

Bilateral Thalamic Glioma: Review of Eight Cases with Personality Change and Mental Deterioration

Gary D. Partlow,^{1,2} Raquel del Carpio-O'Donovan,¹ Denis Melanson,¹ and Terence M. Peters¹

Purpose: To describe the clinical, radiographic, and neuropathologic features of bilateral thalamic glioma. **Methods:** We searched our hospital records (1963 to present) to identify patients diagnosed as having the disease. **Results:** Our search revealed eight patients, ranging in age from 8–63 years, with bithalamic tumor diagnosed by angiography, CT, and/or MR. All patients displayed personality changes and/or mental deterioration, including memory loss, inattention, confusion, hallucination, hyperphagia, or slow mentation. Unilateral motor weakness was also noted in six cases. The tumor always involved the medial aspect of the left and right thalami, but was often more extensive. The pathology was determined to be grades I–IV astrocytoma, confirmed by stereotactic biopsy or autopsy in six. Mild to moderate hydrocephaly occurred in some cases and was considered to be a contributing factor to mental deterioration. No correlation was found between age and type of tumor. **Conclusions:** Bilateral glioma of the dorsomedial and intralaminar nuclei of the thalamus can be a primary cause of dementia that has not been well-recognized in the past. CT and particularly MR should be considered for patients presenting with personality change or dementia, because of the possible presence of this unusual but devastating disease.

Index terms: Glioma; Dementia; Thalamus, neoplasms; Neuropathology

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Thalamic tumors account for approximately 1%–1.5% of all brain tumors (1–3). Reports of bithalamic glioma are unusual, often being mentioned as part of larger reports on the occurrence and treatment of thalamic tumors in general (1–4). In a review of the older literature, Walker (5) concluded that bilateral lesions of the medial thalamic nuclei (and perhaps connections with the hypothalamus) produce severe mental impairment. In a recent case report (6), it was noted that a bilateral thalamic tumor without hydrocephaly can produce alterations in mood and behavior in the relative absence of motor or sensory deficits. The present paper describes eight patients with bithalamic glioma whose main presenting symptom was dementia.

Subjects and Methods

The hospital records for general admissions, radiology, and pathology were searched to identify patients diagnosed as having bithalamic glioma, from 1963 to the present. All data available for each patient, including neurologic reports, the various imaging modalities (angiography, computed tomography (CT), magnetic resonance (MR) imaging) and the histopathology were collected and analyzed. Angiography was performed in three patients and incomplete records did not allow for subtraction films. CT was performed without and with contrast media for the five patients presenting after 1973. The four patients who presented after 1984 underwent MR imaging at 1.5 T. The pulse sequence parameters were spin-echo T2-weighted sequences consisting of >2100/<35, >75/1–2 (TR/TE/excitations); and T1-weighted images, <600/<20/1–2. Gadolinium contrast agent was not used.

Routine histologic techniques had been used for paraffin embedding and hematoxylineosin staining of the biopsy and autopsy material.

Results

Eight patients with bithalamic glioma were identified since 1963. The data are summarized in Table 1. Symptoms of mental impairment such as inattention, confusion, memory loss, and emo-

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¹ Department of Radiology, Montreal Neurological Institute and Hospital, Montreal, Quebec, Canada H3A 2B4.

² Address reprint requests to G.D. Partlow, Department of Biomedical Sciences, University of Guelph, Guelph, Ontario, Canada N1G 2W1.

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TABLE 1: Summary of patients diagnosed with bithalamic glioma

| Case | Age | Sex | Date | Symptoms | Biopsy (B) Autopsy (A) | Diagnosis | Glioma Grade | Hydro- cephaly |
|------|-----|-----|------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|----------------------|-------------------------------------------------|-------------------|
| 1 | 8 | F | 1988 | Slow mentation Difficulty concentrating, inattention Regression of language Strabismus, bradykinesia on left | B | CT, MR | I, II | None |
| 2 | 15 | F | 1990 | Dramatic personality change, disinhibition Untidy, unmotivated, easily distracted Left hemiparesis, ataxia Strabismus | Alive | CT, MR | | None |
| 3 | 15 | F | 1990 | Personality change Hyperphagic, overweight | B | CT, MR | III, IV | Mild |
| 4 | 35 | M | 1963 | Progressive loss of memory for recent events Loss of interest, easily falls asleep Mental confusion, hallucinations Marked increase in appetite, weight gain | B, A | | I, II | Mild |
| 5 | 49 | M | 1973 | Memory loss, confusion, hallucinations Confabulation Motor weakness and slowness on right | A | Angiogram | III, IV | Moderate |
| 6 | 53 | M | 1989 | Personality changes, increased confusion Memory loss, difficulty concentrating Instability of gait | B, A | CT, MR, angiogram | I, II thalamus III, IV frontal lobe | Mild |
| 7 | 67 | F | 1968 | Rapidly progressive dementia Sudden memory loss Disoriented, emotionally unstable Weakness of left arm and leg Dystonia, dysarthria, incontinence | A | | I, II | Mild |
| 8 | 68 | F | 1974 | Disoriented, confusion, memory loss Motor weakness on right, slowness Dysphasia | | CT, angio- gram | | Mild |

