

## MULTICENTRIC SPINAL CORD AND BRAIN GLIOBLASTOMA: A CASE REPORT

Bojan Stanojević<sup>1</sup>, Jovan Ilić<sup>1</sup>, Aleksandar Igić<sup>1,2</sup>, Vesna Nikolov<sup>1,2</sup>,  
Aleksandra Aracki Trenkić<sup>3</sup>, Marija Djordjević<sup>2</sup>, Slavko Živković<sup>1</sup>, Stefan Todorović<sup>4</sup>

Multicentric glioblastomas, which simultaneously involve supra- and infratentorial areas, are rare. In our patient, the magnetic resonance imaging (MRI) of cervical and thoracic spine was performed, which verified the spinal intramedullary tumor at the level of the C6 and from Th1 to Th4 segment. During surgery, the tumor, which had macroscopic characteristics of glioblastoma was encountered and it was partially resected. Pathohistological findings verified that the tumor was IDH-wild type glioblastoma. The MRI of the brain was performed after surgery, which showed the right temporoparietal glioblastoma. The patient underwent the postoperative chemoradiation therapy and came for regular check-up examinations for 6 months, however, the patient's neurological signs and symptoms have gradually worsened to this day. Although diagnostic advancements in neuro-oncology have led to more sensitive and specific diagnosis of multicentric gliomas, this topic is still insufficiently researched and requires our attention.

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**Key words:** glioblastoma, surgical oncology, neurosurgery

<sup>1</sup>University Clinical Center of Niš, Department of Neurosurgery, Niš, Serbia

<sup>2</sup>University of Niš, Faculty of Medicine, Niš, Serbia

<sup>3</sup>University Clinical Center of Niš, Department of Radiology, Niš, Serbia

<sup>4</sup>University Clinical Center of Niš, Department of Neurology, Niš, Serbia

Contact: Jovan Ilić  
112/12 Byzantine Blvd., 18000 Niš, Serbia  
E-mail: jovaniilic94@gmail.com

### Introduction

Glioblastoma multiforme (GBM) represents circa 45.6% of primary malignant brain tumors (PMBT), as well as about 54% of all glial tumors (GT), and infratentorial presentation is unusual (1, 2). Moreover, when it comes to the frequency and aggressiveness, it takes the first place of all PMBT. The average survival rate of treated is only 14.6 months (2). As a grade IV astrocytoma, it consists of tumor cells with rapid and infiltrative growth, while histological methods show characteristic malignant morphology, necrosis of tumor cells and neovascularization (3). Multicentric glioblastomas

(MCGB) represent spatially and temporally separated GBM, which incidence ranges between 0.15 and 10% among GBM. MCGB, which simultaneously involve supra- and infratentorial localization, are rare. Moreover, they represent isolated tumor masses, located in different parts of the central nervous system (CNS), which cannot be explained by local spread, dissemination via cerebrospinal fluid (CSF), blood or through commissural pathways (1, 2). Continuity cannot be demonstrated between tumor masses microscopically or macroscopically, and these do not represent satellite lesions of the primary tumor (3, 4). If the conditions above are not met, then the tumor most likely represents a multifocal glioblastoma (MFGB) (3, 5).

In this case report, we present a patient with MCGB, with consideration of appropriate therapeutic options.

### Case report

A 38-year-old male patient was admitted to the Clinic of Neurosurgery because of the interscapular pain with propagation towards the right shoulder. He also stated that, during the last month, the pain was accompanied by a change in the walking pattern as well as bilateral leg numbness, predominantly in the left. The magnetic resonance imaging (MRI) of the cervical and thoracic spine was performed, which confirmed an intramedullary tumor at the level of the C6 and from Th1 to Th4 medullar

