Thalamic gliomas: A clinical, radiological and pathological study of 39 cases

Suresh Nair N.

Girish Menon

Gopalakrishnan C.V.

Mathew Abraham

Ravi Mohan Rao B.

ABSTRACT

Aim: To analyze the clinical profile, radiological and pathological findings and factors influencing outcome in thalamic gliomas. Materials and methods: A retrospective analysis of the case records of 39 patients with thalamic glioma, operated since Jan 2000 over a period of six years. Variables analysed include: age, sex, surgical procedures, and histology.

Results: The study group included 24 males and 15 females. Raised intracranial pressure was the commonest mode of presentation in 29 (74%) patients followed by hemiparesis, visual deficit and dysphasia. Radiological features varied with the grade of the gliomas and four patients were found to have bilateral thalamic involvement. A radical decompression was attempted in 14 patients while the rest underwent a less radical surgery or biopsy of the tumor. 23 (59%) of the tumors were categorized as high-grade gliomas, and 16 (41%) as low grade. All patients received radiotherapy postoperatively. Of the 32 patients available for follow up, tumor progression/recurrence was observed in all of the high grade and five (12.8%) of the low-grade neoplasms. At the time of last follow up 69.6 % of the patients who underwent decompressive surgery had a good outcome compared to only 37.5 % of those who underwent biopsy.

Conclusion: Age and sex did not influence outcome in our study. Patients with thalamic gliomas who underwent radical cytoreductive surgery followed by adjuvant radiotherapy had a prolonged median survival with acceptable morbidity. High-grade tumors carry a dismal prognosis whatever be the radicality of tumor decompression..

Key words: Thalamus, gliomas, Magnetic resonance imaging

Author's Affiliations: Department of Neurosurgery, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Trivandrum - 695011, Kerala.

Reprint Requests: Dr. Suresh Nair, Prof. & Head, Department of Neurosurgery, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Trivandrum - 695011, Kerala, Phone : 91- 471-2443152(O), 91-471-24348959 (R), Fax : 91 471 2446433, Email: snair@sctimst.ac.in

INTRODUCTION

Thalamic tumors account for about 1- 5% of CNS tumors. Most of these tumors are low grade lesions of astrocytic lineage but because of their relative inaccessibility, and poor response to adjuvant therapy, carry a dismal prognosis. The natural history is unpredictable & optimal management of these tumors is

controversial. We present here a single institution six year experience of 39 consecutive patients with histologically confirmed thalamic glial tumors and attempt to analyze the clinicoradiological features, management strategies and outcome predictors.

MATERIALS & METHODS

We retrospectively analyzed the case records of 39 patients with thalamic glioma, treated in our department from January 2000 over the next six years with at least two years follow up. The criteria used for inclusion in our study were neuroradiographic demonstration of a thalamic tumor and histological confirmation of glioma. Patients whose diagnostic imaging was suggestive of tumor origin from structures other than the thalamus (hypothalamus, pineal, optic chiasm, brainstem, adjacent cortex) based on bulk of disease, were excluded from the study. Bithalamic gliomas were defined by evidence of involvement of both thalamic regions on MRI. The histological diagnosis was established according to revised World Health Organization (WHO) criteria 2007. Progressive disease was defined by symptoms suggestive of tumor recurrence and/or >25% increase in tumor volume. The following variables were assessed for prognostication: age, sex, surgical procedure and histology.

RESULTS

The study included 24 males & 15 females showing a clear male preponderance (male to female ratio of 1.6:1). The age range varied from 7 yrs to 63 with a median age at diagnosis of 13 years (Table 1). The most common symptom was raised intracranial pressure (74%) followed by hemiparesis, visual deficit, dysphasia, seizures and thalamic syndrome (Table 2). MRI documentation of disease was available in thirty-eight patients (97.4%) while one patient was diagnosed based on CT scan. Neuroimaging identified monothalamic involvement in 35 (90%) cases whereas bilateral thalamic involvement was present in 4 (10%) tumors.

Confirmed histopathological examination was possible in all cases. On histological review, 23 (59%) of the tumors were categorized as high-grade gliomas, and 16 (41%) as low grade. While radiographic contrast enhancement was more evident with high-grade tumours (44%), extension into adjacent structures was equally apparent among both low- (38%) & high grade (44%) tumors (Table 3).

