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Rehabilitation of motor dysfunction in primary brain tumor patients†

David S. Kushner and Christina Amidei

Department of Physical Medicine and Rehabilitation, University of Miami Miller School of Medicine, Miami, Florida (D.S.K.); Department of Neurology and Rehabilitation, University of Illinois, College of Medicine (C.A.)

Corresponding Author: David S. Kushner, MD, Department of Physical Medicine & Rehabilitation, University of Miami Miller School of Medicine, 1120 NW 14th Street, CRB 955, Miami, FL 33136 (dkushner@med.miami.edu).

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In 2010 it was estimated that >688 000 Americans were living with a primary brain tumor (PBT) corresponding to a U.S. prevalence rate of approximately 221.8 per 100 000 people. Five-year survival is 96.1% in nonmalignant PBTs, 34% in malignant PBTs for all ages, and 71% in children [1985–2005]. Case fatality rates have decreased in the U.S. since the 1970's for nonmalignant PBTs and for medulloblastoma, oligodendroglioma, and astrocytoma. Statistics of increasing survival highlight the importance of rehabilitation interventions to improve function and quality of life in survivors. PBT motor dysfunction is multifactorial, occurring as a result of direct effects of tumor and/or swelling or as a result of treatments; etiologies include encephalopathy, myopathy, neuropathy, infection, poor nutrition, metabolic factors, emotional factors, impaired perception/vision/cognition and complications of immobility. Motor dysfunction may lead to: impaired mobility, impaired activities of daily living, risk for complications of immobility, falls, pain, anxiety/depression, and loss of functional independence and quality of life. Rehabilitation treatment strategies target specific causes of motor dysfunction to improve functional independence and quality of life. This article reviews current knowledge and controversy regarding the role of rehabilitation for motor disorders in PBT patients.

Keywords: brain tumors, motor skills disorders, quality of life, rehabilitation, survival.

In 2010 it was estimated that >688 000 Americans were living with a primary brain tumor (>138 054 with a malignant tumor and >550 042 with a nonmalignant tumor), corresponding with a U.S prevalence (benign and malignant) of approximately 221.8 per 100 000 people.[1] These statistics do not include the prevalence of patients surviving with metastatic brain tumors. Average 5-year survival is 34% in malignant primary brain tumors for all ages and 71% in children [1985–2005].[2] In contrast, the average 5-year survival is 96.1% in most nonmalignant PBTs.[3] Case fatality rates have decreased in U.S. since the 1970s for nonmalignant primary brain tumors; and for medulloblastoma, oligodendroglioma, and astrocytoma.[4] Statistics of increasing survival highlight the importance of rehabilitation interventions to improve function and quality of life in survivors.

Motor deficits, including unilateral or bilateral weakness, ataxia, spasticity, and loss of complex movement execution due to multiple possible etiologies, can occur during any brain tumor illness. Tumor location, treatment effects, and medications contribute to these deficits. Motor dysfunction has been associated with significant deterioration in health-related quality of life in people with primary and metastatic brain tumors. Significant decrease in median overall survival has been reported in people with motor deficits, possibly due to the complications of immobility, although the exact reasons for this finding are unclear.

Motor deficits, particularly gait impairment, contribute to significant symptom burden at end of life, and are the most common reason for initiation of hospice care. Rehabilitation interventions focus on prevention and amelioration of motor dysfunction throughout the disease course in order to preserve quality of life. Rehabilitation improves quality of life and helps in the prevention of the medical complications of immobility, but the impact of these interventions on long-term functional independence and the prolongation of survival remains controversial, particularly in malignant brain tumor patients. This article will review the current knowledge regarding the rehabilitation of motor dysfunction in primary brain tumor patients and address the role of rehabilitation in malignant tumor patients.

