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Changing Paradigms in the Rehabilitation of Inpatients with Brain Tumors

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Abstract

Neurologic tumors account for over 50% of American acute inpatient rehabilitation facility cancer admissions. WHO Grade IV astrocytoma (also known as glioblastoma multiforme, high grade glioma or GBM) is the most common primary brain tumor in adults and is invariably fatal. The majority of primary brain tumor patients experience neurologic deficits. However, under-referral from oncology to rehabilitation has been reported. This brief narrative review article covers functional, medical and regulatory considerations when rehabilitating brain tumor inpatients.

Keywords

Inpatient; Rehabilitation; Brain; Astrocytoma; Glioma; Glioblastoma

Introduction

Inpatient brain injury rehabilitation can occur in the acute care hospital service (typically under the neurosurgery or neuro-oncology service), acute inpatient rehabilitation facility (IRF), post-acute brain injury rehabilitation facility, skilled nursing facility (SNF), or long term acute care facility (LTAC). SNF's and LTAC's are sometimes referred to as subacute inpatient rehabilitation facilities. The differences in the post-acute care rehabilitation facilities are in the amount of medical care typically given and therapy they receive. Most of the research regarding inpatient brain cancer rehabilitation has been in the IRF setting.

Multiple studies have demonstrated under-referral of cancer patients to rehabilitation. [1, 2, 3] Several studies have also shown under-referral of hospitalized cancer inpatients

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Compliance with Ethics Guidelines

Conflict of Interest

The authors declare that they have no competing interests.

Human and Animal Rights and Informed Consent

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specifically to rehabilitation. [4, 5] In an Italian study, only 12.8% of brain tumor patients received inpatient rehabilitation and only 14.9% received outpatient rehabilitation. [6] This is particularly worrisome, since it has been reported that 75.4% and 39.2% of brain tumor patients have three and more than five concurrent deficits, respectively. [7] Hemiplegia, dysphagia, aphasia, ataxia and cognitive deficits can be encountered depending on tumor location. Barriers to rehabilitation referral include a lack of understanding of what rehabilitation does and failure to recognize functional deficits by oncologists. [8, 9, 10] Rehabilitation may be an afterthought to oncologists or neurosurgeons. After the admitting diagnosis has been treated on the acute care service, it may become apparent that the patient cannot be discharge home safely. This will often trigger a rehabilitation consultation late in the admission or referral to a post-acute inpatient rehabilitation facility. Earlier rehabilitation consultation during the acute care hospitalization, perhaps, could help some patients avoid needing a post-acute care inpatient rehabilitation facility.

In a recently published study by Mix et al. that included 70% of all American acute inpatient rehabilitation facilities, cancer patients accounted for only 2.4% of the total IRF admissions from October 2010 through September 2012. During the study period, 14,780 neurologic primary cancers were admitted to IRF's accounting for over half (52.9%) of the 27,952 total cancer admits. The next largest group of primary cancers was digestive cancers with only 12%. [11] Neurologic primary cancers were also the largest group of cancer patients admitted to the acute inpatient rehabilitation unit in published studies from the Shirley Ryan Ability Lab (formerly known as the Rehabilitation Institute of Chicago) (27.9%) [12] and MD Anderson Cancer Center (17%). [13] Neurologic cancers compared to other cancer subtypes have lower admission FIM scores including lower cognitive FIM subscores. [11]

The predominance of nervous system cancers is striking and could be due to several factors. First, patients with neurologic impairments may be a patient population that most benefits from intensive inpatient rehabilitation. Stroke, traumatic brain injury and spinal cord injury have accounted for a large portion of IRF patients. Second, accepting physiatrists may feel comfortable rehabilitating neurologic impairments common in brain tumor patients including spasticity, hemiplegia, aphasia and dysphagia. The third reason may be the Medicare 60% rule which mandates in order to participate in the Medicare Prospective Payment System, an IRF's patient admissions must have 60% of their admissions possessing one of 13 medical diagnoses. Cancer is not one of the 60% rule diagnoses, however, brain injury is. Brain tumor patients whether due to a primary brain tumor or metastatic brain tumor are general felt to fall under the brain injury diagnosis. [14, 15] Interestingly, MD Anderson Cancer Center is exempt from the Prospective Payment System and does not have to adhere to the 60% rule. Despite this, neurologic tumors were still the largest group of primary tumors admitted to the IRF there (although the proportion was less compared to Shirley Ryan Ability Lab or the national data from Mix et al.).

