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Focused Review

Diagnosis, Treatment, and Rehabilitation for Adult Glioma

Brain Tumor Rehabilitation: Symptoms, Complications, and Treatment Strategy

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HIGHLIGHTS

- Patients with brain tumors experience weakness, cognitive and emotional dysfunction.
- Seizures, headaches, and dysphagia are common complication of brain tumors.
- Multidisciplinary assessment is necessary to treat tumor-related impairment.

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ABSTRACT

Brain tumors are receiving increasing attention in cancer rehabilitation due to their high rate of neurological deterioration. Motor dysfunction, cognitive deterioration, and emotional problems are commonly present in patients with brain tumors. Other medical complications, such as seizures, headache, and dysphagia are also common. An individualized multidisciplinary rehabilitation intervention is necessary to treat functional impairment due to the tumor itself and/or treatment-related dysfunction. Herein, we discuss rehabilitation treatment strategies in relation to the neurological and functional complications that commonly occur in patients with brain tumors.

Keywords: Brain Tumor; Cognitive Dysfunction; Fatigue; Rehabilitation; Weakness

INTRODUCTION

Despite making up a small proportion of all cancers, brain tumors are receiving increasing attention in cancer rehabilitation due to their high rate of neurological deterioration. The degree and type of impairment may depend on the tumor pathology and the lesion site. The majority of brain tumors have poor survivorship and prognoses, and benign tumors might be challenging to treat completely and are likely to recur.

The neurological complications commonly reported in patients with brain tumors in the early rehabilitation setting include cognitive dysfunction (80%), motor dysfunction (78%), visuoperceptual deterioration (53%), sensory problems (38%), and bowel/bladder dysfunction (37%). Three or more impairments were observed in 75% of patients, and five or more impairments in 39% of patients [1].

A rehabilitation intervention is required for more than 80% of patients with central nervous system tumors [2]. However, it can be difficult to communicate with patients and families about brain tumors in a rehabilitation setting because most initial inquiries concern the primary prognostic and treatment considerations for tumors, which are typically the purview of neurosurgery, medical oncology, and/or radiation oncology.

Table 1. Common neurological and physical complications of brain tumors

Neurological complications	Other medical complications
Cognitive dysfunction	Hemodynamic/vascular complications
Memory disorder	Hypertension
Communication difficulties	Arterial thrombotic events
Mood disorder	Venous thromboembolism
Depressive disorder	Pulmonary embolism
Anxiety disorder	Vasogenic edema
Impulse control disorder	Endocrinopathies
Personality disorder	Decreased production: GH, TSH, ACTH, gonadotropins
Seizure	Amenorrhea
Pain	Infections
Headache	Pneumonia
Other neuropathic pain	Urinary infections
Motor dysfunction	
Weakness	
Spasticity	
Dyskinesia	
Dystonia	
Fatigue	
Sensory deterioration	
Sensory impairment	
Proprioception impairment	
Visual disturbance	
Auditory dysfunction	
Dysarthria	
Dysphagia	
Aphasia	
Neurogenic bladder/bowel	
Sexual dysfunction	

GH, growth hormone; TSH, thyroid stimulating hormones; ACTH, adrenocorticotropic hormones.

An individualized multidisciplinary rehabilitation intervention is necessary to treat functional impairment due to the tumor itself and/or treatment-related dysfunction. Herein, we discuss rehabilitation treatment strategies in relation to the neurological and functional complications that commonly occur in patients with brain tumors (**Table 1**).

PHYSICAL PROBLEMS

Motor dysfunction

Motor dysfunction in patients with primary brain tumors can occur due to a variety of causes, including as a direct effect of the tumor's location or swelling or as a side effect of neurosurgery, chemotherapy, radiation, steroids, or other drugs [3]. Myopathy was reported in 10% of patients with brain tumors who received dexamethasone for more than 2 weeks, and approximately two-thirds of these myopathic patients developed symptoms after continuous administration of dexamethasone for 9–12 weeks [4].

Rehabilitation interventions focus on preventing or improving motor dysfunction, and thus preserving or enhancing quality of life [3]. The daily functional improvements made by patients with brain tumors receiving inpatient hospital-based rehabilitation could be comparable to those made by stroke and traumatic brain injury patients [5,6]. A systematic review suggested that exercise is safe and feasible in patients with brain tumors, yielding some benefits in terms of symptom severity and interference. Although the level of evidence is still low, exercise has been shown to improve aerobic capacity, body composition, and levels of physical activity [7].

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Fatigue

Fatigue is commonly present in patients with brain tumors, and its incidence increases with treatment, such as chemotherapy, radiation therapy, and the use of anticonvulsant drugs [8]. The lifelong prevalence of fatigue has been reported in up to 70% of patients [9,10].

Fatigue care can be approached both non-pharmacologically and pharmacologically. As non-pharmacologic treatments, several strategies have been revealed to be effective, such as physical exercise, behavioral management, coping strategies, dietary modifications including adequate hydration, and the management of anemia [8]. Pharmacologically, psychostimulants such as methylphenidate, modafinil, and armodafinil have not demonstrated significant benefits in randomized trials, but may be effective in managing fatigue [9,11,12].

