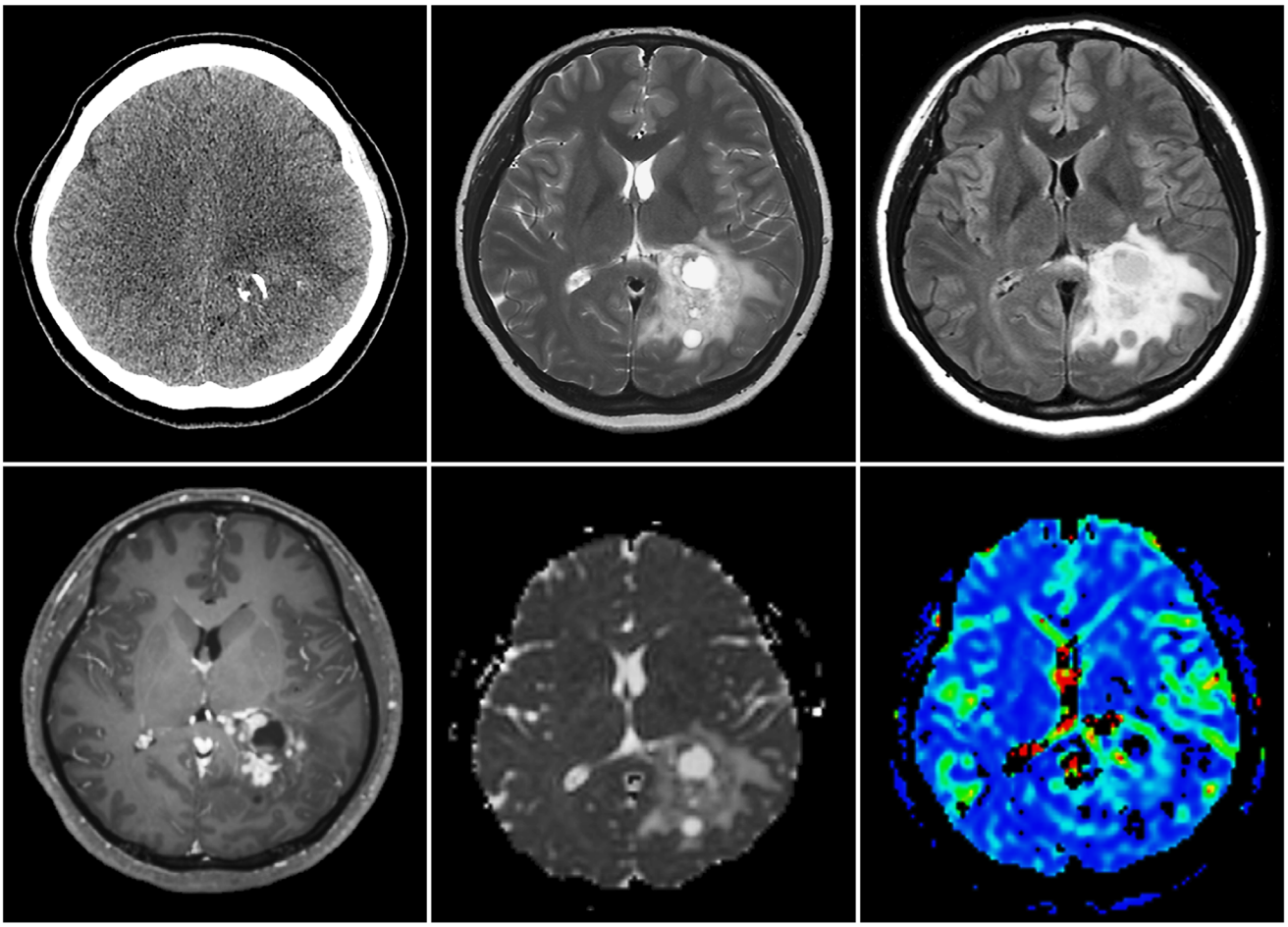

FIGURE 17: Images in a 29-year-old female with extraventricular neurocytoma. On CT, there is a low-attenuating mass with areas of calcification at the left parietal lobe. On MRI, the mass also involves the left temporooccipital lobe with moderate edema. The mass is well-defined, with multiloculated cystic and solid appearance and enhancement at the solid portion. There are foci of slight cellularity increase on ADC map and mild rCBV increase.

