Polymorphous low-grade neuroepithelial tumor of the young

J.Sales-Llopis

Neurosurgery Department, Alicante University General Hospital, Spain.

Latest PubMed Articles

- Glioneuronal tumors PATZ1-fused: clinico-molecular and DNA methylation signatures for a variety of morphological and radiological profiles
- Case report: Polymorphous low-grade neuroepithelial tumor of the young and supratentorial ependymoma diagnosed in an adult male
- Phenotypic and epigenetic heterogeneity in FGFR2-fused glial and glioneuronal tumours
- MAPK pathway alterations in polymorphous low-grade neuroepithelial tumor of the young: diagnostic considerations
- Unraveling morphology, methylation profiling, and diagnostic challenges in BRAF-Mutant pediatric glial and glioneuronal tumors
- Polymorphous Low-Grade Neuroepithelial Tumor of the Young (PLNTY): Scoping Review of Case Reports and Case Series
- Low-grade glioma of the temporal lobe and tumor-related epilepsy in children
- Polymorphous low-grade neuroepithelial tumor of the young (PLNTY): A case report with surgical and neuropathological differential diagnosis

Abstract

Background: Polymorphous low-grade neuroepithelial tumor of the young (PLNTY) is a recently classified CNS WHO grade I neoplasm that predominantly affects children and young adults. Its recognition has expanded our understanding of low-grade gliomas and their molecular drivers. This systematic review provides a comprehensive overview of PLNTY, including its epidemiology, diagnostic criteria, radiological features, genetic and molecular characteristics, and clinical outcomes.

Methods: A systematic review of the literature was conducted, encompassing studies, case reports, and case series published between 2017 and 2023. Data related to PLNTY's clinical presentation, radiological findings, histopathological features, genetic alterations, and treatment outcomes were synthesized.

Results: PLNTY primarily afflicts individuals within a broad age range, typically presenting with seizures. Radiologically, it is characterized by cortical or subcortical masses, often in the temporal lobe, and distinctive calcifications known as the “salt and pepper sign.” Genetic profiling reveals alterations in the MAP kinase pathway, including the BRAF V600E mutation. Surgical resection is often effective in achieving seizure control and favorable clinical outcomes. Although the extent of resection and specific genetic profiles do not significantly correlate with prognosis, contrast enhancement on imaging may impact recurrence and seizure control.

Conclusion: PLNTY is an emerging entity in the realm of CNS tumors, distinguished by its unique molecular and histopathological features. While challenges exist in its diagnosis and classification, advancements in molecular profiling have improved accuracy. Recognizing the radiological hallmarks and genetic alterations of PLNTY is crucial for appropriate management. Further research is needed to comprehensively understand this intriguing tumor and its clinical implications.

Introduction

Polymorphous low-grade neuroepithelial tumors of the young are diffuse low-grade gliomas, classified as CNS WHO grade I neoplasms.

In 2021, the World Health Organization (WHO) Classification of Tumors of the Central Nervous System (CNS) underwent significant restructuring to incorporate additional molecular diagnostics, several newly recognized tumor types, and new grading schemes for existing tumor types. The 2021 CNS WHO classification further elaborates and integrates histopathologic and molecular diagnostic criteria to improve diagnostic classification. Furthermore, it is the hoped that identification of molecular alterations in pediatric and adult tumors facilitates improved prognostic information and the development of novel targeted therapies for adults and children with CNS tumors. In one of the largest changes in the new WHO classification, diffuse gliomas are divided into pediatric-type and adult-type gliomas to highlight our expanding knowledge of their different molecular drivers and prognostic associations. Several new pediatric-type diffuse low-grade gliomas are defined including (I) diffuse astrocytoma, MYB- or MYBL1-altered, (II) polymorphous low-grade neuroepithelial tumor of the young (PLNTY), and (III) diffuse low-grade glioma, MAPK-pathway altered [1)]

Polymorphous low-grade neuroepithelial tumors of the young (PLNTY) were first described in 2017 by Huse et al. [2)] a variant of low-grade neuroepithelial tumors that exhibit infiltrative growth, histopathological variability with frequently prominent oligodendroglioma-like components, intense labeling for CD34, absence of 1p/19q co-deletion, a distinct DNA methylation signature and genetic alterations involving MAP kinase pathway constituents of either the B-Raf proto-oncogene BRAF or fibroblast growth factor receptors 2 or 3 (FGFR2 and FGFR3). [3)].

Epidemiology

Mostly arising in children and young adults, with an age range of 5–32 years (median 16 years) [4) 5)].

Diagnosis

Low-grade neuroepithelial tumors (LGNET) are a diverse group of neoplasms occurring most commonly in children and young adults, often associated with epilepsy and favorable clinical outcomes. They are composed of a spectrum of tumor entities with divergent clinicopathologic

features including ganglioglioma, pilocytic astrocytoma, dysembryoplastic neuroepithelial tumor (DNT), rosette-forming glioneuronal tumor (RGNT), extraventricular neurocytoma (EVN), multinodular and vacuolating neuronal tumor (MVNT), polymorphous low-grade neuroepithelial tumor of the young (PLTNY), myxoid glioneuronal tumor (MGNT), diffuse leptomeningeal glioneuronal tumor (DLGNT), and papillary glioneuronal tumor (PGNT). However, histologically distinguishing between these different LGNET subtypes can be challenging, and molecular profiling is now recognized as critical for accurate classification [6].

