ABSTRACT

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Histone H3.3 G34-mutant Diffuse Gliomas in Adults.

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The characteristics of H3.3 G34-mutant gliomas in adults have yet to be specifically described. Thirty adults with H3.3 G34-mutant diffuse gliomas were retrospectively reviewed for clinical and pathologic information. Molecular profiling using next-generation sequencing was performed in 29 of the 30 H3.3 G34-mutant patients with 1 patient lacking available tumor samples, as well as 82 IDH/H3 wild-type adult diffuse glioma patients. The age at diagnosis of H3.3 G34-mutant diffuse gliomas was significantly younger than IDH/H3 wild-type gliomas (24 vs. 57 y, P<0.001). Overall, 19 of the 30 patients were diagnosed of glioblastoma with the primitive neuronal component, and 8 were glioblastoma. The molecular profiling analysis revealed higher frequencies of Olig-2 loss of expression, TP53 mutation, ATRX mutation, PDGFRA mutation, and MGMT promoter methylation (P<0.05) in H3.3 G34-mutant gliomas than IDH/H3 wild-type gliomas. No TERT promoter mutation and only 1 case of EGFR amplification were detected in the H3.3 G34-mutant cohort, the frequencies of which were significantly higher in the IDH/H3 wild-type cohort. A dismal prognosis was observed in H3.3 G34-mutant patients comparing to IDH/H3 wild-type cohort (overall survival: 14 vs. 22 mo; P=0.026). Univariate and multivariate analyses showed that the extent of resection and TP53 mutation were independently affecting prognosis. The distinct pathologic and molecular features of H3.3 G34-mutant diffuse gliomas in adult patients demonstrated the clinical importance of detecting H3.3 G34R/V mutations. The dismal prognosis of this rare high-grade glioma disease we reported here would further promote the investigation of dedicated therapeutic strategies.

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