tional disturbances dominated the clinical picture. Motor deficits were common but were of secondary importance. Typical clinical signs of increased intracranial pressure, such as headache and vomiting, were absent, although the lateral ventricles were mildly enlarged in five patients and moderately enlarged in one.

The bithalamic tumor was detected with angiography, CT, and MR (Figs. 1 and 2). Both symmetrical and asymmetrical appearance of the tumor mass was observed (Figs. 1 and 2). In all cases in which MR was used (cases 1, 2, 3, and 6), the tumor was readily identified (Figs. 1-3). However, with CT, the tumor occasionally appeared isodense with surrounding gray matter, and thus was more difficult to identify (compare Figs. 1A and 2A). Because of the sequence of

presenting signs, ie, personality changes first and motor deficits secondarily, and because of examples such as case 6 where the tumor is confined to the thalamus only (Fig. 3), it was concluded that the tumor originates within the thalamus itself. In the malignant form, it can rapidly spread into the basal ganglia and internal capsule (Fig. 3B), and eventually into the cerebral cortex (Fig. 3C). In cases 2 and 6, this evolution occurred within 1 year.

At autopsy, the tumor can be seen as a large mass occupying the left and right thalami, particularly the medial aspects (Fig. 4A). In some, but not all cases, the third ventricle is obliterated (compare Figs. 1, 2, and 4). In six cases, a tissue diagnosis confirmed the presence of low to high grade astrocytoma (eg, Fig. 4B). In case 6, the

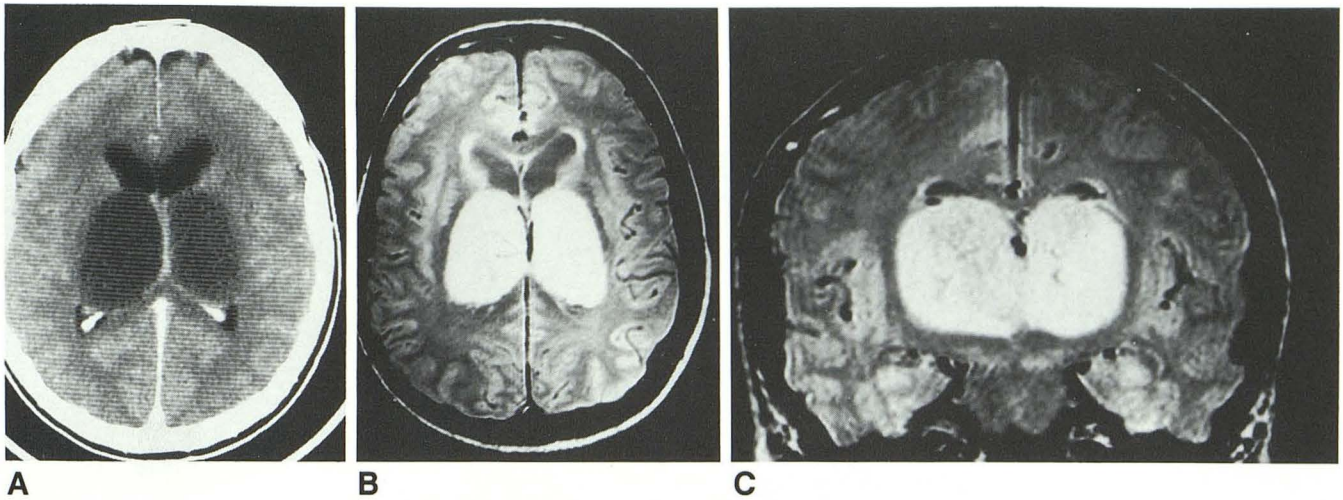


Fig. 1. Case 6; symmetrical appearance of bithalamic tumor.