Of the estimated 17,000 primary brain tumors diagnosed in the United States each year, approximately 60% are GBM). They are the most common primary brain tumors in adults. [16, 17] The median lifespan for GBM patients is 12-15 months with fewer than 25% surviving up to 2 years and fewer than 10% surviving up to 5 years. [18, 19] Metastatic brain tumors will develop in 20-40% of cancer patients. Lung, breast, colon, kidney and

melanoma cancers can commonly metastasize. More than half of patients with metastatic brain tumors have multiple intracranial lesions. [20] Surgical resections and radiation are often treatments given. Leptomeningeal disease (LMD) or carcinomatous meningitis consists of metastatic cancer cells within the cerebrospinal fluid lining the surfaces of the central nervous system. The treatment for LMD is often intrathecal chemotherapy delivered via lumbar puncture or an Ommaya reservoir. [21] LMD patients often suffer from neurologic impairments and functional deficits but they can be challenging. Many experience neurologic fluctuations which may make rehabilitation planning difficult.

Functional Improvement

In the IRF setting, one may notice significant neurologic return in the first weeks post craniotomy and tumor resection. This rapid neurologic recovery is likely due in part to reduced resection site inflammation and intracranial pressure. When compared to other brain injury etiologies, brain tumor rehabilitation inpatients improve at a similar speed as their traumatic brain injury [22] and stroke counterparts.[23, 24] (as measured by the Functional Independence Measure efficiency or FIM efficiency). The FIM efficiency is calculated as change in FIM from admission to discharge from rehabilitation divided by length of inpatient rehabilitation stay. Mean FIM efficiencies have been reported between 0.72-1.5. [25, 26] It has also been shown in multiple studies that brain tumor patients tend to have shorter lengths of stay. The need to resume cancer treatment or the more limited prognosis may lead to establishing more modest rehabilitation goals and quicker discharge from the IRF. Because of the similar FIM efficiency but shorter length of stay, overall changes in FIM scores tend to be less. Studies comparing low grade with high grade astrocytomas [27] and comparing astrocytoma, meningioma and metastatic brain cancer patients [26] also found no statistically significant differences in FIM efficiency. Upon completing inpatient rehabilitation, between 82-90% of IRF brain tumor patients are discharged home. [24, 25, 27]

Unlike other brain injury populations, such as traumatic brain injury and stroke, brain tumors are dynamic lesions. These dynamic lesions, depending on the cancer aggressiveness, can recur. Also the effects of cancer treatments, particularly radiation necrosis which may be delayed, can lead to new neurologic symptoms months to years after initial diagnosis. Recurrence and brain cancer recurrence/progression may lead to a return or worsening of neurologic symptoms requiring more rehabilitation. It is not unusual for a brain tumor patient to be admitted multiple times to inpatient rehabilitation during their cancer treatment course. Follow-up after inpatient rehabilitation discharge is strongly recommended due to the high likelihood of future neurologic decline. [28] Figure 1 demonstrates a functional graph of a glioblastoma patient.

Radiation necrosis, brain cancer progression/recurrence and damage from repeated craniotomies and resections can result in an accumulation of brain injuries. Patients sometimes expect functional improvement to return like prior inpatient rehabilitation admissions. However, it is typically harder for these patients to recover at the same speed and level that they did before. The functional decline and the inability to “bounce back” as they remembered several months to years earlier can be discouraging for patients. [28]

Medical Complications and Return to the Primary Acute Care Service

It has been shown that cancer IRF patients are transferred back to the primary acute care service significantly more frequently than their non-cancer counterparts. A study of cancer IRF patients matched to non-cancer control IRF patients found a return to primary acute care rate of 21% versus only 9.7% respectively. [29] Hematologic malignancy IRF patients have had reported return to the primary acute care service rates of between 26-38%. [30, 31, 32, 33] Brain cancer IRF patient return to the primary acute care service rates have been lower than general and hematologic cancer patients between 7.5% and 24%. [25, 26, 27] The differences in the composition of brain tumor patients in the studies likely played a role for the wide range. Transfer to the primary acute care service of stroke and traumatic brain injury IRF patients have been reported as 7.1% [34] and 20% [35], respectively.

