PERSPECTIVE


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# See the whole picture

To understand brain cancer fully, it is imperative to pay more attention to the neurological symptoms of patients, says **Terri S. Armstrong**.

Glioma, a broad category comprising tumours that originate in the brain, is the most common primary cancer of the central nervous system in adults. Almost all cases of glioma relapse despite intensive treatment, and those affected often die of the disease. In contrast to other types of solid-tumour cancer, people with glioma have a disease trajectory that encompasses both a cancer and a neurological disorder. The discovery of glioma typically follows the development of neurological signs and symptoms. Such an onset can occur suddenly, with those affected requiring urgent or emergency medical care, or more insidiously, with neurological signs and symptoms that slowly progress in severity and extent. These symptoms, which include headaches, seizures, neurocognitive dysfunction and deficits in motor or language skills, have wide-reaching effects that can affect a person's ability not only to work, but also to care for themselves.

Most neuro-oncologists, however, have not focused their research on the clinical manifestations of glioma. Instead, researchers and even clinicians have concentrated almost exclusively on the biology that underlies such tumours, which has been codified through extensive molecular profiling[1,2].

But glioma is not merely a set of tumour types, and the disease cannot be defined solely by the biological changes with which it is associated. The reality is that the clinical presentation and trajectory of glioma's neurological symptoms form an integral part of the biological behaviour of the disease. I propose an alternative way of thinking about glioma that I hope will lead to better outcomes for patients.

Glioma should be considered as a disease process that is defined by two sequences of change that run in parallel — one relating to glioma's biological causes and effects (at the level of cells and tissues) and the other relating to its symptoms and impact on function. If we can understand the biological processes that lead to the cancer and to its symptoms, and then target those processes, perhaps we can prevent the symptoms from occurring, altogether.

Shifting conventional thought on glioma in this way is important because, more so than in many other types of cancer, symptoms of the disease play a key part in the disease process. In cases of high-grade glioma, the severity of a person's neurological symptoms at diagnosis and how soon worsening occurs have been shown to predict both disease progression and survival time[3,4].

Clinicians, however, routinely offer fewer treatment options to people who have many or extreme symptoms, or whose functions have been limited considerably, in the belief that their tolerance of therapies will be poor and that they will be unlikely to respond. Such people are also infrequently recruited to clinical trials. In effect, care providers are neglecting to consider the symptoms of patients with glioma as being integral to treatment decisions, or as useful biomarkers of the response to treatment. The present focus on the biology of glioma has limited the development of therapies that are designed to improve symptoms and functioning — a particular shame, given that most people with brain cancer express the desire for a treatment that attenuates symptoms in addition to helping them to live longer[5].

A symptom-sensitive approach to glioma care could offer great benefit to those with the disease. When combined with the analysis of biological samples, it could point the way to the optimal therapeutic regimen — and might even be a useful marker of the response to treatment. For example, it has been shown that treating people with a certain subtype of glioma can help to reduce the occurrence of seizures. However, most clinicians continue to define success in clinical trials of potential therapies by the conventional outcomes of tumour shrinkage or extended survival times, rather than by the alleviation of neurological symptoms. Essentially, we do not use such symptoms as biomarkers that define glioma and its subtypes, or a person's response to treatment. Recognizing glioma's symptomatic subtypes at diagnosis, as well as including measures to define disease trajectory over time, forces us to consider glioma's clinical course as being integral to the disease. This shift will facilitate the development of treatments that are directed at easing the burden of symptoms.

**GLIOMA'S NEUROLOGICAL SYMPTOMS FORM AN INTEGRAL PART OF THE DISEASE'S BIOLOGICAL BEHAVIOUR.**

Given the mandate from patients to develop treatments that improve or stabilize symptoms, as well as the evidence to show that symptoms can be relevant predictors of a person's prognosis and treatment response, it is imperative that the identification of glioma subtypes takes into account the presentation and trajectory of symptoms.

The main reason that this is not already standard practice is the cost and effort that would be required to collect such patient-centric information — a burden that would have to be shared by patients, care providers and healthcare systems. So far, gathering these data in clinical trials has often been optional and is hampered by archaic collection methods such as pen and paper, leading to major gaps in our knowledge.

The good news is that mechanisms and validated instruments have been developed that facilitate the brief, standardized and electronic collection of symptomatic data in people with glioma. There is also evidence from people with other solid-tumour cancers that the collection of these data correlates with fewer visits to emergency medical facilities and hospitalizations[6]. It would be ill-advised to evaluate the status of a person's glioma without sampling the tumour and performing neuroimaging. It seems equally short-sighted to ignore the contribution that symptoms can make to choosing the best therapeutic approach. ■

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