PRIMARY INTRAMEDULLARY GLIOBLASTOMA MULTIFORME OF THE SPINAL CORD: REPORT OF EIGHT CASES

Péter Banczerowski*, Magdolna Simó†, László Sipos*, Felícia Slowik*, György Benoist*, Róbert Veres*
*Országos Idegsebészeti Tudományos Intézet, Budapest
†Semmelweis Egyetem, Általános Orvostudományi Kar, Neurológiai Klinika, Budapest

Primary glioblastoma multiforme located intramedullary in the spinal cord is a very rare entity. The authors report eight cases and discuss the clinical features, the possibility of diagnosis, combinated treatment and pathomorphological signs focusing on the relevant literature and their experience.
Clin Neurosci/Ideggy Szle 2003;56(1–2):28–32.

Keywords: *glioblastoma multiforme, intramedullary, spinal cord*

ELSŐDLEGES GERINCVELŐI GLIOBLASTOMA MULTIFORME: NYOLC ESET ISMERTETÉSE
Banczerowski P, MD; Simó M, MD; Sipos L, MD, PhD; Slowik F, MD, PhD; Benoist Gy, MD; Veres R, MD, PhD

Az elsődleges gerincvelői glioblastoma multiforme világirodalmi ritkaság. A szerzők összegzik nyolc esetük és az irodalom áttekintése kapcsán a betegség klinikai megjelenését, a diagnózis lehetőségeit, a kombinált kezeléssel kapcsolatos tapasztalataikat és a daganat patomorfológiai tulajdonságait.

Kulcsszavak: *glioblastoma multiforme, intramedullaris, gerincvelő*

Levelező szerző/Correspondence: Dr. Banczerowski Péter
Országos Idegsebészeti Tudományos Intézet, 1145 Budapest, Amerikai út 57.
Telefon: (1) 251-2999, fax: (1) 251-5678, e-mail: bancpet@ethernet5.oiti.hu
Közlésre érkezett: 2002. november 11. Elfogadva: 2002. november 25.

Intramedullary tumours account for 16% of all spinal intradural tumours[1, 2]. Out of these 29% are astrocytomas[2–7], but malignant astrocytomas [Kernohan grades III and IV, i. e. glioblastoma (GBM)] are less frequent, with 7.5%[1, 4, 8]. Intramedullary spinal cord astrocytomas account for 6-8% of all primary spinal cord tumours[1, 4, 5, 7, 8].

Intramedullary glioblastomas (GBM) are very rarerly described in the literature, each publicated few cases only[1, 3–5, 7, 9–12], while GBM account for more than 50% of all primary adult intracerebral gliomas. The authors report their experiences with eight cases of primary spinal intramedullary glioblastoma multiforme treated between 1959 and 1995.

Clinical material and methods

PATIENT POPULATION

Eight patients with histologically proved primary intramedullary glioblastoma multiforme were treated at the National Institute of Neurosurgery, Budapest since 1959 **(Table 1).** Six out of them were operated on. In two patients due to poor general and neurological condition radiotherapy or adjuvant chemotherapy was used. In these cases the post mortem examination detected GBM histologically. One patient due to her relatively good neurological condition and young age had reoperation because of tumour recurrance four month following the first operation.

There were five male (62.5%) and three female (37.5%) patients. The mean age of male patients was 43.2 (range 31–56) and female 17 (range 12–25) years. Two out of the female patients were 12 and 14 years old. In four patients the tumour was found at the level of conus medullaris, one was located in the midthoracic region and three in the cervical region. Signs and symptoms were related to tumour localisation and consisted of backache, motor, sensory and autonomic deficits below the level of the tumour.

The mean duration of symptoms from onset to the time of diagnosis was 3.0 (range 0.5–8) months.

