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Bilateral thalamic tumors in children

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Abstract *Introduction:* The actual incidence of thalamic tumors is not known, but the frequency of the bilateral tumoral involvement of both thalami is even less defined. *Case report:* In the present paper we report 4 new pediatric cases of primary bilateral thalamic tumors (PBTTs) observed in the Pediatric Neurosurgery Section at the Catholic University Medical School, Rome. Neuroimaging studies could not detect the presence of abnormal neoplastic tissue at the level of the midline basal subependymal region of the third ventricle, in the midbrain, and in the pineal gland in any of these 4 patients, thus apparently excluding the diffusion of a firstly unilateral thalamic tumor to the contralateral thalamus. In all of the patients, the lesions appeared as large symmetrical masses on both sides of the third ventricle, a feature that seems to further exclude the contralateral growth of a previously unilateral tumor. PBTTs appear to remain confined to the thalamic nuclei for a long time, and, unlike the unilateral form, the border between gray and white matter may not be violated for a relatively long time. Unlike in adults, PBTTs do not present with dementia in children. Signs and symptoms of increased intracranial pressure (3 cases) and movement disorders (tremor, 2 cases) were the presenting clinical manifestations in our 4 patients. *Conclusions:* The diffuse and bilateral involvement of both thalami makes surgical therapy barely feasible, even at the present time. Today, the main role of surgery is still to obtain a histological diagnosis. Generally, PBTTs are low-grade astrocytomas (grade II in the WHO classification), but limited anaplastic areas may be found in some patients, so that grade III and IV astrocytomas may be expected in a significant proportion of cases.

Keywords Thalamus · Thalamic tumors · Brain tumors

Introduction

Thalamic tumors in children are rare, though their actual incidence has not yet been established. Two recent reports provide figures ranging from 0.84% [7] to 5.2% [5] of all intracranial tumors. This broad discrepancy in incidence is mainly related to the difficulty in differentiating primary thalamic tumors from those lesions that only secondarily involve the thalamic structures, originating primarily from the cerebral hemispheres, the caudate nuclei, the pineal gland, and the brain stem. The secondary invasion of both thalamic nuclei is not uncommon, especially in the late phases of the progression of the neoplastic process, and the phenomenon may be observed in up to a third of the patients [5]. On the other hand, primary bilateral thalamic tumors (PBTTs) are considerably less common; their description is confined only to anecdotal single case reports, both in adult and pediatric populations [2, 3, 4, 5, 6, 7, 8]. Although the morphological features of PBTTs are quite typical, characterized by the

Table 1 Synopsis of the series

Patient	Sex	Age	Presenting clinical manifestations	Symptoms/signs at admission	Neuroimaging studies	Surgical management	Histological diagnosis	RX therapy	Outcome
1	Female	10 years	Headache and vomiting, right hemiparesis	Mild right hemiparesis	CT scan: bilateral thalamic tumor	Stereotactic biopsy	Astrocytoma grade II	Curie therapy	Death 7 months after surgery due to progression of the disease
2	Male	6 years	Headache and vomiting	Mild bilateral papilledema	MRI: bilateral thalamic tumor developing in the atrium of both lateral ventricles. No post-contrast enhancement. No mass effect. No hydrocephalus	Stereotactic biopsy into the right thalamus	Astrocytoma grade II	Hyperfractionated radiotherapy (47 Gy)	Death 10 months after surgery due to progression of the disease
3	Male	3 months	Bulging anterior fontanel, torticollis, nystagmus, bilateral tremor	Bulging anterior fontanel, nystagmus, torticollis, mild degree of intentional tremor	US scan, MRI, CT scan: bilateral thalamic tumor. Mild ventricular dilation	Stereotactic biopsy (right thalamus)	Astrocytoma grade II	No	Death 12 months after surgery due to progression of the disease
4	Male	10 years	Intentional and at rest tremor on the left arm	Tremor at rest in the left arm aggravated by intentional movement. Extrapyramidal hypertone in the same arm	CT scan, MRI: bilateral thalamic tumor developing into the atrium of the lateral ventricles. No enhancement after contrast	Craniotomy. Partial tumor excision through an interhemispheric transcallosal approach	Astrocytoma grade III	Hyperfractionated radiotherapy (46 Gy)	Alive 8 months after surgery. Tremor immodified. Tumor stable

nearly symmetrical enlargement of both thalamic nuclei without any apparent interconnecting tumoral tissue, their incidence, clinical manifestations, natural history, and prognosis remain relatively obscure. In this report we describe 4 cases of PBTTs with the goal of contributing further to the definition of these rare tumors and providing information concerning their management and outcome.