Motor Deficits and Primary Brain Tumors

Table 1 shows the incidence rates of the most common primary brain tumors. Primary and metastatic brain tumors may occur

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Table 1. Distribution of common primary brain tumors by histological subtype

Meningiomas: most common, 34% of all brain tumors
Gliomas: 30% of all brain tumors and 80% of all malignant tumors
Glioblastomas: 17% of all brain tumors and 54% of gliomas
Astrocytomas: 7% of all brain tumors
Nerve sheath tumors: 9% of all brain tumors
Pituitary tumors: 13% of all brain tumors
Lymphomas: 2% of all brain tumors
Oligodendrogliomas: 2% of all brain tumors
Medulloblastomas: 1% of all brain tumors

anywhere in the brain and cross neuro-anatomic boundaries. Motor dysfunction in primary brain tumor patients may be multifactorial, occurring as a result of direct effects of tumor location and/or swelling, and/or as a result of treatments such as surgery, chemotherapy, radiation, steroids and/or other pharmacotherapy.

Table 2 summarizes potential impairments that may contribute to motor dysfunction in primary brain tumor patients. The most common impairments include cognitive deficits, weakness, visual-perceptual deficits, and sensory loss, followed by cranial neuropathies, diplopia and ataxia. In one study three or more deficits were seen in 75% of patients and five or more deficits in 39%, highlighting the multifactorial etiology of motor dysfunction in these patients.[5]

Motor deficits may impair quality of life, functional independence, and safety and may result in falls and injuries and/or the complications of immobility such as venous-thromboembolism (VTE), pneumonia, skin ulcerations and joint contractures, all of which may contribute to mortality. The subsections below will outline the potential causes of motor dysfunction in patients with primary brain tumors, as well as VTE, which is the most common complication of immobility resulting in hospital readmissions and mortalities. Motor dysfunction etiologies and manifestations in primary brain tumor patients are targeted for rehabilitation interventions.

Table 2. Possible etiologies for motor dysfunction in brain tumor patients

Muscle weakness
Central weakness
Myopathy-related weakness
Neuropathy-related weakness
Cognitive impairments
Memory for task
Comprehension
Apraxia
Attention/Concentration
Impaired executive function
Psychomotor Delay/Delayed response time
Emotional Impairments
Depression
Anxiety
Fear of Falling
Apathy/Abulia
Abnormal Tone/Spasticity
Abnormal synergy patterns
Abnormal range of motion
Sensory Impairments
Numbness
Impaired Proprioception
Impaired Perception
Visuospatial impairments
Hemineglect
Impaired vision/Hemianopia
Physical Impairments
Pain
Fatigue
Contractures
Ataxia/Incoordination/Imbalance

Tumor Location

Various motor dysfunction syndromes may occur as a direct result of tumor location. The effects of hemisphere tumors may vary depending on whether the right or left side of the brain is affected, and depending on the lobar location. Frontal lobe involvement may cause impaired executive functions, impulsiveness, apraxia, and emotional lability. Parietal tumors may cause hemineglect, spatial disorientation, apraxia, impaired vision (optic pathway involvement), and/or contralateral proprioceptive agnosia and other sensory impairments. Temporal lobe involvement may cause impairments of visual fields (optic pathway), memory, comprehension, and behavior. Occipital effects involve various vision impairments. Suprasellar tumors in the area of the pituitary may also result in visual field impairments such as bitemporal hemianopsia.

Motor effects of tumors of the thalamus may vary. For example, tumors of the supra-posterolateral portion of the thalamus may result in astasia, the inability to stand in the absence of motor weakness or marked sensory loss, causing a tendency to fall backwards or toward the side contralateral to the lesion.[6] Interestingly, midline cerebellar tumors could present with symptoms similar to those seen with supra-posterolateral thalamic lesions.[6] In addition, because thalamic tumors may involve all of the thalamus or various nuclei within the thalamus, other findings may include impairments of arousal, high-level cognition, mood and motivation, and/or contralateral pain, sensory loss, ataxia, hemiparesis, and hemineglect.[7,8]

Tumors occurring in the region of the basal ganglia may variably cause apathy, abulia, hemiparesis, dystonia, and impaired cognition.[8] Brainstem tumors may variably cause deficits that correspond with involvement of various ascending and descending white matter pathways producing ataxia, incoordination, weakness and/or sensory loss; and involvement of cranial nerve nuclei may cause diplopia, imbalance, dysphagia and other findings that would correspond with the specific cranial nerve. Cerebellar tumors may cause ipsilateral or midline ataxia/incoordination, dysmetria, and dysarthria, but also may result in cognitive and affective symptoms.[9]

