Pediatric low-grade glioma case series

2023

61 patients with PLGGs were included in this retrospective study, which was divided into a training set and an internal validation set at a ratio of 2:1 based on the molecular subgroups or the molecular marker. The patients were classified into low-risk and intermediate/high-risk groups, BRAF fusion positive and negative groups, respectively. We extracted 5929 radiomic features from multiparametric MRI. Thereafter, we removed redundant features, trained random forest models on the training set for predicting the molecular subgroups or the molecular marker, and validated their performance on the internal validation set. The performance of the prediction model was verified by 3-fold cross-validation.

They constructed the classification model differentiating low-risk PLGGs from intermediate/high-risk PLGGs using 4 relevant features, with an AUC of 0.833 and an accuracy of 76.2% in the internal validation set. In the prediction model for predicting KIAA1549-BRAF fusion using 4 relevant features, an AUC of 0.818 and an accuracy of 81.0% were achieved in the internal validation set.

The current study demonstrates that MRI radiomics is able to predict molecular subgroups of PLGGs and KIAA1549-BRAF fusion with satisfying sensitivity [1)]

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Mobark et al. profiled a targeted panel of cancer-related genes in 37 Saudi Arabian patients with pLGGs to identify genetic abnormalities that can inform prognostic and therapeutic decision-making. They detected genetic alterations (GAs) in 97% (36/37) of cases, averaging 2.51 single nucleotide variations (SNVs) and 0.91 gene fusions per patient. The KIAA1549-BRAF fusion was the most common alteration (21/37 patients) followed by AFAP1-NTRK2 (2/37) and TBLXR-PI3KCA (2/37) fusions that were observed at much lower frequencies. The most frequently mutated) genes were NOTCH1-3 (7/37), ATM (4/37), RAD51C (3/37), RNF43 (3/37), SLX4 (3/37) and NF1 (3/37). Interestingly, they identified a GOPC-ROS1 fusion in an 8-year-old patient whose tumor lacked BRAF alterations and histologically classified as low-grade glioma. The patient underwent gross total resection (GTR). The patient is currently disease-free. To the author's knowledge, this is the first report of GOPC-ROS1 fusion in PLGG. Taken together, they revealed the genetic characteristics of pLGG patients can enhance diagnostics and therapeutic decisions. In addition, we identified a GOPC-ROS1 fusion that may be a biomarker for pLGG [2)].

Fukuoka et al. performed genome-wide methylation analysis on 136 pediatric low-grade gliomas, identifying a unique cluster consisting of three tumors with oligodendroglioma-like histology, BRAF p.V600E mutations and recurrent whole chromosome gains of 7 and loss of 10. Morphologically, all showed similar features, including a diffusely infiltrative glioma composed of round nuclei with perinuclear halos, a chicken-wire pattern of branching capillaries and microcalcification. None showed astrocytic features or characteristics suggestive of high-grade tumors including necrosis or mitotic figures. All tumors harbored multiple chromosomal copy number abnormalities (>10 chromosomes

altered), but none showed 1p/19q co-deletion or IDH1 p.R132H mutation. Hierarchical clustering and t-stochastic neighbor embedding analyses from DNA methylation data cluster them more closely to previously described pediatric-type low-grade gliomas and separate from adult gliomas. These tumors exhibit distinct clinical features; they are temporal lobe lesions occurring in adolescents and young adults with a prolonged history of seizures and all are alive with no recurrence (follow-up 3.2 to 13.2 years). We encountered another young adult case with quite similar pathological appearance and molecular status except for TERT promoter mutation. Although the series is small, these may represent a new category of IDH wild-type low-grade gliomas which may be confused with “molecular GBM.” Further, they highlight the heterogeneity of IDH wild-type gliomas and the relatively indolent behavior of “pediatric-type” gliomas [3].

A study collected population-based follow-up information for all PLGG patients diagnosed in Ontario, Canada from 1985 to 2012 (n = 1202) and determined factors affecting survival. The impact of upfront radiation treatment on overall survival (OS) was determined for a cohort of Ontario patients and an independent reference cohort from the Surveillance, Epidemiology, and End Results database.

At a median follow-up of 12.73 years (range, 0.02-33 years), only 93 deaths (7.7%) were recorded, and the 20-year OS rate was 90.1% ± 1.1%. Children with neurofibromatosis type 1 had excellent survival and no tumor-related deaths during adulthood. Adverse risk factors included pleomorphic xanthoastrocytoma (P < .001) and a thalamic location (P < .001). For patients with unresectable tumors surviving more than 5 years after the diagnosis, upfront radiotherapy was associated with an approximately 3-fold increased risk of overall late deaths (hazard ratio [HR], 3.3; 95% confidence interval [CI], 1.6-6.6; P = .001) and an approximately 4-fold increased risk of tumor-related deaths (HR, 4.4; 95% CI, 1.3-14.6; P = .013). In a multivariate analysis, radiotherapy was the most significant factor associated with late all-cause deaths (HR, 3.0; 95% CI, 1.3-7.0; P = .012) and tumor-related deaths (HR, 4.4; 95% CI, 1.3-14.6; P = 0.014). A similar association between radiotherapy and late deaths was observed in the independent reference cohort (P < .001). In contrast to early deaths, late mortality was associated not with PLGG progression but rather with tumor transformation and non-oncological causes.

The course of PLGG is associated with excellent long-term survival, but this is hampered by increased delayed mortality in patients receiving upfront radiotherapy. These observations should be considered when treatment options are being weighed for these patients [4].

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