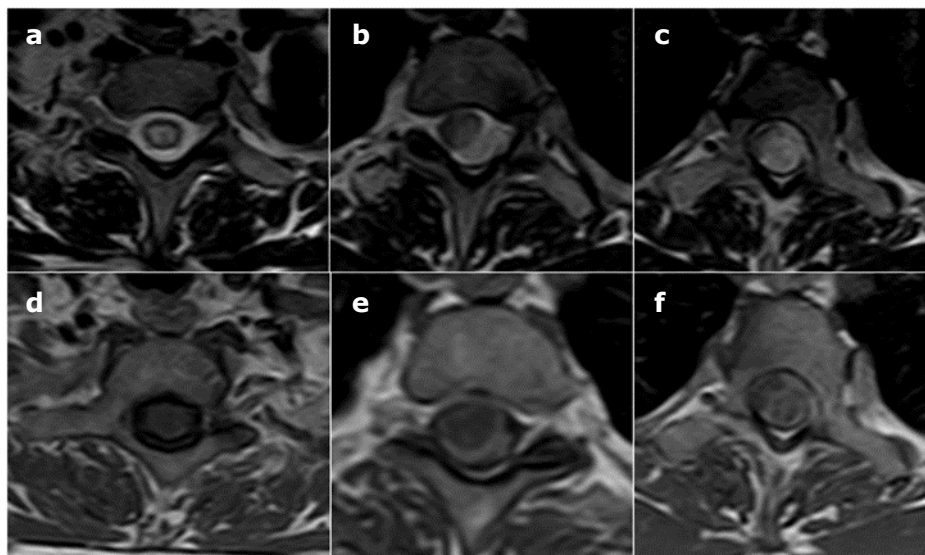
segment, which pushed the rest of the spinal medulla to the right (Figure 1, 2).

At the admission, the neurological examination showed the Glasgow Coma Scale score of 15. Postural tremor of the right hand was noted, while the walking pattern was bizarre. Lazarević's sign was positive bilaterally at about 40 degrees. The

patellar and ankle reflexes were amplified on both sides. Ankle and knee clonus were positive. Babinski's sign was bilaterally positive, and hypoesthesia was also recorded for dermatomes from L1 to S3 on the left.



**Figure 1.** Preoperative sagittal T2W tomograms detect an intradural and predominantly extramedullary lesion at the C6 level, on the left posterolateral side, which cannot be clearly delineated from the spinal cord; from levels Th1 to Th4, predominantly on the left posterolateral side, an intradural tumor lesion is detected with consequent compression of the spinal cord, dislocating it contralaterally in the cranial aspect, while the caudal part of the tumor infiltrates and expands the spinal cord. Diffuse myelopathic type changes of medullary signal in the cranial and caudal part of the tumor are noted.

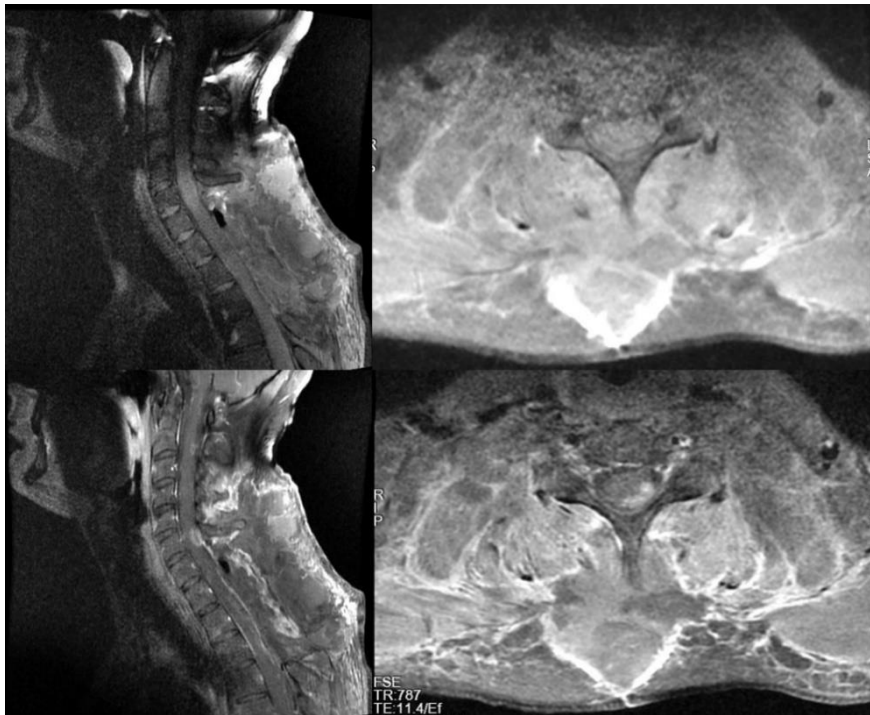


**Figure 2.** Preoperative axial T2W (a, b, c) and T1W postcontrast (d, e, f) tomograms indicate intradural and intramedullary lesions with extramedullary propagation