Steroid Myopathy

Corticosteroids reduce brain tumor-associated edema and related neurologic deficits while minimizing side effects and/or the risk of encephalopathy in patients undergoing radiation therapy.[10] However, corticosteroids may cause multiple potential side effects including steroid myopathy, which causes weakness that predominantly affects the proximal limb musculature and impairs ability to stand up from sitting as well as stair climbing. Reportedly 10% of primary brain tumor patients receiving daily dexamethasone for 2 or more weeks are at risk for developing steroid myopathy, particularly if they develop Cushingoid features.[10,11] Corticosteroids may also cause osteoporosis, which makes falls from motor dysfunction more likely to result in fractures.

Radiation Therapy Encephalopathy

Radiation is commonly used in the treatment of patients with high-grade gliomas, as this has been shown to improve survival.[12] However, there is a risk of radiation encephalopathy, which may manifest with neurocognitive deficits and/or radiation-induced necrosis. The exact incidence of radiation necrosis may range from 7% to 24% particularly following stereotactic radiosurgery.[12–14] Pathophysiology of radiation necrosis of the brain involves coagulative and fibrinoid necrosis and cortical irritation with associated vasogenic cerebral edema that impairs surrounding brain function.[14] Radiation encephalopathy may occur as an acute, subacute, or chronic complication. It may be reversible when it is a complication of recent radiotherapy, however it may also result in permanent neurologic impairments. Acute radiation encephalopathy is often treated with steroids for the edema. Motor dysfunction may be one of the manifestations of radiation encephalopathy in brain tumor patients.

Chemotherapy Encephalopathy

Chemotherapy for malignant brain tumors, and other cancers, may result in neurocognitive impairments and somatoform symptoms including fatigue, malaise, depression, and anxiety.[15] Impaired memory, attention, and executive control are the most common of the cognitive manifestations that have been correlated with gray and white matter volume reductions and altered white matter tract microstructure on neuroimaging studies.[16] Motor dysfunction may also be one of the indirect manifestations of chemotherapy encephalopathy in brain tumor patients.

Venous Thromboembolism (VTE)

Malignant brain tumor patients are at a high risk for VTE complications,[17] particularly following craniotomies for high-grade oligodendroglioma, high-grade glioma, lymphoma, and lesions of metastatic or mixed pathology.[18] The reported incidence of VTE in this post-surgical group reportedly ranges from 3.0% to 13.7%.[18,19] VTE is one of the main reasons for unplanned hospital readmissions in brain tumor patients; rates of readmission for VTE range from 19.7% to 22%.[20,21] Patients readmitted to a hospital within 30 days of a craniotomy for reasons that may include VTE had twice the risk of mortality compared with patients who were not readmitted[20]; and readmitted glioblastoma patients had shorter overall survival rates than those not readmitted.[21] Immobility and pre-operative motor deficits increase the risk for VTE.[19] Early post-craniotomy mobilization therapies in combination with mechanical and/or pharmacologic prophylaxis have been shown to reduce VTE complications.[22] Evidence-based VTE prophylaxis in compliance with American College of Chest Physicians (ACCP) guidelines during inpatient rehabilitation have been shown to reduce the incidence of symptomatic VTE by 6-fold in at-risk patients.[23]

Rehabilitation

Most patients are referred to rehabilitation following neurosurgery, initial or subsequent to recurrence, for motor and/or cognitive impairments. Though still controversial,[24] rehabilitation has been shown to be useful in improving motor and cognitive function, and/or survival and quality of life in malignant primary brain tumor patients, although mostly in observational studies rather than randomized controlled studies (RCTs) or clinical controlled trials (CCTs).[16,25–33] Motor dysfunction leads to impairments of mobility and activities of daily living, risk for complications of immobility and falls, pain, anxiety and/or depression, loss of functional independence, and reduced quality of life. Rehabilitation targets the causes of motor dysfunction as well as its effects on physical function, well-being, and quality of life. Daily functional gains made by primary brain tumor patients undergoing inpatient rehabilitation may be similar to those made by traumatic brain injury and stroke patients matched by age, gender, and admission functional status.[16,25,26] Perioperative motor deficits in glioblastoma patients have been demonstrated to have a deleterious impact on mobility and quality of life, contributing to decreased survival.[27,28] However, a recent CCT showed that malignant glioma survivors at a median time of 2 years since initial diagnosis can improve function with multidisciplinary rehabilitation, with some gains maintained up to 6 months, particularly in the Functional Independence Measure (FIM) domains of sphincter control, communication, and cognition.[29] Motor FIM score gains averaging 10 points during rehabilitation is a significant predictor of longer survival in patients with brain metastases and glioblastomas.[31]

