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Ganglioglioma with anaplastic/high-grade transformation: Histopathologic, molecular, and epigenetic characterization of 3 cases

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Abstract

Ganglioglioma (GG) with anaplasia (anaplastic ganglioglioma) is a rare and controversial diagnosis. When present, anaplasia involves the glial component of the tumor, either at presentation or at recurrence. To date, most published cases lack molecular characterization. We describe the histologic and molecular features of 3 patients presenting with BRAF p. V600E-mutant GG (CNS WHO grade 1) with high-grade glial transformation at recurrence. The tumors occurred in pediatric patients (age 9-16 years) with time to recurrence from 20 months to 7 years. At presentation, each tumor was low-grade, with a BRAFV600E-positive ganglion cell component and a glial component resembling pleomorphic xanthoastrocytoma (PXA) or fibrillary astrocytoma. At recurrence, tumors resembled anaplastic PXA or high-grade astrocytomas without neuronal differentiation. CDKN2A homozygous deletion (HD) was absent in all primary tumors. At recurrence, 2 cases acquired CDKN2A HD; the third case showed loss of p16 and MTAP immunoexpression, but no CDKN2A/B HD or mutation was identified. By DNA methylation profiling, all primary and recurrent tumors either grouped or definitely matched to different methylation classes. Our findings indicate that malignant progression of the glial component can occur in GG and suggest that CDKN2A/B inactivation plays a significant role in this process.

Keywords: BRAF p. V600E-mutant; CDKN2A/B inactivation; Anaplasia; Ganglioglioma; Methylation class PXA; Whole-genome DNA methylation profiling.