Gliomas

Gliomas are tumors of glial cells, the non-neuronal cells of the brain and spinal cord. They are the most common tumors of the central nervous system (CNS) tissue. Gliomas occur in both adults and children and their prognosis depends on the underlying subtype and grade, i.e. how malignant the tumor is. A tentative diagnosis can be made using neuroimaging techniques (e.g. MRI) but the gold standard for diagnosis is the microscopic examination of tumor tissue following a surgical biopsy. The microscopic examination may be complemented by molecular tests. Only a trained specialist, a neuropathologist who has detailed knowledge of the many different diseases of the nervous system, should carry out the microscopic examination. This is important because several other CNS diseases including multiple sclerosis, CNS infections, metastases of peripheral tumors or even an infarct can present with tumor-like signs. The neurosurgeon in theatre is more relaxed and can work better if there is specialist support especially intraoperatively.

The microscopic examination of the tumor tissue (histology) reveals the tumor type. Gliomas are named after the normal glial cells each subtype appears to share morphological similarities with. The main glial cell types of the CNS are astrocytes and oligodendrocytes. A third common glial cell type, the microglia, populate the CNS during embryonic and early postnatal development and cause tumors so rarely that there is no official classification entry yet. Ependymal cells line the fluid-filled spaces in the brain that are called ventricles. Ependymal cells are related to astrocytes. Tumors thought to arise from ependymal cells are called ependymomas. They infiltrate the brain tissue less diffusely than the other gliomas and this is one main reason for their overall less malignant behavior. In other words, ependymomas are more “solid” than astrocytomas and oligodendrogliomas and this is also visible upon microscopic inspection.

A grade that predicts the biological behavior of a glioma, which may be malignant, is only assigned once the type of tumor has been recognized. The WHO classification of CNS tumors distinguishes the following subtypes of glioma:

Astrocytic tumors

Pilocytic astrocytoma (I)
- Pilomyxoid astrocytoma (II)

Subependymal giant cell astrocytoma (I)

Pleomorphic xanthoastrocytoma (II)

Diffuse astrocytoma (II)
- Fibrillary astrocytoma
- Gemistocytic astrocytoma

Protoplasmic astrocytoma
Anaplastic astrocytoma (III)
Glioblastoma (IV)
Giant cell glioblastoma
Gliosarcoma
Gliomatosis cerebri (III)

Oligodendroglial tumors
Oligodendroglioma (II)
Anaplastic oligodendroglioma (III)

Oligoastrocytic tumors
Oligoastrocytoma (II)
Anaplastic oligoastrocytoma (III)

Ependymal tumors
Subependymoma (I)
Myxopapillary ependymoma (I)
Ependymoma (II)
Cellular
Papillary
Clear cell
Tanycytic
Anaplastic ependymoma (III)

After the type of tumor has been identified based on morphological criteria, which are applied to routine histological stains and sometimes complemented by immunohistochemistry, a grade is assigned. The tumor grade, which indicates the biological behavior of the tumor to the clinician, is very important for the choice of therapeutic regimen.

The grades of the different glioma subtypes, or variants, are shown as Roman numerals in brackets behind the respective glioma subtype in the above list. Therefore, the WHO classification of CNS tumors essentially represents a malignancy scale aimed at helping the clinician to choose the right treatment. It is not always strictly logical in a biological sense, which can be confusing to researchers who may not be aware of this. For instance, there is no pilocytic astrocytoma grade II and there is no diffuse astrocytoma grade I. These two entities are very different biologically but share the common family name, astrocytoma.

A tumor is referred to as grade I if the biopsy shows only very few dividing cells and the chances of the patient being cured by the surgical resection alone are high. A grade II tumor in contrast is likely to recur and may even worsen over time. This is called tumor progression and is usually the case for diffuse astrocytoma, oligodendroglioma and oligoastrocytoma. Histological signs of such a malignant or WHO grade III glioma include so-called atypical nuclei and the presence of dividing cells. The biological term for cell division is mitosis. Tumor means literally "swelling" or too much tissue, which is due to too many cells. The more cells a tumor generates the faster it grows and the more mitoses are visible in the microscope. Generally, patients with grade III tumors are treated by adjuvant radiation and/or chemotherapy. Some tumors infiltrate the brain tissue extensively, which makes them even more difficult to treat. This applies to the diffusely growing gliomas: astrocytoma, oligodendroglioma, oligoastrocytoma and notably glioblastoma. Glioblastoma is an example of a WHO grade IV tumor. In addition to malignant looking cells and lots of mitoses, such tumors tend to show large areas of cell death (necrosis) because they grow so rapidly that the blood supply cannot keep up with their growth rate. However, grade IV tumors also stimulate the formation of new blood vessels (neoangiogenesis) and the presence of the latter is another histological sign of their malignancy.

In summary, the grade of a brain tumor can be used as a prognostic factor. Survival of more than five years is common for patients with a WHO grade II glioma whereas 2-3 years are typical for a WHO grade III tumor. The outcome is much worse for WHO grade IV glioblastoma where less than half of patients survive for more than one year.

Most contemporary research focuses on the analysis of the glioma as such but since the infiltrative behavior of gliomas is a critical factor for their prognosis, new knowledge gained in the neurosciences on what the brain does or does not do to glioma is increasingly appreciated. One promising avenue for new therapies to take may be to target the brain's defense cells, the microglia, which appear to be controlled by the glioma. However, such research is in its infancy.

Author:

PROFESSOR MANUEL B. GRAEBER MD PhD FRCPath
Neuropathologist
Barnet-Cropper Chair of Brain Tumour Research
The Brain and Mind Research Institute
UNIVERSITY OF SYDNEY
100 Mallett Street, Camperdown NSW 2050