Posterior fossa ependymoma outcome

Patients with incompletely resected EPN_PFA tumors had a very poor outcome despite receiving adjuvant radiation therapy, whereas a substantial proportion of patients with EPN_PFB tumors can be cured with surgery alone [1].

The PFA molecular subgroup of posterior fossa ependymomas (PF-EPNs) shows poor outcome. H3K27me3 (me3) loss by immunohistochemistry (IHC) is a surrogate marker for PFA wherein its loss is attributed to overexpression of Cxorf67/EZH2 inhibitory protein (EZHIP), C17orf96, and ATRX loss. We aimed to subgroup PF-EPNs using me3 IHC and study correlations of the molecular subgroups with other histone related proteins, 1q gain, Tenascin C and outcome. IHC for me3, acetyl-H3K27, H3K27M, ATRX, EZH2, EZHIP, C17orf96, Tenascin-C, and fluorescence in-situ hybridisation for chromosome 1q25 locus were performed on an ambispective PF-EPN cohort (2003-2019). H3K27M-mutant gliomas were included for comparison. Among 69 patients, PFA (me3 loss) constituted 64%. EZHIP overexpression and 1q gain were exclusive to PFA seen in 72% and 19%, respectively. Tenascin C was more frequently positive in PFA ($p = 0.02$). H3K27M expression and ATRX loss were noted in one case of PFA-EPN each. All H3K27M-mutant gliomas ($n = 8$) and PFA-EPN ($n = 1$) were EZHIP negative. C17orf96 and acetyl-H3K27 expression did not correlate with me3 loss. H3K27me3 is a robust surrogate for PF-EPN molecular subgrouping. EZHIP overexpression was exclusive to PFA EPNs and was characteristically absent in midline gliomas and the rare PFA harbouring H3K27M mutations representing mutually exclusive pathways leading to me3 loss [2].

Chen et al. found that nucleolin was an unfavorable prognostic predictor for ependymomas. Moreover, the findings show a subset of aggravating outcomes in anaplastic ependymoma and infratentorial ependymoma. [3].

1)
Ramaswamy V, Taylor MD. Treatment implications of posterior fossa ependymoma subgroups. Chin J Cancer. 2016 Nov 15;35(1):93. doi: 10.1186/s40880-016-0155-6. PMID: 27846874; PMCID: PMC5111181.
2)
Nambirajan A, Sharma A, Rajeshwari M, Boorgula MT, Doddamani R, Garg A, Suri V, Sarkar C, Sharma MC. EZH2 inhibitory protein (EZHIP/Cxorf67) expression correlates strongly with H3K27me3 loss in posterior fossa ependymomas and is mutually exclusive with H3K27M mutations. Brain Tumor Pathol. 2020 Nov 1. doi: 10.1007/s10014-020-00385-9. Epub ahead of print. Erratum in: Brain Tumor Pathol. 2021 Jan 9;: PMID: 33130928.
3)
Chen C, Chen L, Yao Y, Qin Z, Chen H. Nucleolin overexpression is associated with an unfavorable outcome for ependymoma: a multifactorial analysis of 176 patients. J Neurooncol. 2015 Nov 28. [Epub ahead of print] PubMed PMID: 26615563.