ventricle. Calcification and oligodendroglioma-like honeycomb architecture is noted,[83,84] thus before advances in neuronal immunohistochemical characteristics it was historically termed as intraventricular oligodendroglioma before the 1980s. However, the 1p/19q codeletion that is characteristic of oligodendroglioma is absent. Central neurocytomas usually show strong staining for synaptophysin. The exact molecular feature of this tumor is unknown. Most patients are diagnosed between the ages of 20 and 40 years.[85] Prognosis is usually favorable, especially with gross total resection. Adjuvant therapy should be considered for tumors with higher Ki-67 index values, although the exact cutoff value is debatable.[85,86]

Central neurocytomas are most commonly located in the anterior portion of the lateral ventricles, usually attached to the septum pellucidum near the foramen of Monro causing obstructive hydrocephalus.[87] It has a characteristic "soap-bubble" (multicystic) appearance on T2 images with heterogeneous enhancement. "Scalloping sign," which refers to an appearance resembling a scallop and consisting of cysts on the periphery of the tumor and the wavy walls of the hemorrhage may be seen.[84] Calcification is common. On ADC map, the ADC values are low, which may resemble high-grade gliomas,[88] and rCBV is reported be moderately high among intraventricular tumors.[89] Figure 16 shows a representative case in a patient with central neurocytoma.

EXTRAVENTRICULAR NEUROCYTOMA. Extraventricular neurocytoma is a rare well-circumscribed neuronal neoplasm that arises throughout the CNS outside the ventricular system (hence named as "extraventricular"). Histopathological characteristics resemble those of central neurocytoma but demonstrate a much wider morphological spectrum. *FGFR1::TACC1* fusions are frequent. It commonly occurs in adults in the third to fourth decades. Prognosis is usually favorable, especially with gross total resection.

Majority of extraventricular neurocytomas locate in the cerebral hemispheres. The best diagnostic clue is a well-circumscribed, heterogeneously enhancing, cystic and solid mass

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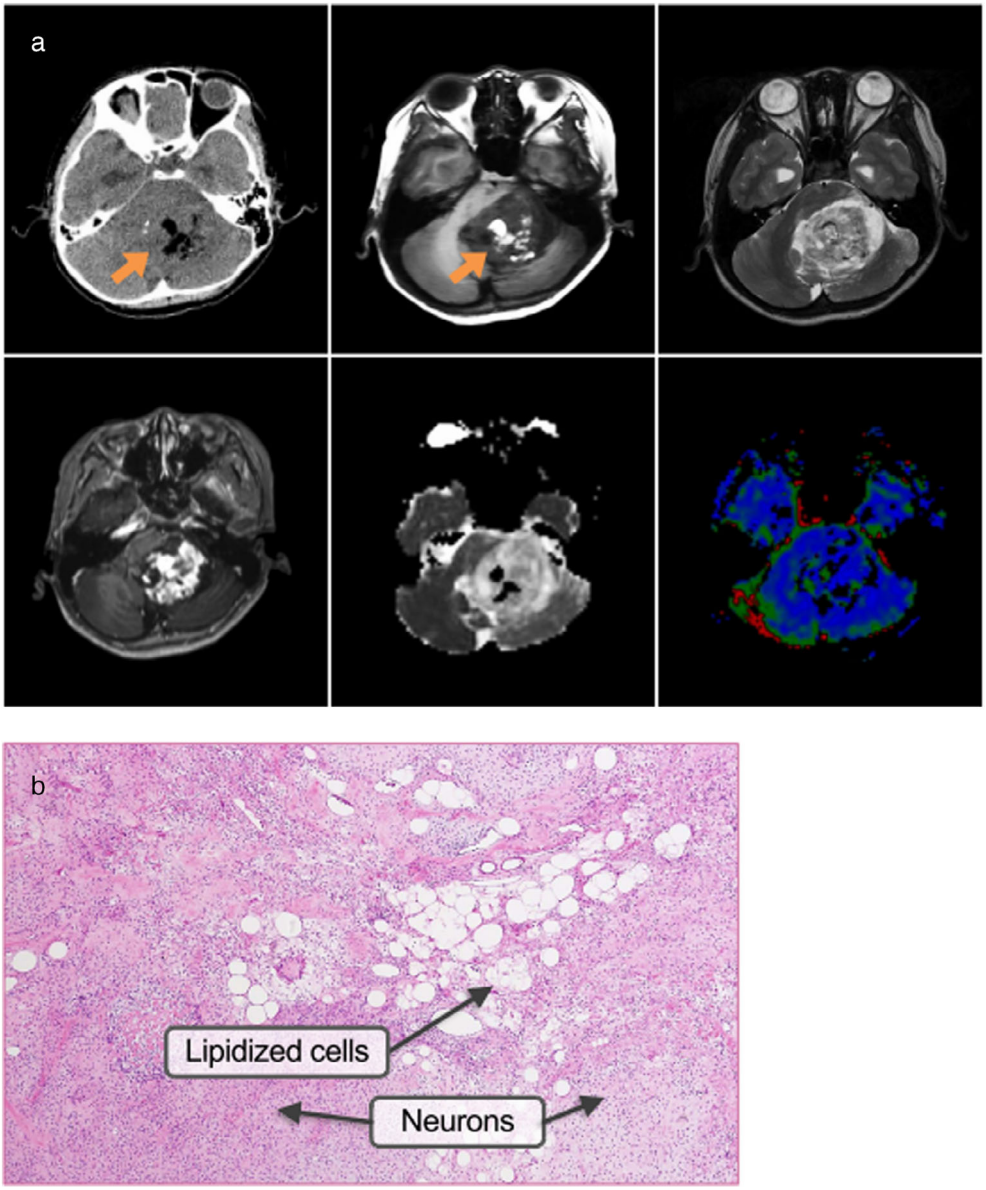