PLNTYs demonstrate characteristic calcification, subcortical location, and frequent temporal lobe localization, features that may allow radiologists to prospectively suggest the diagnosis in the proper clinical setting [7]

The main radiological features included cortical or subcortical masses (95.8%) in the temporal lobe (66.7%), calcification (83.3%), well-defined margins (72.7%), solid and cystic components (66.6%), and T2-weighted imaging (T2WI) hyperintensity (50.0%). The duration of seizure was significantly longer (positive vs. negative (median [range]), 24 months [6 - 96 months] vs. 5 months [1 - 12 months], p = 0.042), and the presence of cortical dysplasia was significantly more frequent (3/8 vs 0/16, p = 0.042) in the patients with transmantle-like sign.

PLNTY typically represents a calcified, well-defined mass in the supratentorial cortical or subcortical regions. The radiological findings defined here could facilitate the diagnosis of PLNTY [8].

The imaging hallmark of PLNTYs is centrally located dense calcifications, often described as a salt and pepper sign. Most PLNTYs show no enhancement in contrast to enhanced T1-weighted sequences, although a patchy mild enhancement is found in a minority of the cases [9].

Systematic reviews

2023

A total of 16 studies were included in the systematic review. The final cohort was composed of 51 patients. The extent of resection (EOR) and outcome is not significantly associated with the different genetic profiling (p = 1), the presence of cystic intralesional component, calcification (p = 0.85), contrast-enhancing and lesion boundaries (p = 0.82). No significant correlation there is between EOR and remission or better control of epilepsy-related symptoms (p = 0.38). The contrast enhancement in the tumor is significantly associated with recurrence or poor control of epileptic symptoms (p = 0.07).

In PLNTYs, contrast enhancement seems to impact prognosis, recurrence, and seizure control much more than radiological features, genetic features, and type of resection of the tumor [10]

2022

Eight patients underwent surgical treatment in our center between December 2017 and December 2020, and the postoperative pathology was diagnosed as PLNTY. Their clinical data, imaging, pathological, molecular characteristics, and seizure outcome were retrospectively analyzed. Follow-up evaluations and a literature review were performed.

The 8 patients included 1 woman and 7 men, aged between 5 and 51 years old (mean = 31.6, median = 29). The preoperative symptoms of all 8 cases were seizures. Four tumors were situated in the temporal lobes, and one of the four extratemporal tumors was in the occipital lobe and three were in the frontal lobe. Enlarged and gross total resections were performed in 2 cases and the other 6 cases, respectively. All cases exhibited intense labeling of CD34, and absence of 1p/19q codeletion and IDH1 or IDH2 mutation. B-Raf proto-oncogene (BRAF) V600E mutation was presented in 4 (66.7%) of 6 detected cases. The postoperative seizure outcome of Engel class I was achieved in 6 cases (75%).

PLNTY represents distinctive histologic, immunophenotypic, and biomolecular features, and has high epileptogenicity. Early surgical intervention and enlarged resection of PLNTY associated with epilepsy will help to improve the postoperative seizure-free rate [11)].

Kurokawa et al. assessed the demographic, clinical, and neuroradiological features of PLNTY.

Literature data were extracted from database searches in MEDLINE and SCOPUS databases up to June 10, 2021. Studies reporting on pathologically proven PLNTY with neuroradiological findings were included. After reviewing 103 abstracts, 9 articles encompassing 19 cases met the inclusion criteria. We also added five patients from our hospital. The correlations between the presence of a “transmantle-like sign” and the following three factors: duration of seizures; tumor size; and pathologically proven cortical dysplasia, were examined.

The median patient age was 15.5 years (range, 5-57 years), and 15/24 (62.5%) were female. All tumors were localized supratentorial. The main radiological features included cortical or subcortical masses (95.8%) in the temporal lobe (66.7%), calcification (83.3%), well-defined margins (72.7%), solid and cystic components (66.6%), and T2-weighted imaging (T2WI) hyperintensity (50.0%). The duration of seizure was significantly longer (positive vs. negative (median [range]), 24 months [6 - 96 months] vs. 5 months [1 - 12 months], $p = 0.042$), and the presence of cortical dysplasia was significantly more frequent (3/8 vs 0/16, $p = 0.042$) in the patients with transmantle-like sign.

PLNTY typically represents a calcified, well-defined mass in the supratentorial cortical or subcortical regions. The radiological findings defined here could facilitate the diagnosis of PLNTY [12)]

A review of the literature revealed that there are 31 cases of PLNTY reported in the literature, most of which are children or young adults. The present case represents the second PLNTY diagnosed in a middle-aged adult to the best of our knowledge, suggesting that PLNTY should always be included in the differential diagnosis of low-grade brain tumors, as well as in adult patients [13)]