Radiotherapy was administered postoperatively irrespective of the grade of the tumor as achieving a radical total decompression in such an eloquent area was improbable. Radiation fields were chosen to encompass tumor volumes & sites of extension. Aggressive surgical resection was attempted only in focal, monothalamic gliomas without evidence of local infiltration. Lesser degrees of resection or biopsy were utilized for bilateral or diffuse tumors (Table 4). A radical decompression was attempted in 14 patients while the rest underwent a less radical surgery or biopsy of the tumor.

Thirty two of the 39 cases (82%) came for follow up (18 high grade & 14 low grade cases). Among the prognostic variables, the impact of histopathological grade was maximum .Tumor progression/ recurrence was observed in all the high grade tumors within 1 year and 5/14 (35.7%) of the low-grade neoplasms. None of the patients with high grade lesions were alive 2yrs after diagnosis; where as the 2yr survival for patients with low grade gliomas was 57%. Patients who underwent decompressive cytoreductive surgery fared better (GOS 1 or 2) in comparison to those who underwent only biopsy (69vs31%; p <0.05). Surgical morbidity with radical surgery was relatively high and the common post operative complications included motor deficits in six patients, dysphasia in two, visual field cut in one and seizures in one.

DISCUSSION

Diencephalic gliomas account for about 5% of childhood CNS tumors and have been

Table 1: Clinical & radiological features based on glioma grade

	Total sample	Low-grade histology No (%)	High-grade histology No (%)
All patients	39	16 (41%)	23 (59%)
Sex			
Males	24	10 (62%)	14 (61%)
Females	15	06 (38%)	09 (39%)
Age at diagnosis			
= 20	21	07 (44%)	14 (61%)
21-40	08	05 (31%)	03 (13%)
= 41	10	04 (25%)	06 (26%)
Laterality			
Unithalamic	35	12 (75%)	23 (100%)
Bithalamic	04	04 (25%)	
Extension beyond thalamus			
Present	16	6 (38%)	10 (44%)
Absent	23	10 (62%)	13 (56%)
Contrast enhancement			
Present	27	6 (38%)	21 (92%)
Absent	08	7 (43%)	1 (04%)
Not done	04	3 (19%)	1 (04%)

Table 2: Surgical procedures performed

Procedure	Number
Shunt & endoscopic biopsy	1
Stereotactic biopsy (STB)	11
STB + shunt/ETV	4
Decompression	14
Shunt/ETV + Decompression	9
Total	39

