Survival and low-grade glioma: the emergence of genetic information.


Abstract

Significant gaps exist in our understanding of the causes and clinical management of glioma. One of the biggest gaps is how best to manage low-grade (World Health Organization [WHO] Grade II) glioma. Low-grade glioma (LGG) is a uniformly fatal disease of young adults (mean age 41 years), with survival averaging approximately 7 years. Although LGG patients have better survival than patients with high-grade (WHO Grade III or IV) glioma, all LGGs eventually progress to high-grade glioma and death. Data from the Surveillance, Epidemiology and End Results (SEER) program of the National Cancer Institute suggest that for the majority of LGG patients, overall survival has not significantly improved over the past 3 decades, highlighting the need for intensified study of this tumor. Recently published research suggests that historically used clinical variables are not sufficient (and are likely inferior) prognostic and predictive indicators relative to information provided by recently discovered tumor markers (e.g., 1p/19q deletion and IDH1 or IDH2 mutation status), tumor expression profiles (e.g., the proneural profile) and/or constitutive genotype (e.g., rs55705857 on 8q24.21). Discovery of such tumor and constitutive variation may identify variables needed to improve randomization in clinical trials as well as identify patients more sensitive to current treatments and targets for improved treatment in the future. This article reports on survival trends for patients diagnosed with LGG within the United States from 1973 through 2011 and reviews the emerging role of tumor and constitutive genetics in refining risk stratification, defining targeted therapy, and improving survival for this group of relatively young patients.

KEYWORDS: GBM = glioblastoma; GWAS = genome-wide association study; HGG = high-grade glioma; LGG = low-grade glioma; MDA = MD Anderson Center; MGMT = O6-methylguanine-DNA methyltransferase; PCV = procarbazine, CCNU, and vincristine; RCT = randomized clinical trial; SEER; SEER = Surveillance, Epidemiology, and End Results; SNP = single-nucleotide polymorphism; TCGA = The Cancer Genome Atlas; TMZ = temozolomide; UCSF = University of California, San Francisco; epidemiology; genes; glioma; low grade; survival; treatment