Eur. J. Oncol., vol. 17, n. 2, pp. 00-00, 2012

Large medulloblastoma with brain-stem invasion in an adult: case report and review of the literature

Grande medulloblastoma con interessamento del cervello staminale in persona adulta: resoconto di un caso e revisione della letteratura

Pavel Haninec, Radek Kaiser

3rd Faculty of Medicine, Charles University, Department od Neurosurgery, University Hospital Kralovske Vinohrady, Prague, Czech Republic

Summary

We report the case of a 43-year-old woman with a large midline medulloblastoma invading the brain-stem. She underwent a radical resection followed by radio- and chemotherapy. The follow-up period was 2.5 years; she is now without recurrence of the tumor, but neurological deficits, mostly in the form of cerebellar dysfunction, persist. The aim of this case report is to increase awareness of the incidence, treatment and prognosis of primitive neuroectodermal tumors in adults. Medulloblastomas are rare and compared to the pediatric population, have a relatively good prognosis. The most important prognostic factors are completeness of the resection and presence of metastases. Eur. J. Oncol., 17 (2), 99-104, 2012

Key words: **medulloblastoma, PNET, posterior fossa, radiotherapy, tumor**

Riassunto

Riportiamo il caso di una donna di 43 anni affetta da grande midline medulloblastoma che ha invaso il cervello-staminale. È stata sottoposta a radicale resezione seguita da radio e chemioterapia. Il periodo di follow-up è stato di 2 anni e mezzo. Non ci sono state recidive del tumore ma persistono deficit neurologici, principalmente sotto forma di disfunzioni cerebellari. Attraverso il resoconto di questo caso clinico si intende aumentare la consapevolezza dell'incidenza, del trattamento e della prognosi dei tumori primitivi neuroectodermali negli adulti. I medulloblastomi sono rari e se rapportati alla popolazione pediatrica, hanno una prognosi relativamente buona. I fattori più importanti legati alla prognosi sono la completezza della resezione e la presenza di metastasi. Eur. J. Oncol., 17 (2), 99-104, 2012

Parole chiave: **medulloblastoma, PNET, fossa posteriore, radioterapia, tumore**

Received/Pervenuto 9.1.2012 - Accepted/Accettato 1.6.2012
Address/Indirizzo: Prof. Pavel Haninec, M.D., Ph.D., 3rd Faculty of Medicine, Charles University, Department od Neurosurgery, University Hospital Kralovske Vinohrady, Srobarova 50, 100 34 Prague 10, Czech Republic - Tel. 00420 267 168 540 - Fax 00420 267 168 448 -
E-mail: pavel.haninec@fnkv.cz

Introduction

Medulloblastoma (MB), which is more typical in the pediatric population, is a highly malignant tumor of pluripotent cells, usually in the posterior cranial fossa, and accounting for 20-25% of all childhood brain tumors. It is the most common brain malignancy in children (mean age 5 years). It accounts for the majority of the primitive neuroectodermal tumors (PNETs) and is frequently associated with the cerebellar vermis. Tumors growing in the lateral part of the cerebellum are uncommon. Supratentorial or spinal PNETs are rare, although much more aggressive (1, 2). MB was firstly described in 1925 by Bailey and Cushing as an embryonic tumor growing from "medulloblasts", which were thought to be glial and neuronal precursor cells. It was later demonstrated that these cells do not exist and the etiology of the tumor remains unknown (3, 4). MBs are uncommon in adults older than 16 years and account for approximately 1% of all brain tumors (5, 6). Tumor frequency decreases with age, although a case of a 73-year-old woman with this tumor has been described (7). Owing to this sparse data, the outcome and prognosis are less clear than in children. The literature suggests that MBs in adults have a better prognosis and recurrences are typically late, appearing more than two years after resection in 60% of cases as compared to pediatric tumors, which recur, during the first two years, in 75% of cases. Almost 50% of MBs are located in the cerebellar hemispheres, which offers the potential for a more radical excision (in contrast to less than 10% in children); the desmoplastic type of tumor is present in 50% of adult cases and 15% of childhood cases (5, 6, 8). The most common clinical signs are headache, nausea, vomiting, and gait instability resulting from intracranial hypertension due to obstruction of the flow of cerebrospinal fluid (CSF). The average duration of symptoms is from 7 to 9 weeks. MB is characterized by development of implantation metastases, usually in CSF pathways, and/or more rarely, in extra-neuraxial structures. As in childhood, males are more often affected than females (2, 9). Currently, MBs are divided into four sub-groups, each with a unique biological behavior (10).