Fig. 1: Age distribution
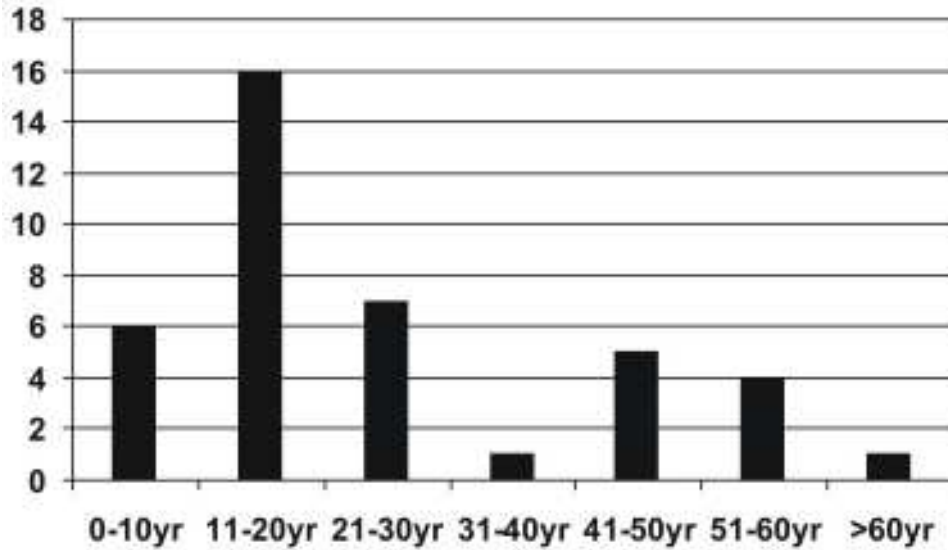
Fig 2: Clinical presentation
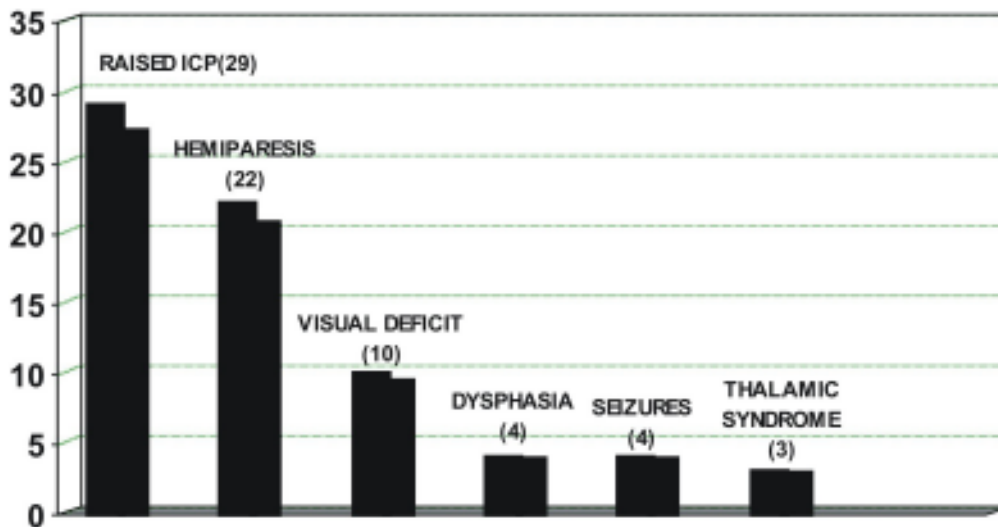
broadly grouped into two categories (10,13). The first group includes optic pathway/ hypothalamus gliomas (OPG) that have been further sub-classified into three anatomic subcategories: anterior, chiasmatic & chiasmatic/ hypothalamic. These tumours are seen in the younger pediatric age group with a mean age at diagnosis being 4.5yrs and approximately 20 to 30% of children having NF-1. Treatment is initiated early as most of these children present with major visual impairment or the diencephalic syndrome. Children with OPG have an excellent long-term prognosis with a 10yr survival of over 85%. (2,8,11,12,17).

Thalamic gliomas constitute the second group of diencephalic tumours and differ from the first group in several aspects (13). The reported incidence of pure thalamic lesions varies from 1-5% in various institutional series (810,11,12,17). Their true incidence is however, is not known as they are often grouped with tumors arising from other diencephalic structures. Thalamic gliomas are known to have a bimodal age distribution .The first peak occurs among children & adolescents (less than 20yrs old) & the second in those older than 40 years. We too observed a similar pattern with sixteen patients in the second decade and ten patients above the age

of forty. Although we noticed a male preponderance in our series, we could not establish its influence on prognosis.

Symptoms and signs at presentation in thalamic tumors are related to the size and extent of the tumor and the presence of increased intracranial tension. The common presenting symptoms apart from raised intracranial pressure include focal motor and sensory deficits, movement disorder, neuropsychological symptoms and occasional seizures (8). Surprisingly the "classic thalamic syndrome of Dejerrine and Roussy" is rarely seen with thalamic tumours. Fernandez et al (2) suggest that oligodendrogliomas lead to severe intracranial hypertension before motor weakness appears contrary to astrocytomas where motor weakness is the predominant symptomatology. This is possibly because oligodendrogliomas are known to grow in an infiltrative manner, initially without destruction of the underlying structures, which is why they may be voluminous in spite of the lack of motor deficit. In our observation the most common symptoms were raised intracranial pressure and hemiparesis.

Astrocytomas account for majority of thalamic tumours. Pilocytic astrocytomas, fibrillary astrocytomas, anaplastic astrocytomas, and glioblastomas represent more than 90% of reported cases, the percentage of high-grade lesions varying from 33 to 56% (2). Infiltrating fibrillary astrocytomas are prone to malignant progression from grade II to grade IV & extension into adjacent structures such as the basal ganglia & the brainstem is not uncommon. Although thalamic gangliogliomas and oligodendrogliomas have been reported only very occasionally, Fernandez et al (2) report a high incidence of oligodendroglioma in their series and suggest that analysis of 1p/19q status can be useful to support the diagnosis of oligodendroglioma even if loss on 1p and/or 19q is infrequent in children compared to adults. We did not have any cases of ganglioglioma or oligodendroglioma in our series.

