The genetic landscape of anaplastic astrocytoma.


Department of Pathology, Duke University Medical Center, The Preston Robert Tisch Brain Tumor Center at Duke, and Pediatric Brain Tumor Foundation Institute at Duke, Durham, NC.

Abstract

Anaplastic astrocytoma WHO grade III (A3) is a lethal brain tumor that often occurs in middle aged patients. Clinically, it is challenging to distinguish A3 from glioblastoma multiforme (GBM) WHO grade IV. To reveal the genetic landscape of this tumor type, we sequenced the exome of a cohort of A3s (n=16). For comparison and to illuminate the genomic landscape of other glioma subtypes, we also included in our study diffuse astrocytoma WHO grade II (A2, n=7), oligoastrocytoma WHO grade II (OA2, n=2), anaplastic oligoastrocytoma WHO grade III (OA3, n=4), and GBM (n=28). Exome sequencing of A3s identified frequent mutations in IDH1 (75%, 12/16), ATRX (63%, 10/16), and TP53 (82%, 13/16). In contrast, the majority of GBMs (75%, 21/28) did not contain IDH1 or ATRX mutations, and displayed a distinct spectrum of mutations. Finally, our study also identified novel genes that were not previously linked to this tumor type. In particular, we found mutations in Notch pathway genes (NOTCH1, NOTCH2, NOTCH4, NOTCH2NL), including a recurrent NOTCH1-A465T mutation, in 31% (5/16) of A3s. This study suggests genetic signatures will be useful for the classification of gliomas.

PMID: 24140581 [PubMed - as supplied by publisher]