Case series

2022

Five cases of PLNTY diagnosed at the First Affiliated Hospital and Affiliated Brain Hospital of Nanjing Medical University, Nanjing, China from 2019 to 2021 were collected. All cases were evaluated using clinical and imaging data, histology, immunohistochemical staining and molecular genetics. The relevant literature was reviewed. Results: There were two male and three female patients, aged 10 to 39 years, with an average age of 25 years. Clinically, the tumors were in the temporal lobe (3 cases), the lateral ventricle (1 case) and the left head of caudate nucleus (1 case). The clinical manifestations included epilepsy in 3 cases, right visual disturbance in 1 case, and post-trauma incidental finding in 1 case. Microscopically, the lesions were characterized with infiltrative growth, cellular pleomorphism (oligodendroglioma-like cells were always present, with low-grade, pleomorphic nuclei) and variable calcifications. Immunohistochemically, the tumor cells were positive for GFAP and Olig2. They also showed intense and diffuse expression of CD34 while CD34 expressing ramified neural elements were present in regional cortex. Ki-67 proliferation index was less than 3%. Molecular genetics showed the BRAF V600E mutation in 2 cases, the PAK5-Q337R missense mutation in 1 case, the FGFR2-CTNNA3 fusion in 1 case, and the FGFR2-INA and FGFR2-PPRC1 concomitant fusion in 1 case. No postoperative chemoradiotherapy was given. Follow-up intervals ranged from 3 to 29 months while no recurrence or metastasis was identified. Conclusions: PLNTY is uncommon. A definite diagnosis of PLNTY relies on histopathological examination and molecular genetics. It is important to distinguish PLNTY from high grade gliomas and avoid overtreatment. The recently reported the PAK5-Q337R missense mutation and the FGFR2-PPRC1 gene fusion in PLNTY may help diagnose and understand the pathogenesis of PLNTY [14)].

2021

Ida et al. molecularly profiled 13 cases with diagnostic histopathological features of PLNTY (10 female; median age, 16 years; range, 5-52). Patients frequently presented with seizures (9 of 12 with available history) and temporal lobe tumors (9 of 13). MAPK pathway-activating alterations were identified in all 13 cases. Fusions were present in the 7 youngest patients: FGFR2-CTNNA3 (n = 2), FGFR2-KIAA1598 (FGFR2-SHTN1) (n = 1), FGFR2-INA (n = 1), FGFR2-MPRIP (n = 1), QKI-NTRK2 (n = 1), and KIAA1549-BRAF (n = 1). BRAF V600E mutation was present in 6 patients (17 years or older). Two fusion-positive cases additionally harbored TP53/RB1 abnormalities suggesting biallelic inactivation. Copy number changes predominantly involving whole chromosomes were observed in all 10 evaluated cases, with losses of chromosome 10q occurring with FGFR2-KIAA1598 (SHTN1)/CTNNA3 fusions. The KIAA1549-BRAF and QKI-NTRK2 fusions were associated respectively with a 7q34 deletion and 9q21 duplication. This study shows that despite its name, PLNTY also occurs in older adults, who frequently show BRAF V600E mutation. It also expands the spectrum of the MAPK pathway activating alterations associated with PLNTY and demonstrates recurrent chromosomal copy number changes consistent with chromosomal instability [15)].

A 50-year-old woman suffering from epilepsy since the 1st year of her life. A computed tomography scan and magnetic resonance imaging of the brain documented the presence of a calcified mass involving the left temporal lobe. The tumor was surgically excised and the histological examination showed a hypocellular and massively calcified neoplasm with morphological and immunohistochemical features consistent with the diagnosis of “PLNTY.” [16)]

2020

3 cases diagnosed as PLNTY by pathology in the hospital during the last 10 years, with an average age of 15. They were all suffered from different degrees of epilepsy. All of them underwent magnetic resonance (MR) imaging and 2 of them underwent computer tomography (CT) imaging. The PLNTYs all appear as a solid or solid-cystic cortical mass with little mass effect and unclear boundary with normal brain tissue. They are all shown as hyperintensity in T2WI and iso-/hypointensity in T1WI with slight or no enhancement after contrast enhancement in MR imaging. The “salt and pepper sign” in T2WI and grit calcification in CT images might be specific characteristics of PLNTY. All of them recovered after the excision of the tumors. The gene tests revealed fibroblast growth factor receptors 3 (FGFR3)-TACC3 fusion and FGFR3 amplification in one case, and the B-Raf proto-oncogene (BRAF) V600E mutation in another case.

In the image, the partial ill-marginated cortical mass with a “salt and pepper sign” in T2WI or grit calcification in CT imaging might be the typical imaging characteristics of PLNTY. They also prove that the BRAF V600E mutation as well as the FGFR2 and FGFR3 have a close relationship with PLNTY [17)]

Dysembryoplastic neuroepithelial tumors (DNT) lacking key diagnostic criteria are challenging to diagnose and sometimes fall into the broader category of mixed neuronal-glial tumors (MNGT) or the recently described polymorphous low-grade neuroepithelial tumor of the young (PLNTY). We examined 41 patients with DNT, MNGT, or PLNTY for histologic features, genomic findings, and progression-free survival (PFS). Genomic analysis included sequence and copy number variants and RNA-sequencing. Classic DNT (n = 26) was compared with those with diffuse growth without cortical nodules (n = 15), 6 of which exhibited impressive CD34 staining classifying them as PLNTY. Genomic analysis was complete in 33, with sequence alterations recurrently identified in BRAF, FGFR1, NF1, and PDGFRA, as well as 7 fusion genes involving FGFR2, FGFR1, NTRK2, and BRAF. Genetic alterations did not distinguish between MNGTs, DNTs, or PLNTYs; however, FGFR1 alterations were confined to DNT, and PLNTYs contained BRAF V600E or FGFR2 fusion genes. Analysis of PFS showed no significant difference by histology or genetic alteration; however, numbers were small and follow-up time short. Further molecular characterization of a PLNTY-related gene fusion, FGFR2-CTNNA3, demonstrated oncogenic potential via MAPK/PI3K/mTOR pathway activation. Overall, DNT-MNGT spectrum tumors exhibit diverse genomic alterations, with more than half (19/33) leading to MAPK/PI3K pathway alterations [18)].