DIAGNOSTIC EVALUATION

Patients were evaluated between 1959–82 with lipid-soluble and later water-soluble contrast material myelography. In most of the cases the cerebrospinal fluid examination was useful and showed high protein level, streched passage and some of the cases tumour cells, but citology was not specific. After the advent of computer tomography (CT) into our department in 1982, CT was used either with or without myelography. The last few years the magnetic resonance imaging (MRI) became the diagnostic procedure of choice **(Figure 1)** and since then all of the patients underwent MRI before and after surgery. MRI was useful for follow-up the

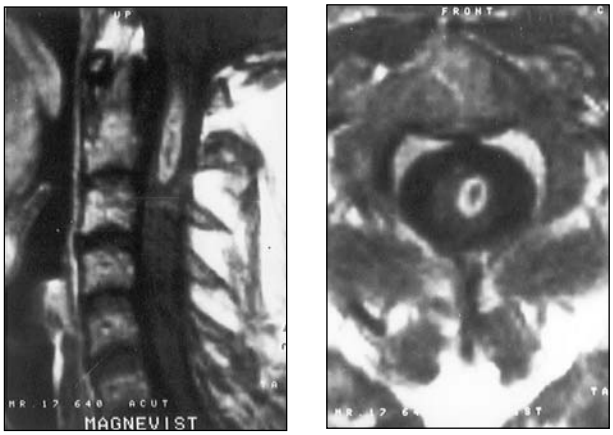

Figure 1. *Contrast-enhanced sagittal and horizontal T1 magnetic resonance imaging scans show the intramedullary tumour at cervical region.*

Table 1. *Summary of clinical course of patients with primary GBM of the spinal cord.*

Case No. /Year	Age/Sex	Duration of symptoms (month)	Location	Surgery	Radio-therapy	Chemo-terapy	Preopera-tive state	Results (early)	Survival time (month) operation/ onset
1. (1959)	56/M	56/M8	conus	biopsy+ decompr.	yes	no	poor	fair	8/16
2. (1960)	31/M	6	thoracic	subtotal	yes	no	fair	good	6/12
3. (1965)	12/F	1.5	cervical	partial	no	no	good	poor	4.5/6
4. (1967)	41/M	2.5	conus	subtotal	no	no	fair	poor	0.5/3
5. (1969)	25/F	3,	cervical	no	yes	no	poor	death	0/26
6. (1986)	14/F*	0,5	conus	partial	no	yes	fair	fair	10/10.5
7. (1993)	46/M	0,5	cervical	no	no	no	poor	fair	0/2
8. (1995)	42/M	2	conus	subtotal	yes	yes	fair	fair	10/

operation: from the time of operation to death; onset: from the time of onset to death,*reoperation was carried out four monthes following the first operation

tumour behavior after surgery and adjuvant therapy. Spinal cord angiography was not performed in any of the cases.

OPERATIVE TECHNIQUE

Patients with cervical lesions were operated on in sitting and at the level of midthoracic or conus medullaris in prone position. Laminectomy and tumour removal or biopsy were performed. In any of the cases total tumour removal was not possible. In some of the cases intraoperative ultrasound was used to localize the lesion accurately. The spinal cord was opened in the midline and Cavitron Ultrasonic Surgical Aspirator (CUSA) and bipolar coagulation were used under operating microscope after the advent of these equipments. Repeated intraoperative ultrasonography was used to control the extent of tumour removal. A watertight dural closure was made in most of the patients. High dose intravenous methylprednisolon (first 20 minutes 30 mg/kg, and during the following 24 hours 5.4 mg/kg/hour) was used intra- and postoperatively by last times.

ADJUNCTIVE TREATMENT

One patient received postoperativ chemotherapy only. Drugs used were methotrexat (10 mg/5 days/month) and 1.3-bis(2-chloroethyl)-1-nitrosurea (BCNU) (80 mg/m^2/3 days). This patient was treated after surgical removal of tumour with BCNU and steroid therapy and four month later underwent repeated surgery for partial removal of recurrance of tumour at the level of conus medullaris.

Three patients received radiotherapy only between 20–36 Gy after surgical removal of the tumour. One patient received combinated radiotherapy (36 Gy) and chemotherapy (methotrexat) with steroid therapy together following surgery. This patient was followed by MRI postoperatively after radiotherapy and chemotherapy and the regression of residual tumour was observed **(Figure 2).**

One patient received steroid therapy only.

In two cases surgery was not followed by adjuvant therapy due to worsened neurological and general condition.

