Model of growth and surgical treatment glioblastoma multiforme tumors localized in the motor zone of the brain-use of the direct electrocorticostimulation in the prevention of motor deficit

INTRODUCTION

Glioblastoma multiforme localized in the motor area is the surgical challenge because of the need for more radical resection in order to extend the life of the patient, and the other due to the risk that radicalism could lead to additional-crippling neurological deficit. Method. We present a series of 26 patients with Glioblastoma multiforme localized in and around the motor area in front of the central sulcus who were hospitalized from October 2004 to February 2009. During all operations we conducted cortical electrostimulation on displayed area of the brain, to the anatomical location of M1 segment of the motor cortex. Results. Distance of the central sulcus in relation to the coronary suture, measured by magnetic resonance imaging (MRI) was 18.38 mm±9.564 mm. The volume of electricity required for a motor response was 9.26±1.286 mA(min. 7mA, max. 11mA), with increasing distance from the coronary suture the amplitude required to explicit motor responses decreased (p<0.01). Conclusion: The method of direct cerebral cortex electro-stimulation is simple and safe method and a binding protocol to the patient safe operation glioblastoma multiforme localized in the motor area of the brain.

Key words: glioblastoma multiforme, cerebral motor cortex, electrocorticostimulation

INTRODUCTION

Malignant gliomas cause a total of 2.5% of cancer deaths per year and the third cause of death from cancer at the age of 15 to 34 years of age. Actual position on low grade glioma brain tumors is that they are classified as malignant, with an average survival of 4 to 9 years. Results of group of authors indicate that radical surgical resection may postpone malignant transformation and prolong survival time.

Neurosurgeons consider brain tumors as active lesions for which they need to find a solution, because if the rest of tumor tissue is smaller after surgical resection, the period of survival is longer. Therefore it is necessary to know the natural course of brain tumors in their initial, intermediary and terminal stage. Despite the maximum radical surgical resection and additional oncological protocols which combines radio and chemotherapy, overall survival for patient with glioblastoma multiforme is between one and two years. The functions of human cortex, despite the anatomical boundaries are organizationally related and surgical resection can be basically considered as a brain injury. Preoperative and intraoperative brain mapping separates the normal from the abnormal function and allows resection of lesions that previously could not even been imagined. Current studies recommend standard use of intraoperative electrical stimulation of the brain during operations in eloquent brain zone as a method that improves postoperative functional outcome.

Direct cortical electrostimulation is safe, accurate and easy to perform method for identification of eloquent cortical and subcortical field.

MATERIALS AND METHODS

Our study included a total of 26 patients with supratentorial glioblastoma multiforme localized in and around the motor area in front of the central sulcus, who were hospitalized at the Institute of Neurosurgery, Clinical Center of Serbia in Belgrade from October 2004 to February 2009. Assessment of pre and post operative status of the patients was validated by Karnofski index scale. From the study we excluded patients with recurrent tumors and patients whose Karnofski index at admission was less than 70. In order to achieve a clear preoperative orientation, especially in the present cases of infiltrative...
tumor growth with no visible boundaries to the surrounding brain, we performed measurement of the distance of the central sulcus (the longest in the high parietal sulcus sections) compared to the coronary suture on the MRI images, based on diagnosed and planned operations.

All patients were operated under general anesthesia using the general intravenous anesthesia, without the addition of volatile anesthetics. For the induction of anesthesia in the bolus propofol (1-2mg/kg) and fentanyl (5-10µg/kg) were used. Anesthesia was maintained with continuous administration of propofol (75-125µg/kg). Intraoperative analgesia was achieved by remifentanil (0.25mg/kg/min). Neuromuscular blockers were used only for intubation (rocuronium from 0.3 to 0.4 mg/kg or mivacurium 0.2 mg/kg) but not during the surgery (neuromuscular blockade was effective only 15-25 minutes during intubation).

Prophylactically every patient's was provided by preoperative peroral antibiotic (2g Nilacef to 12 pm), dexamethasone in a single dose of 8 mg iv in 6 hours and anticonvulsant therapy Mazepin 3x200mg.

During all operations electrostimulation was conducted on display area of the brain to reach the anatomical location of M1 segment of the motor cortex. For electrical stimulation of the cortex were used 3-contact strip electrodes (AD-Tech® strip electrodes, AD Tecnica, WI, USA). Upon identifying the motor fields the distance from the coronary suture was measured and performed by comparison with the values obtained from the preoperative measurement of the distance of the central sulcus of the coronary suture on the MRI image. The data were processed by computer aided SPSS 12.0 software package.

RESULTS

Histopathologic analysis confirmed the existence of GBM in 26 cases.