A, Contrast-enhanced axial CT scan. Both thalami are enlarged and hypodense contrary to their normal appearance which is isodense to gray matter.

B and C, T2-weighted MR images (2100/30) in axial and coronal planes. The tumor presents as a homogeneous, hyperintense mass occupying both thalami. Hydrocephaly appears mild according to ventricular size, but hyperintensity of periventricular walls is suggestive of transependymal fluid resorption.

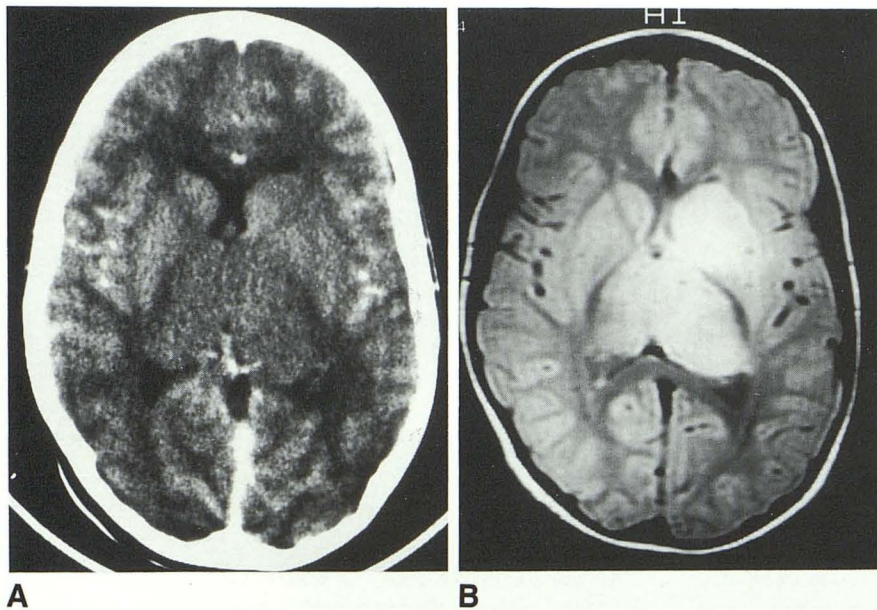


Fig. 2. Case 1; asymmetrical appearance of bithalamic tumor.

A, Contrast-enhanced axial CT scan. The subtle tumor mass is isodense with surrounding gray matter.

B, T2-weighted MR image (2500/20) in axial plane. Prominent homogeneous hyperintense bilateral thalamic tumor, displacement, and outer bowing of posterior limbs of internal capsules. On the left side, the tumor extends into the striatum.

tumor was determined to be a low grade astrocytoma at biopsy, but subsequent autopsy 1 year later indicated that the tumor had evolved into a high grade glioblastoma multiforme. In two cases, (cases 4, and 7), tissue was not available and only a presumptive diagnosis was made.

Discussion

Bilateral thalamic glioma is rare. Its occurrence has been mentioned in the past as part of larger studies on thalamic gliomas (1-4). However, only two recent case reports have directly described

this phenomenon (6, 7). It is possible that bithalamic glioma are beginning to occur more frequently. Four out of eight cases in this report were presented in the past 3 years. However, with the advent of routine use of CT and MR for diagnosis of neurologic disorders, it may simply be that such tumors are more readily detected. In the past, often a more conservative approach was taken rather than using the more invasive angiogram or ventriculogram for diagnosis. Currently, angiography is not required for the diagnosis of thalamic tumor. It is primarily used for the assessment of vasculature when stereotactic

