Diffuse midline glioma H3 K27M-mutant MRI

T1: decreased intensity

T2: heterogeneously increased

T1 C+ (Gd): usually minimal (can enhance post-radiotherapy)

DWI/ADC: usually normal, occasionally mildly restricted

Extensive spread is relatively frequent, both craniocaudally to involve the cerebral hemispheres and spinal cord, as well as leptomeningeal spread [1)]

A study included 66 cases (40 in men, 26 in women) of H3 K27M-mutant glioma in adult patients. Tumors were found in the following sites: thalamus (n = 38), brainstem (n = 6), brainstem with cerebellar or thalamic involvement (n = 4), whole-brain (n = 8), corpus callosum (n = 3), hypothalamus (n = 1), hemispheres (n = 2), and spinal cord (n = 4). All pure brainstem lesions were located posteriorly, and all corpus callosal lesions were in the genu. Most spinal tumors were long-segment lesions. Hemispheric lesions mimicked gliomatosis cerebri in presentation, with the addition of traditional midline structure involvement. Most tumors were solid with relatively uniform signals on plain MRI. Of the 61 cases with contrast-enhanced MR images, 36 (59%) showed partial to no enhancement, whereas 25 (41%) showed diffuse or irregular peripheral enhancement. Hemorrhage and edema were rare. Most lesions were solid and showed mild diffusion restriction on diffusion-weighted imaging. Tumor dissemination to the leptomeninges (n = 8) and subependymal layer (n = 3) was observed.

Qiu et al. described the MRI features of diffuse midline glioma with H3 K27M mutation in the largest study done to date in adult patients. Tumors were found in both midline and nonmidline structures, with the thalamus being the most common site. Although adult H3 K27M-mutant gliomas demonstrated highly variable presentations in this cohort of patients, the authors were able to observe shared characteristics within each location [2)].

The radiographic features of diffuse midline gliomas with histone H3 K27M mutation were highly variable, ranging from expansile masses without enhancement or necrosis with large areas of surrounding infiltrative growth to peripherally enhancing masses with central necrosis with the significant mass effect but little surrounding T2/FLAIR hyperintensity. When we compared diffuse midline gliomas on the basis of the presence or absence of histone H3 K27M mutation, there was no significant correlation between enhancement or border characteristics, infiltrative appearance, or presence of edema [3)]

Zhuo et al. from the Beijing Tiantan Hospital aimed to predict H3K27M mutation status by Amide proton transfer imaging (APTw) and radiomic features.

Methods: Eighty-one BSG patients with APTw imaging at 3T MR and known H3K27M status were retrospectively studied. APTw values (mean, median, and max) and radiomic features within manually delineated 3D tumor masks were extracted. Comparison of APTw measures between H3K27M-mutant

and wildtype groups was conducted by two-sample Student's T/Mann-Whitney U test and receiver operating characteristic curve (ROC) analysis. H3K27M-mutant prediction using APTw-derived radiomics was conducted using a machine learning algorithm (support vector machine) in randomly selected train (n = 64) and test (n = 17) sets. Sensitivity analysis with additional random splits of train and test sets, 2D tumor masks, and other classifiers were conducted. Finally, a prospective cohort including 29 BSG patients was acquired for validation of the radiomics algorithm.

Results: BSG patients with H3K27M-mutant were younger and had higher max APTw values than those with wildtype. APTw-derived radiomic measures reflecting tumor heterogeneity could predict H3K27M mutation status with an accuracy of 0.88, the sensitivity of 0.92, and specificity of 0.80 in the test set. Sensitivity analysis confirmed the predictive ability (accuracy range: 0.71-0.94). In the independent prospective validation cohort, the algorithm reached an accuracy of 0.86, the sensitivity of 0.88, and specificity of 0.85 for predicting H3K27M-mutation status.

Conclusion: BSG patients with H3K27M-mutant had higher max APTw values than those with wildtype. APTw-derived radiomics could accurately predict an H3K27M-mutant status in BSG patients [4].

Piccardo et al., from Genoa, retrospectively analyzed 22 pediatric patients with DMG histologically proved and molecularly classified as H3K27M-mutant (12 subjects) and wild-type (10 subjects) who underwent DWI, Proton magnetic resonance spectroscopic imaging, and ASL performed within 2 weeks of 18F-FDOPA PET. DWI-derived relative minimum apparent diffusion coefficient (rADC min), Proton magnetic resonance spectroscopic imaging data choline/N-acetylaspartate (Cho/NAA), choline/creatine (Cho/Cr), and presence of lactate and relative ASL-derived cerebral blood flow max (rCBF max) were compared with 18F-DOPA uptake Tumor/Normal tissue (T/N) and Tumor/Striatum (T/S) ratios, and correlated with histological and molecular features of DMG. Statistics included Pearson's chi-squared test and Mann-Whitney U tests, Spearman's rank correlation and receiver operating characteristic (ROC) analysis.

The highest degrees of correlation among different techniques were found between T/S, rADC min and Cho/NAA ratio ($p < 0.01$), and between rCBF max and rADC min ($p < 0.01$). Significant differences between histologically classified low- and high-grade DMG, independently of H3K27M-mutation, were found among all imaging techniques ($p \leq 0.02$). Significant differences in terms of rCBF max, rADC min, Cho/NAA and 18F-DOPA uptake were also found between molecularly classified mutant and wild-type DMG ($p \leq 0.02$), even though wild-type DMG included low-grade astrocytomas, not present among mutant DMG. When comparing only histologically defined high-grade mutant and wild-type DMG, only the 18F-DOPA PET data T/S demonstrated statistically significant differences independently of histology ($p < 0.003$). ROC analysis demonstrated that T/S ratio was the best parameter for differentiating mutant from wild-type DMG (AUC 0.94, $p < 0.001$).

Advanced MRI and 18F-DOPA PET characteristics of DMG depend on histological features; however, 18F-DOPA PET-T/S was the only parameter able to discriminate H3K27M-mutant from wild-type DMG independently of histology [5].

References

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