Thalamic gliomas have wide range of imaging characteristics that can be grouped into four patterns (3).

PATTERN I

A solid tumor, hypodense on unenhanced CT, hypo-isointense on T1-WI, and hyperintense on T2-WI, with moderate/absent edema, and without contrast enhancement. These features strongly suggest diffuse non-anaplastic astrocytoma. Similarly, when there is extensive infiltration involving adjacent structures or both thalami, despite the lack of contrast enhancement, the most reliable diagnosis is anaplastic astrocytoma. Gliomatosis cerebri may be suggested when the tumor involves other cortical/subcortical areas besides the thalamus.

PATTERN II

A solid tumor, with or without cystic counterparts, that appears hypodense on unenhanced CT, hypointense on T1-WI, hyperintense on T2-WI, and with contrast enhancement. This pattern is encountered in many tumors with dramatically different prognoses, but considering the following "sub-patterns" can provide correct diagnosis:

1. If the margins of the tumor are well defined and areas of contrast enhancement appear homogeneous, the most reliable diagnosis is pilocytic astrocytoma or ganglioglioma (less common)

2. If the margins are ill defined, with infiltrative behavior, and contrast enhancement is patchy and/or nonhomogeneous, anaplastic astrocytoma is the most reliable diagnosis

3. If the features described above are associated with necrosis, hemorrhage, and extensive edema, glioblastoma multiforme is the most likely diagnosis; as an alternative, atypical rhabdoid tumor may be proposed in infants.

PATTERN III

A solid tumor, with or without cystic components, with calcifications on CT, non-homogeneous hypointensity on T1-WI and hyperintensity on T2-WI, and with contrast enhancement. Oligodendroglioma or mixed oligo-astrocytoma is possible diagnoses, but astrocytoma or anaplastic astrocytoma cannot be excluded.

PATTERN IV

A solid or predominantly solid tumor, hyperdense on unenhanced CT, hypo/isointense on T1-WI, isointense or hypointense on T2-WI, with contrast enhancement infiltrating the walls of the posterior third ventricle. This pattern is strongly suggestive of a diagnosis of germ cell tumor, even if the pineal area is not involved; however, lymphoma should be considered as the second option.

The management policy for thalamic gliomas has evolved from initiation of radiotherapy without prior tissue diagnosis to open biopsy or partial resection and more recently image guided gross total resection. With increasing availability of newer surgical tools the high rates of morbidity associated with open decompression of thalamic tumours has decreased considerably and almost all contemporary series advocate cytoreductive surgery prior to adjuvant therapy based on definite statistical survival benefit. Moreover surgical intervention is often necessary to relieve the raised intracranial pressure as well as to establish a diagnosis. However controversy exists on the type of surgical approach to be adopted as well as the extent of decompression to be attempted. One of the early results which allow some statistical conclusions with regard to the outcome after resection of thalamic astrocytomas came from the analysis of Krouwer and Prados (8) who concluded that the prognostic factors for a favorable outcome include histological diagnosis of low grade astrocytoma, age under 18 years, and cytoreductive surgery. Patients who underwent total or subtotal resection in Pathys series (12) had a significantly prolonged median survival in comparison to those who did not undergo surgery (p = 0.0087). Similarly Grigsby (6) and others (1,9,14,16,18) in their analysis of thalamic and brain stem gliomas have highlighted the fact that the patients undergoing subtotal resection had a relatively good prognosis. Our observation is similar with patients undergoing cytoreductive surgery having a definite benefit over those undergoing simple biopsy. Based on these data it appears likely that surgical tumor reduction provides definite benefit for deep-seated astrocytomas that can be approached and removed with a small risk as defined by the adjacent functional structures.