Case reports

Only a very few cases have been reported so far and have been incorporated in the World Health Organization (WHO) Central Nervous System Classification of Tumors

2023

Nair et al. report a rare case of PLNTY which closely resembles DNET (Dysembryoplastic neuroepithelial tumor) with plenty of interesting findings which would otherwise go unnoticed resulting in a nonspecific or misclassified diagnosis.

Case report: A 12-year-old boy presented to the Neurosurgery OPD with seizures for the past five years and was given multiple antiepileptics for the same. Magnetic resonance imaging (MRI) showed a well-defined lobulated cortical mass with T1 hypo intensity and T2 hyperintensity in the left temporal lobe measuring 2.1 × 2 × 1.3 cm suggesting a DNET. Left temporal craniotomy and excision of the lesion were done. The frozen section showed features of a low-grade glial neoplasm. Routine sections demonstrated polymorphous findings including oligodendroglia-like features, neuronal nuclear pleomorphism, spindled astroglial elements, perivascular rosettes, calcification, and vascular mineralization. By immunohistochemistry (IHC), the tumor cells were diffusely positive for GFAP and CD34.Ki67 labeling index was low. A final diagnosis of PLNTY was made based on the above findings. The child has been epilepsy free since the past one-month post-surgery and is on follow-up

PLNTY is a newly discovered distinct pediatric low-grade glial neoplasm that was earlier grouped into nonspecific forms of DNET. It is characterized morphologically and molecularly by the presence of oligodendroglial component, CD34 expression, BRAFV600E mutation, and alterations in the MAP kinase pathway. They are known to behave in a low-grade fashion amenable to control by excision with occasional cases of recurrence reported. It is important to recognize and report similar tumors to determine the long-term risk of recurrence and create a more complete understanding of their radiology and molecular genetics [19].

A 45-year-old man was treated with awake surgery with a confirmed diagnosis of PLNTY, reporting the radiological and surgical characteristics through imaging and intra-operative video [20]

Two cases of PLNTY, one in a 14-year-old female and the other in a 66-year-old female. The pediatric tumor showed typical clinical course and histopathology with BRAF p.V600E mutation, whereas the elderly tumor was unusual because of non-epileptic onset clinically and ependymal differentiation histopathologically harboring KIAA1549-BRAF fusion. There might be unusual but possible PLNTY, as in the elderly case [21].

2022

A 31-year-old female with intractable epilepsy was found to have a temporal mass and diagnosed with PLNTY after histopathologic and molecular testing. We describe the radiographic, histologic, and genetic features in relation to the epileptic and oncologic outcomes of this patient. Then, we compare these features and outcomes to other cases of PLNTY described in the literature [22].

A case report provides the first description of SEEG-recorded seizures in PLNTY to provide insight into its surgical strategy.

Spontaneous clinical seizures were recorded with SEEG in a young adult patient with drug-resistant epilepsy associated with a PLNTY in the left lateral temporal cortex. The seizure onset was characterized by low-voltage fast activity (LVFA) and showed eccentric localization with respect to the tumor: LVFA was localized in the anterior portion of the tumor and spread toward the adjacent polar cortex. The language risks associated with the resection of the posterior temporal cortex could thus be minimized.

PLNTY can show a focal and eccentric seizure-onset zone around the tumor. The present findings serve to improve the functional and seizure outcomes using the staged invasive approach in PLNTY [23].

2021

A PLNTY case in a young woman presenting with seizures due to a parietal brain tumor and to provide an analysis of the literature. Histopathologically the tumor was consistent of oligodendroglioma-like neoplastic cells showing almost diffuse CD34 and olig-2 staining, retained ATRX expression, p53-negativity, and a low Ki67 index with no necrosis or microvascular proliferation.

1p/19q status was analyzed with FISH; IDH1 and IDH2 mutations were analyzed with mini-sequence analysis. Translocations, mutations, and expression analyses were studied for 18, 19, and 21 genes via targeted new-generation deep RNA sequencing, respectively.

The tumor did not carry 1p/19q codeletion, was IDH wild-type and had radiological features compatible with the diagnosis of PLNTY. The tumor did not show BRAF or FGFR alterations but had an EGFR c.2342A>G (p.Asn781Ser) mutation which was likely a non-driver mutation due to its low allele frequency of 4%.

PLNTYs are rare brain tumors, and their accurate diagnosis is important to avoid improper management. Their prognosis shall be stratified according to their mutations [24].

One case of malignant transformation in a recurrent PLNTY has so far been reported, suggesting a broad molecular spectrum [25].

Liu S, Chen P, Yang H, Xie T, Liu T, Li C, Yang L, Li Z, Huang J, Gao Y, Xie Q, Yu Y, Hu F, Zhang X. Role of endoscopic third ventriculostomy in patients undergoing resection of pulvinar area lesions: Preliminary clinical results. J Clin Neurosci. 2023 Sep 27;117:61-67. doi: 10.1016/j.jocn.2023.09.018. Epub ahead of print. PMID: 37774635.

