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Repetitive transcranial magnetic stimulation for the treatment of major depression in a patient with an intracranial space occupying lesion: A case report of safety

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Abstract

This is the first case report of safety of therapeutic repetitive transcranial magnetic stimulation (rTMS) in a patient with an intracranial space occupying lesion (ICSOL) who suffered from recurrent major depression. In this case, the ICSOL was a mixed cystic and solid enhancing pineal region mass measuring approximately 16.9 mm × 12.2 mm × 15.5 mm. The patient remitted from depression with 36 sessions of dorso-lateral prefrontal cortex rTMS treatments over a six week period. During the rTMS treatment course, patient's medication list included bupropion that potentially can increase the risk of a seizure and topiramate that potentially can reduce the risk of seizure associated with the treatment. Patient tolerated the rTMS treatment well, reporting only transient headache and discomfort at the site of stimulation after the treatment. She tolerated the procedure well and had no incidental seizure activity throughout her treatment sessions.

Keywords

Transcranial Magnetic Stimulation; rTMS; Seizure; Brain Tumor; Intracranial Space Occupying Lesion

Background

Repetitive transcranial magnetic stimulation (rTMS) is approved by the Food and Drug Administration (FDA) for the treatment of major depressive disorder (MDD) (1). The common side effects of rTMS are headache and pain at the stimulation site. From its inception, TMS has been associated with the infrequent occurrence of a seizure during administration of the treatment (2). The risk of seizure with TMS is very low in general and just slightly higher with rTMS at high frequency (>5hz), longer train duration and shorter intertrain intervals because of hypersynchronized discharges of groups of neurons in the

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gray matter caused by increased excitatory synaptic activity compared to the inhibitory activity (3,4). In contrast, low frequency stimulation has been shown to reduce interictal spike frequency and amplitude in patients with epilepsy (3).

Other factors that influence the risk of seizure from rTMS are discussed below. A meta-analysis estimated the risk of a seizure from rTMS in subjects with previous history of epilepsy is 1.4% (5). Such low risk in this subject group can be attributed to concurrent use of antiepileptic medications. Use of antiepileptic drugs for treatment of epilepsy can offer protection against rTMS-induced seizures (3). Similarly, rTMS should be used with caution in conjunction with medications that might lower seizure threshold, such as bupropion (6). Preexisting neurological disorders (e.g., history of head injury with loss of consciousness, brain surgery and congenital brain malformations), sleep deprivation, use of proconvulsant drugs and recent withdrawal of anticonvulsant drugs, are other factors that increase the risk of seizure in patients undergoing rTMS (3).

Brain tumor is listed as a condition of increased or uncertain risk to develop seizures as a side effect in patients undergoing rTMS (3). We report a case of an individual with MDD treated with rTMS, who tolerated the procedure well, without any adverse events and was discovered to have an intracranial space-occupying lesion (ICSOL) during the treatment course. Additionally, the patient received bupropion and topiramate throughout the treatment course.

Case Report

A 39 year old female with history of recurrent depressive illness, hypertension and hyperlipidemia presented with relapse in depression symptoms of 3–4 months duration. She had switched her antidepressant from bupropion to fluoxetine and the dose of fluoxetine was increased from 20mg to 40mg 2 months prior to beginning rTMS. She was referred to a psychiatrist for pharmacotherapy management by her psychologist due to worsening of depression symptoms. Her symptoms included sadness, early morning awakening, feeling worse in the morning, concentration problems, loss of libido, inefficiency at work and agitation. She reported poor sleep in spite of spending more time in bed than usual. She had normal appetite with no weight changes. She denied having any suicidal ideations and did not report any kind of psychotic symptoms. She was drinking 1–2 alcoholic beverages to help her sleep and denied all other substance abuse. She has no history of manic episode, previous hospitalization or a suicide attempt. Her family psychiatric history was significant for depressive illness in mother and sister, and her sister has a history of suicide attempt. The Beck Depression Inventory (BDI) score was 20 during the initial evaluation. Her medical history was remarkable for chronic headaches, hypertension and hyperlipidemia.

Patient responded well to initial trial of combined psychotherapy and pharmacotherapy (duloxetine 60mg, aripiprazole 5mg, zolpidem CR 6.25mg). She also received topiramate 75mg at bedtime for headaches. She met remission criteria with BDI score of 3 after 3 months with above treatment. She had a complete relapse of depression after 2 months and returned to BDI of 20, now accompanied by subtle auditory hallucinations of perceiving murmuring voices when the airflow was on from her home's central air conditioner. This

psychotic symptom led to a more general discussion to elicit whether she was experiencing somatic delusions, and she reported the belief that there was something wrong with her brain. Bupropion 150mg twice daily was added to the pharmacotherapy regimen, a brain MRI was ordered, and she was referred for rTMS treatment.