The average age of patients with glioblastoma multiforme was 40.47 ± 12.854 years. In all cases the diagnosis of intracranial expansive lesion located in the region of the central sulcus of the brain was made by recording the nuclear magnetic resonances imaging (MRI). In 58.9% (20) findings of the lesions were localized in the right supratentorial hemisphere, and 41.1% (14) in the left supratentorial hemisphere. In order to achieve a clear preoperative orientation, especially in the present cases, infiltrative tumor growth, with no visible boundaries to the surrounding brain tumors, we performed to measure the distance of the central sulcus (the longest in the high parietal sulcus sections) in relation to the coronary suture on MRI images, based on diagnosed and planned operations. The average distance of the central sulcus in relation to the coronary suture was 18.38 mm ± 9.564 mm; minimum distance amounted to 7 mm and a maximum of 42 mm. (Table 1)

All patients were operated under general anesthesia, and during all operations conducted electrostimulation display area of the brain for anatomical location of M1 segment of the motor cortex. The average value of electric current intensity needed to obtain motor responses was 9.26±1.268 mA (min. 7mA, max. 11mA). Longer distance from the coronary suture imply decreased strength of current intensity required to explicit motor responses (r =- 0.574, p <0.01).

The average strength of electric current needed to explicit motor responses in patients suffering from glioblastoma multiforme was 8,115 ± 1.479 mA which is an average of 1.149 mA less than the average amount of

### Table 1

<table>
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<th>N</th>
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<th>Median</th>
<th>Min</th>
<th>Max</th>
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### Table 2

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<td>Glioblastoma</td>
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</table>
TABLE 3

THE VALUE OF THE INDEX KARNOFSKI PRE-POST OPERATIVE

<table>
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<th>HP exam</th>
<th>Karnofski index - pre op</th>
<th>Karnofski index - post op</th>
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<tbody>
<tr>
<td>N</td>
<td>Arithmetic mean</td>
<td>Median</td>
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<td>34</td>
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current needed to elicit motor responses in patients in whom the slow-growing glioma brain (9.265 ± 1.286 mA). This difference highly statistically significant (p < 0.01, Table 2). Statistical analysis showed a statistically significant (p < 0.05) lower amperage required for the identification of motor areas of tumors where the degree of surgical resection was a subtotal to the level of reduction - 8.273 ± 1.162 mA compared the radical operation - 9.079±1.549 mA. The nominal value of the average difference was 0.810 mA.

Single view in relation to the histological group of tumors, show a numerical increase of Karnofski index (CI) after surgery compared to the situation before surgery. The mean value of KI before surgery for low grade glioma was 90.59 ± 10.133 and postoperative 92.94 ± 8.359. (Table 3).

DISCUSSION

Surgery of lesions localized in the motor cortex is a challenging because of the accompanying risk of de novo occurrence of motor deficit. Intrinsic tumors may affect cortical and subcortical structures, with no signs of functional deterioration. On the other hand a clear presentation of the vast area of the tumor in a patient without neurological deficits before surgery may not be a guarantee that the tumor can be removed radically without the possibility of subsequent motor deficit 16. Group of authors is of opinion that the length of survival after surgery is directly dependent on the degree of resection as the low grade and high grade gliomas in the brain, and if the resection include the supplementary motor field there can be the full Iniencephaly 17. Electrical stimulation of the cortex in infiltrating glioma of the brain localized in the motor cortex prevents damage to functionally important parts of the cortex and allows radicalism operations 17. Skriboll emphasizes that it is difficult to determine whether additional postoperative neurological deficits is caused by intratumoral localization of motor fibers or due to manipulation of surgical zone near the motor or both reasons 18.

Tumor invasion of functional cortex, the compression effect and functional organization of the cortex raises the need for finding the shortest safe access to the tumor in order to achieve a higher degree of radicalism. Sir Victor Horsley identified centres for arms and legs by performing an experimental electrical stimulation of the cortex of monkeys 19. Fritisch and Hitzing (1870) conducted the first controlled electrical stimulation of cerebral cortex - the front half of the supratentorial hemisphere of dog, connecting a source of direct galvanic current with a bipolar electrode. Direct cortical stimulation DC galvanic current human cerebral cortex gaining sensory and motor response was made by Robert Bartholow (1874), placing wires in the pulp chamber abscess localized in the left convexity supratentorial hemisphere and watched the observed contraction of the right shoulder and leg. Until the present time the primary method experienced modifications, including the current electrostimulation waking patients, conceived by Gruenbaum-and Cushing and confirmed by the Penfield-in the form of recommendations for a safe surgical approach to lesions localized in eloquent areas of the brain 20-22.

The rapid growth of the tumor causes compression and movement of motor cells, so that after surgical removal it gives a quick recovery of neurological deficit and considerably wider presentation of the motor field, with the possibility of obtaining an identical motor response in the different parts of M1 segment of the cortex, and the absence of motor deficit before surgery with fast-growing malignant tumor is explained by the synergistic action of M1 segment of the opposite hemisphere through collateral connections 23.

