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Molecular Mutations Identified in Oligodendrogliomas with Leptomeningeal Spread and Distant Metastasis

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Introduction

Oligodendroglioma is a low-grade glioma (LGG) of central nervous system (CNS) with disease burden frequently restricted to local advancement. Although rare, both disseminated CNS and distant corporal metastasis of LGG have been reported in literature. Identification of oligodendroglioma with increased metastatic potential will provide the opportunity to optimize clinical management for this lethal subtype.

Over the past decade, molecular and genetic characterization of tumor specimen have become routine in guiding treatment of newly diagnosed LGG. The 1p/19q codeletion, isocitrate dehydrogenase 1 (IDH1) mutation, and methylation of the O6-methylguaninemethyltransferase (MGMT) promoter are genetic changes associated with improved progression-free survival.

We provide the first description of molecular mutations identified in multiple oligodendrogliomas with CNS dissemination despite favorable genetic characteristics including IDH1 mutation, 1p/19q codeletion, and MGMT promotor methylation.

Methods

We vetted 460 oligodendroglioma and anaplastic oligodendroglioma cases in our database and identified two cases of metastatic spread. We retrospectively performed genomic analysis of our tumor specimen for mutations which are likely to have contributed to metastatic potential.

Results

Our tumor specimens demonstrated favorable mutations at IDH1, 1p/19q (codeletion), and MGMT promoter. Further genetic analysis of one original tumor specimen revealed mutations in MED12, CDH20, CDK12, FRS2, and RET. Specimen from second tumor patient demonstrated mutations in MTOR, PIK3CA, H1047R, CDKN2A/B, FAM123B, LRP1B, LZTR1, NOTCH1, PIK3R1, SOX2, and TERT promoter.

Conclusions

Mutations involving cell motility (CDH20, FRS2, PIK3CA), modulation of gene expression (MED12, CDK12, MTOR, SOX2), cell cycle regulation (CDKN2A/B, LZTR1, NOTCH1, TERT promotor), or others (H1047R, FAM123B, LRP1B, PIK3R1) may have contributed to metastatic spread of oligodendroglioma were present in our patient's tumor specimens. Prospective utilization of a predictive molecular subclass of metastatic potential in oligodendroglioma may add value in patient counseling, disease surveillance, and surgical management.

Learning Objectives

By the conclusion of this session, participants should be able to appreciate metastatic potential of oligodendroglioma, and possible novel genetic markers that may be used to identify this special subset of oligodendroglioma.

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