Materials and methods

In the last 20 years (January 1981–December 2000) 700 children, varying in age from 0 to 15 years, were treated at the Pediatric Neurosurgical Section due to an intracranial tumor. Sixty-four of these tumors were classified as thalamic on the grounds of the computed tomography (CT) scan and/or magnetic resonance (MR) imaging. Out of these 64 tumors, four were PBTTs. Age, sex, clinical presentation at admission, results of the neuroimaging studies, modalities of treatment, and outcomes of these 4 children are reported in Table 1.

Results

Three out of the 4 children presented with symptoms and signs of increased intracranial pressure, though none of them had an impaired level of consciousness. Focal neurological signs, namely mild hemiparesis, tremor, nystagmus and torticollis were present in 3 patients.

CT scan, MRI, and, in the youngest child, echoencephalography, revealed the symmetrical involvement of the thalamic nuclei (Figs. 1, 2, 3). Characteristically, these lesions did not enhance after contrast enhancement. Calcifications were not detected in any of the patients. Associated mild ventricular dilation was evident only in the youngest child.

Stereotactic (3 cases) and direct partial tumor excision (1 case, Fig. 3) allowed us to obtain the histological diagnosis (astrocytoma grade II in 3 children and grade III in 1). Three out of the 4 children underwent radiant therapy: implant of 131I in 1 patient and hyperfractionated external radiotherapy in 2 patients. Adjunctive therapies were refused by the parents of 1 patient. Three of the 4 children died 7, 10, and 12 months after the diagnosis; the remaining child is still alive 8 months after completing the radiotherapy treatment.

Discussion

The existence of PBTTs, i.e., the bilateral onset of a neoplastic process at the level of both thalami, is not widely accepted. Some authors consider the bilateral involvement of the thalamic nuclei to be the result of either the spreading of a glioma from the one side to the other [1], or the lateral sprouting of a tumor originating in the subependymal region of the third ventricle [2]. According to

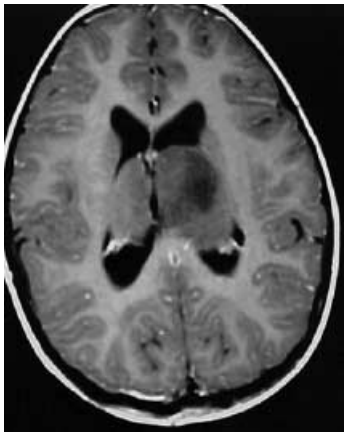

Fig. 1 Axial MRI of a bilateral thalamic astrocytoma after contrast administration. The tumor does not involve the head of caudate nuclei, and does not violate the border between gray and white matter

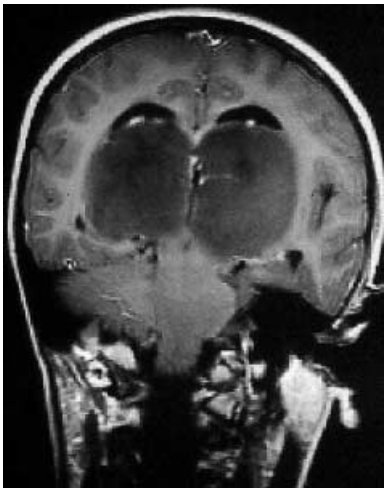

Fig. 2 Coronal MRI of a bilateral thalamic glioma in both the thalamic nuclei after contrast administration; the midbrain is free from tumoral involvement

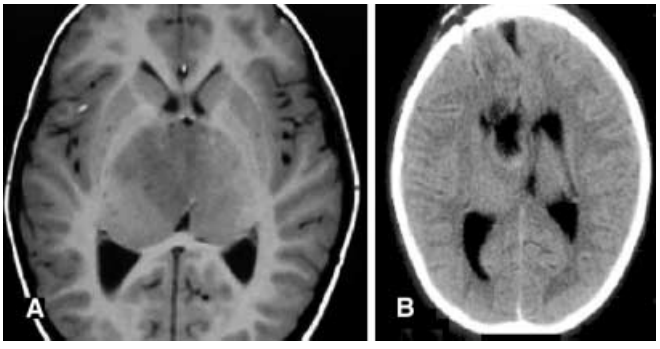

Fig. 3 **A** Pre-operative MRI T1-weighted images of a primitive bilateral thalamic astrocytoma. **B** Immediate post-surgical CT scan image after partial tumoral removal through a transcallosal approach

a third hypothesis, both thalami might be involved by means of the cranial diffusion of a contiguous midbrain tumor [2]. Although the hypotheses mentioned above might easily account for the commonly occurring asymmetrical tumoral invasion of the thalamic regions, which may be observed in cases of mesencephalic tumors, they are more difficult to accept in cases of symmetrical tumoral enlargement of the thalamic nuclei, which in some instances seem to remain almost completely distinct on the CT scan or MR imaging studies. Indeed, the neuroradiological investigations did not detect any sign of tumor at the level of the midbrain, the pineal gland, and the midline basal subependymal region of the III ventricle in our 4 patients (Fig. 2).