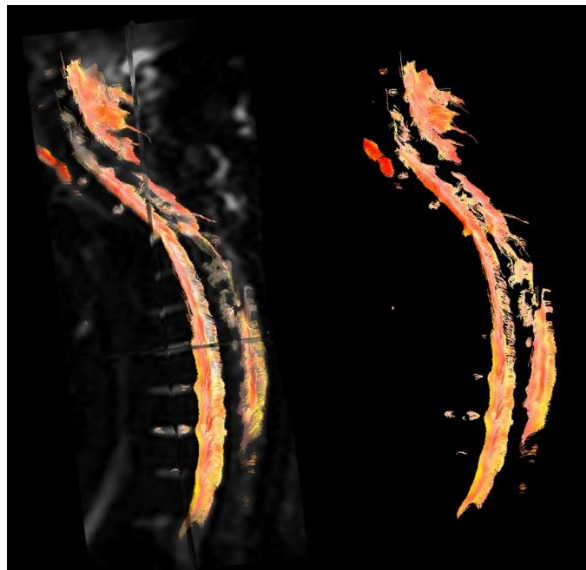
After adequate preoperative examination, surgical treatment of the patient was planned. Laminectomy was performed from the Th1 to Th4 vertebrae and the dura matter was opened in the middle. The tumor was encountered, which was adherent to the spinal cord and without noticeable borders towards the spinal cord, and was partially resected. The roots of the Th2 and Th3 spinal nerves were resected as well. The postoperative course went with severe spastic paraparesis and loss of sensitivity for all types of somatosensory senses, from the dermatome Th2 below. After two weeks of conservative treatment and physical therapy, the patient's neurological status improved, achieving the MRC (Medical Research Council scale) grade of 3 for both legs. Deep sensibility recovered gradually, while hypoesthesia persisted at the previously mentioned level. Control computed tomography (CT) of the thoracic spine showed a subcutaneous hematoma in the operative region, which resolved spontaneously. Thereafter, a control MRI of the cervical and thoracic spine was performed, which showed

vaguely tumor masses at the level of the C2 and C3 vertebrae, measuring about 7 x 3 mm, as well as tumor mass at the level of the C6 vertebra, measuring 17 x 8 x 5 mm, which could not be clearly differentiated from the spinal medulla (Figure 3, 4).

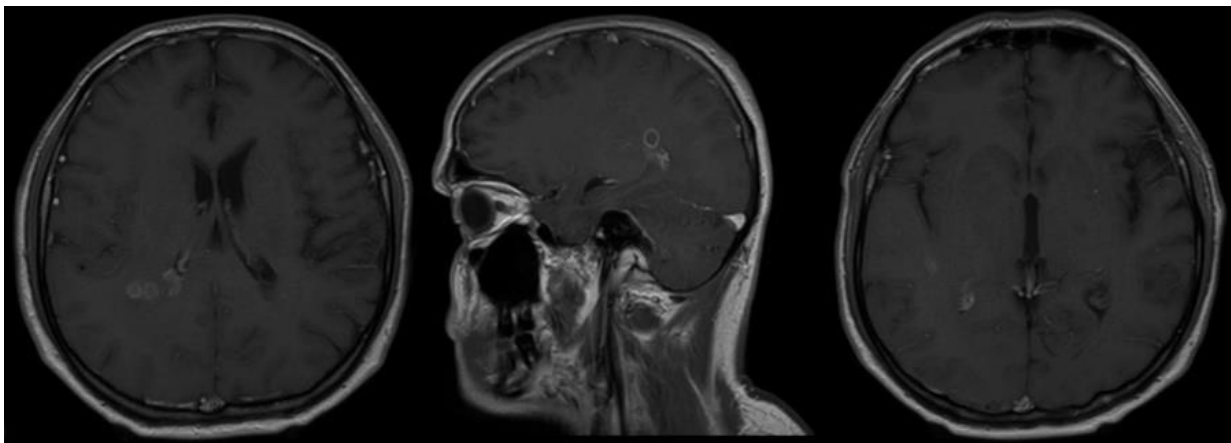
Afterwards, the patient underwent a rehabilitation treatment for one month with moderate paraparesis. The MRI of the brain was performed, which recorded the right temporoparietal tumor with transcallosal invasion, as well as the signs of Wallerian degeneration (Figure 5). Pathohistological findings verified that the tumor was IDH-wild type Glioblastoma (WHO grade IV). Consequently, daily concomitant temozolomide at 75 mg/m<sup>2</sup> as an adjunct to craniospinal radiotherapy (302 Gy/460 Gy of the involved field) followed by up to six cycles of temozolomide at 150-200 mg/m<sup>2</sup> on 5 out of 28 days was indicated. The patient came for regular checkup examinations for 6 months, however, the patient's neurological signs and symptoms have gradually worsened to this day.



