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Original Article

Clinical Characteristics and Long-Term Outcomes of Movement Disorders in Childhood Thalamic Tumors

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ABSTRACT

BACKGROUND: We studied the outcomes of movement disorders that were associated with childhood thalamic tumors. **METHODS:** We retrospectively reviewed 83 children with thalamic tumors treated at our institution from 1996 to 2013 to document the incidence and outcome of movement disorders. Magnetic resonance imaging was used to analyze the involvement of thalamic nuclei, and three instruments were used to rate the severity of the disorders. **RESULTS:** Nine (11%) patients had one or more of the following movement disorders: postural tremor, resting tremor, ballism, dystonia, myoclonus, and athetosis. Median age at tumor diagnosis was seven years (range, 0.25 to 11 years), and the average age at movement disorder onset was eight years (range, 1.5 to 11 years). Movement disorders developed at a median of 1.5 months (range, 0 to 4 months) after surgical resection. The severity of the disorders was either unchanged or slightly improved during follow-up. The red nuclei were the only thalamic structures that showed tumor involvement in all nine patients. **CONCLUSIONS:** No specific injury of the thalamic nuclei was associated with movement disorders in children with thalamic tumors, and the severity of these disorders did not change over time.

Keywords: thalamic tumors, childhood, movement disorder, outcome

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Introduction

Thalamic tumors are uncommon in children and may comprise 0.84% to 5.2% of all intracranial childhood tumors.[1] This discrepancy is because of difficulty in distinguishing between primary thalamic tumors (i.e., those that originate from the thalamus) and secondary thalamic tumors that arise from adjacent structures (i.e., caudate nuclei, brainstem, or pineal gland). These neoplasms are usually low-grade gliomas, but they can have histologic properties of grade III and IV astrocytomas. However, other tumor pathologies also have been reported.[1,2] Confirmation of diagnosis requires tumor biopsy or resection.[3] Puget et al.[4] found that patients with low-grade thalamic tumors experience better survival when more than 90% of the tumor is resected and the duration of symptoms is longer than two months. Bernstein et al.[3] found that patients with thalamic malignancy survived approximately one year, regardless of the extent of resection. Bilateral thalamic tumors are even rarer and may have a worse prognosis.[5] The clinical signs and symptoms of thalamic tumors can be burdensome and include sensory syndrome, motor disorders, oculomotor deficits, increased intracranial pressure, seizures, and movement disorders.

Movement disorders occur infrequently in patients with thalamic tumors; their prevalence ranges from 1% to 33% in pediatric and adult studies.[2,3,6,7] Also, the data on

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the severity and outcome of movement disorders in these individuals are inadequate. The symptoms of movement disorders are typically associated with large thalamic low-grade astrocytomas and most likely result from surgical injury or the tumor compressing the neurons or neuronal pathways in the thalamic relay center.[8-11] Movement disorders reported in thalamic tumors include tremor, dystonia, chorea, ballism, and myoclonus.[9] No one has systematically correlated the anatomic locations of thalamic tumors or surgical lesions with the development of movement disorders and their outcomes. Therefore we studied movement disorders in children with thalamic tumors and attempted to identify specific injuries to the thalamic nuclei that were associated with these disorders.

Methods

This retrospective review was approved by the St. Jude Institutional Review Board. Our query of the hospital's neuro-oncology database for thalamic tumors identified 83 patients who were 18 years or younger at diagnosis and treated at our institution from 1996 to 2013.

All 83 medical records were first reviewed by a study nurse to identify patients who may have had a movement disorder. These charts were then reviewed by a study neurologist (R.B.K.), who did not know the magnetic resonance imaging (MRI) data, to determine whether a movement disorder was present, and if so, its severity, response to therapy, and long-term outcome. MRI scans of all patients were reviewed by the other study neurologist (Z.S.S.), who was not aware of the clinical data, to define the surgical injury to thalamic nuclei and involvement with tumor. The anatomic locations of lesions seen on MRIs were assessed using a neuroanatomy atlas with corresponding coronal, sagittal, and axial slices to identify nuclei-specific injuries.[12] All tumors were histologically confirmed after stereotactic biopsy, subtotal resection, or gross total resection. Tumors were graded according to the classification system of the World Health Organization.[13]

