Gliomatosis cerebri: Disparities beyond molecular similarities

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INTRODUCTION: Gliomatosis cerebri (GC) is a diffuse and extensive growth pattern that involves three contiguous lobes and mimics a low-grade lesion by imaging. It was considered at separate entity for gliomas until 2016, but molecular profiling differences did not warrant the separation. Survival is greatly diminished in these patients, and tumor behavior is markedly aggressive. We provide clinical basis to explore novel biomarkers of aggressive behavior in gliomas, and describe management and survival outcomes of the diagnosis.

METHODS: Cases were identified through the National Cancer Database (NCDB) from 2004-2014 using the ICD-O3 code 9381 as NCDB uses the 2007 World Health Organization Classification of Tumors of the Central Nervous System. We compared clinical characteristics and survival patterns of GC to grade III and IV gliomas (high-grade gliomas, HGG).

RESULTS: 397 cases of GC were identified and compared to 3.798 HGG. The median age of GC patients was 63 years, significantly older compared to HGG (51 years, p<0.01). There was a male predominance in both groups (56.2% and 57.3%, respectively). Twenty-three (5.8%) patients were younger than 19 years of age in the GC group, compared to 3.9% in the HGG group. Patients were more commonly white (86.9%, and 88.7%), with 5.8% and 6.7% Hispanics, and 6.3% and 6.2% blacks in the GC and HGG group. Over 25% of the GC cases were graded as WHO grade III, 15.4% as grade II, and 4% as grade IV. In the HGG group, 69.7% were grade III, and 30.3% were grade IV. WHO grade was not reported in 55.2% of the GC patients. In GC, the preferred treatment modality was watchful waiting (35.3%), followed by radiation and chemotherapy (17.9%), and radiation, chemotherapy and surgery (14.9%). Over 43% of GC patients received radiation, and over 45% received chemotherapy. Treatment was more aggressive in HGG with 52% receiving surgery, plus chemotherapy and radiation, and over 70% receiving radiation or chemotherapy. Surgical resection was performed in 28.5% of GC patients, compared to 75.4% of HGG. Chemotherapy only offered the best 5-year survival advantages for GC patients. Median survival in GC patients was 11.9 months significantly shorter than 31.6 months of HGG (p<0.0001). Grade IV was the only significant risk factor for mortality identified for GC patients.

CONCLUSION: The large extension of GC limits surgical and radiation approaches. Treatment is based on radiation and chemotherapy, with a high risk of neurotoxicity. Over 35% of patients did not receive any form of treatment. Survival was significantly impaired compared to other HGG, with no significant risk factor identified. We believe there is a biological explanation for the aggressiveness of these tumors that overlaps any other known risk factor, and confers treatment resistance that warrants further investigation.