Further points in favor of the possible existence of PBTTs, apart from their homogeneous CT and MR features, are the rapid fatal evolution after diagnosis (3 out of our 4 children died in times shorter than those commonly observed in children with brainstem tumors), and the complete unresponsiveness of the tumors to the radiotherapy treatment, delivered either intratumorally or from an external source. Further support is provided by the topographic characteristics of these lesions, which remain confined within the thalamic nuclei for a long time, and, unlike unilateral thalamic tumors, do not tend to violate the border between gray and white matter (Figs. 1, 2, 3). The radiological characteristics, i.e., the homogeneous aspect, the compact epicenter, the absence of contrast enhancement which corresponds to an intact blood-brain barrier boundary, as well as the rapidly fatal clinical course, associate PBTTs with the considerably more frequent primitive pontine gliomas. Only in the late phases of their evolution may these tumors grow to infiltrate the temporal lobe through the connections with the amygdaloid nuclei [3] or the brain stem [2].

The clinical picture of PBTTs is also quite typical: symptoms and signs may remain surprisingly mild even in patients with large tumors. Consequently, in the early stages of the disease, a correct clinical diagnosis is difficult. The vagueness of the symptoms, coupled in some cases with difficulties in interpreting the neuroradiological findings, may in fact lead to misdiagnosis, going as far as diagnosing chronic encephalitis or necrotizing encephalopathy [7]. Age distribution is not different as regards the unilateral gliomas, but the severe dementia and the personality modification observed in adults affected by PBTTs [3] are rarely reported in pediatric patients, even if also in children the dorsomedial nuclei are also involved in the lesion in children. Damage to these thalamic nuclei is believed to be the reason for the dementia and the personality changes because of their connections with the temporal and the frontal lobes. At present these differences between adults and pediatric patients have not yet been explained. Intracranial hypertension is not related to hydrocephalus, which is usually absent, but it is secondary to the direct action of the neoplastic occupying space mass. Other symptoms and signs may be protean and non-specific because of the complex and various anatomical and functional connections of the thalamic structures. Hemiparesis, sensory disturbances, tremors, dysmetria, and unsteady gait may be present. In case 3, the torticollis and the nystagmus are justified by the involvement of the cerebello-rubro-thalamic tracts.

MRI is the best radiological examination for demonstrating these lesions, which appear as hyperintense areas on T2-weighted images and isointense on T1-weighted images without enhancement. Interestingly, PBTTs may show an increased creatine-phosphocreatine peak on MR spectroscopy, a pattern specific to these lesions [2] that is not present in unilateral thalamic gliomas; this suggests that these tumors have a different metabolic pattern, and confirm that they are a peculiar type of brain neoplasm.

The diffuse and bilateral involvement of the thalamic nuclei by the tumor makes surgical therapy very problematical, even today. Neuronavigation and stereotactic surgery, the modern technologies applied to neurosurgery, are still limited by the size and the site of these gliomas. Theoretically, a radical removal may be possible only for the most benign and non-infiltrative neoplasms, those that displace more than infiltrate the brain parenchyma, such as gangliocytomas or most juvenile pilocytic astrocytomas, but, to our knowledge, no such cases have been described in the literature. Consequently, the main role of surgery is still to obtain a histological diagnosis. Generally, these gliomas are low-grade astrocytomas (grade II of the WHO classification), but limited anaplastic areas may be found, and grade III and IV astrocytomas may be diagnosed. Radiotherapy and chemotherapy are sometimes utilized as adjuvant therapy, but their role is questionable. In our series, it was not possible to correlate histological diagnosis and modality of treatment with outcome (Table 1), which is generally poor, independently of the therapy that was utilized.

Conclusion

Bilateral thalamic gliomas are rare neoplasms, yet their actual incidence is unknown. Probably they are not simply unilateral thalamic tumors that grow on both sides, but are distinct lesions, as proved by their specific neuroradiological and metabolic properties, as well as a rapidly fatal clinical evolution. The unresponsiveness of these tumors to radiotherapy and chemotherapy treatment contributes further to distinguishing these extremely rare tumors from the relatively more common unilateral thalamic neoplasms.

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