Results

PATHOLOGICAL FINDINGS

At surgery the intramedullary GBM was reddish-gray, the interface with normal spinal cord tended to be more indistinct, more vascular then benign astrocytomas and the tumour was partially necrotized.

In three cases autopsy was performed at our institution.

All tumour specimens were embedded in paraffin and stained by routine methods. In some of the cases immunhistochemical investigations were carried out for detection of glial fibrillary acidic protein (GFAP) using peroxidase-antiperoxidase (PAP) method. All of the cases the diversity of the cells were encountered histologically. The tumours showed dense cellularity, focal necroses and vascular endothelial proliferation. The number of mitosis was variable. Besides the small, poorly differentiated fusiform cells, large, multinucleated astrocytic cells were present. In one case a highly cellular pleiomorphic tumour contained large number of giant and multinucleated cells with irregular nuclei **(Figure 3)**. In two cases the seeding of the tumour-cells by the cerebrospinal pathways could be found and infiltration of leptomeninges around the spinal cord **(Figure 4)**, the brain stem and on the surface of the cerebral hemisphere could be detected. At the post mortem examination in one case intramedullary cavities were associated with the presence of GBM.

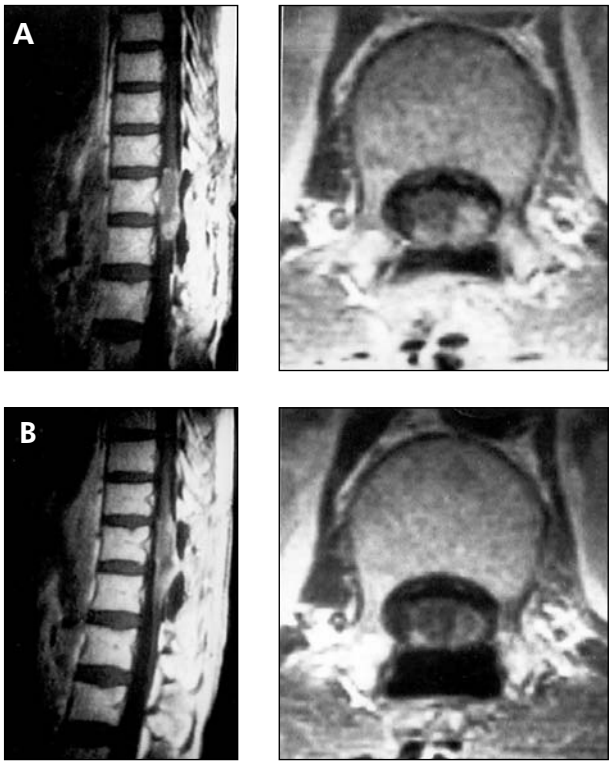

Figure 2. *Contrast-enhanced sagittal and horizontal T1 magnetic resonance imaging scans.* **A** *The residual intramedullary glioblastoma after operation,* **B** *regression of tumour after radio- and chemotherapy*

A median survival time from operation to death was 6.5 months with a range of 0.5 to 10 months. The median survival time from onset of symptoms until death was 10.94, months with a range of 2 to 26. The longest survival time following the surgery was ten months. Early results after surgery were as follows: two improved, two unchanged, two worsened. Two patients underwent both surgery and radiotherapy (Cases 1., 2.) and they neurological condition improved (early results). Two patients underwent surgical procedure only, one of them became tetraplegic and appeared respiratory plegia (Case 3.), while another soon died due to paralytic ileus (Case 4.). Two patients was not operated on because of poor condition and received adjunctive therapy only (Cases 5., 7.). One of them started radiotherapy and died after the second cycle due to worsening neurological condition (Case 5.), while another one received only steroid therapy, improved for a short time, but died two month later due to respiratory problems because of tumour progression (Case 7.). One patient received only chemotherapy (BCNU) and steroid therapy after the operation and her early neurological condition was unchanged. Four months later she underwent reoperation and her neurological condition unchanged (Case 6.). One patient (Case 8.) received combinated surgical, radiotherapy (36 Gy) and chemotherapy (methotrexat) and steroid therapy. This patient's early neurological state was unchanged and alived ten months following the operation. His early postoperative MRI showed the regression of residual tumour **(Figure 2).**

