A focus on psychological needs of brain tumor patients and leveraging epidemiology

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In this issue of *Neuro-Oncology Practice*, 2 overarching themes are explored: the psychological needs of patients with brain tumors, and disparities in brain tumor treatment and outcome.

Brain tumor patients rely on health care providers to provide the prognostic information they need to make medical, personal, and financial decisions. Forst and colleagues (p. 490) conducted a prospective survey of patients with malignant glioma and their caregivers, finding that although both groups considered knowledge of prognosis to be very important, they reported that prognosis was infrequently discussed during oncology visits. Furthermore, patients and caregivers often held inaccurate perceptions regarding prognosis. For example, a large majority of patients reported their tumors were curable, and almost one-third reported that their oncologists' primary goal was curative. Notably, patients who reported their cancer as incurable experienced greater depressive symptoms.

Continuing with the theme of the psychological effects of awareness of mortality, Loughan and colleagues (p. 498) evaluated death-related distress in a prospective single-institution study, finding that most primary brain tumor patients endorsed moderate to severe death-related distress, the presence of which was associated with symptoms of generalized anxiety and depression. Death-related anxiety, a subdomain of death-related distress, was observed at a much higher rate in brain tumor patients than in prior reports of patients with other advanced cancers. Together these studies show that achieving optimal patient-clinician communication regarding prognosis and providing support for patients struggling with the psychological implications of having a life-limiting illness are areas of unmet need in neuro-oncology.

Neuropsychiatric challenges within neuro-oncology are not limited to the glioma patient population. Maurer and colleagues (p. 507) used a health care claims database to evaluate the association between mental health disorders (MHDs) and untreated meningioma, reporting that 33.5% of patients carried a diagnosis of MHD prior to meningioma discovery and 16.1% were diagnosed with MHDs in the subsequent year. Regardless of the suspected direction of causality (ie, whether distress over meningioma discovery triggered MHDs or whether meningioma was incidentally discovered during

an evaluation that would have inevitably resulted in a diagnosis of MHD), it is clear that this patient group has a significant burden of psychological comorbidity.

Each of these studies illustrates that patients with brain tumors have important psychological needs that must be met as part of comprehensive neuro-oncologic care. Although medication therapy is just one aspect of addressing such needs, antidepressants may be useful for some patients with glioma and comorbid psychological symptoms. In fact, some antidepressants have demonstrated antitumor activity in preclinical studies. Gramatzki and colleagues (p. 514) conducted a retrospective study to evaluate the use of antidepressants in patients with glioblastoma within the Canton of Zurich, Switzerland. They report that 16.1% of patients took antidepressants at some point during their disease course. However, no association with survival was observed either in the glioblastoma patient group as a whole or when stratified by *MGMT* mutation status, so the hypothesis that antidepressant therapy may have clinically significant antitumor activity in addition to its symptomatic benefits was not supported.

Leggiero and colleagues (p. 477) explored a more novel strategy for physical and psychological symptom management in cancer patients by conducting a systematic review of the use of virtual reality (VR) interventions. They found that although little has been published on VR interventions in patients with brain tumors specifically, supportive data exist for use of VR strategies in cancer patients generally, with benefits including decreased anxiety, physical discomfort, and distress. The authors conclude that VR may be a promising tool in the brain tumor patient population and that more research is warranted.

Disparities in health care delivery remain an issue of great societal importance, and differences between groups in brain tumor incidence rates, treatment, and outcome continue to be examined in neuro-oncology. Lu and colleagues (p. 522) used a large cancer database to evaluate demographic factors associated with the treatment of elderly patients with glioblastoma in the United States. They found that the odds of receiving "triple therapy" including tumor resection, radiation, and chemotherapy varied by region and was significantly reduced in

older patients, female patients, Hispanic patients, and by various markers of low socioeconomic status (SES).

Several studies have reported that glioma risk increases with SES, a seemingly paradoxical finding in that many other cancers demonstrate an inverse relationship with SES. Fischer and colleagues (p. 531) studied a German patient group using health insurance status as a surrogate for SES. They found that private insurance, a marker of high SES, was associated with increased malignant glioma risk, and that the association was independent of patient age or sex.

Rogers and colleagues (p. 541) performed a retrospective study evaluating the association between metabolic syndrome and glioblastoma incidence as well as survival. They found that the rate of metabolic syndrome in their glioblastoma cohort was slightly higher than in the US population as a whole, though not necessarily higher than in the rate in their local geographic region. Further, they report that patients with metabolic syndrome demonstrated a trend toward poorer overall survival, an association that became significant in subgroup analyses. Because the prevalence of medical comorbidities such as metabolic syndrome varies with race and SES, future analyses including all of these factors will be important in understanding predictors of glioma survival.

Achey and colleagues (p. 549) used cancer registry data from the United States to evaluate the incidence and survival of ependymoma. They report that anaplastic ependymoma is most common in children aged 4 years and younger, whereas ependymoma not otherwise

specified is more common in adults. Ependymoma incidence was significantly higher in white populations compared to any other racial group. Though black individuals had a much lower incidence of ependymoma, black patients experienced a 78% increased risk of death compared to white patients. Additional predictors of poorer survival included adult age at diagnosis, anaplastic tumors, subtotal surgical resection, and nonspinal tumor location.

Reflecting significant recent interest in this topic, Montoya and colleagues (p. 465) provide a thorough but concise introduction to immunotherapeutic approaches to brain tumor treatment, including the rationale for the immunotherapy and challenges specific to the brain tumor population. Treatment paradigms reviewed include the spectrum of tumor vaccines, immune checkpoint inhibitor therapy options, oncolytic viruses, and CAR-T (chimeric antigen receptor T-cell) treatment. The authors acknowledge that results of glioma immunotherapy trials to date have fallen well short of early hopes, and conclude with a discussion of potential paths forward such as investigation of combination therapy approaches.

Central neurogenic hyperventilation is a rare but important manifestation of brainstem involvement by CNS tumors. Briard and colleagues (p. 559) present a case of its successful treatment, and review the literature to identify 31 reports totaling 33 cases of this condition. They conclude that although symptomatic medical management may be of benefit, definitive treatment of the underlying neoplasm is needed for durable control.