Rehabilitation of Multifactorial Motor Symptoms

One of the roles for rehabilitation clinicians is to determine causes of motor symptoms that may then be targeted for specific rehabilitation treatments. For example, in primary brain tumor patients, balance dysfunction may be caused by factors such as impairments of vision, vestibular or sensory paths, brainstem or cerebellar pathways; parasagittal or sensory cortex tumors; poor nutrition; anemia; postural hypotension; dehydration; temporal or posterior fossa radiation; and/or medication side effects. Some of the potential causes for vestibular/balance dysfunction may respond rapidly to an intervention, such as the discontinuation of a particular medication, while other physical therapy interventions may gradually help in the recovery of balance. Vestibular therapeutic regimens may include practical activities that challenge postural stability and balance, eye-hand-head coordination activities, virtual reality techniques, and/or use of special equipment/devices; progress may be tracked with FIM scores and/or posturography.[34–36] Postoperative imbalance/vestibulopathy associated with certain tumors such as schwannomas or cerebellar tumors may respond to vestibular therapies, particularly when the treatment is initiated in the early postoperative period.[34,36]

Fatigue and poor endurance or exercise tolerance may be caused by adverse effects of chemotherapy, radiation, medications, deconditioning, metabolic problems, infection, anemia, depression, impaired sleep, and/or nutritional factors. Some of these problems are more easily treated than others. Fatigue occurs in approximately 80% of primary brain tumor patients who undergo cranial irradiation, and in nearly 40% of low-grade glioma survivors.[37–40] Fatigue, cognitive impairments, and depression are common and often co-morbid symptoms,[37] all of which may respond to various pharmacologic and nonpharmacologic therapeutic interventions. Nonpharmacologic interventions for fatigue that have been proven to be effective in the general cancer patient population include physical therapy and exercise, psychosocial and nutritional interventions, pain management, and treatment of anemia, altered sleep hygiene, and comorbid conditions, such as thyroid dysfunction.[37,40,41] Rehabilitation exercise programs that were successful for fatigue treatment in general cancer patients included mild-to-moderate intensity walking and resistance training;[40,41] however, randomized controlled trials in primary brain tumor patients have not yet been performed.[37]

Cognitive deficits that may impair motor function include problems with comprehension, memory, attention, initiation, apraxia, psychomotor delay, and/or perception. Approximately 80% of primary brain tumor patients may have cognitive impairments.[5] Causes of impaired cognition may include: direct effects of tumor, surgical resection, radiation, chemotherapy, medications, fatigue, depression, and/or anxiety, and medication side effects. Depression and anxiety have been reported to occur in 16% to 50% of primary brain tumor patients,[42] may be difficult to distinguish from fatigue, and may interfere with concentration, attention, and cognition. Cognitive multidisciplinary rehabilitation treatment targets deficits in communication, comprehension, expression, social interaction, problem solving and memory. Gains in cognition may be maintained for up to at least 6 months in malignant glioma survivors at median time of 2 years since initial diagnosis per a recent CCT.[29]

Rehabilitation in Acute Care

Rehabilitation interventions should begin in primary brain tumor patients during an acute care hospitalization after the diagnosis and/or treatment is established, any life-threatening problems are controlled, and/or the patient is stabilized after surgery. The highest priorities during acute care are the prevention of medical complications; regulation and management of general health functions such as nutrition, hydration, bowel/bladder function, sleep, and homeostasis; and encouragement of early mobilization and the resumption of self-care activities.[43] Therapeutic interventions to encourage mobility may be started in stable patients after neurosurgery. However, mobilization should be approached with caution or delayed in patients with altered consciousness, evolving neurological signs, recent intracranial bleeding, persistent orthostasis, and/or any other acute medical complications.[43] Early mobilization in brain tumor patients helps to prevent complications of immobility such as VTE, skin breakdown, contracture development, constipation, orthostasis, and/or pneumonia, while promoting early ambulation and the performance of activities of daily living. Self-care activities should be encouraged in stable brain tumor patients because early participation in self care increases strength, endurance, awareness, communication, problem solving, and social activity.[43] Rehabilitation goals prior to the discharge from acute care include: determining the need for further rehabilitation, selecting the best post-acute living environment or rehabilitation setting, and assisting with patient and family education on the clinical effects of the brain tumor, potential complications, and the need and rationale for further treatments and rehabilitation.