Case report

A previously healthy 43-year-old woman without a personal or family history of cancer, working as manager, was examined for left sided hemiparesthesia persisting for almost one year, with acute progression and development of blurred vision during the two weeks prior to examination. The neurological exam revealed central paresis of the right 7th cranial nerve (CN) and neo- and paleo-cerebellar symptoms. A MRI showed a large tumor in the central part of posterior fossa. The tumor had invaded the pons, mesencephalon and cerebellar vermis and had grown cranially to the level of 3rd ventricle. Its size was 48 x 35 x 30 mm and it was enhanced by contrast (fig. 1 A, B).

The Resection

The tumor was approached through a suboccipital craniotomy while the patient was in a semi-sitting position. After dissection of the cerebellar vermis, a grey-violet tumourous mass with pathological vessels was found (Fig. 2 A, B). A significant part of the tumor was resected using an ultrasonic surgical aspirator. The resection extended to the mesencephalon cranially and under the temporal lobe, to the tentorium on the left side, and medially and ventrally under the 4th ventricle. The resection was large but was still thought to be incomplete due to the absence of distinct borders between the tumor and normal brain tissue. The cavity was overlaid with Surgicel®, the dura was sutured and the bone plate was fixed in its original position. Histopathological examination demonstrated a desmoplastic medulloblastoma with proliferative activity of 40-50%, WHO Grade IV. The tumor was classified as T4 M0 on the Chang scale (tab. 1)

Post-operative care

The patient was observed in the intensive care unit and after a few days was transferred to a standard room. Post-procedure, the patient developed the following symptoms: (1) a palsy of the 3rd and 4th CN on the right and the 3rd CN on the left, (2) a palsy of

