Papillary glioneuronal tumor

In 2007, WHO classified Papillary glioneuronal tumor (PGNT) as grade I neuronal-glial tumor because of the characteristic papillary architecture and bipartite (astrocytic and neuronal/neurocytic) cell population.

Papillary glioneuronal tumor (PGNT) is a WHO-defined brain tumor entity that poses a major diagnostic challenge.

SLC44A1-PRKCA fusions have been described in PGNT.

Low-grade epilepsy-associated neuroepithelial tumors (LEATs) create a diagnostic challenge in daily practice and intraoperative pathological consultation (IC) in particular. Intraoperative squash smear cytology are extremely useful for accurate diagnosis; however, the knowledge on cytopathologic features of LEATs is based on individual case reports. Kurtulan et al. discuss the 3 most common and well-established entities of LEATs: gangliоglioma (GG), dysembryoplastic neuroepithelial tumor (DNT), and papillary glioneuronal tumor (PGNT).

Thirty patients who underwent surgery for GG, DNT, and PGNT between 2001 and 2021 were collected. Squash smears prepared during intraoperative consultation were reviewed by 1 cytopathologist and an experienced neuropathologist.

Among the 30 tumors, 16 (53.3%) were GG, 11 (36.6%) DNT, and 3 (10%) PGNT. Cytomorphologically, all of the 3 tumor types share 2 common features such as dual cell population and vasculocentric pattern. GG smears were characteristically composed of dysplastic ganglion cells and piloid-like astrocytes on a complex architectural background of thin- to thick-walled vessels. DNT, on the other hand, showed oligodendroglial-like cells in a myxoid thin fibrillary background associated with a delicate capillary network. Common cytological features of PGNT were hyperchromatic cells with narrow cytoplasm surrounding hyalinized vessels forming a pseudopapillary pattern and bland cells with neuroendocrine nuclei dispersed in a neuropil background.

A higher diagnostic accuracy can be obtained when squash smears are applied with frozen sections. However, it is important to integrate clinical and radiologic features of the patient as well as to know the cytopathologic features of the LEAT spectrum in the context of differential diagnosis to prevent misinterpretation in the IC [1)].

Hou et al., subjected 28 brain tumors from different institutions histologically diagnosed as PGNT to molecular and morphological analysis. Array-based methylation analysis revealed that 17/28 tumors exhibited methylation profiles typical for other tumor entities, mostly dysembryoplastic neuroepithelial tumor and hemispheric pilocytic astrocytoma. Conversely, 11/28 tumors exhibited a unique profile, thus constituting a distinct methylation class PGNT. By screening the extended Heidelberg cohort containing over 25,000 CNS tumors, they identified three additional tumors belonging to this methylation cluster but originally histologically diagnosed otherwise. RNA sequencing for the detection of SLC44A1-PRKCA fusions could be performed on 19 of the tumors, 10 of them belonging to the methylation class PGNT. In two additional cases, SLC44A1-PRKCA fusions were confirmed by FISH.

They detected fusions involving PRKCA in all cases of this methylation class with material available for analyses: the canonical SLC44A1-PRKCA fusion was observed in 11/12 tumors, while the remaining case exhibited a NOTCH1-PRKCA fusion. Neither of the fusions was found in the tumors belonging to other methylation classes. The results point towards a high misclassification rate of the morphological diagnosis PGNT and clearly demonstrate the necessity of molecular analyses. PRKCA fusions are highly diagnostic for PGNT, and detection by RNA sequencing enables the identification of rare fusion partners. Methylation analysis recognizes a unique methylation class PGNT irrespective of the nature of the PRKCA fusion [2].

1)
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2)
Hou Y, Pinheiro J, Sahm F, Reuss DE, Schrimpf D, Stichel D, Casalini B, Koelsche C, Sievers P, Wefers AK, Reinhardt A, Ebrahimi A, Fernández-Klett F, Pusch S, Meier J, Schweizer L, Paulus W, Prinz M, Hartmann C, Plate KH, Reifenberger G, Pietsch T, Varlet P, Pagès M, Schüller U, Scheie D, de Stricker K, Frank S, Hench J, Pollo B, Brandner S, Unterberg A, Pfister SM, Jones DTW, Korshunov A, Wick W, Capper D, Blümcke I, von Deimling A, Bertero L. Papillary glioneuronal tumor (PGNT) exhibits a characteristic methylation profile and fusions involving PRKCA. Acta Neuropathol. 2019 Feb 13. doi: 10.1007/s00401-019-01969-2. [Epub ahead of print] PubMed PMID: 30759284.