Cancer Related Symptoms

Cognitive deficits are commonly encountered in brain tumor patients depending on tumor location. At MD Anderson Cancer Center, all IRF patients receive a speech therapy cognitive screening evaluation at inpatient rehabilitation admission. During psychiatric consultation, cognitive deficits should be taken into consideration when determining an appropriate rehabilitation setting. Some patients with significant persistent cognitive and behavioral issues at IRF discharge may benefit from post-acute brain injury rehabilitation programs. It is important to note that these programs are only covered by some private insurance policies and not Medicare or Medicaid. Because cancer is a disease of older people, many are on Medicare when they are diagnosed.

Cancer patients can suffer from a variety of other symptoms due to the cancer and its treatment including radiation and chemotherapy. Insomnia during inpatient rehabilitation is commonly encountered while on inpatient rehabilitation due to the brain injury itself but also due to the use of steroids post-operatively. Steroids may also contribute to steroid psychosis and agitation. Cancer related fatigue, pain, depression, nausea, and poor appetite are also often encountered. Greater than 80% of brain tumor patient experience cancer related fatigue during treatment. [36] Neurostimulants such as methylphenidate have been shown to help patients with cancer related fatigue. [37] Appetite stimulants such as mirtazapine and dronabinol can be used. The use of megestrol can be concerning in these patients who are already susceptible to hypercoagulability. Constipation while on opioids for post-operative pain is frequent. Monitoring bowel movements and the use of scheduled laxatives may be useful. Two studies have shown that cancer rehabilitation inpatients have improved cancer symptomatology at discharge compared to admission. [38, 39] Reasons could be due to the symptom suppressing effects of physical activity but also psychiatric medical interventions. Many cancer symptoms can affect function and therapy participation which triggers medication optimization, injections or other treatments by the psychiatrist.

Deep Venous Thrombosis Prophylaxis

Studies have shown that between 17 and 26% of patients with glioblastoma develop a venous thromboembolic event (VTE). [40, 41] Relative immobility and a cancer related

hypercoagulable state can contribute to an increased risk of VTE. The risk of symptomatic bleeding in high grade gliomas has been reported between 1 to 3 percent without pharmacologic DVT prophylaxis. [42, 43, 44] The risk of symptomatic bleeding in patients with brain metastases varies by primary cancer. Melanoma, renal cell carcinoma and thyroid carcinoma may be more prone to bleeding. [45] The American College of Chest Physicians recommendations published in 2012 include mechanical prophylaxis and the initiation of pharmacologic VTE prophylaxis once adequate hemostasis has been achieved. [46]

In our practice, all brain tumor patients are ordered Thrombo-Embolic-Deterrent (TED) hose and sequential compression devices unless there is a medical contraindication. With respect to primary brain tumor patients, we ask the treating neurosurgeon or neuro-oncologist (whichever was involved in their care last) when to and what kind of pharmacologic VTE prophylaxis to initiate. Anecdotally, the timing of the initiation of the use of VTE prophylactic medications varies significantly between our 14 cancer neurosurgeons perhaps due to differing opinions on when adequate hemostasis is obtained. With respect to metastatic brain tumors, we evaluate recent brain imaging. If there is any sign of hemorrhage, we do not initiate pharmacologic DVT prophylaxis. Otherwise, we ask the last treating oncologist. Often, these patients are already initiated on DVT prophylaxis on the acute care service prior to transfer to inpatient rehabilitation. If there is any doubt about whether or not to start DVT prophylaxis, we consult a hematologist.