**Figure 3.** Postoperative sagittal and axial pre- and postcontrast T1W tomograms with fat suppression of the cervicothoracic segment of the spine indicate the presence of intradural, extramedullary lesions in the posterolateral left segment of the canal with marginal contrast capture, without delineation in relation to C2 and C6 medullary level; on the segment of Th1-Th4 spinal cord, in the operative field, is an expanded lesion, with T1W hyposignal, as well as discrete linear and "patchy" post-contrast signal amplification, in favor of probable remnant and post-therapeutic sequelae.



**Figure 4.** Postoperative cervical and thoracic MRI tractography shows the preservation and continuity of most of the fibers with partial destruction in the posterior part, predominantly at the levels of Th2 and Th3 of spinal cord.



**Figure 5.** Postcontrast postoperative T1W tomograms show marginal pathological signal enhancement of oval confluent lesions, typical for high-grade gliomas.

## Discussion

Most MCGB are localized supratentorially, and simultaneous supra- and infratentorial localizations are less common, while infratentorial MCGB mostly occur in the cerebellum or brainstem (4). According to some authors, MCGB are defined by supra- and infratentorial localization (5, 6).

To the best of our knowledge and according to the literature we reviewed, this is the first described case of MCGB that simultaneously affects the brain, cervical and thoracic part of the spinal cord.

Various hypotheses and theories on the origin of multicentric gliomas have been proposed, but the etiopathogenesis has not yet been fully elucidated (7, 8). Conhein et al. hypothesized that multicentric gliomas occur when there are multiple embryonic residues in different parts of the CNS (9). Willis et al. considered the possibility of developing multicentric gliomas in two phases. During the first phase, there is a neoplastic transformation of CNS tissue, which covers a large area, whereas in the second phase, there is a neoplastic proliferation at different sites of the CNS (10, 11). Other authors believe that multicentric gliomas are actually metastatic in nature, but

the spreading path from primary glioma to secondary tumor mass has not yet been proven (12). Some authors have highlighted the importance of the calcium-binding protein Mts1/S100A4 in migration, invasiveness, dissemination and interactions of high-grade glioma cells with the surrounding brain tissue (13). They obtained the results that supported the hypothesis that higher levels of Mts1/S100A4 protein in glioma cells and astrocytes positively correlated with the invasiveness and dissemination of glioma cells (13).

The spread of tumor cells via the cerebrospinal fluid (CSF) has been considered as a potential mechanism for the development of MCGB (14), but cytological examination of the CSF in our patient did not reveal the presence of tumor cells. Existing techniques for revealing tumor cells in CSF are known to have limitations in terms of sensitivity and specificity, so other techniques are being developed, such as immunohistochemistry, flow cytometry, PCR as well as non-cellular biomarkers and other *in vivo* methods, which could provide more credible results in the future (15). Jomin et al. considered that multicentric gliomas were of low-grade malignancy, while high-grade gliomas metastasized early and represented multifocal gliomas (16). Contrary to this, our patient with multicentric glioma had pathohistologically confirmed IDH-wild type glioblastoma.

Some authors have described MCGB on the MRI as tumor masses outside the cortical-subcortical boundaries, or localized in the deep white matter of the brain. The same authors believe that these MCGB are presented as solid tumor masses of irregular nodular shape without central necrosis, which differs significantly from metastasis (12). Contrary to this, the brain MRI in our patient showed the presence of oval and confluent lesions with necrotic central part within the deep white mass, as well as extensive surrounding vasogenic edema extending along the corpus callosum and contralaterally, with signs of Valerian degeneration and mild mass effect. Some other authors support the fact that MCGB appear deeper within the white matter of the brain on MRI images, bind contrast more densely, and that compared to metastasis, the surrounding vasogenic edema is more extensive, which is in accordance with our results.

Earlier, neuroimaging methods for the detection of MCGB had serious limitations and over time have further developed and become more sensitive. There is a reasonable suspicion that many cases of MCGB would have been diagnosed as multifocal by using modern neuroimaging, including the FLAIR MRI sequence. Probably because of this, some authors considered that there was no practical value of differentiation between multicentric and multifocal gliomas (17, 18).

