Malignant glioma with primitive neuroectodermal tumor-like component (MG-PNET): novel microarray findings in a pediatric patient.


Abstract

Central nervous system (CNS) tumors exhibiting dual features of malignant glioma (MG) and primitive neuroectodermal tumor (PNET) are rare and diagnostically challenging. Previous studies have shown that MG-PNET carry MYCN or MYC gene amplifications within the PNET component concomitant with glioma-associated alterations, most commonly 10q loss, in both components [9]. Here we confirm and extend the profile of molecular genetic findings in a MG-PNET involving the left frontal lobe of a 12-year-old male. Histologically, the PNET-like component showed morphological features akin to anaplastic medulloblastoma highlighted by widespread immunoreactivity for βIII-tubulin (TUBB3) and nonphosphorylated neurofilament protein, and to a lesser degree, Neu-N, synaptophysin, and CD99, whereas the gliomatous component was demarcated by glial fibrillary acidic protein (GFAP) labeling. Immunohistochemical labeling with an anti-H3K27M mutant-specific antibody was not detectable in either gliomatous and/or PNET-like areas. Interphase fluorescent in situ hybridization (FISH) study on touch preparations from frozen tumor and formaldehyde-fixed, paraffin-embedded histological sections showed amplification of MYC in both PNET-like and gliomatous areas. Single nucleotide polymorphism (SNP) microarray analysis revealed that the tumor carried gains of multiple chromosomes and chromosome arms, losses of multiple chromosomes and chromosome arms, gains of multiple chromosomal segments (not limited to amplification of chromosomal segments 4q12 including PDGFRA, and 8q24.21 including MYC), and a hitherto unreported chromothripsis-like abnormality on chromosome 8. No mutations were identified for IDH1, IDH2, or BRAF genes by sequence analysis. The molecular genetic findings support the presence of a CNS-PNET as an integral part of the tumor coupled with overlapping genetic alterations found in both adult and pediatric high-grade gliomas/glioblastoma. Collectively, microarray data point to a complex underpinning of genetic alterations associated with the MG-PNET tumor phenotype.

PMID: 27781423 DOI: 10.5414/NP300942

[PubMed - in process]