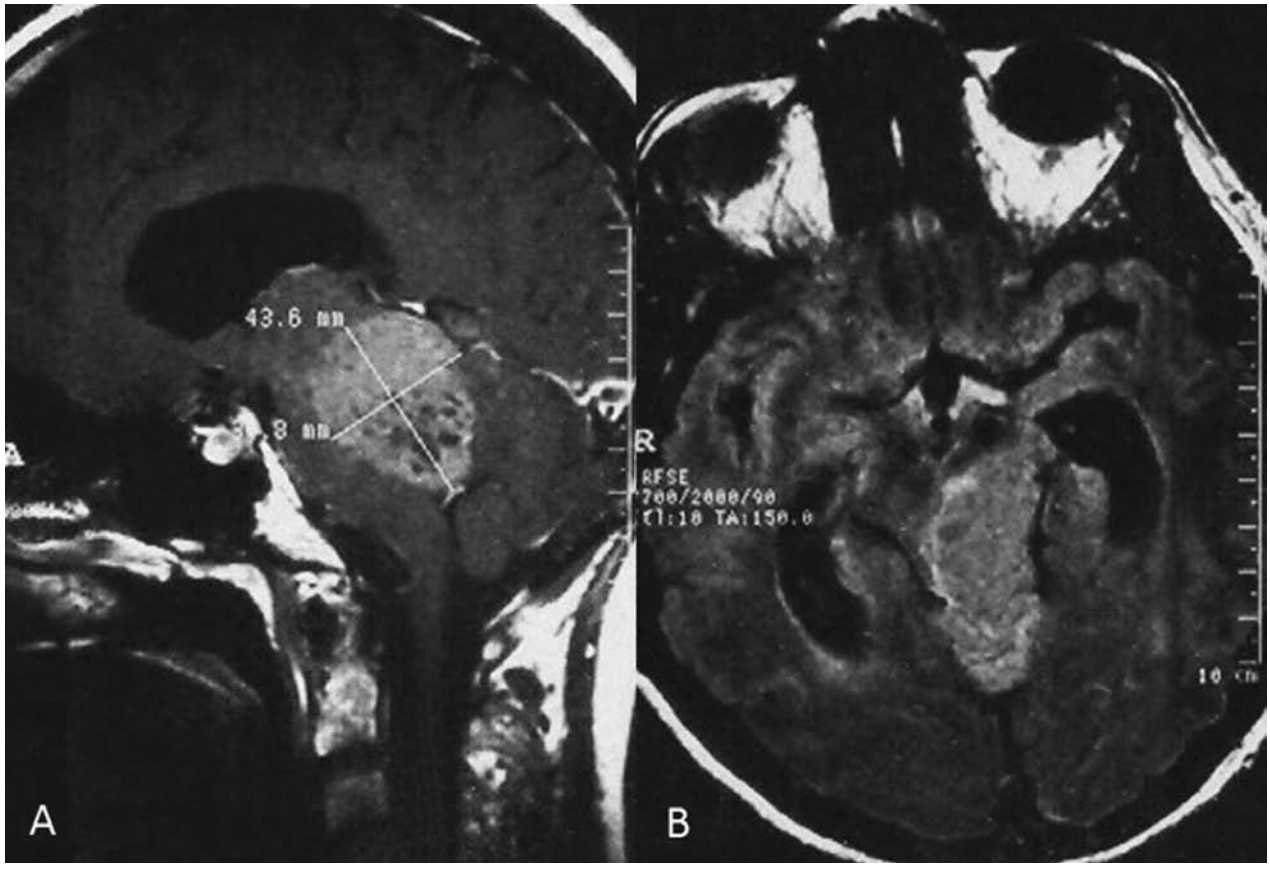

Fig. 1. Pre-operative MRI, sagittal (A) + axial (B) scan, tumor located in the 4th ventricle and invading the brain-stem

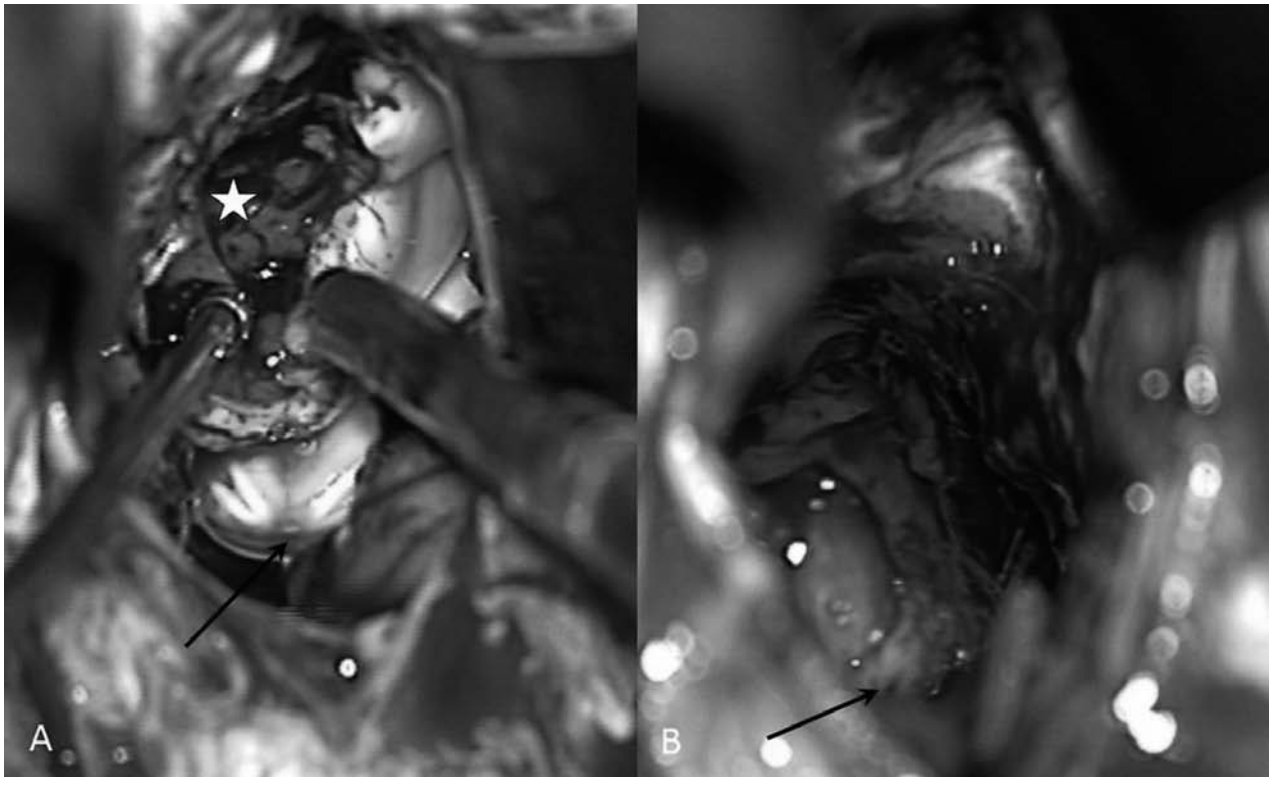

Fig. 2. Intra-operative photography, arrow aims at the obex of the 4th ventricle, * - tumor