FIGURE 18: (a) Images in a 9-year-old boy with cerebellar liponeurocytoma. On CT, there is a lobulated mass involving bilateral cerebellar hemispheres with an area of marked hypoattenuation corresponding to fat density. On MRI, the fat component show T1 hyperintensity while the remaining mass shows T1 hypointensity. The mass shows heterogeneous T2 hyperintensity with heterogeneous enhancement, with a focal low ADC value which may be due to fat producing a restricted diffusion on ADC map. Mild rCBV increase is seen. (b) On histopathology, neurocytes with lipidized tumor cell are noted (H&E; ×40).

with moderate edema.[90] Calcification and hemorrhage are common.[91] A representative case is shown in Fig. 17.

CEREBELLAR LIPONEUROCYTOMA. Cerebellar liponeurocytoma is a rare cerebellar tumor with advanced neuronal or neurocytic differentiation, variable glial differentiation, and focal lipoma-like changes. *TP53* missense mutations are relatively frequent (4 in 20 cases).[92] Most patients are diagnosed in adults. Prognosis is usually favorable, especially with gross total resection and adjuvant radiotherapy.

Cerebellar liponeurocytoma most commonly involves the cerebellar hemispheres, but it can also be located in the paramedian region or vermis and extend to the cerebellopontine angle or fourth ventricle. A fat-containing cerebellar mass raises possibility of the diagnosis. On CT, a cerebellar tumor with focal areas of marked hypoattenuation corresponding to fat attenuation is seen. Focal areas of T1 hyperintensity are seen within T1 hypointense lesions, corresponding to high lipid content.[93] Heterogeneous enhancement is seen and edema is rare.[94] Calcification may be seen. Reported cases show diffusion restriction due to high cellularity on ADC map and increased rCBV in the solid portion.[91] A representative case with imaging and pathological findings is shown in Fig. 18.

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Conclusion

The key points in 2021 WHO classification and imaging features of glioneuronal and neuronal tumors were reviewed and summarized in a radiologist's viewpoint. We hope this article serves as an opportunity for radiologists to understand the histopathologic and molecular approach to this frequently neglected tumor category, and bear in mind how we could assist clinicians in the diagnostic process. The current state of knowledge reflected in this review is incomplete and the integrative diagnosis based on molecular features will continue to evolve. Nonetheless, full acknowledgement of the current context of classification will improve the quality of radiologists for daily interpretation and communication with clinicians. We hope this review series serves as a motivation for our fellow radiologists to fully elucidate the classification system and imaging of glioneuronal and neuronal tumors.

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