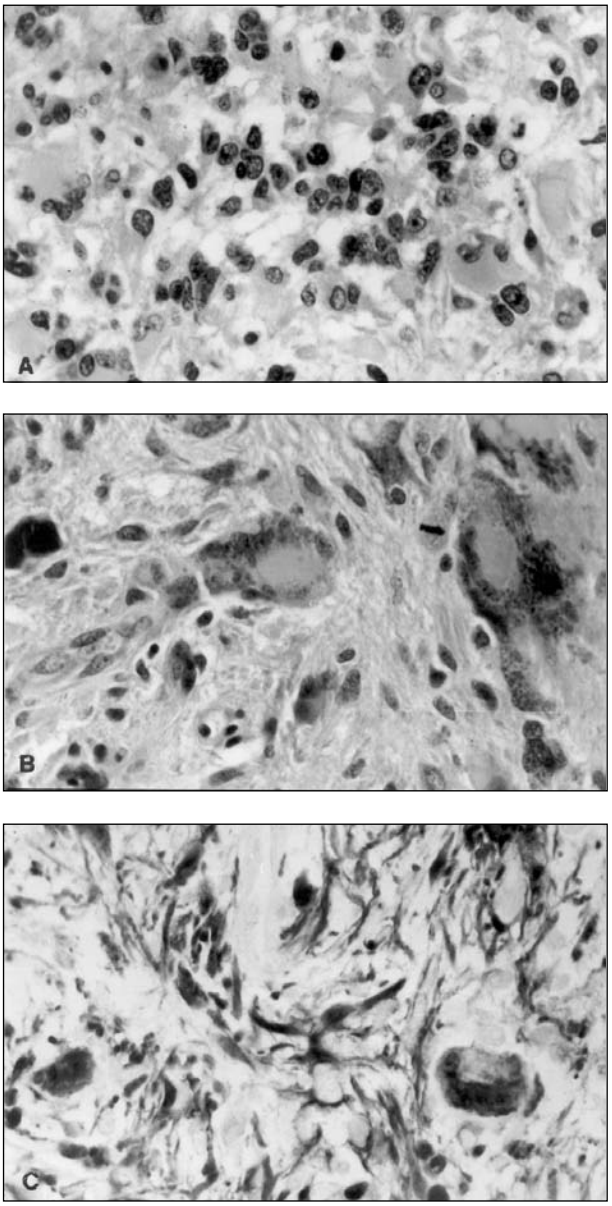

Figure 3. *Histology of the spinal cord GBM.* **A** *The tumour is built up by polymorphic cells (Case 7.), HE 280×.* **B** *Glioblastoma contain numerous, bizarre multinucleated giant cells (Case 6.), HE 280×.* **C** *The cells of the monstrocellular glioblastoma showing positive reaction for GFAP (Case 6.), 280×.*

Discussion

Primary GBM make up a small amount of intramedullary spinal cord tumours and carry a very dismal prognosis. There is a short time from onset to the time of diagnosis and is followed by progressive neurological deterioration and death. There is a clinical history of less than one year, when it is longer it might be associated with cases of well differentiated astrocytoma that later degenerate into GBM[4]. The operated patients died after a median survival time of only 6.5 month following the surgical intervention. One operated patient lived more than one year from the onset of sympoms. Only two patients improved following surgery for a short time.

Hydrocephalus occured in only two patients, but in literature the incidence of development of hydrocephalus is more frequent[4]. The cause of hydrocephalus is obscure, but it has been suggested that the elevated protein level leads to decreased CSF reabsorption[4].

