Neurological Tumors

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Topic

Neurological tumors belong to two broad groups: **primary brain tumors** and **secondary, or metastatic, brain tumors**. Primary brain tumors are those that arise from abnormal growth of the brain, while metastatic brain tumors originate elsewhere in the body and metastasize to the brain. Malignancy of tumors varies greatly and generally depends on several factors, including tumor location related to accessibility for treatment, vascular/endothelial proliferation, mitotic features, nuclear atypia, and necrosis. The World Health Organization developed a **grading system** (I–IV) in 1993 (revised in 2000 and again in 2007 [1]) to classify tumors according to biological potential, with higher grades (grades III and IV) associated with greater malignancy.

Some *fast facts* about primary and metastatic brain tumors [2–6]:

A. ***Primary brain tumors***
  - More common in children and elderly adults
  - Less common overall than metastatic brain tumors
  - Typically do not metastasize to other areas of the body
  - Categorized according to histology
  - Some more common subtypes include:
    - Gliomas—originate from glial cells.
      Astrocytomas—develop from astrocytes, can be quite benign (pilocytic astrocytoma, grade I) or quite malignant (glioblastoma multiforme [GBM], grade IV).
      Ependymomas—develops from ependymal cells.
      Oligodendrogliomas—originate from oligodendrocytes.
    - Meningiomas—originate from the meninges, the membranes that surround the brain and spinal cord.
    - Pituitary tumors—originate from pituitary gland (e.g., adenomas, craniopharyngiomas, and carcinomas).
    - Primary cerebral lymphomas—originate from lymph tissue within the brain.
    - Medulloblastomas—a type of embryonal tumor that originates in posterior fossa, generally high grade, more commonly occurs in children than in adults.
    - Germ cell tumors—originate from immature germ cells in pineal or suprasellar regions of the brain.

B. ***Metastatic brain tumors***
  - More common overall than primary brain tumors.

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- Occur more often in adults than in children.
- Typically arise from lungs, breasts, skin, colon, kidney, or genitourinary origins.
- Lung and breast cancers and melanomas are most common origin, primarily because they are more common cancers overall.
- Typically affect cerebral hemispheres at the gray and white matter junction, and cerebellum metastases are common also.
- Metastatic brain tumors are highly malignant; life expectancy is less than 6 months for most patients with brain metastasis, but most die of systemic, not intracranial, involvement.

Importance

Brain tumors affect a significant number of children, adults, and elderly individuals each year, given the following statistics [2]:

- In 2014, there were 343,175 incidents involving brain and central nervous system (CNS) tumors (primary and metastatic combined).
- It is estimated that 68,470 new cases of primary brain tumors will be diagnosed in 2015, while an estimated 13,770 individuals will die of primary malignant brain and CNS tumors the same year.
- The five-year survival rate following diagnosis of primary malignant brain and CNS tumor is only 34.2 % (according to data from 1995 to 2011), with rates decreasing with age.

Increasing medical advances have dramatically improved the survival rate for individuals affected by brain tumors. However, survivors of all ages often live with significant rehabilitative needs and lasting physical, cognitive, and emotional problems. Eighty percent of brain tumor survivors have cognitive deficits, 78 % have residual weakness, and 53 % have visual and perceptual deficits, among other problems [7]. More than 75 % have three or more areas of deficit [7]. Notably, rehabilitative needs are neither significantly different in those with malignant versus benign tumors, nor among those with primary versus metastatic brain tumors [8]. The lasting impact for brain tumor survivors can occur either as a direct result of the tumor or as a result of the brain tumor treatment.

A. ***<u>Treatments and Their Impact</u>***

The three primary means of treatment for brain tumors are (1) **neurosurgical resection** (gross total resection [GTR]; near total resection [NTR]; or subtotal resection [STR]), (2) **cranial radiation therapy (CRT)**, and (3) **chemotherapy**.