2020

Two cases of PLNTY diagnosed from January 2016 to December 2019 were collected from Ningbo Diagnostic Pathology Center, Zhejiang, China. The clinical features, histopathological characteristics, and immunohistochemical and molecular genetic findings were analyzed and the relevant literature was reviewed. Results: The two patients were both female, at the ages of 14 and 25 years, respectively. Both patients presented with seizure attacks. The imaging study showed a mixed signal in the cerebral cortex, located in the occipital and temporal lobes, respectively. Microscopically, the tumors were characterized by the invariable presence of oligodendroglioma-like appearance, often with calcification. Immunohistochemically, the tumors were diffusely and intensely CD34-positive with ramified, CD34-expressing neural elements in the regional cortex. The tumors were positive for GFAP, Olig2 and ATRX, and negative for IDH1, Neu N, nestin and EMA. The Ki-67 labeling index was less than 2%. Case number 2 harbored the BRAF V600E mutation, while case number 1 was negative for both the BRAF V600E mutation and 1p/19q codeletion. Both patients recovered very well and were free of

seizures after the follow-up of 2 and 24 months, respectively. Conclusions: PLNTY is an uncommon neuroepithelial tumor. Histopathologic and immunohistochemical examinations are necessary for establishing the diagnosis and for excluding oligodendroglioma. PLNTY should be considered a benign tumor corresponding to WHO Grade I. The prognosis is overall good after complete tumor resection [26].

A 14-year-old boy with tumor-associated refractory epilepsy. Positron emission tomography imaging demonstrated a region with heterogeneous high 11C-methionine uptake and a region with homogenous low 18F-fluorodeoxyglucose uptake within the tumor. Histopathological and genomic analyses confirmed the tumor as a BRAF V600E-mutated polymorphous low-grade neuroepithelial tumor of the young (PLNTY). Within the high-methionine-uptake region, we observed increased protein levels of L-type amino acid transporter 1 (LAT1), a major transporter of methionine; c-Myc; and constituents of the mitogen-activated protein kinase (MAPK) pathway. We also found that LAT1 expression was linked to the BRAF V600E mutation and subsequent activation of MAPK signaling and c-Myc. Pharmacological and genetic inhibition of the MAPK pathway suppressed c-Myc and LAT1 expression in BRAF V600E-mutated PLNTY and glioblastoma cells. The BRAF inhibitor dabrafenib moderately suppressed cell viability in PLNTY. Collectively, our results indicate that BRAF V600E mutation-activated MAPK signaling and downstream c-Myc induces specific metabolic alterations in PLNTY, and may represent an attractive target in the treatment of the disease [27].

Benson et al. present the imaging and pathologic findings of such a tumor as well as the surgical approach and clinical management [28].

Polymorphous low-grade neuroepithelial tumor of the young: a case report [29]

2019

A 30-year-old, right-handed man was diagnosed with intractable epilepsy at 22 years of age. Magnetic resonance imaging revealed T2 signal hyperintensity and corresponding T1 signal hypointensity within the subcortical white matter of the right middle temporal gyrus. The positron emission tomography scan demonstrated hypometabolism in the right anterior temporal region. Electroencephalography and stereo-electroencephalography monitor localized seizures to the right temporal lobe, allowing the patient to undergo right temporal lobectomy. Histologic sections demonstrated cortical dysplasia, white matter heterotopia, and hippocampal reactive gliosis without neuronal loss. Interestingly, an approximately 6-mm subcortical neoplasm was identified in the temporal lobectomy. It was composed of well-differentiated oligodendroglial-like cells but exhibited mild-to-moderate nuclear variability and pleomorphism, and mild infiltration into the overlying cortex without perineuronal satellitosis. No mitotic activity, microvascular proliferation, or necrosis was identified, and the Ki-67 labeling index was less than 1%. The tumor was diffusely CD34 positive with moderate glial fibrillary acidic protein retained ATRX staining, and demonstrated the presence of the BRAF V600E mutation. The tumor was negative for reticulin condensation, synaptophysin, SMI31, neuronal nuclei immunostains, and both the IDH1 mutation and 1p19q codeletion. Overall histologic findings were most consistent with PLNTY.

The correct diagnosis of PLNTY and its distinction from closely resembling low-grade neuroepithelial

tumors is important. They hoped the proposed diagnostic features would aid in its proper diagnosis and management [30].

A previously healthy, 19-year-old man presented with new onset of seizures. Imaging showed an intracranial mass, which was treated with surgical removal. Preoperative and postoperative magnetic resonance imaging, histopathologic examination, genetic testing, and immunohistochemical staining all supported a diagnosis of PLNTY.

Diagnostic investigation of PLNTY shows many similarities with oligodendroglioma, and thus these entities can be mistaken for one another. Certain studies are needed to distinguish PLNTY and other dysembryoplastic neuroepithelial tumors, such as oligodendroglioma [31].

2018

Bitar et al. report a newly diagnosed case of PLNTY involving the temporal lobe in a 31-year-old man with chronic focal epilepsy. This tumor had histologic and immunophenotypic features similar to the recently described PLNTY and proved BRAF V600E mutant. Biomolecular profiling is becoming increasingly important in characterizing neuroepithelial tumors. Furthermore, biomolecular features such as CD34 expression and BRAF mutation have been reported to be significantly associated with the clinical behavior of these tumors. Like other low-grade neuroepithelial tumors, PLNTYs appear to be generally indolent with excellent seizure relief after total surgical resection. It is important to recognize cases of PLNTY in order to guide clinical management including the indication for surgery [32].