Patient was treated using Magventure X100 rTMS device and the motor threshold was estimated to be 60% using the TMS Motor Threshold Assessment Tool Software (7). Dorso-lateral prefrontal cortex was the stimulation site, determined using the Beam F3 calculation method and confirmed with the 6 cm rule (8,9). We administered a sample of 10 HZ and 20 HZ stimulation to the patient. Patient tolerated 20 HZ stimulation better than 10 HZ stimulation. Hence, the patient was treated with 20 HZ, 2s trains and 110% of motor threshold with an intertrain interval duration of 15 sec. She received a total of 3000 pulses daily for 30 sessions over a six week period. The chosen stimulus parameters were in the safety range as discussed in the application guidelines for the use of TMS in clinical practice, except use of slightly longer duration of pulse trains (2s vs 1.6s) (3). Patient tolerated the treatment well, reporting only transient headache and discomfort at the site of stimulation after the treatment.

Midway through the rTMS treatment sessions, after her BDI score had decreased to 13, the patient's brain MRI results became available. Unexpectedly, her brain imaging showed mixed cystic and solid enhancing pineal region mass (measuring approximately 16.9 mm anteroposterior, 12.2 mm craniocaudal and 15.5 mm in transverse dimensions) with mild compression of the superior midbrain tectum with primary differential considerations include pineocytoma and germ cell tumor (Figure). Neurosurgical consultation was obtained and the consultant did not recommend any further intervention. Further discussion with the patient produced her recollection that she had undergone a brain imaging procedure as a child because of chronic sinusitis, and at that the time the image revealed a calcified pineal mass. In retrospect, the most recent imaging findings had been present for more than 20 years.

The imaging results were reviewed with patient and were explained about the increased risk of rTMS-induced seizure in the presence of preexisting neurological condition. Patient felt the benefits associated with the rTMS treatment outweighed risk of seizure, and she consented to continue with rTMS treatment. She completed 36 rTMS treatment sessions with improvement of depression with BDI of 5. She tolerated the procedure well and had no incidental seizure activity throughout her treatment sessions.

Discussion

We discuss above a case of MDD treated with rTMS, completed the treatment course and met remission criteria. The patient had two risk factors that potentially increased the risk of a seizure. She was discovered to have an ICSOL (mixed cystic and solid enhancing pineal region mass) that potentially can increase the risk of a seizure. The patient was also on a proconvulsant medication bupropion that could again further raise the risk of a seizure. On the other hand, our patient received topiramate, an anticonvulsant that potentially can reduce the risk of seizure associated with the treatment. The patient tolerated the entire rTMS

treatment course with no complaints other than the common side effects of transient headache and local pain at the site of the stimulation. She had no major side effects from the treatment and in particular, no seizures.

Intracranial mass is also a relative contraindication for electroconvulsive therapy (ECT), primarily because ECT is associated with significant, transient increase in blood pressure and correspondingly with an increase in intracranial pressure that could lead to brain herniation (10,11). The risk of serious side effects from ECT in the presence of intracranial mass varies with the characteristics of the tumor, including the tumor's size, location, and any associated peri-tumor edema (10,11). Indeed, some types of brain tumor, such as a small, anteriorly placed meningioma with no associated edema or shift, seem to pose minimal risk for complications (12). It seems likely that the risk of seizures in rTMS associated with intracranial mass will also be related to the location, size, and other characteristics of the particular tumor. In a study using navigated rTMS to test the feasibility of preoperative language mapping in brain tumor patients, about 17000 rTMS trains of 5, 7 and 10 Hz were applied at 114% of resting motor threshold. There was no incidental seizures in any of the patients and 34% of the patients in the study were suffering from epilepsy (13).

In the present report, the tumor was of modest size, probably slow growing over a period of decades, with no associated edema, and with minimal distortion of neighboring brain structures. These characteristics were likely associated with lower risk for complications. In conclusion, this is the first case report of safety of therapeutic rTMS in a patient with an ICSOL who suffered from recurrent major depression. Further studies and reports of other types of ICSOLs are warranted to characterize the safety profile of rTMS to use rTMS with comorbid depressive disorders.

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MRI Brain – Sagittal (top) and Axial (Bottom) views showing mixed cystic and solid enhancing pineal region mass

Figure 1.

MRI Brain – Sagittal (top) and Axial (Bottom) views showing mixed cystic and solid enhancing pineal region mass