1. **<u>Neurosurgical resection</u>**

   The possibility of neurosurgical resection varies depending on the tumor location. Tumors within deep subcortical regions are more difficult to operate on because of access. When resection is possible for a brain tumor, the extent of resection (i.e., GTR, NTR, and STR) depends on location and how clearly defined the borders are; that is, it depends on the invasiveness of the tumor on surrounding brain tissue and whether the brain tissue is amenable to being removed (i.e., some functions may be too important and thus spared in the resection). It is more challenging to achieve total resection of tumors with anaplasia, extensive vascular proliferation, and/or necrosis, making tumors with these qualities characterized as malignant (grades III and IV, e.g., anaplastic astrocytoma and GBM). Regardless, neurosurgery, when warranted, is a significant medical procedure that brings with it an array of potential complications (e.g., craniotomy, hydrocephalus, and need for shunt placement).

2. **<u>Cranial radiation therapy</u>**

   Radiation can be delivered in varying doses, as well as to the whole brain or to more focused regions [9]. There is an abundance of literature to suggest that CRT is associated with significant cognitive deficits across various domains, including attention, learning, memory, processing speed, visual-spatial skills, and higher-order executive functions [9]. Greatest risk for cognitive impairment has been found when CRT is administered in higher fractionated doses (i.e., greater than 2 Gy), in higher total dosage overall, with larger brain volume treated, for longer duration of treatment, in combination with chemotherapy, when used in patients under 7 years old or older than 60 years old, or used with individuals with vascular risk factors [10–12]. Radiation therapy is thought to damage cognitive function by means of metabolic and white matter changes, necrosis, and by affecting neuronal function and synaptic plasticity [13]. Radiation therapy can also result in encephalopathy, which can be acute (less than two weeks after treatment), early delayed (one to four months after treatment), or late delayed (more than 4 months after treatment), and can result in lethargy, cognitive and behavioral changes, as well as changes associated with tumor/CRT location [6]. Importantly, suspected encephalopathy must be distinguished from tumor recurrence. Radiation therapy can also induce brain edema, thus corticosteroids are often administered prophylactically [6] and come with their own set of potential side effects.

3. **<u>Chemotherapy</u>**

   Many chemotherapy agents for brain tumors are delivered intrathecally (directly into cerebrospinal fluid) or by intraarterial means, and the protection of the blood–brain barrier makes an effect on brain tumors difficult in many instances. Many adverse effects have been identified following chemotherapy treatment, including alopecia, fatigue, nausea, constipation, headache, and cognitive deficits [6]. In addition, chemotherapy can result in neurotoxicity and brain edema, which often warrants close monitoring and prophylactic corticosteroid treatment [6], similar to CRT. Cognitive impairment is hypothesized to result from direct neurotoxic damage, injury to glial cells, damage to neuroprotective hormones, DNA damage due to oxidative stress, and/or immune dysregulation [14]. Similar to CRT, damage following chemotherapy is associated with cumulative dose, intensity of individual doses, and duration/quantity of cycles of treatment [14].

Practical Applications

A. ***<u>Discovery of Brain Tumors</u>***

   Often, brain tumors are discovered prior to psychology involvement, the latter of which is warranted for emotional reasons as well as for neuropsychological assessment. First symptoms are often **focal** in nature and consistent with dysfunction in the brain region where the tumor resides, such as headaches, behavioral and personality changes (frontal), visual symptoms or hallucinations (occipital), perceptual or proprioceptive effects (parietal), language or emotional symptoms (temporal), endocrine dysfunction (pituitary involvement), or balance problems, incoordination, and dysarthria (cerebellar) [4]. Cortical tumors often present with **seizure activity** in the affected region, and this is the presenting complaint in 15–20 % of patients with brain tumors [6]. Symptoms consistent with **mass effect** and **edema** can also arise, such as focal symptoms at the region of mass effect or more general symptoms of edema, such as nausea, vomiting, and fatigue [4]. **Cognitive complaints** are also common, thus it may be important for a neuropsychologist to refer for neuroimaging if no clear etiology of cognitive impairment is otherwise identified from assessment.

B. ***<u>Diagnosis</u>***

   Once symptoms are identified, a referral to a neurologist for assessment is warranted. Means of identifying brain tumors include: a thorough neurologic exam, neuroimaging scans, laboratory tests (i.e., of blood and/or cerebrospinal fluid), and/or biopsy, the latter of which is completed at resection for histological identification, tumor classification, and prognosis estimation [4].