Discussion

Polymorphous low-grade neuroepithelial tumor of the young (PLNTY) is a recently recognized entity in the classification of central nervous system (CNS) tumors, bringing about new insights into the world of low-grade gliomas. This systematic review has provided a comprehensive overview of PLNTY, encompassing various aspects of its epidemiology, clinical presentation, diagnostic criteria, radiological characteristics, genetic alterations, and clinical outcomes.

PLNTY predominantly affects children and young adults, typically presenting with seizures, and it is often characterized by radiological features such as cortical or subcortical masses, predominantly in the temporal lobe, and distinctive calcifications referred to as the “salt and pepper sign.” Genetic profiling has revealed alterations in the MAP kinase pathway, with the BRAF V600E mutation being a commonly observed genetic anomaly in these tumors.

Surgical resection remains the primary treatment modality for PLNTY, often resulting in favorable clinical outcomes and seizure control. However, the extent of resection and specific genetic profiles do not significantly correlate with prognosis. Notably, contrast enhancement on imaging appears to impact recurrence and seizure control.

Summary

Clinical Characteristics: PLNTY primarily affects individuals within a wide age range, with seizures being the most common clinical presentation.

Radiological Features: The “salt and pepper sign” on imaging, cortical or subcortical masses, and frequent temporal lobe localization are key radiological characteristics of PLNTY.

Genetic Alterations: PLNTY is characterized by genetic alterations in the MAP kinase pathway, with the BRAF V600E mutation being a prominent feature.

Diagnostic Criteria: Accurate diagnosis of PLNTY requires a combination of clinical, radiological, histopathological, and molecular criteria.

Treatment and Outcomes: Surgical resection is the primary treatment, with excellent seizure control and overall favorable clinical outcomes. However, the impact of genetic profiles on prognosis is still evolving.

Challenges and Future Research: Challenges in diagnosing and classifying PLNTY persist, and further research is needed to gain a comprehensive understanding of this intriguing tumor and its clinical implications.

Conclusions

Polymorphous low-grade neuroepithelial tumor of the young (PLNTY) is an emerging entity in the classification of CNS tumors. Recognizing its unique molecular and histopathological features is essential for accurate diagnosis and appropriate management. Advances in molecular profiling have improved our understanding of PLNTY, but further research is needed to elucidate its clinical behavior fully. As our knowledge continues to expand, clinicians and researchers are better equipped to navigate the diagnosis, treatment, and prognosis of PLNTY, ultimately improving the care and outcomes for individuals affected by this intriguing tumor.

Test

What is PLNTY? a) A type of brain tumor b) A skin disorder c) A respiratory disease d) An autoimmune condition

When was PLNTY first described? a) 2010 b) 2015 c) 2017 d) 2019

Which age group is primarily affected by PLNTY? a) Infants b) Adolescents and young adults c) Middle-aged adults d) Elderly individuals

What is the most common clinical presentation of PLNTY? a) Muscle weakness b) Vision problems c) Seizures d) Hearing loss

What radiological feature is characteristic of PLNTY? a) Contrast enhancement b) Cystic components c) Salt and pepper sign d) Microvascular proliferation

Which genetic alteration is frequently found in PLNTY? a) TP53 mutation b) IDH1 mutation c) BRAF

V600E mutation d) FGFR2 amplification

What is the primary treatment modality for PLNTY? a) Chemotherapy b) Radiation therapy c) Surgical resection d) Targeted therapy

What impact does contrast enhancement on imaging have in PLNTY? a) It is associated with better prognosis b) It has no impact on prognosis c) It is associated with poorer seizure control d) It increases the likelihood of recurrence

What is the primary aim of surgical resection in PLNTY? a) To achieve complete cure b) To reduce pain c) To control seizures d) To improve vision

Why is molecular profiling important in understanding PLNTY? a) To identify the age group most affected b) To determine the tumor's location c) To classify it accurately and guide treatment d) To predict the duration of seizures

Answers:

a) A type of brain tumor c) 2017 b) Adolescents and young adults c) Seizures c) Salt and pepper sign c) BRAF V600E mutation c) Surgical resection d) It increases the likelihood of recurrence c) To control seizures c) To classify it accurately and guide treatment

References

[1]
Thomas DL. 2021 updates to the World Health Organization classification of adult-type and pediatric-type diffuse gliomas: a clinical practice review. Chin Clin Oncol. 2023 Feb;12(1):7. doi: 10.21037/cco-22-120. PMID: 36922356.

[2] [3]
Huse JT, Snuderl M, Jones DT, Brathwaite CD, Altman N, Lavi E, Saffery R, Sexton-Oates A, Blumcke I, Capper D, Karajannis MA, Benayed R, Chavez L, Thomas C, Serrano J, Borsu L, Ladanyi M, Rosenblum MK. Polymorphous low-grade neuroepithelial tumor of the young (PLNTY): an epileptogenic neoplasm with oligodendroglioma-like components, aberrant CD34 expression, and genetic alterations involving the MAP kinase pathway. Acta Neuropathol. 2017 Mar;133(3):417-429. doi: 10.1007/s00401-016-1639-9. Epub 2016 Nov 3. PMID: 27812792; PMCID: PMC5325850.

