Genomic characterization of recurrent high-grade astroblastoma.


Abstract

Astroblastomas are rare primary brain tumors, diagnosed based on histologic features. Not currently assigned a WHO grade, they typically display indolent behavior, with occasional variants taking a more aggressive course. We characterized the immunohistochemical characteristics, copy number (high-resolution array comparative genomic hybridization, OncoCopy) and mutational profile (targeted next-generation exome sequencing, OncoPanel) of a cohort of seven biopsies from four patients to identify recurrent genomic events that may help distinguish astroblastomas from other more common high-grade gliomas. We found that tumor histology was variable across patients and between primary and recurrent tumor samples. No common molecular features were identified among the four tumors. Mutations commonly observed in astrocytic tumors (IDH1/2, TP53, ATRX, and PTEN) or ependymoma were not identified. However one case with rapid clinical progression displayed mutations more commonly associated with GBM (NF1(N1054H/K63)*, PIK3CA(R38H) and ERG(A403T)). Conversely, another case, originally classified as glioblastoma with nine-year survival before recurrence, lacked a GBM mutational profile. Other mutations frequently seen in lower grade gliomas (BCOR, BCORL1, ERBB3, MYB, ATM) were also present in several tumors. Copy number changes were variable across tumors. Our findings indicate that astroblastomas have variable growth patterns and morphologic features, posing significant challenges to accurate classification in the absence of diagnostically specific copy number alterations and molecular features. Their histopathologic overlap with glioblastoma will likely confound the observation of long-term GBM "survivors". Further genomic profiling is needed to determine whether these tumors represent a distinct entity and to guide management strategies.

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