Assessment of movement disorders

The severity of movement disorders was determined using clinical information obtained by chart review and retrospectively applying the Karnofsky Performance Scale (KPS),[14] Extrapyramidal Symptom Rating Scale (ESRS),[15] and Clinical Global Impression of Severity (CGI-S)[16] at the first and last follow-up visits. Our institution has had a systematic neurological evaluation scale in place since 2001. All the patients included in this study were seen by a neurologist, and most of them had findings recorded on paper or electronic chart based on the scale. All patients had at least one examination available in their charts. The KPS, which ranges from 0 (dead) to 100 (no evidence of motor weakness or impaired function), indicates the patient's functional status. ESRS, which ranges from 0 (absent) to 6 (extremely severe), includes subscales for assessing tremor (eight body parts summed to a maximum score of 48), dyskinesia (10 body parts summed to a maximum score of 60), and dystonia (seven items summed to a maximum score of 42).[15] CGI-S scores range from 0 (absent) to 8 (extremely severe), which assess overall severity of tremor, dyskinesia, and dystonia in disease.[16]

We defined tremor as rhythmic uncontrollable shaking of a body part. Postural tremor appeared when the patient was directed to sustain a posture, such as stretching one's arms out. Dystonia was defined as a sustained contraction of a single or group of muscles. Myoclonus was defined as a sudden, single involuntary muscle jerk. Chorea was irregular, jerky spontaneous movements predominantly in proximal limb muscles, and athetosis was slower writhing movements predominantly in distal limb muscles. Finally, ballism was more explosive, jerky, and higher amplitude flinging of a proximal limb(s).

Results

Clinical characteristics

After chart review of 83 patients with thalamic tumors, we identified nine (11%) who experienced at least one type of movement disorder during the course of their illness. Median age at tumor diagnosis was seven years (range, 0.25 to 11 years), and median age at movement disorder onset was eight years (range, 1.5 to 11 years). Median time to first neurological evaluation was four months (range, one to 36 months) after movement disorder onset, and median time to last follow-up was three years (range, 0.2 to 11 years) after movement disorder onset. None of the patients had a family history of movement disorder, as determined by their answer to a question about whether any family member had ever been diagnosed with abnormal body movements or gait. All patients also had a normal early development.

Movement disorders included postural tremor (n = 7), resting tremor (n = 2), ballism (n = 4), dystonia (n = 2), myoclonus (n = 2), athetosis (n = 4): five patients had more than one type of movement disorder present concurrently. Both low- and high-grade tumors were present in patients with movement disorders (Table 1). Movement disorder developed in eight patients at a median of 1.5 months (0 to 4 months) after surgery; one patient had movement disorder onset 11 months before surgery. The extent of tumor resection ranged from stereotactic biopsy (n = 5) to subtotal resection (n = 3) and to complete tumor resection (n = 1). Conformal radiation therapy (54 to 59.4 Gy) was used as an adjuvant treatment in eight patients at a median time of 2.5 years (range, 0.83 to 5 years) after tumor diagnosis. Six of the eight patients received adjuvant chemotherapy as well. Four patients required a second surgery at a median time of four years (range, 1 to 12 years) after the first surgery; this procedure did not influence the intensity or morphology of the movement disorder in any patient (Table 1). Two patients had bithalamic tumors and seven had unilateral tumors. In the latter group, the movement disorder was contralateral to the tumor site. Six patients had tumors confined to the thalamus, whereas three had tumor extension into surrounding structures (i.e., corpus callosum, lateral ventricle, basal ganglia, internal capsule, and midbrain) (Tables 1 and 2).

The postoperative MRIs showed surgical lesions in the pulvinar (n = 4), mediodorsal (n = 2), ventrolateral (n = 2), centromedian (n = 1), anterior (n = 1), and laterodorsal (n = 1) regions of the thalamus and in the substantia nigra (n = 1), and red nucleus (n = 1) (Figure). Of the seven unilateral thalamic tumors, four invaded the entire thalamus, and three invaded all except the anterior region. All nine patients had tumors involving the red nucleus, and six had tumors involving the substantia nigra (Table 2). Postoperative intratumoral hemorrhage developed in one patient three weeks after the biopsy. Movement disorder appeared a week after the hemorrhage in this patient.

Movement disorder severity and outcomes

Postural tremor was unilateral and in one extremity in six patients; it was bilateral in one patient and involved