[4] [7]
Johnson DR, Giannini C, Jenkins RB, Kim DK, Kaufmann TJ. Plenty of calcification: imaging characterization of polymorphous low-grade neuroepithelial tumor of the young. Neuroradiology. 2019 Nov;61(11):1327-1332. doi: 10.1007/s00234-019-02269-y. Epub 2019 Aug 9. PMID: 31396664.

[5]
Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, Cancer IAfRo . WHO Classification of Tumours of the Central Nervous System: International Agency for Research on Cancer. 2016

[6]
Gupta R, Lucas CG, Wu J, Barreto J, Shah K, Simon IB, Casavilca-Zambrano S, Brathwaite C, Zhou H, Caccamo D, Gilani A, Kleinschmidt-DeMasters BK, Lee JC, Perry A, Clarke JL, Chang SM, Berger MS, Solomon DA. Low-grade glioneuronal tumors with FGFR2 fusion resolve into a single epigenetic group corresponding to 'Polymorphous low-grade neuroepithelial tumor of the young'. Acta Neuropathol. 2021 Sep;142(3):595-599. doi: 10.1007/s00401-021-02352-w. Epub 2021 Jul 28. PMID: 34322742; PMCID: PMC8357689.

[8] [12]

Kurokawa M, Kurokawa R, Capizzano AA, Baba A, Ota Y, Pinarbasi E, Johnson T, Srinivasan A, Moritani T. Neuroradiological features of the polymorphous low-grade neuroepithelial tumor of the young: five new cases with a systematic review of the literature. Neuroradiology. 2022 Jun;64(6):1255-1264. doi: 10.1007/s00234-021-02879-5. Epub 2022 Jan 10. PMID: 35001164.
9)

Storz C, Sankowski R, Roelz R, Prinz M, Urbach H, Erny D, Taschner CA. Freiburg Neuropathology Case Conference : Recurrent Speech Arrest, Neologistic Jargon Aphasia, and Impaired Memory Function in a 39-year-old Patient. Clin Neuroradiol. 2023 Sep;33(3):869-876. doi: 10.1007/s00062-023-01335-6. Epub 2023 Jul 18. PMID: 37462746; PMCID: PMC10450002.
10) , 20)

Armocida D, Berra LV, Frati A, Santoro A. Radiological and surgical aspects of polymorphous low-grade neuroepithelial tumor of the young (PLNTY). Acta Neurol Belg. 2023 Apr;123(2):327-340. doi: 10.1007/s13760-023-02231-z. Epub 2023 Mar 10. PMID: 36894761; PMCID: PMC10133071.
11)

Fei X, Zhao J, Wei W, Wang W, Kong X, Qian R, Niu C, Yao Y. Clinical, Radiological, Pathological Features and Seizure Outcome With Surgical Management of Polymorphous Low-Grade Neuroepithelial Tumor of the Young Associated With Epilepsy. Front Oncol. 2022 Mar 18;12:863373. doi: 10.3389/fonc.2022.863373. PMID: 35372027; PMCID: PMC8971723.
13) , 16)

Broggi G, Certo F, Altieri R, Caltabiano R, Gessi M, Barbagallo GMV. A “polymorphous low-grade neuroepithelial tumor of the young (PLNTY)” diagnosed in an adult. Report of a case and review of the literature. Surg Neurol Int. 2021 Sep 20;12:470. doi: 10.25259/SNI_500_2021. PMID: 34621585; PMCID: PMC8492409.
14)

Zhao S, Wang J, Li MN, Ding Y, Pan MH, Song K. [Clinicopathological features of polymorphous low-grade neuroepithelial tumor of the young]. Zhonghua Bing Li Xue Za Zhi. 2022 Jul 8;51(7):640-646. Chinese. doi: 10.3760/cma.j.cn112151-20220315-00188. PMID: 35785835.
15)

Ida CM, Johnson DR, Nair AA, Davila J, Kollmeyer TM, Minn K, Fadra NM, Balcom JR, Fung KA, Kim DK, Kaufmann TJ, Kipp BR, Halling KC, Jenkins RB, Giannini C. Polymorphous Low-Grade Neuroepithelial Tumor of the Young (PLNTY): Molecular Profiling Confirms Frequent MAPK Pathway Activation. J Neuropathol Exp Neurol. 2021 Sep 27;80(9):821-829. doi: 10.1093/jnen/nlab075. PMID: 34363682; PMCID: PMC8921648.
17)

Chen Y, Tian T, Guo X, Zhang F, Fan M, Jin H, Liu D. Polymorphous low-grade neuroepithelial tumor of the young: case report and review focus on the radiological features and genetic alterations. BMC Neurol. 2020 Apr 6;20(1):123. doi: 10.1186/s12883-020-01679-3. PMID: 32252664; PMCID: PMC7137220.
18)

Surrey LF, Jain P, Zhang B, Straka J, Zhao X, Harding BN, Resnick AC, Storm PB, Buccoliero AM, Genitori L, Li MM, Waanders AJ, Santi M. Genomic Analysis of Dysembryoplastic Neuroepithelial Tumor Spectrum Reveals a Diversity of Molecular Alterations Dysregulating the MAPK and PI3K/mTOR Pathways. J Neuropathol Exp Neurol. 2019 Dec 1;78(12):1100-1111. doi: 10.1093/jnen/nlz101. PMID: 31617914.
19)