COGNITIVE AND EMOTIONAL PROBLEMS

Cognitive dysfunction

Cognitive dysfunction and attentional deterioration commonly accompany brain tumors and can interfere with rehabilitation plans. Brain tumors in the frontal or temporal lobe can deteriorate attention, lower executive ability, and/or decrease the speed of information processing. These deteriorations may be exacerbated or prominently manifested by chemotherapy and radiation therapy [4]. Cognitive changes after chemotherapy are primarily associated with the effects of high levels of cytokines, DNA damage, and neurotoxic damage of brain white matter. Fatigue, depression, and psychosomatic effects can also play a secondary role in cognitive dysfunction [13]. It has been reported that 50% to 90% of brain tumor patients who survived for more than 6 months after radiation therapy have radiation-induced cognitive dysfunction [14]. Radiation-induced encephalopathy can occur in the acute or late phase and is related to injuries of neural cells themselves or vascular endothelial cells [14].

Meyers and colleagues found methylphenidate to be effective in improving cognitive function, including memory, expressive speech function, and executive function in patients with brain tumors [15]. Other agents that have been studied to enhance cognitive function include donepezil, modafinil, hyperbaric oxygen, and bevacizumab [16]. Neuropsychological rehabilitation interventions should be incorporated into the treatment plan, according to Janda and her colleagues, who analyzed the unmet needs of patients and caregivers with brain tumors for supportive care [17]. A randomized clinical study by Gehring and colleagues found that patients who participated in a cognitive rehabilitation program including executive function, memory, and attention compensatory skills training, as well as computer-based attention retraining, performed better on neuropsychological tests, had better attention and memory, and experienced less psychological fatigue [18].

Mood disorders

When a brain tumor is detected, up to 42% of patients have major depressive disorder, which can deteriorate over time [19]. Depression is related to cognitive dysfunction and functional impairment, which reduce the quality of life.

Antidepressants have been shown to be safe, without unsafe drug interactions with other chemotherapeutic agents. However, medications known to lower the seizure threshold, such as bupropion and clomipramine, should be avoided [4,20]. Limited data exist regarding the

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efficacy of psychosocial interventions combined with other treatments, such as cognitive and/or physical therapies [21].

OTHER COMPLICATIONS

Seizures

Seizures commonly occur in patients with brain tumors, being reported in 20%–40% of patients with high-grade tumors, 50%–85% of those with low-grade tumors, and 15%–20% of those with brain metastasis [3,22]. It is crucial to treat a number of triggering factors, including tumor growth, brain edema, intracranial pressure, metabolic problems, and other tumor-related factors, in order to achieve optimal seizure management [4].

Treatment for epilepsy often requires a lifetime commitment. However, antiepileptic drugs (AEDs) can be discontinued in carefully selected patients who have been seizure-free for a long time and have a low risk of tumor progression [23]. Adverse effects of AEDs should prompt consideration of discontinuation. In several previous studies, the incidence of adverse events brought on by prophylactic AEDs was rather significant, reaching 34%. Significantly, serious side effects such as toxic epidermal necrolysis and lowered levels of consciousness were documented [24-26]. A decreased level of consciousness can be a major obstacle to rehabilitation treatment.

Prospective studies and a meta-analysis on seizure-free brain tumor patients have not found seizure-prophylactic effects of AEDs [27-29]. More recently, the European Association of Neuro-Oncology and Society for Neuro-Oncology practice guideline update on anticonvulsant prophylaxis in brain tumors also warned against the use of preventive anticonvulsants [30]. According to the guideline, in seizure-free individuals with newly diagnosed brain tumors, AEDs should not be prescribed to reduce the risk of seizures (grade of recommendation: A). In patients with brain tumors undergoing surgery, there is not enough evidence to recommend the prescription of AEDs to reduce the risk of seizures in the perioperative or postoperative period (grade of recommendation: C).

Headache

In 53% of patients with brain tumors, headaches have been reported; 77% of these patients experience tension headaches, the most prevalent type of headache [7,31]. Local traction on pain-sensitive tissues, such as the cranial nerves, venous sinuses, arteries, and sections of the dura has been suggested as potential headache triggers.

Appropriate treatment is necessary because headache can act as a hindrance to rehabilitation and reduce motivation. Corticosteroids (particularly when there is a rise in intracranial pressure), surgical procedures, or radiation therapy can be used for the management of headache. Typically, after a craniotomy, analgesics are needed.

Dysphagia

The lifelong prevalence of dysphagia in patients with brain tumors has been reported to be as high as 85% [32]. When dysphagic patients with stroke and brain tumors were matched, both had statistically similar incidence rates and patterns of dysphagia. In addition, there was no significant difference in swallowing functions between patients with benign and

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malignant brain tumors [33]. Dysphagia may be caused by focal neurological deficits, or more commonly, deteriorated consciousness [34].

The inability to swallow affects nutrition, hydration, and medical therapy. No systematic research has been done on the effects of hydration and tube feeding in patients with brain tumors, but a study reported that swallowing function was improved in most patients with supratentorial and infratentorial tumors by swallowing therapy and chemoradiotherapy [33].

CONCLUSION

Patients with brain tumors have a high rate of neurological impairment, resulting in functional deficits. Individualized comprehensive rehabilitation management is necessary with treatments that have been demonstrated to be beneficial, but some medical treatment and rehabilitation interventions require more supporting evidence. What matters most is a multidisciplinary team approach and frequent communication with patients and their families.

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