Post-acute Rehabilitation Settings

There are specific criteria that are used to determine further rehabilitation. For example, the threshold criteria for admission to any active inpatient or outpatient rehabilitation program that would involve active patient participation would include medical stability, one or more persistent disabilities, the ability to learn, and the endurance to sit supported for at least 1 hour per day.[43] Primary brain tumor patients who would qualify for intense interdisciplinary inpatient rehabilitation programs have the ability to tolerate 3 hours of therapy daily and would require total-to-moderate assistance in either mobility or activities of daily living.[43] Patients having complex medical needs who are unable to tolerate 3 hours of active therapy daily may benefit from subacute rehabilitation treatment in a skilled nursing facility. Candidates for outpatient rehabilitation would require supervision to minimal assistance in mobility and activities of daily living and would have limited functional deficits.[34] Home health care therapy programs vary in capabilities and services; advantages include the convenience and familiarity of the home setting, while disadvantages include the potential of increased burden on family caregivers.

Post-acute Rehabilitation Process

Regardless of the setting, a rehabilitation plan of care should be developed for all primary brain tumor patients. A rehabilitation plan of care would include a clear description of the patient's impairments, disabilities and strengths, explicit short- and long-term functional goals, and treatment strategies to achieve goals and prevent complications.[43] Goals in rehabilitation for motor dysfunction in primary brain tumor patients include the prevention of secondary complications, treatment to reduce neurological impairments, and the teaching of compensatory strategies for residual disabilities. Tumor type, location, deficits, and time since diagnosis are important considerations in setting the goals. Importantly, even newly diagnosed glioblastoma patients who are status post an initial resection craniotomy are likely to make significant gains in mobility and self-care following a course of inpatient rehabilitation.[30] If prognosis is poor or there are severe cognitive deficits that preclude learning, then the emphasis would be on caretaker education, adjustments to a living environment to facilitate care, and improving the patient's capacity for bed transfers.

Goals may change over the clinical course and may be different for benign versus malignant tumors. Initial concerns are specific impairments and functional abilities. Later concerns may include survival, progression of impairments, and complications of treatments. In regard to motor impairments, patients with some voluntary motor control are encouraged to use an affected limb in functional tasks. Patients with persistent functional deficits are taught compensatory strategies. Absence of volitional movement in a limb at more than four weeks post onset of deficit suggests that recovery of volitional movement is unlikely.[43] Adaptive devices and braces are used if more natural methods are not available or cannot be learned. Lower extremity orthotic devices are indicated in a patient having persistent weakness, such as complete foot drop or knee instability, if ankle or knee stabilization will help the patient to walk. Impairments of cognition and perception also contribute to motor dysfunction in primary brain tumor patients; treatments emphasize retraining, substitution of intact abilities, and compensatory approaches. Persistent cognitive deficits that preclude learning are a contraindication to active rehabilitation. Impairments of language, including expression, comprehension, and/or hemineglect, may also contribute to motor dysfunction such as through an inability to express needs, which can lead to falls; an inability to understand motor commands, impairing motor rehabilitation; or a lack of awareness usually of the left hemi-body and left visual field. Treatment of aphasia is targeted at comprehension deficits, improving functional communication, and using strategies to compensate for persistent problems. Treatment for hemineglect and other right hemisphere language disorders focuses on increasing awareness of deficits, reinstating the pragmatics of nonverbal communication, and the teaching of compensatory strategies such as scanning to the affected side.