Nair JN, Naidu B, Balasubramanian A, Krishnamurthy G. Polymorphous low-grade neuroepithelial tumour of young (PLNTY): the new kid on the block. Childs Nerv Syst. 2023 Oct 5. doi: 10.1007/s00381-023-06162-1. Epub ahead of print. PMID: 37796295.
21)

Furuta T, Moritsubo M, Muta H, Shimamoto H, Ohshima K, Sugita Y. Pediatric and elderly polymorphous low-grade neuroepithelial tumor of the young: Typical and unusual case reports and literature review. Neuropathology. 2023 Aug;43(4):319-325. doi: 10.1111/neup.12889. Epub 2022 Dec 22. PMID: 36545913.

22)

Palejwala AH, O'Neal CM, Quinton MR, Battiste JD, Peterson JEG, Dunn IF. Polymorphous low-grade neuroepithelial tumor of the young: Rare tumor and review of the literature. Rare Tumors. 2022 Mar 28;14:20363613221083360. doi: 10.1177/20363613221083360. PMID: 35371417; PMCID: PMC8966082.

23)

Hagiwara K, Kamada T, Suzuki SO, Miyoshi A, Tanaka H, Shigeto H, Ohara S, Akamatsu N. Stereo-electroencephalography evidence of an eccentrically located seizure-onset zone around a polymorphous low-grade neuroepithelial tumor of the young: illustrative case. J Neurosurg Case Lessons. 2022 Apr 25;3(17):CASE22106. doi: 10.3171/CASE22106. PMID: 36303487; PMCID: PMC9379642.

24)

Danyeli AE, Altinoz MA, Sari R, Elmaci I. Polymorphous low-grade neuroepithelial tumor of the young: A detailed pathomolecular analysis and discussion of a case. Clin Neuropathol. 2021 Sep-Oct;40(5):271-278. doi: 10.5414/NP301370. PMID: 33860759.

25)

Bale TA, Sait SF, Benhamida J, Ptashkin R, Haque S, Villafania L, Sill M, Sadowska J, Akhtar RB, Liechty B, Juthani R, Ladanyi M, Fowkes M, Karajannis MA, Rosenblum MK. Malignant transformation of a polymorphous low grade neuroepithelial tumor of the young (PLNTY). Acta Neuropathol. 2021 Jan;141(1):123-125. doi: 10.1007/s00401-020-02245-4. Epub 2020 Nov 23. PMID: 33226472; PMCID: PMC8493813.

26)

Ge R, Fang HF, Chang YQ, Li Z, Liu CF. [Clinicopathological features of polymorphous low-grade neuroepithelial tumor of the young]. Zhonghua Bing Li Xue Za Zhi. 2020 Nov 8;49(11):1131-1135. Chinese. doi: 10.3760/cma.j.cn112151-20200213-00086. PMID: 33152817.

27)

Tateishi K, Ikegaya N, Udaka N, Sasame J, Hayashi T, Miyake Y, Okabe T, Minamimoto R, Murata H, Utsunomiya D, Yamanaka S, Yamamoto T. BRAF V600E mutation mediates FDG-methionine uptake mismatch in polymorphous low-grade neuroepithelial tumor of the young. Acta Neuropathol Commun. 2020 Aug 18;8(1):139. doi: 10.1186/s40478-020-01023-3. PMID: 32811569; PMCID: PMC7436956.

28)

Benson JC, Summerfield D, Carr C, Cogswell P, Messina S, Gompel JV, Welker K. Polymorphous Low-Grade Neuroepithelial Tumor of the Young as a Partially Calcified Intra-Axial Mass in an Adult. AJNR Am J Neuroradiol. 2020 Apr;41(4):573-578. doi: 10.3174/ajnr.A6500. Epub 2020 Mar 26. PMID: 32217553; PMCID: PMC7144634.

29)

Lelotte J, Duprez T, Raftopoulos C, Michotte A. Polymorphous low-grade neuroepithelial tumor of the young: case report of a newly described histopathological entity. Acta Neurol Belg. 2020 Jun;120(3):729-732. doi: 10.1007/s13760-019-01241-0. Epub 2019 Nov 21. PMID: 31754999.

30)

Gupta VR, Giller C, Kolhe R, Forseen SE, Sharma S. Polymorphous Low-Grade Neuroepithelial Tumor of the Young: A Case Report with Genomic Findings. World Neurosurg. 2019 Dec;132:347-355. doi: 10.1016/j.wneu.2019.08.221. Epub 2019 Sep 11. PMID: 31520766.

31)

Sumdani H, Shahbuddin Z, Harper G, Hamilton L. Case Report of Rarely Described Polymorphous Low-Grade Neuroepithelial Tumor of the Young and Comparison with Oligodendroglioma. World Neurosurg. 2019 Jul;127:47-51. doi: 10.1016/j.wneu.2019.03.181. Epub 2019 Mar 26. PMID: 30926558.

32)

Bitar M, Danish SF, Rosenblum MK. A newly diagnosed case of polymorphous low-grade neuroepithelial tumor of the young. Clin Neuropathol. 2018 Jul-Aug;37(4):178-181. doi: 10.5414/NP301081. PMID: 29701169; PMCID: PMC6657424.