Table 1 - Chang TM classification of medulloblastomas (13)

T1	< 3 cm in diameter
T2	> 3 cm in diameter
T3a	> 3 cm in diameter with spread
T3b	> 3 cm in diameter with definite spread into the brain stem
T4	> 3 cm in diameter with extension up past the aqueduct of Sylvius and/or down past the foramen magnum
M0	No gross subarachnoid or hematogenous metastasis
M1	Microscopic tumor cells found in cerebrospinal fluid
M2	Gross nodular seeding in cerebellum, cerebral subarachnoid space, or in the third or fourth ventricles
M3	Gross nodular seeding in spinal subarachnoid space
MX	Extraneuraxial metastasis

the 9th -12th CNs on the left, (3) a horizontal and vertical nystagmus, (4) right sided hemiparesis with ataxia, and (5) left sided dystaxia. Clinical signs of most cranial nerves palsies disappeared within two weeks, only the dysphagia persisted. MR imaging of the whole spine and CSF tests were both negative. The patient underwent radiotherapy – 36 Gy on the cerebrospinal axis and 59.4 Gy on the posterior fossa; the patient also underwent seven cycles of chemotherapy (cisplatine + vincristine + lomustine). Repeated MR examinations did not show recurrence of the tumor (fig. 3 A, B). Now, 2.5 years post-operative, and after continuous rehabilitation, the patient is able to manage many tasks of daily living unassisted. Although she cannot walk, because of ataxia, she is able to stand. Additionally, paleo- and neo-cerebellar syndromes are present with atactic speech, adiadochokinesis, hypermetry and ataxia of all extremities.

Discussion

We report a case of an adult patient with a relatively rare PNET in the posterior fossa, which invaded the brain stem and had grown cranially to the level of the 3rd ventricle. It was, from a pathological point of view, the worst possible variant, i.e. a Chang T4. Now 30 months post-operative, no evidence of local relapse is present, which is typical of the biological behavior of these tumors in adults. Permanent