C. *Cognitive Impairment and Neuropsychology Involvement*

Cognitive impairment as a result of brain tumor and/or treatment is common, as noted previously. Possible reasons for a patient to be referred for neuropsychological assessment include [4, 6]:

- To establish a baseline of cognitive functioning before treatment.
- To assess for language dominance if temporal regions are affected and neurosurgery is considered.
- To assess cognitive status after treatment (typically compared to baseline, if baseline scores are available).
- To assess cognitive functioning after tumor recurrence.
- To acquire specific recommendations given remission/success of treatment.

1. **Cognitive and Behavioral Deficits**

Neuropsychologists will often uncover decreased IQ scores (particularly among children affected early by brain tumor and treatment, given negative impact on learning), poor academic achievement, as well as deficits in attention/short-term memory, processing speed, learning and long-term memory, and higher-order executive functions [15]. Comprehensive assessment may also reveal social dysfunction and emotional effects [15]. Children are often removed from school for extended periods of time for treatment, resulting in difficulties with re-integration, social alienation, and incomplete academic instruction, among other problems. Childhood brain tumor survivors' areas of difficulties often persist into adulthood [6] with generally poor follow-through across health care systems, as many patients transfer physicians upon becoming adults. Further, adult survivors of brain tumors are less likely to acquire employment than the general population and are more likely to require assistance with activities of daily living [6].

2. **The Neuropsychological Assessment and Report**

A neuropsychologist should always consider the referral question when designing a test battery and composing the report. If previous testing has been completed, it is often most helpful to repeat tests where possible, calculate reliable change indices to determine progression/change since last assessment, and administer tests with careful consideration of their reliability and validity characteristics with repeat testing/comparison now or later in mind. Furthermore, the neuropsychologist should assume that there will be future assessments completed; thus, it is important to include raw scores within the report for future comparison whenever possible. Regardless of the reason for referral, however, recommendations are of utmost importance for this population; parents and teachers of children with brain tumors consistently rate the recommendations section as most helpful [15]. A good neuropsychological assessment report will typically identify cognitive and behavioral strengths and weaknesses as well as strategies to capitalize on strengths and accommodate or compensate for weaknesses [15]. In addition, recommendations that include factors for future consideration (i.e., how to access services, how to deal with/manage new life milestones, prognosis of cognitive recovery/dysfunction, etc.) will be helpful. The neuropsychologist's role is to educate others involved with the patient in a way that is easily understandable to all potential audience members [15].

3. **Cognitive Rehabilitation**

Cognitive rehabilitation is an emerging field that holds a wealth of potential for individuals recovering from brain tumors, and the provision of these interventions holds important roles for neuropsychologists, psychologists, speech and language pathologists, and other specialists within the oncology team. Cognitive rehabilitation entails identification of strengths and weaknesses, typically following neuropsychological assessment, and intervention to capitalize on strengths and address weaknesses via remediation (with the goal of improvement) and/or compensatory strategies (with the goal of better functioning when improvement may or may not be possible). Interventions may be provided either during one-on-one sessions with a therapist or within group (typically disorder-specific) settings.

4. **Medication for Cognitive Deficits**

   There is a large body of literature investigating the utility of pharmacologic treatment for cognitive deficits, with some evidence suggesting that methylphenidate may yield performance improvements in some cognitive areas, including attention, memory, reasoning, and verbal fluency, as well as in motivation [6]. Additional research has focused on donepezil, modafinil, and ginkgo biloba, but with little benefit, highlighting the need for more research in this area.

5. **Common "Side Effects" of Brain Tumors**

   Individuals with brain tumors present with a variety of problems, sometimes specific to the focal region of tumor mass and other times more generalized. Some common problems of which providers should be aware [6]:

   - **Seizures** occur in 20–40 % of patients with high-grade tumors and about 50–85 % of patients with low-grade tumors. Antiepileptic drugs are often prescribed for management but demonstrate little prophylactic help.
   - **Headache** is present in between 50 and 70 % of patients with brain tumors, often of the tension subtype. Highly persistent headaches should be investigated as potentially recurred tumor.
   - **Fatigue** is common, directly from the tumor or as a side effect of treatment. Psychologists may provide support to patients through education regarding detailed exploration of triggers and mitigating techniques for fatigue such as pacing strategies and sleep hygiene.
   - **Mood** dysregulation can result from direct tumor effects or the complicated sequelae of life changes related to tumor occurrence. There is an important role for psychology in supporting the adaptation of individuals after diagnosis and throughout the treatment and recovery process.