The ideal surgical approach to a thalamic tumour is again controversial (1,9,14,16,18). Although the conventional approach involves a transfrontal or transcallosal approach Steiger (16) et al in their extensive series prefer either a parieto-occipital transcortical transventricular approach or an infratentorial supracerebellar route from the contralateral side. Although the infratentorial way of access is less invasive because it is completely extra-axial, the window between the two basal veins of Rosenthal is limited, and this route cannot remove lesions with a lateral extent to more than approximately 1 cm from the midline. Thus this approach is suitable only for small tumors originating from the habenula or the medial aspect of the pulvinar thalami. For tumors extending more laterally, Steiger (16) prefers a parietooccipital transventricular approach over an anterior transfrontal transventricular or a transcallosal approach. We prefer either a transcortical /transsulcal approach or an interhemispheric approach depending on the lateral extent of the lesion. With the availability of image guidance we have adopted a more radical approach at decompression preferably through a temporal or parietal transcortical approach. We do not have any experience with the infratentorial supracerebellar approach for thalamic gliomas described by Steiger (16).

The conventional dose of 50-55 Gy does not seem to be beneficial as reported by several authors (5,12) and the current trend is

towards hyperfractionation and an effort to increase the total radiotherapy dose to 76 Gy - 78 Gy in order to achieve better local control. Prados et al (8) have reported a better median survival of 12.7 months by administering this higher dose. Similarly Halperine (7) have reported no added advantage in local control by whole brain radiation and radiation therapy fields encompassing CT definition of tumor, surrounded by an adequate margin is sufficient.

Several authors have assessed the complication of treatment and quality of survival and in most of the series majority of surviving children seem to have good functional results and relatively normal life (2,6,12,15). In our series complications following surgery were confined to visual deficits, worsening of contralateral motor power and speech disturbances. This experience corresponds to the report of Drake and co-workers who stated a minimal morbidity in their small series. The most likely source for speech disturbances is the pulvinar since it represents the site of the neurons projecting to the peri-sylvian language centers. Disturbances of the state of consciousness and frontal like syndromes are known to occur with ischemic lesions of the anterior and central thalamic nuclei and are more common with transfrontal or transcallosal approaches for thalamic lesions. Long term complications of hyperfractionated radiotherapy, however do exist and these include schooling difficulties, seizure disorder, hearing loss and stunted growth.

The natural history of thalamic tumours is extremely poor as reported by, Franzini and co-authors. In their analysis of 70 patients with biopsy confirmed thalamic gliomas 43% died within 3 years after diagnosis. Grigsby (6) et al report an overall 5 year survival in thalamic tumors in pediatric patients of 59.5% which is better than in adults (20.9%) (p = 0.006). Mean survival ranges from 91 weeks to 21.4 weeks in grades 2 to 4. Pathy et al (12) quote a 28% disease free survival at 2 years, and an overall 5-year survival of 73%. Multimodality therapy is frequently ineffective & overall 4-year survival for all cases with thalamic primary tumors is 37% (13). Summarizing the available literature, age at diagnosis, tumour histology and cytoreductive surgery appear to be important prognostic parameters. We could not establish any relation between young age and a favourable prognosis as reported in some series. In our series, among the prognostic variables, the impact of histopathological grade was the highest. Tumor progression/ recurrence was observed in all the high-grade tumors within 1 year and 5/14 (35.7%) of the low-grade neoplasms. None of the patients with high-grade lesions were alive 2yrs after diagnosis; where as the 2yr survival for patients with low-grade gliomas was 57%. Patients who underwent decompressive cytoreductive surgery fared better than those who underwent only biopsy. Bithalamic gliomas are aggressive & have a prognosis similar to that of brainstem diffuse gliomas.

Many authors believe that bilateral thalamic gliomas are not simply unilateral thalamic tumors that grow on both sides, but are distinct lesions, as proven by their specific neuroradiological and metabolic properties, as well as a rapidly fatal clinical evolution (4). However one of our patients, who underwent treatment for unilateral lesion showed clear documentation of contralateral progression on serial follow up scans. These tumours are reported to be a possible, although infrequent, cause of cerebellar symptoms and of cranial nerve and sensory deficits although none of our four patients with bilateral lesions had such a presentation. 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.

Given the retrospective nature of the study, no conclusion could be drawn regarding impact of radiation therapy or efficacy of chemotherapy in this patient population. Aggressive attempts at resection may have a significant impact on outcome & the evolution of image-guided neurosurgery can contribute to effective resection with decreased incidence of complications. Recent advances in radiotherapy and chemotherapy may contribute to a better outcome.