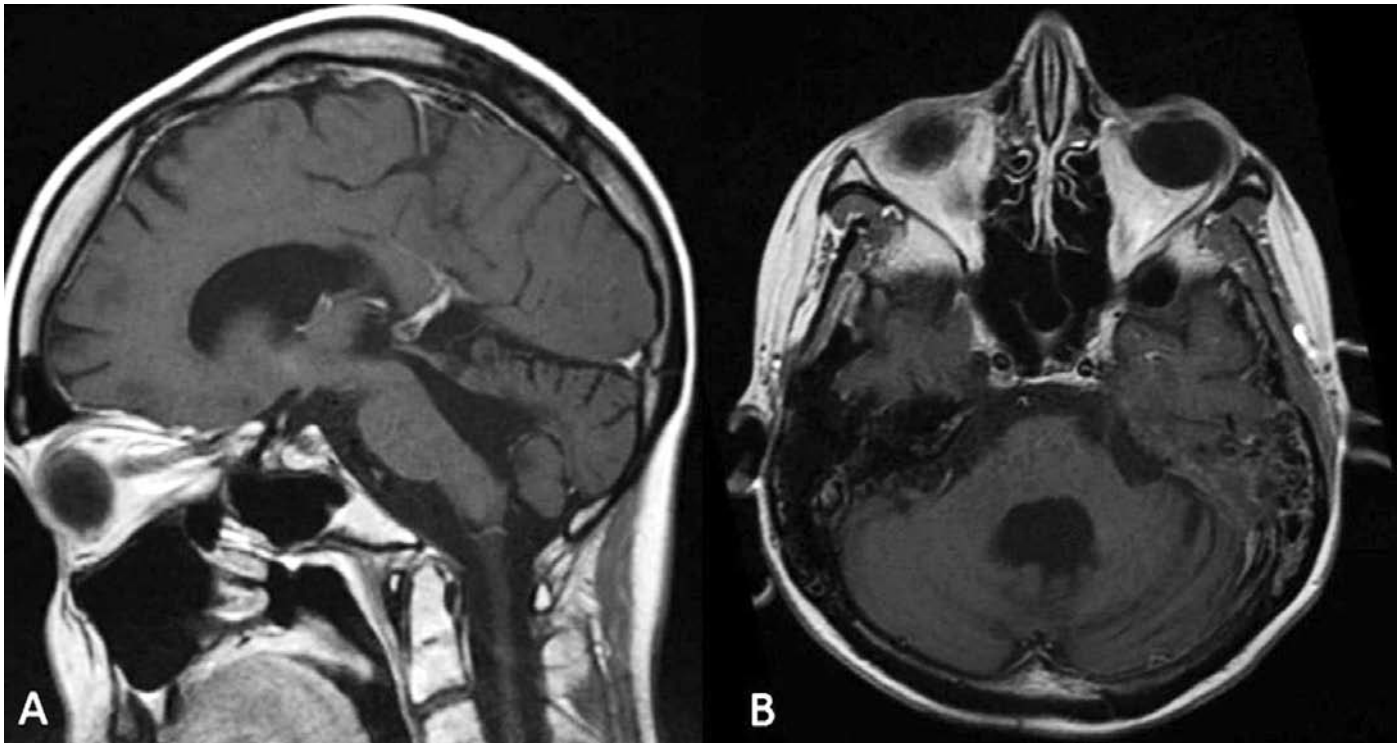

Fig. 3. Sagittal (A) and axial (B) MRI control scan 30 months after the operation without any residuum

neurological deficits from the cerebellar lesion persist, which are similar to the preoperative deficits, however, because the procedure was both life saving and life extending, and in light of its radical nature we think that this level of impairment is acceptable.

The extent of resection is a prognostic factor. Generally, a successful operation involves resection of more than 90% of tumourous mass or a residuum smaller than 1.5 cm^3. This leads, in accordance with some studies, to longer survival (11). Other studies have shown good outcomes even when less radical operations were performed. But it is widely accepted, that survival is dependent on a radical resection of the tumor. It is important to find a compromise between the extent of the resection and neurological deficits (5).

Other factors, such as sex, brain-stem invasion, age, and chemotherapy are differently assessed in various publications, although none were studied in a large homogenous group. Except for the extent of resection, postoperative radiotherapy and the presence of metastases, no other defined factors may dramatically influence the outcome (4, 5). Classic and desmoplastic MBs are equally represented (12). Initially, the desmoplastic variant seemed to be less aggressive but long-term results have not confirmed this condition. Today, it is generally accepted, that desmoplastic malignity in adults is as high as the classic variant (4, 5, 11).

Riffaud et al. published a study on a group of 27 patients, age 16-54 years, treated over a 28 year period. The tumor invaded the brain-stem in only four cases and of these, only two were classified as T4. Five-year survival was achieved in 81% of patients, 10 and 20 year survival was 62 and 43%, respectively. The authors did not identify the influence of age, duration of symptoms, Karnofsky scale, hydrocephalus, tumor localization, brain-stem invasion, histological variant or chemotherapy on the prognosis. On the other hand, metastases are a definite risk factor: 87% of the patients who were classified as M0 were alive 5 years after surgery, while no one classified as M2 or M3 reached 5 years. In the M0 group 18 relapses in 11 patients were observed, which developed, on average, 4.2 years post-operative (0.7-18 years); on average, these patients died 2.5 years after relapse (9).

It is necessary to classify each tumor using the Chang scale (13). An MRI of the whole spine and a CSF examination should be performed to reveal implantation metastases and micrometastases, respectively. A patient becomes high risk when less than 90% of tumourous mass is resected and/or a metastasis is present. Metastases after 10 years are not uncommon and it is generally felt that if relapses or metastases do not appear before 8 years, then long-term survival is expected (5, 11).

Although MB is the most common extra-neuraxial metastatic brain tumor (2-3%), these metastases are still very rare, so whole body screening is not routinely recommended. Targeting the examination to a specific organ is indicated when symptoms develop from an insult to the organ. Bones, lymph nodes, lungs and/or liver are usually affected, though breast and pancreas metastases have also been reported. Most of these tumors are found in the first two years after establishment of a diagnosis, with approximately 12% after four years (10). In general, uncommon cases with metastatic dissemination, at the time of the primary surgery, have a very bad prognosis (9, 13). A second tumor in the central nervous system is found in approximately 50% of patients with extra-neuraxial metastasis. Dissemination outside CNS is possible not only by the blood and lymphatic route, but also along nerve roots and artificially implanted ventriculoperitoneal or atrial shunts (9). Using a shunt, to manage obstructive hydrocephalus, before removal of the tumor, is contra-indicated. In cases of rapid deterioration of clinical status, acute decompression of the posterior fossa is indicated (11).