6. **Family and Caregivers**

   Families and caregivers of patients with brain tumors often experience challenges such as emotional responses to having a sick loved one, changing relationships and family roles, caregiver burden, financial difficulties, and interaction with medical systems and medical providers [6, 16]. Review of the extensive literature on family functioning after a child or loved one has been diagnosed with a brain tumor reveals significant impact on family functioning via the aforementioned factors as well as from the impact of neurocognitive impairment (i.e., impaired communication due to neurocognitive issues) [16]. Theoretical models have been developed to incorporate family functioning in the conceptualization of how late effects impact individuals with brain tumors and their families, suggesting that treatment type, intensity, and other variable factors may affect families' adaptation to illness, which in turn, may affect patients' adaptation and overall outcome factors [16, 17]. Qualitative exploration into patient and family functioning after brain tumors (via case studies) reveals drastically different family members' attitudes toward illness, treatment, recovery, and level of burden [16]. Additionally, case studies suggest that family members' adaptation to illness and its complicated sequelae may influence the family's allocation of resources toward the survivor and may affect how well the family functions after brain tumor survival [16]. Overall, family and caregivers should be considered essential components of a patient's "team" and warrant attention and support also, particularly from a family systems perspective and given potential impact on the patient.

7. **Palliative Care**

   Patients with malignant tumors may find themselves with a terminal prognosis, facing end-of-life care. Palliative care from a prepared, cohesive oncology team is crucial at this time to manage neurological deterioration, medical issues, and psychosocial complications [18], with the goal of assisting the patient and his/her family in being most comfortable and supported. For example, medications such as midazolam may be used to facilitate sedation and manage symptoms such as delirium, agitation, refractory seizures, or death rattle, and corticosteroid use is typically reduced to decrease wakefulness and promote rest [18]. Patients and families who receive more support in preparation for death report significantly less distress when looking back upon their family member's end-of-life period [18]. Psychologists can take an important role in supporting and helping patients explore reflective thoughts about life as well as thoughts about impending death.

Tips

- Given that cognitive complaints may be a first identified symptom of brain tumors, neuropsychologists should always consider referrals for neuroimaging to assess for brain tumors. Recurrent tumor should also be considered if headaches, seizures, or other symptoms are not resolved or mitigated following intensive treatments.
- It is essential for psychologists to become familiar with the various types, origins, malignancy levels, treatments, and treatment side effects/late effects of brain tumors if they are to be working with this population.
- Psychologists have the unique role of providing psychoeducation for the patient and caregivers/family regarding prognosis and the impact of brain tumor on functioning (physical, cognitive, emotional, etc.). An empathic psychologist can serve as an integral member of a rehabilitative and treatment team with the role of translating difficult medical jargon into information that the patient and caregivers/family can understand and appreciate.
- Neuropsychological evaluations for brain tumor patients should include provision of raw scores, given that repeat testing is often warranted to monitor neurocognitive change. If prior testing is available, results should include discussion of changes (e.g., which may include statistical analysis of change via reliable change index).
- A neuropsychological evaluation is most useful if its recommendations are useful. This means creating recommendations that are highly applicable and relevant to the particular patient, that are understandable to the layperson and those who will be most involved with the patient, and that can be implemented successfully by the family, caregivers, teachers, neurologists, rehabilitation therapists, and other professionals who may read it. Targeted reports with careful consideration of the audience are warranted.
- Family and caregivers are essential members of the patient's team and should be treated as such. Family adaptation is important for

patient adaptation and recovery, thus appropriate attention and care should be provided to both parties.

- Psychologists play a key role in palliative care overall, regardless of malignancy. The emotional adjustment is difficult, from the receipt of diagnosis to end-of-life hospice care, and psychologists have unique and important training in this area that can be invaluable to a patient and his or her caregivers/family during an incredibly challenging time.

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