Discharge planning begins at the time of admission to any active rehabilitation program and it involves the interdisciplinary team, the patient, and the family. Discharge planning concerns are shown in Table 3. Discharge occurs when reasonable treatment goals have been achieved, or if there has been an absence of progress over 1 to 2 successive weeks, which would suggest the need to reconsider the treatment regimen and/or the rehabilitation setting. Patients who are unable to tolerate rehabilitation interventions in an active rehabilitation setting may still benefit from more passive interventions in another setting such as at home with home therapies or in a skilled nursing center.

Potential Barriers for PBT Patient Access to Rehabilitation

In principle rehabilitation would seem to be a service easily provided to primary brain tumor patients, but in reality implementing rehabilitation for people with brain tumors can be challenging due to insurance coverage issues, potential physical/cognitive barriers to participation, and absence of rehabilitation as a component of a multidisciplinary clinical care pathway and/or lack of a multidisciplinary care approach. Health insurance providers may not cover rehabilitation services due to defined benefits and/or lack of RCTs that demonstrate improved outcomes in malignant primary brain tumor patients.[24] RCTs that address long-term outcomes or cost benefits of rehabilitation for those with malignant brain disease are also lacking.[24]

Table 3. Rehabilitation discharge planning concerns

Home accessibility needs
Home equipment needs
Driving issues
Handicap parking needs
Medical follow-up
Outpatient or home therapy needs
Caretaker education
Referral to appropriate community services and support groups

A second issue is that physical, cognitive and/or emotional symptoms caused by the tumor and/or its treatment may decrease a patient's ability or motivation to participate in rehabilitation programs. Active patient participation, medical stability, one or more persistent disabilities, the ability to learn, and the endurance to sit supported for at least one hour a day are minimum requirements for admission to any active inpatient or outpatient program.[43] Patients that do not meet these criteria would not be candidates for an active rehabilitation program.

Finally, absence of rehabilitation as a component of a multidisciplinary clinical care pathway or lack of a multidisciplinary care approach to identifying patients that might benefit from rehabilitation are other important barriers. A multidisciplinary team approach is resulting in improved patient access to surgery, better post-surgical outcomes, shorter post-surgical, acute-care hospital length-of-stays, and improved coordination of chemotherapy and/or radiation therapy treatments, but not access to rehabilitation services.[44–48]

Currently, national data are unavailable regarding the proportion of primary brain tumor patients who are referred to rehabilitation, and of these, what proportions are accepted or rejected, and for what reasons. Perhaps a survey of the Society of Neuro-Oncology members about perceptions of potential barriers to rehabilitation access might be useful in clarifying the most common of these issues or other potential issues not discussed here.

Controversy Regarding Rehabilitation in PBT Patients

There is general agreement that rehabilitation is beneficial for motor functional recovery and the prevention of complications in patients with low-grade or benign brain tumors;[16,25–33] however, there is continued controversy regarding the benefits of rehabilitation for patients with high-grade malignant tumors and a relatively short life expectancy. This controversy stems from a paucity of RCTs that demonstrate improved functional outcomes, survival, or cost benefits.[24] Two recent studies, one RCT and one CCT, have demonstrated that rehabilitation benefits glioblastoma patients.[29,33] Increasing survival rates for malignant glioma patients have been reported,[4,29,45] which highlights an increasing need for rehabilitation in this population to improve motor function and quality of life while preventing the complications of immobility such as VTE. Malignant brain tumor patients are at a high risk of developing VTE,[17–19] and this risk may be reduced as much as 6-fold by rehabilitation interventions to improve mobility in combination with recommended ACCP guidelines.[22,23] The lack of RCTs and CCTs does not suggest the ineffectiveness of multidisciplinary rehabilitation services but rather highlights the need for well-designed studies in primary brain tumor patients to clarify best practices, optimal settings, type, intensity, duration of therapy, and cost-effectiveness.

Conclusion

Increasing survival highlight the importance of rehabilitation interventions to improve function and quality of life in PBT survivors. Motor dysfunction is common and occurs as the result of multiple possible causes in PBT patients. Rehabilitation is beneficial in the prevention of the medical complications of immobility such as VTE and in improving motor function, cognition, and overall functional independence for people having PBTs, including those patients having malignant brain tumors. Rehabilitation RCT studies are needed in PBT patients to clarify best practices, optimal settings, type, intensity, duration of therapy, and cost-effectiveness.

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