Integrated Prognostication of Molecular Oligodendroglioma in The Cancer Genome Atlas

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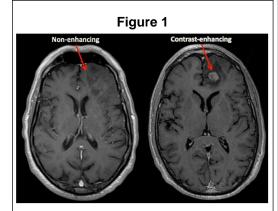EMORY UNIVERSITY SCHOOL OF MEDICINE

Learning Objectives

By the conclusion of this session, participants should be able to:

- Identify the molecular signature of oligodendroglioma
- Understand the importance of histological grading and radiographic features in the new paradigm of molecular classification for lower-grade gliomas
- Appreciate the role of image-based analysis in quantifying and better prognosticating brain tumors

Introduction

Lower-grade gliomas with IDH-mutations and 1p/19q co-deletion, or oligodendroglioma, represent an important subset with unpredictable clinical courses. Disease progression can be monitored with magnetic resonance imaging (MRI), most notably by the presence of contrast-enhancement and radiographic necrosis (Figure 1). We investigated molecular markers associated with radiographic features of disease progression in oligodendroglioma to help explain variations in clinical course.

Figure 1

Non-enhancing   Contrast-enhancing

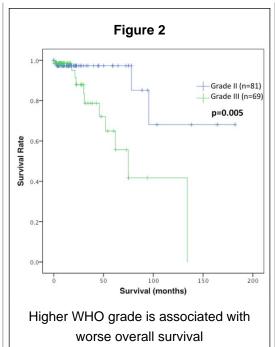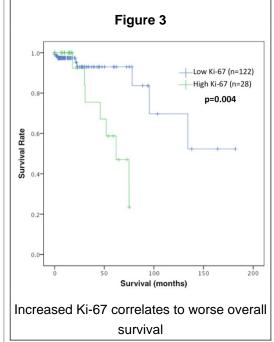Continuum of non-enhancing to contrast-enhancing oligodendroglioma

Results

Patients with CE+ (n=35) outnumbered those non-CE (n=20) patients; 10 CE+ tumors demonstrated rNec. Distribution of WHO grade was nearly even (grade II n= 29; grade III n=25). CE+ and rNec were associated with higher WHO histological grade (p<0.001), increased Ki-67 expression (p=0.003), and worse overall survival (log-rank p=0.04) (Figure 2 and 3). Tumors with NOTCH1 mutations were almost exclusively CE+ (13 of 14). 77.8% (14 of 18) of tumors with PI3K mutations and 82.4% (14 of 17) with FUBP1 mutations were CE+. CIC mutations were evenly distributed in both CE+ (n=16) and non-CE (n=9) groups. Key CNEs included gain of chromosomes 7p (n=7), 11p (n=9), and loss of chromosome 15q (n=9). Tumors with these CNEs were exclusively CE+.
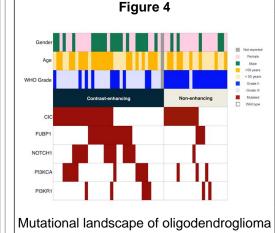
Methods

Fifty-five patients with oligodendroglioma were selected from The Cancer Genome Atlas with pre-operative MRIs available from The Cancer Imaging Archive. MRIs were reviewed for unequivocal contrast enhancement (CE+) and radiographic necrosis (rNec). Statistical analysis was performed to identify relationships between CE and rNec and WHO histological grade, cellular proliferation (based on Ki-67 expression), key genetic alterations, and copy number events (CNE).

Figure 2

Grade II (n=81)
Grade III (n=69)
p=0.005

Higher WHO grade is associated with worse overall survival

Figure 3

Low Ki-67 (n=122)
High Ki-67 (n=28)
p=0.004

Increased Ki-67 correlates to worse overall survival

Figure 4

Mutational landscape of oligodendroglioma

Conclusions

The use of radiographic contrast-enhancement as a surrogate for disease progression in this investigation revealed key genetic alterations and copy number variations that may help predict aggressive behavior in oligodendroglioma. These genetic signatures can better inform prognostication and may contain potential progression-related targets for future drug therapies.

References

1. Cancer Genome Atlas Research N, Brat DJ, Verhaak RG, et al. Comprehensive, Integrative Genomic Analysis of Diffuse Lower-Grade Gliomas. N Engl J Med. Jun 25 2015;372(26):2481-2498