Concurrent Oncologic Treatment Considerations

The initial treatment for glioblastoma multiforme is the Stupp Regimen. Patient's first receive a surgical craniotomy with maximal possible resection. The patient's incision site is allowed to heal. Approximately seven days post-operatively, pathology results confirm the diagnosis. When the sutures have been removed (typically 10-14 days) and the surgical incision is sufficiently healed (typically 14-21 days), chemoradiation is initiated. This consists of six weeks (Monday through Friday, 2 Gray per fraction) of concurrent radiation (60 Gray total) with oral temozolomide followed by 28 day cycles of temozolomide with 5 days on and 23 days off of the medication. [47] This is generally continued until tumor recurrence occurs or toxicities prevent continuation. During the five days of oral temozolomide patients may feel fatigued and nauseated which may affect therapy performance and tolerance. During outpatient rehabilitation, one may try to avoid scheduling therapy during the five days of oral temozolomide to maximize therapy visits.

During inpatient rehabilitation, the ongoing radiation and chemotherapy may present both financial and logistical issues. Under the Medicare Prospective Payment System, the cost of concurrent radiation or chemotherapy may lead to reduced margins or perhaps losses during IRF admissions. For traditional brain injury IRF patients, diagnostic and treatment procedures are completed before transfer to IRF. However, given the timeline of the Stupp Regimen as well as other treatments for recurrent GBM or other brain tumors, patients may need to receive radiation or chemotherapy while on inpatient rehabilitation. [28]

With respect to ongoing radiation treatments, patients typically can be transitioned from inpatient to outpatient radiation (in the middle of the Stupp Regimen) within the same

institution. However, it can be difficult to transition to a completely new radiation center in the middle of the radiation treatment regimen. The future or ongoing radiation treatment plan should be taken into consideration when triaging primary brain tumor patients to post-acute inpatient rehabilitation facilities. The goal of inpatient rehabilitation may be to improve function so that the patient can make it to his/her radiation treatments. Unlike most stroke and traumatic brain injury patients, the logistics of ongoing cancer treatment need to be considered beyond home discharge disposition.

IRF institutional policies, nurse credentialing, availability of chemotherapy and concomitant monitoring may be obstacles to administering oral or intravenous chemotherapy in a post-acute inpatient rehabilitation facility. While radiation treatment is relatively short, scheduling transportation to and from the radiation machine (in particular if off site and requiring an ambulance) can lead to reduced time available for therapies. Many patients experience radiation related fatigue. The fatigue often is not felt after the first radiation fraction, but after three to five fractions. If possible, asking the radiation oncology schedulers, to schedule the patient as one of the last radiation treatments of the day may be beneficial. The post-radiation fraction fatigue will worsen at the end of the day after rehabilitation therapy is completed. Hopefully, patients will be more energized the next morning and ready to participate in rehabilitation. It also may prevent the return transportation logistical time from radiation to the inpatient rehabilitation unit from interfering in the therapy schedule.

Pathology Reports While in Post-Acute Care Inpatient Rehabilitation

Cancer related discussions that address morbidity and mortality may be unfamiliar to physiatrists. After a craniotomy and tumor resection, a pathology specimen is sent for analysis. The final pathology report typically takes over a week and by that time patients often are already transferred from the acute care hospital to a post-acute inpatient rehabilitation facility. In a freestanding inpatient rehabilitation facility, due to distance or lack of hospital privileges, oncologists may be unable to discuss the pathology results and the ramifications of their diagnosis in person. In a freestanding inpatient rehabilitation, the physiatrist is often the only physician caring for a newly diagnosed brain tumor patient. Questions regarding prognosis may be directed at the physiatrist who may have limited knowledge of the latest research and treatments. [28]

Conclusion

Neurologic tumors are the most common primary cancer type admitted to acute inpatient rehabilitation. They demonstrate similar rates of functional improvement, are a 60% rule diagnosis, present with neurologic findings similar to other brain injury populations and are relatively medically stable compared to other cancer populations. Reimbursement and logistical concerns regarding ongoing cancer treatment, managing toxicities and symptoms related to the cancer and its treatment, and under-referral from oncology services are co.

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Figure 1.
Graphical Representation of a Glioblastoma Multiforme Brain Tumor Patient Functional Course