The absence of neurological deficits with low grade glioma is a common finding, which is explained by many authors as a local regroup of functional networks of neurons, allowing total removal of lesions without inducing neurological sequelae 24-25. It is also pointed out that functional neural tissue can be detected within the tumor which causes limited surgical resection 26-27.
The modification in the spatial organization and direction of tumor growth can be caused by previous surgery and a tumor itself can cause functional peritumor reorganization of the motor cortex with the absence of neurological deficit even though the part of eloquent areas located within the boundaries of the tumor and/or induce compensatory function of other ipsilateral regions in charged for the same function.11,14,24,26

This phenomenon is explained by the type III spatial configuration of low grade glioma described by Dau mas-Dupont and associates with tumor cells surrounding and infiltrating the brain without loss of essential connections or function.21

The explanation of the return of function can be found in the assumption that the M1 field is detected and protected during the operation but not the other fields that have the function of excitation or inhibition on the M1 region, which causes transient neurological deficit that may be improved by secondary compensatory mechanisms.5,28

Surgical resection of the tumor can be basically considered as brain injury, and can induce GABA inhibition and NMDA receptor-dependent excitation in the region of cavity, leading to synaptic plasticity and reorganization by speeding heterosynaptic long term potentiation.24 These changes in local synaptic activity can trigger pre-existing regional functional centers and distant cortical connections.23,24 Mechanisms of reorganization and motor somatosensor organizations have been confirmed in experimental animal studies.29 It has been shown that the initial rapid reorganization, sometimes transient can become permanent by recurrent training.30 Practical application of this model is reflected in the use of transcranial magnetic stimulation for excitation or inhibition.

Yoshiura et al identified increased activity in contralateral motor area on fMRI in patients with brain tumor in the motor zone.21 Schiffbauer and Thiel models emphasize the dynamic functional reorganization in the surrounding peritumour brain, creating compensatory motor fields, which explains the absence of motor deficits in tumors localized in the motor area of cerebral cortex, and also the emergence of the deficit immediately after operation, with a tendency to complete recovery within 3 months postoperatively.16,32 Suess analyzed 225 surgically treated tumors out of which 121 in direct contact, and 134 over the primary cortex showing a correlation between the use of electrocortical stimulation procedures in order to identify the primary cortex and the degree of surgical radicality. In 11 cases patients had delayed motor deficit in the period of 8 hours to 3 days after surgery, which completely recovered within three months.13

Duffau recommends the standard use of intraoperative electrical stimulation of the brain during operations in eloquent areas of the brain as a method which improves postoperative functional outcome.10,11,24,34 Direct cortical electrostimulation is safe, accurate and easy to perform method for identification of eloquent cortical and subcortical field.13,14 Functional neural tissue can be detected inside the tumor which causes a limited surgical resection.18,26 Modification in the spatial organization and direction of tumor growth can be caused by previous surgery and tumor itself can cause functional peritumoral reorganization of motor cortex with the absence of neurological deficit, although part of the eloquent area located within the boundaries of the tumor and/or induce compensatory function of other ipsilateral regions responsible for the same function.11,14,24,26

CONCLUSION

Direct electrostimulation of cerebral cortex is a reliable method for identification of motor areas of the brain, and a requirement for additional prevention - iatrogenic neurological deficit.

Our results and review of the literature impose direct electrostimulation as binding intraoperative procedure for all lesions localized in the region of the motor cortex.

SUMMARY

MODEL RASTA I HIRURŠKO LEĆENJE GLOIOBLASTOMA MULTIFORME TUMORA LOKALIZOVANIH U MOTORNOJ ZONI MOZGA - KORIŠĆENJE TEHNIKE DIREKTNE ELEKTROKORTIKOSTIMULACIJE U PREVENCIJI MOTORNOG DEFICITA

Multiformni glioblastomi, lokalizovani u motornoj zoni predstavljaju aktuelni hirurški izazov, zbog potrebe za što radikalnijom resekcijom u cilju produženja života pacijenta, i sa druge strane zbog opasnosti da bi radikalnost mogla dovesti do dodatnog neurološkog deficita.


Rezultati. Udaljenost centralnog sulkusa u odnosu na koronarnu suturu, merena magnetskom rezonancom iznosila je 18,38mm±9,564mm. Jačina struje potrebne za dobijanje motornog odgovora iznosila je 9,26±1,286 mA, sa povećanjem odstojanja od koronarne suture je jačina struje potrebna za izazivanje motornog odgovora manja (p<0,01)

Zaključak: Metoda direktnih elektrokortikostimulacije moždanog korteksa je jednostavna i sigurna metoda i predstavlja obavezujući protokol u cilju po pacijenta bezbedne operacije tumora lokalizovanih u motornoj zoni mozga.

Ključne reči: glioblastoma multiforme, motorni korteks mozga, elektrokortikostimulacija
BIBLIOGRAPHY


