Glioblastoma multiforme (GBM)

Glioblastoma multiforme (also referred to as glioblastoma, GBM or grade IV astrocytoma) is an uncommon cancer yet accounts for more than half of all diagnosed *primary malignant* brain *tumours*. *Primary* tumours are those that have arisen at the site they are detected, as opposed to secondary tumours (or metastases) which have arisen elsewhere and spread to the site they are detected, generally via the blood or lymphatic system. *Malignant* tumours are those that show evidence of having invaded into surrounding tissue. *Tumours* are any abnormal growth of cells. GBM may also be referred to as high grade glioma, a general term for either type III or IV brain tumours.

Most often GBM is diagnosed in middle-aged adults, but it can also occur in young adults and children. It occurs slightly more often in men than women.

It is not known what causes GBM in most people. Exposure to ionising radiation (X-rays and gamma rays) is a known risk factor, but this is a very rare cause. Other risk factors include ageing and being male, and in very rare cases inherited genetic susceptibility (e.g. people with neurofibromatosis type I or II, Li-Fraumeni syndrome or Turcot syndrome). There is no strong evidence that non-ionising radiation (radio waves, microwaves, ultraviolet waves or infrared radiation) causes GBM, including the use of mobile phones.

GBM cancer cells most resemble a type of brain cell called an astrocyte. These are abundant in the brain and are thought to support and aid the function of nerve cells. Whether GBM arises in mature astrocytes or in a less mature cell that later in its development can become an astrocyte is still unclear. Current research suggests that gene mutations are the molecular basis for GBM and the exact nature of these mutations likely influences the behaviour of the tumour (e.g. rate of growth and response to treatment).

Symptoms that people experience before being diagnosed with GBM vary from person to person and often depend on where the tumour is located, how large it is and how quickly it is growing. Headache, confusion, memory loss and seizures (fits) are common. Sometimes symptoms are similar to a stroke, such as numbness and difficulty speaking. Symptoms can develop slowly (over weeks to months) or quickly (such as a first seizure).

GBM is generally first detected with a CT (computed tomography) scan. A contrast-enhanced MRI (magnetic resonance imaging) scan (one performed with the injection of a dye into a vein) is usually performed as well to better visualise the extent of the tumour.

While a CT or MRI scan may suggest a GBM, the only way to confirm the diagnosis is to have a pathologist examine the tumour under a microscope. A small piece of tumour can be removed by a needle biopsy, but more commonly surgery is performed to remove as much of the tumour as possible at an open resection and a larger biopsy specimen or specimens is collected for examination by a pathologist.

Following a diagnosis of GBM, the choice of what to do next will involve careful consideration and important decisions. This will involve the patient, their family or carers and a team of specialists and other health care workers involved in the patient's care.

If the patient hasn't already had an open resection for diagnostic purposes, is fit to undergo an operation and the tumour is of a size and in a location suitable for resection, surgery is recommended to remove as much of the tumour as possible to improve survival. Surgery often

involves stereotactic guidance to accurately locate the tumour, and in some cases the patient may need to be awake to help the neurosurgeon avoid damaging regions of the brain with important functions.

Generally GBM cannot be completely removed by surgery. This is generally because of the infiltrative nature of these tumours and the need to preserve as much healthy brain as possible. Radiotherapy is generally recommended for patients well enough to receive it to improve survival. A dose of 60 Gy is usual, given as 30 daily doses of 2 Gy over approximately six weeks.

Chemotherapy is also generally recommended for patients well enough to receive it. Temozolomide is commonly used, beginning at the same time as radiotherapy and continuing for six months. Alternatively, carmustine (Gliadel) chemotherapy wafers may be inserted at the time of surgery when the tumour is removed.

Despite the combination of surgery, radiotherapy and chemotherapy, the outlook for GBM is generally not good. Only half of patients survive more than 14 months and 1 in 5 more than five years.

After treatment, patients are generally monitored with MRI to watch for recurrence of their tumour. If GBM does recur there is no clear evidence for the best course of action. Further surgery and chemotherapy with temozolomide or another drug (e.g. bevacizumab, irinotecan or thalidomide) may be considered. Patients also may be offered the opportunity to participate in clinical trials of new treatments.

This overview of the clinical aspects of GBM is offered only as general advice for patients, their carers and other interested parties seeking a summary of some of the issues faced by a person diagnosed with GBM. For a more in depth discussion the interested reader is referred to the excellent publication, “Cancer Council Australia. Adult gliomas (astrocytomas and oligodendrogliomas): a guide for patients, their families and carers. Sydney: Cancer Council Australia / Clinical Oncological Council of Australia; 2011”.

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