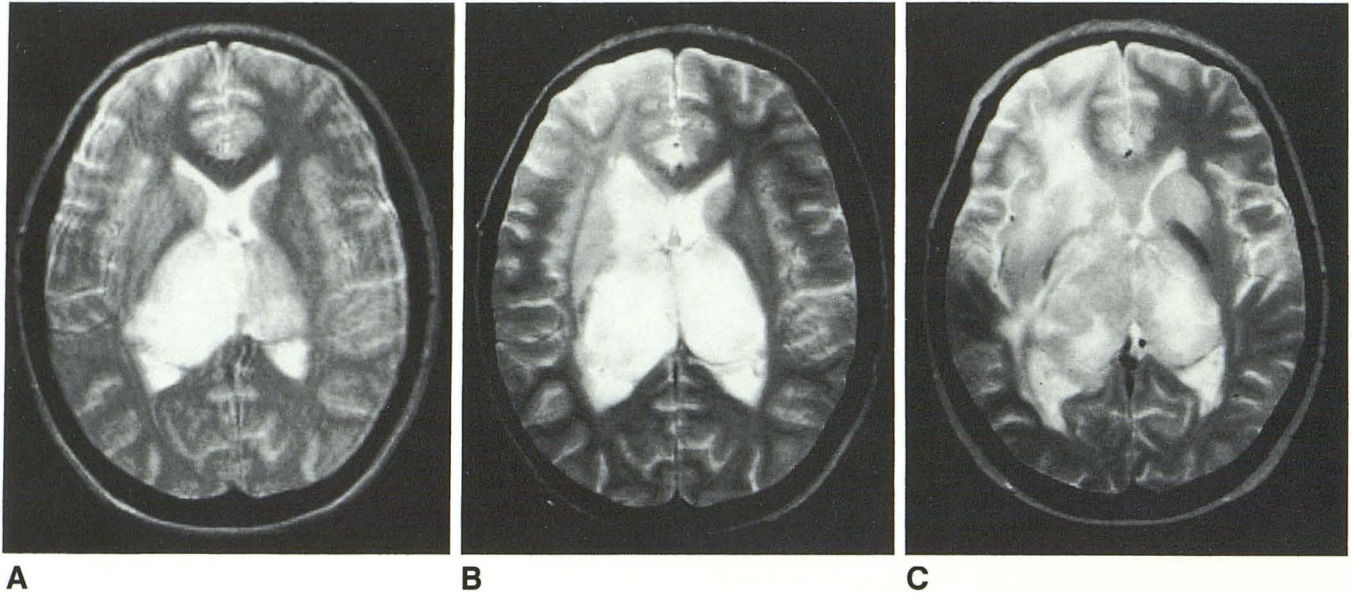


Fig. 3. Case 2; evolution of rapidly progressing, aggressive tumor with predominance on right; T2-weighted axial MR images (2100/80).

- A, Upon initial presentation, tumor mainly involves both thalami, but is more hyperintense and larger on the right.
 B, Nine months later, the left thalamic component has increased in size and become more hyperintense, while the right has spread into basal ganglia and internal capsule.
 C, One year from first diagnosis, tumor has spread into the left striatum, while the right also occupies the cerebral hemispheres, primarily frontal lobe.

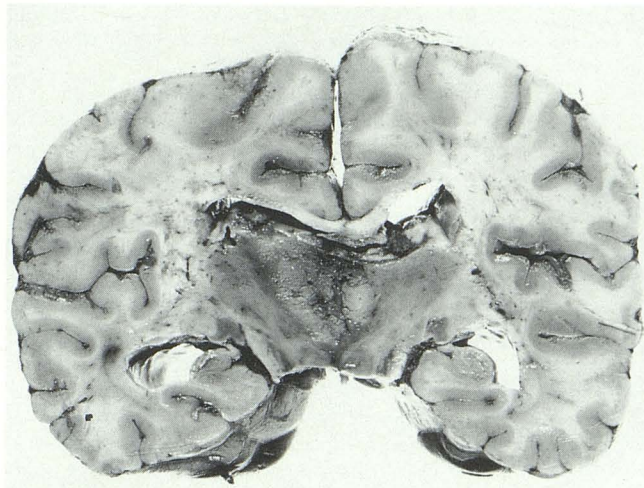
biopsy is being considered. However, recognition of early venous shunting does provide some diagnostic value regarding high grade glioma (Villemure JG, personal communication).

A high incidence of increased intracranial pressure has been reported in studies of thalamic tumor (1-3). Symptoms associated with hydrocephaly, such as headache and vomiting, were common, as well as signs of mental deterioration. Although it was suggested (1, 2) that the dementia seen in such cases was a result of increased intracranial pressure, other reports have distinctly attributed these personality changes to the tumor itself, particularly when signs of hydrocephaly were absent (3, 5, 6, 8). In the present study, the primary clinical symptoms involved personality changes, including confusion, memory loss, apathy, emotional lability, and hyperphagia. In six cases, there was little or no indication of increased intracranial pressure. The ventricles were of normal size or only slightly enlarged; there was no evidence of herniation of brain tissue below the tentorium (which would result in coma and subsequent death); and, typical clinical signs of headache and vomiting were absent. Consequently, it appears that the interventricular foramina were patent and that cerebrospinal fluid could escape to the third and fourth ventricles. Therefore, the