The incidence of giant-cell variation of spinal glioblastomas is low[5], but in one case it was detected in our material **(Figure 3. B, C).**

The spinal cord GBM is often dissaminated and the tumour cells spread in the subarachnoid space with a local or distant involvement of lep-

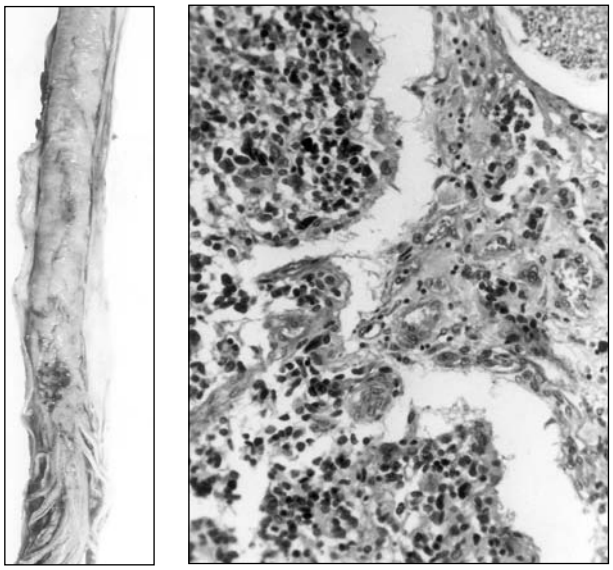

Figure 4. *Macro- and microscopic photographs show the invasion of the spinal leptomeninges by intramedullary glioblastoma cells (Case 5.).*

tomenings[1, 4, 8, 9] **(Figure 4).** This was observed in 50% (four out of eight) of our cases. In two out of our cases the tumour ivolved the subarachnoid space and the spinal roots already at the time of surgery. The seeding of intracranial GBM along the spinal cord is common, about 25%[4, 6, 8–10], while the reverse way is extremly rare[6, 10].

According to literature we suppose that the treatment is primarily debulking of the tumour, but it cannot be radical in most of the cases. When surgery is followed by irradiation and chemotherapy the survival time can be improved, though GBM is not really chemo-sensitive. In our early cases the treatment principles of treated intramedullary spinal GBM was not standardized and the therapy was individual. Since the spinal GBM is a very rare lesion, there is still not enough experience with effective irradiation and chemotherapy, while multicentre cooperative study would be useful. MRI was very helpful for follow-up the tumour behaviour after surgery and adjuvant therapy.

REFERENCES

1. *Ciapetta P, Salvati M, Capoccia G, Artico M, Raco A, Fortuna A*. Spinal Glioblastomas: report of seven cases and review of the literature. Neurosurgery 1991;28:302-6.
2. *Simeone F*. Intradural tumours. In: *Rothman RH, Simeone FAWB. (eds)* The spine (3rd edition). Saunders Co. 1992; pp. 1515-28.
3. *Alvisi C, Cerisoli M, Giulioni M*. Intramedullary spinal gliomas: long-term results of surgical treatments. Acta Neurochir 1984;70:169-79.
4. *Cohen AR, Wisoff JH, Allen JC, Epstein F*. Malignant astrocytomas of the spinal cord. J Neurosurg 1989; 70:50-4.
5. *Grisold W, Pernetzky G, Jellinger K*. Giant-cell glioblastoma of the thoracic cord. Acta Neurochir 1986;58:121-6.
6. *Kopelson G, Linggood RM*. Intramedullary spinal cord astrocytoma versus glioblastoma. Cancer 1982;50:732-5.
7. *Mortara R, Parker JC Jr, BrooksWH*. Glioblastoma multiforme of the spinal cord. Surg Neurol 1974;2:115-9.
8. *Johnson DL, Schwarz S*. Intracranial metastases from malignant spinal-cord astrocytoma. J Neurosurg 1987; 66:621-5.
9. *Andrews AA, Enriques L, Renaudin J, Tomiyasu U*. Spinal intramedullary glioblastoma with intracranial seeding. Arch Neurol 1978;35:244-5.
10. *Kendrick FD, Bonnin JM, Garcia JH.* Metastases of a spinal glioblastoma multiforme into an intracranial arachnoid cyst. Neurosurgery 1987;20:780-3.
11. *Rosberg C, Litzenberger J*. Intramedullares Glioblastoma multiforme mit ungewohnlicher, intrakranieller Meningeosis neoplastica. Nervenartz 1988;59:401-4.
12. *Yasui T, Hakuba A, Katsuyama J, Nishimura S*. Microsurgical removal of intramedullary spinal cord tumours: Report of 22 cases. Acta Neurochir 1988;43(Suppl.): 9-12.