Posterior Fossa Ependymoma Classification

The current 2021 update mainly comprises molecular subtypes. More precisely, the types of subependymomas (SE), myxopapillary ependymomas (MPE), and RELA-fusion-positive (now: ZFTA-fusion-positive) ependymomas have been maintained in the 2021 classification, although some changes have been applied. The previously used terms ependymoma and anaplastic ependymoma are not used to define an entity anymore. Instead, Posterior fossa ependymoma group PFA and Posterior fossa type B ependymoma, YAP1-fusion-positive ependymoma in the cerebrum, and spinal ependymoma, as well as spinal ependymoma, MYCN-amplified, in the spinal cord, have been newly defined. This not only provides an objective molecular basis for the diagnosis and classification of ependymomas but is also intended to better predict the clinical outcome of the patients. Notably, first studies on tumor relapse samples indicate that this molecular classification might be more stable in the course of the disease than histology alone.

Posterior fossa ependymoma comprise three distinct molecular variants:

Posterior fossa ependymoma group PFA

Posterior fossa type B ependymoma

Subependymoma of the fourth ventricle

The majority of intracranial ependymomas (60%) are located in the posterior fossa (infratentorial), usually arising from the lateral recess of the fourth ventricle (molecular subgroup: Posterior Fossa type A ependymoma) and midline inferior fourth ventricle floor near the obex (molecular subgroup: Posterior Fossa type B ependymoma) [1) 2) 3)].

Group A patients are younger, have laterally located tumors with a balanced genome, and are much more likely to exhibit recurrence, metastases at recurrence, and death compared with Group B patients

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Clinically, they are very disparate and PFB tumors are currently being considered for a trial of radiation avoidance. However, to move forward, unraveling the heterogeneity within PFB would be highly desirable. To discern the molecular heterogeneity within PFB, we performed an integrated analysis consisting of DNA methylation profiling, copy-number profiling, gene expression profiling, and clinical correlation across a cohort of 212 primary posterior fossa PFB tumors. Unsupervised spectral clustering and t-SNE analysis of genome-wide methylation data revealed five distinct subtypes of PFB tumors, termed PFB1-5, with distinct demographics, copy-number alterations, and gene expression profiles. All PFB subtypes were distinct from PFA and posterior fossa subependymomas. Of the five subtypes, PFB4 and PFB5 are more discrete, consisting of younger and older patients, respectively, with a strong female-gender enrichment in PFB5 (age: $p = 0.011$, gender: $p = 0.04$). Broad copy-number aberrations were common; however, many events such as chromosome 2 loss, 5 gain, and 17 loss were enriched in specific subtypes and 1q gain was enriched in PFB1. Late relapses were common across all five subtypes, but deaths were uncommon and present in only two subtypes (PFB1 and PFB3). Unlike the case in PFA ependymoma, 1q gain was not a robust marker of poor progression-free survival; however, chromosome 13q loss may represent a novel marker for risk stratification

across the spectrum of PFB subtypes. Similar to PFA ependymoma, there exists a significant intertumoral heterogeneity within PFB, with distinct molecular subtypes identified. Even when accounting for this heterogeneity, extent of resection remains the strongest predictor of poor outcome. However, this biological heterogeneity must be accounted for in future preclinical modeling and personalized therapies [4)].

The relationship between microanatomical localization and postoperative survival in posterior fossa ependymomas has been used to classify posterior fossa ependymomas into three types:

Midfloor, roof, and lateral.

“Plastic ependymomas” are thought to be the lateral type. The survival rate of the lateral-type ependymomas is significantly lower than the other two types, regardless of histological malignancy, due to the difficulty in achieving total surgical resection in the lateral-type ependymomas.

Fourth ventricle ependymoma

see Fourth ventricle ependymoma.

Cerebellopontine angle ependymoma

see Cerebellopontine angle ependymoma.

Posterior fossa type A Ependymoma

see Posterior fossa type A Ependymoma.

Posterior fossa type B Ependymoma

Posterior fossa type B Ependymoma.

Pediatric posterior fossa ependymoma

Pediatric posterior fossa ependymoma.

The more common infratentorial tumors may produce nausea, vomiting (particularly when the area postrema is involved), and manifestations of cerebellar compression, mainly ataxia and nystagmus.

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