Postoperative radiotherapy is an essential part of treatment and should begin as early after wound healing as possible (6). It is accepted, that the 5-year survival rate is highly dependent on the length of radiotherapy when the same cumulative dose is used. Much better outcomes have been achieved when radiotherapy is completed between post-operative day 45 and 48 (81-89%) in contrast to delayed completion periods (51-68%) (5). Use of chemotherapy is still controversial. It seems to be effective, especially in high risk patients, where reduces the risk of relapse and prolongs survival times. Considering the possibility of extra-neuraxial dissemination, a systemic treatment with chemotherapy seems to be a logical step. However, extra-neuraxial dissemination is (although more frequent than in children) very

infrequent, so routine chemotherapy, considering its toxicity, remains controversial (9). Germanwala *et al.* has published the first results involving the use of a gamma knife for treatment of the residual mass of the tumor. Effectiveness was similar to conventional methods. Four of 12 patients died from progression of residual tumors, which, however, were more extensive than in the other eight cases (8).

Conclusion

Medulloblastoma is relatively rare in adult patients. It is a highly malignant tumor, capable of growing to large sizes. MBs manifest mostly with signs of intracranial hypertension syndrome. Despite its biological behavior, it is highly radio- and chemosensitive and it has a relatively good prognosis, which is far superior to the prognosis in children. With regard to the correlation between life expectancy and the extent of the resection, it is important to surgically remove as much of the tumor as possible. Standard post-operative treatment includes radiotherapy; however, while routine in pediatric patients, chemotherapy in adult MB cases is still controversial.

Acknowledgements

This study was supported by Charles University in Prague, PRVOUK P34.

References

1. Gliemroth J, Kehler U, Knopp U, *et al.* A multifocal cerebellar and supratentorial medulloblastoma in an adult. Acta Neurochir (Wien) 1998; 140 (7): 723-4.
2. Radovnický T., Sameš M. Cereberal mutism after resection of a medulloblastoma - A case report. Cesk Slov Neurol N 2008; 71 (4): 483-6.
3. David KM, Casey AT, Hayward RD, *et al*. Medulloblastoma: is the 5-year survival rate improving? A review of 80 cases from a single institution. J Neurosurg 1997; 86 (1): 13-21.
4. Jakacki RI. Treatment strategies for high-risk medulloblastoma and supratentorial primitive neuroectodermal tumors. Review of the literature. J Neurosurg 102 (1 Suppl): 44-52.
5. Chan AW, Tarbell NJ, Black PM, *et al*. Adult medulloblastoma: prognostic factors and patterns of relapse. Neurosurgery 2000; 47 (3): 623-31.
6. Iaconetta G, Lamaida E, Rossi A, *et al*. Cerebellar medulloblastoma in adults: report of 15 cases and review of the literature. Acta Neurol (Napoli) 1994; 16 (1-2): 38-45.
7. Kepes JJ, Morantz RA, Dorzab WE. Cerebellar medulloblastoma in a 73-year-old woman. Neurosurgery 2005; 21 (1): 81-3.
8. Germanwala AV, Mai JC, Tomycz ND, *et al*. Boost Gamma Knife surgery during multimodality management of adult medulloblastoma. J Neurosurg 2008; 108 (2): 204-9.
9. Krouwer HG, Vollmerhausen J, White J, *et al*. Desmoplastic medulloblastoma metastatic to the pancreas: case report. Neurosurgery 1991; 29 (4): 612-6.
10. Raffel C, Rutka JT. Central nervous system primitive neuroectodermal tumors: still a useful classification? Neurosurg Focus 2011; 30 (1): Introduction.
11. Belza MG, Donaldson SS, Steinberg GK. *et al*. Medulloblastoma: freedom from relapse longer than 8 years-a therapeutic cure? J Neurosurg 1991; 75 (4): 575-82.
12. Riffaud L, Saikali S, Leray E, *et al*. Survival and prognostic factors in a series of adults with medulloblastomas. J Neurosurg 2009; 111 (3): 478-87.
13. Chang CH, Houseplan EM, Herbert C. An operative staging system for a megavoltage radiotherapeutic technique for cerebellar medulloblastoma. Radiology 1969; 93: 1351-9.