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Volumetric response and pattern of failure of histone altered high grade glioma in adults following management with radiation therapy

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Abstract

Purpose: H3K27M- and H3G34R-mutant gliomas are recently-classified subgroups of high-grade gliomas (HGGs) affecting younger adults. This study aimed to describe patterns of infiltration and failure, and the volumetric response of these tumours to radiotherapy.

Methods: Patients with histone-mutant gliomas aged 16-50 years, managed from 2009 to 2021 were identified and clinical, radiological and histopathological characteristics collected. Tumour volume was assessed on MRI at diagnosis, pre-radiotherapy, month + 1, + 3 and + 5 post-radiation and at relapse.

Results: Of 538 IDH1/2 wild-type HGGs, 18(15%) had a histone alteration. Eleven were H3K27M- and 7 H3G34R-mutant respectively. Median age at diagnosis was 20 years (range17-48 years). Median overall survival was 20 months (95%CI 14-29 months). Both H3K27M- and H3G34R-mutant tumours exhibited extensive T2F infiltration involving a median of 4 neuroanatomical subsites at diagnosis. Median volume of disease pre-radiotherapy on T1gd and T2F respectively was 0.5cm^3 (IQR:0-1.7cm^3) and 11.9 cm^3 (IQR:7.5-29.6cm^3) for H3K27M and 0.9cm^3 (IQR:0-8.4cm^3) and 43.8cm^3 (IQR:25.2-86.6 cm^3) for H3G34R tumours. T2F volume reduction > 50% was observed 3-months post-IMRT in 7(64%) patients with H3K27M and 1(14%) with H3G34R tumours. Fourteen patients had relapsed. Relapse was local-only, distant-only and both in 4(44%), 3(33%) and 2(22%) H3K27M-mutant and 1(20%), 2(40%), and 2(40%) H3G34R-mutant tumours. On last scan before death, leptomeningeal spread was present in 4/8(50%) and 1/5(20%) and subependymal spread in 4/8 (50%) and 0/5 H3K27M- and G34R-mutant cases respectively.

Conclusion: H3K27M-mutant gliomas are highly responsive to radiotherapy but exhibit high propensity for subsequent leptomeningeal and subependymal spread. H3G34R-mutant tumours exhibit lesser early volumetric response to radiotherapy and propensity for distant in-brain failure.

Keywords: Adults; Glioma; Histone-altered; Radiotherapy; Volume.