Multiple tumor masses, that are also spatially separated, reflect on the patient's performance status, and treatment with aggressive tumor resection is less common. Since these tumors are more often located in the deep white matter of the brain or in the posterior fossa, and they can affect the opposite hemisphere, the survival prognosis is poor. Furthermore, patients with multiple tumor masses limited to one brain compartment have a similar survival prognosis as patients with a solitary lesion. Moreover, maximal tumor resection is rarely achieved in patients with multifocal and multicentric gliomas, so these patients have a worse prognosis (18, 19).

Since on the preoperative MRI of the cervical and thoracic spine, the tumor masses were presented intradurally and extramedullary, we opted for a total resection of these tumors. After laminectomy from the level of Th1 to Th4 vertebrae, we found a tumor mass that was presented differently intraoperatively compared to the MRI presentation, as a vaguely limited intramedullary tumor that was predominantly necrotic and macroscopically corresponded to a high-grade glioma. Therefore, during surgery, we changed the decision on treatment and decided on the maximum reduction of tumor mass only at that level, without operating on at the level of C6 segment of the spinal cord, until the results of pathohistological analyzes were delivered. Considering that this is a very rare localization of MCGB, more precisely, that we have not been able to find such a case described in the literature, MRI of the brain was performed only after obtaining the pathohistological results. We did not opt for preoperative CT or MRI of the brain because the initial clinical presentation could have been explained by the localization of MCGB in the cervical and thoracic part of the spinal cord. Had we performed a preoperative MRI of the patient's brain, our team of neurosurgeons would have probably opted for other approach, such as a biopsy. However, it turned out that we made the right treatment decision because the patient had short-term clinical and neurological improvement after the operation. Finally, we believe that comprehensive diagnostic analyzes and procedures are necessary when diagnosing MCGB.

## Conclusion

Although advances in diagnostic technology of brain tumors have led to more sensitive and specific diagnosis of multicentric and multifocal gliomas, this topic is still insufficiently researched and requires our attention. The clinical presentation and prognosis of patients with MCGB, in comparison with patients with solitary GBM, is worse.

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**Prikaz bolesnika****UDC: 616.83-006.4-089-036.1**  
**doi:10.5633/amm.2022.0310****MULTICENTRIČNI GLIOBLASTOM SPINALNE I KRANIJALNE  
LOKALIZACIJE: PRIKAZ SLUČAJA**

*Bojan Stanojević<sup>1</sup>, Jovan Ilić<sup>1</sup>, Aleksandar Igić<sup>1</sup>, Vesna Nikolov<sup>1,2</sup>,  
Aleksandra Aracki Trenkić<sup>3</sup>, Marija Đorđević<sup>2</sup>, Slavko Živković<sup>1</sup>, Stefan Todorović<sup>4</sup>*

<sup>1</sup>Univerzitetski klinički centar Niš, Klinika za neurohirurgiju, Niš, Srbija

<sup>2</sup>Univerzitet u Nišu, Medicinski fakultet, Srbija

<sup>3</sup>Univerzitetski klinički centar Niš, Klinika za radiologiju, Niš, Srbija

<sup>4</sup>Univerzitetski klinički centar Niš, Klinika za neurologiju, Niš, Srbija

*Kontakt:* Jovan Ilić

Vizantijski bulevar 112/12, 18000 Niš, Srbija

E-mail: jovanilic94@gmail.com

Multicentrični glioblastomi, koji se istovremeno nalaze supratentorijalno i infratentorijalno, retko nastaju. Kod našeg bolesnika, urađena je magnetna rezonanca (MR) vratne i torakalne kičme, kojom je otkriven spinalni intramedularni tumor na nivou C6 i od Th1 do Th4 segmenta. Tokom operacije, prikazan je tumor, koji je imao makroskopske karakteristike glioblastoma i obavljena je parcijalna resekcija istog. Patohistološkim nalazom potvrđeno je da se radi o glioblastomu IDH divljeg tipa. Nakon operacije, odrađena je MR mozga, kojom je evidentiran desni temporoparietalni glioblastom. Bolesnik je potom podvrgnut postoperativnoj hemioradijaciji i redovno su obavljani kontrolni pregledi tokom 6 meseci, ali su se, do danas, neurološki znaci i simptomi kod bolesnika postepeno pogoršavali. Uprkos napretku dijagnostike u neuroonkologiji, a posledično i u postavljanju dijagnoze multicentričnih glioblastoma, ova tema je još uvek nedovoljno istražena i smatramo da su potrebna dodatna istraživanja u ovoj oblasti.

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**Ključne reči:** glioblastom, onkološka hirurgija, neurohirurgija