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Отдел нейроонкологии.

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Histologically distinct neuroepithelial tumors with histone 3 G34 mutation are molecularly similar and comprise a single nosologic entity.

Korshunov A[1,2,3], Capper D[4,5,6], Reuss D[4,5,6], Schrimpf D[4,5], Ryzhova M[7], Hovestadt V[8], Sturm D[9,10], Meyer J[4,5], Jones C[11], Zheludkova O[12], Kumirova E[13], Golanov A[14], Kool M[6,9], Schüller U[15], Mittelbronn M[16], Hasselblatt M[17], Schittenhelm J[18], Reifenberger G[19], Herold-Mende C[20], Lichter P[6,8], von Deimling A[4,5,6], Pfister SM[6,9,10], Jones DT[6,9].

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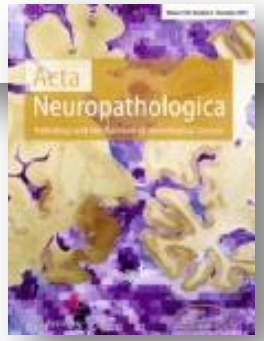
Abstract

In contrast to the relative morphological uniformity of histone H3 K27-mutant high-grade gliomas, H3 G34-mutant tumors present as a histopathologically heterogeneous group of neoplasms, with microscopic characteristics typical of either glioblastoma (GBM) or central nervous system primitive neuroectodermal tumors (CNS-PNET). In the current study, we performed an integrative clinical, histopathological and molecular analysis of 81 G34-mutant CNS tumors. Routinely prepared tumor tissues were investigated for genomic and epigenomic alterations. Despite their divergent histopathological appearance, CNS tumors with H3.3 G34 mutations displayed uniform epigenetic signatures, suggesting a single biological origin. Comparative cytogenetic analysis with other GBM subtypes disclosed a high frequency and high specificity of 3q and 4q loss across G34-mutant tumors. PDGFRA amplification was more common in cases with GBM than with PNET morphology (36 vs. 5 %, respectively), while CCND2 amplifications showed the opposite trend (5 vs. 27 %). Survival analysis revealed the presence of amplified oncogene(s) and MGMT methylation as independent prognostic markers for poor and favorable outcomes, respectively. No difference in outcome was found between morphological variants (GBM vs. PNET). Thus, different histological variants of G34-mutant CNS tumors likely comprise a single biological entity (high-grade glioma with H3 G34 mutation, HGG_G34), which should be outlined in future diagnostic and therapeutic classifications. Screening for H3.3 G34 mutation should therefore be recommended as a routine diagnostic marker for supratentorial CNS tumors across a broad histological spectrum.

KEYWORDS: G34 mutation; Glioblastoma; Methylation; PNET; Prognostic; Subgroup; Survival



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