Gliomatosis cerebri

The term gliomatosis cerebri has been dropped by the World Health Organization Classification of Tumors of the Central Nervous System 2016. Now, widespread brain invasion involving ≥ 3 lobes, frequently with bilateral involvement and often with posterior fossa extension, is considered a special pattern of spread within several diffuse glioma subtypes.

see Multiple gliomas.

Gliomatosis cerebri (GC) was an uncommon brain tumor defined as a diffuse neoplastic glial cell infiltration of the brain, involving more than two cerebral lobes and, occasionally, the infratentorial structures or the spinal cord.

Growth pattern

A growth pattern with extensive involvement of one cerebral hemisphere (≥ 3 lobes) or both cerebral hemispheres was once considered a separate nosological category but is now classified as a growth pattern with widespread involvement.

It may be seen with any of the diffuse gliomas, but is most commonly observed with anaplastic astrocytomas. There are no distinct molecular markers for this.

These malignancies consist of infiltrative threads that spread quickly and deeply into the surrounding brain tissue, or into multiple parts of the brain simultaneously, making them very difficult to remove with surgery or treat with radiation.

Gliomatosis cerebi behaves like a malignant tumor that is very similar to Glioblastoma. GC of the oligodendroglial phenotype is extremely rare, especially in the paediatric setting [1)].

While gliomatosis cerebri can occur at any age, it is generally found in the third and fourth decades of life.

It may affect any part of the brain or even the spinal cord, optic nerve and compact white matter. Clinical manifestations are indefinite, and include headache, seizures, visual disturbances, corticospinal tract deficits, lethargy, and dementia. A case of gliomatosis cerebri presenting as rapidly progressive dementia and Parkinson's disease like symptoms has been described in an 82 year old woman.

Diagnosis

Before the advent of MRI, diagnosis was generally not established until autopsy. Even with MRI, however, diagnosis is difficult.

Typically, gliomatosis cerebri appears as a diffuse, poorly circumscribed, infiltrating non-enhancing

lesion that is hyperintense on T2-weighted images and expands the cerebral white matter. It is difficult to distinguish from highly infiltrative anaplastic astrocytoma or Glioblastoma.

Management

All patients in whom GC is radiographically suspected should have a histopathologic confirmation. Given the diffuse involvement of a large brain volume, the role of surgery primarily lies in securing a tissue diagnosis. Some patients undergo partial resection of an area of T2-signal abnormality or T1 contrast-enhancement to secure sufficient amount of tissue to overcome sampling error. When patients are symptomatic due to edema and mass effect, partial resection can be done with an aim of tumor debulking. It is unclear if extent of surgical resection provides any survival benefit. Perkins et al. reported outcomes in 30 GC patients of which 19 received biopsy and 11 had a partial resection. The median survival (21 versus 18 months, p value = 0.96) did not reach statistical significance [2].

Outcome

The prognosis for gliomatosis cerebri is generally poor.

Surgery is not practical considering the extent of the disease, standard chemotherapy (nitrosourea) has been unsuccessful, and while brain irradiation can stabilize or improve neurologic function in some patients, its impact on survival has yet to be proven.

In 2014, Weill Cornell Brain and Spine Center launched an international registry for Gliomatosis Cerebri, where tissue samples can be stored for genomic study.

Case series

47 patients with histological diagnosis of WHO grade 2 glioma or WHO grade 3 glioma and Gliomatosis cerebri (GC) imaging pattern were identified. GC criteria were confirmed by an independent review. Patients with WHO grade II or III glioma with non-GC pattern served as control cohort (n = 343).

Within the GC patient cohort, lower WHO grade, mutated isocitrate dehydrogenase 1 (IDH1) status, and absence of contrast enhancement were associated with better OS. Compared to the control cohort, patients with GC had significantly shorter OS independent of histological diagnosis or IDH1 mutation status. Patients with GC preferentially received chemotherapy alone (62 vs. 18%), and less frequently radiochemotherapy (21 vs. 27%). OS was significantly shorter in the GC cohort compared to the non-GC cohort both for chemotherapy (3.9 vs. 7.6 years, p = 0.0085) and for combined radiochemotherapy (1.1 vs. 8.4 years, p < 0.0001). However, when only patients who received biopsy plus chemotherapy were analyzed, the differences lost statistical significance (3.5 vs. 6.6 years, p = 0.196).

They found major differences in the selection of first-line therapies of GC versus non-GC patients. These results suggest that these differences may partly account for the worse prognosis of GC patients [3].

Case reports

2011

Mitchell et al. describe an unusual case of oligodendroglial GC diagnosed in a 16-year-old boy with Ollier disease. This is the first case of GC reported in a child with Ollier disease [4].

[1] [4]

Mitchell RA, Ye JM, Mandelstam S, Lo P. Gliomatosis cerebri in a patient with Ollier disease. J Clin Neurosci. 2011 Nov;18(11):1564-6. doi: 10.1016/j.jocn.2011.03.025. Epub 2011 Aug 24. PubMed PMID: 21868231.

[2]

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5545748/

[3]

Divé I, Steidl E, Wagner M, Filipski K, Burger MC, Franz K, Harter PN, Bähr O, Fokas E, Herrlinger U, Steinbach JP. Gliomatosis Cerebri Growth Pattern: Association of Differential First-Line Treatment with Overall Survival in WHO Grade II and III Gliomas. Oncology. 2021 Jan 20:1-10. doi: 10.1159/000512562. Epub ahead of print. PMID: 33472203.