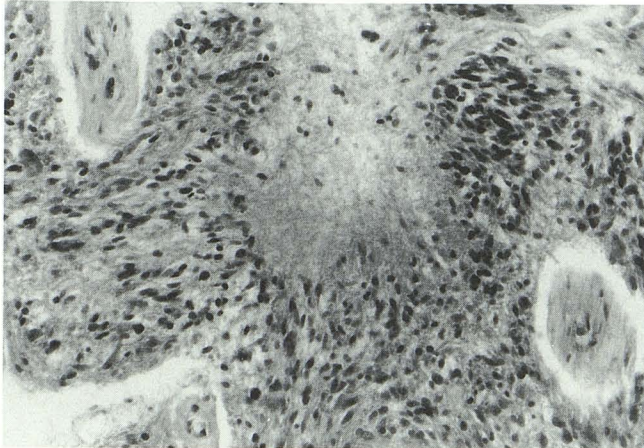
cause of personality changes and dementia was attributed to the bithalamic tumor and not increased intracranial pressure. Such a conclusion is further confirmed by reports of nonhemorrhagic infarcts or atrophy of the thalamus without hydrocephaly or edema (9-11). When the medial aspect of the thalamus was affected bilaterally, patients were characterized by mood and behavioral changes, as well as memory loss. Nevertheless, because of the subjective nature of assessing ventricular size, hydrocephaly cannot be completely ruled out as a contributing factor to mental deterioration.

In two cases of the present study (cases 3 and 4), vegetative dysfunctions, generally associated with the hypothalamus (12, 13) were observed, eg, increased appetite and weight gain (hyperphagia). This may be the result of mass effect from the thalamic tumor upon the hypothalamus, or interruption of the hypothalamic connections that pass through the medial aspect of the thalamus (5). Direct tumor involvement of the hypothalamus cannot be ruled out. Other autonomic dysfunctions associated with thalamic tumor have been reported (eg, incontinence) (2, 14), as was seen in case 7 of the present study.

Many aspects of behavior and personality have been anatomically associated with the medial



A



B

Fig. 4. Case 5; pathology of bithalamic tumor.

A, Gross anatomy shows a large bilateral mass involving the medial aspect of the left and right thalamus.

B, Photomicrograph of high grade glioma (glioblastoma multiforme) with central necrosis. The tumor is highly cellular with marked pleomorphism and prominent vascularity (abnormal vessels in upper left and lower right corners); hemotoxylineosin stain.

aspects of the thalamus. Studies have shown that the mediodorsal nucleus plays a role in mood, memory, sleep, language, and learning (5, 7, 9, 10–12, 14–18). It influences complex behavior and higher mental functions by means of connections with the prefrontal cortex (5, 16, 19). In addition, Macchi (17) ascribed to the intralaminar nuclei a contribution to the attentive, discriminating, and integrative activity in the waking state.

Primary thalamic glioma may originate in the subependymal glia, and hence have primary relation to the medial areas of the thalamus (8). The tumor can spread across the midline via the interthalamic adhesion and the roof or floor of

the third ventricle (1, 8). This would account for the initial appearance of a larger tumor on one side (case 1), but subsequent development of a symmetrical bilateral mass (case 6). In some cases, the tumor also spreads into the lateral nuclear group of the thalamus and eventually the internal capsule and basal nuclei, resulting in sensory and/or motor deficits secondarily (1, 3, 8).

Although several reports have attempted to correlate the occurrence of thalamic glioma with age, there is such discrepancy in the literature that no trend can be determined (1–4, 20). Similarly, in the present study, albeit a small sample size, no age correlation was apparent.

A spectrum of tumors was observed, ranging from grade I–IV. In some situations, it seems that the low grade tumor progressed into the malignant form (cases 2 and 6). The tendency of astrocytomas to dedifferentiate is well-recognized (21).

No correlation of tumor type with age was observed. However, it has been suggested that low grade astrocytoma is more common in younger individuals (<40 years), and high grade in older patients (20), whereas others have reported equal numbers of benign versus malignant thalamic tumors in individuals less than 30 years old (4, 22).

In conclusion, it is important for radiologists to recognize that bithalamic glioma is a possible, although infrequent, cause of personality change and dementia due to destruction of the medial and intralaminar nuclei. Knowledge of this association is helpful for early diagnosis and for prompt therapy to prevent or delay the devastating results of bithalamic glioma.

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