CONCLUSION

Thalamic gliomas constitute a relatively rare group of intracranial neoplasms with distinct clinicoradiological characteristics and poor long-term outcome. Although surgical approach needs to be tailored on a case-to-case basis, attempts at radical cytoreductive surgery definitely leads to a better outcome with acceptable morbidity. In addition to extent of surgical decompression, histology is another important prognosticator with patients having high-grade tumors carrying a much dismal prognosis compared to low-grade tumours.

REFERENCES

1.   Albright A.L. Feasibility and advisability of resections of thalamic tumors in pediatric patients. J Neurosurg 100(5 Suppl Pediatrics). 2004; 468-72.

2.   Carla Fernandez & André Maues de Paula ,Carole Colin & Benoît Quilichini,Corinne Bouvier-Labit & Nadine Girard ,Didier Scavarda, Gabriel Lena,Dominique Figarella-Branger. Thalamic gliomas in children: an extensive clinical, neuroradiological and pathological study of 14 cases. Childs Nerv Syst. 2006; 22 (12) : 1603-10.

3.   Colosimo C , di Lella G.M., ·Tartaglione T. .Neuroimaging of thalamic tumors in children. Childs Nerv Syst. 2002; 18 (8): 426-39.

4.   Concezio Di Rocco Aldo Iannelli. Bilateral thalamic tumors in children. Child's Nerv Syst. 2002; 18: 440-444.

5.   Eifel PJ, Cassady JR, Belli JA . Radiation therapy of tumors of the brainstem and midbrain in children : Experience of joint center for radiation therapy and children's hospital medical centre ,1971-1981. Int J Radia Oncol Biol Phys. 1987; 13: 847-852.

6.   Grigsby PW, Thomas PR, Schwartz HG et al.Multivariate analysis of prognostic factors in pediatric and adult thalamic and brain stem tumors. Int J Radiat Oncol Biol Phys. 1989; 16: 649-655.

7.   Halperine EC. Pediatric brain stem tumors : Pattern of treatment failure of their implication for R.T. Int J Radia Oncol Biol Phys. 1985; 11: 1293-1298.

8.   Hendrikus G.J. Krower, Michael D.Prados .Infiltrative astrocytomas of the thalamus. J Neurosurg. 1995; 82 (4): 548-57.

9.   Ishii R, Suzuki Y, Watanabe A, et al. Gross total removal of gliomas in the pulvinar and correlative microsurgical anatomy. Neurol Med Chir (Tokyo). 2002; 42 (12): 536-45.

10.   Jeffrey C. Allen. Initial management of children with hypothalamic and thalamic tumors and the modifying role of neurofibromatosis-1. Pediatr Neurosurg. 2000; 32 (3): 154-62.

11.   Nishio S, Morioka T, Suzuki S, et al. Thalamic gliomas: a clinicopathologic analysis of 20 cases with reference to patient age. Acta Neurochir (Wien). 1997; 39 (4): 336-42.

12.   Pathy S, Jayalakshmi S, Chander S et al. Prognostic factors influencing the outcome of thalamic glioma. Neurol India. 2002; 50: 37-40.

13.   Peter C. Burger, Kenneth J.Cohen, Marc K.Rosenblum et al. Pathology of diencephalic astrocytomas. Pediatr Neurosurg. 2000; 32(4): 214-9.

14.   Selvapandian S. Endoscopic management of thalamic gliomas. Minim Invasive Neurosurg. 2006; 49 (4): 194-6.

15.   Siffert J, Allen JC. Late effects of therapy of thalamic and hypothalamic tumors in childhood: vascular, neurobehavioral and neoplastic. Pediatr Neurosurg. 2000; 33 (2): 105-11.

16.   Steiger H J, Goetz C , Schmid-Elsaesser R. Thalamic Astrocytomas: Surgical Anatomy and Results of a Pilot Series Using Maximum Microsurgical Removal Acta Neurochir (Wien). 2000; 142: 1327-1337.

17.   Souweidane MM, Hoffman HJ. Current treatment of thalamic gliomas in children. J Neurooncol. 1996; 28 (2-3): 157-66.

18.   Villarejo F. ,Amaya C, Perez Diaz C, et al. Radical surgery of thalamic tumors in children. Childs Nerv Syst. 1994; 10 (2): 111-4.