COMPARATIVE CHARACTERISTICS OF SURGICAL TREATMENT WITH SUBSEQUENT RADIOTHERAPY FOR BRAIN TYPICAL AND ATYPICAL MENINGIOMAS

Treatment option for meningiomas is their maximum radical surgical resection. Despite the radical resection, recidives of benign meningiomas develop up to 15 years approximately in 28% of patients. This research was designed to study the quality of life after the second surgery with subsequent radiation and chemotherapy in patients with recidives of brain meningiomas. Carrying out routine irradiation for atypical meningiomas can prolong the life of patient, stop tumor growth, while the quality of life does not deteriorate substantially.

**Keywords:** Brain meningioma, recidives, radiotherapy.

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**Introduction**

According to Astanbekov et al. (2006), meningiomas account for approximately 18-34% of all brain tumors and are the second leading cause of morbidity and mortality after gliomas. Antonov et al. (2002) noted that brain meningioma frequently occur in middle and old age patients, but they also develop in children and has more aggressive course. Gorbunova et al. (2000) observed multiple meningiomas in almost 10% of patients. Kozlov (2001) defined brain meningioma as benign tumor having the typical structure.

According to the International Histological Classification of Tumors of the Central Nervous System, there are a number of structure types of tumors, the most common of them are meningothelial, fibroblastic, and mixed (Korshunov et al., 2002). On the degree of malignancy, brain meningiomas are classified as typical (I grade of malignancy), atypical (II grade), and anaplastic (III grade) (Martynova, 2009). Mambetova et al. (2009) noted that atypical forms are relatively rare illnesses, which occur in 20% of patients (often in men than in women (Oleshkevich et al., 2006)), characterized by the individual signs of malignancy, often recur, and trend to grow rapidly. Identification of the correlative relationships between histological types of meningiomas, the frequency of their continued growth and recurrence is considered by Olyushin et al. (2008) to be not always reliable. Olyushin et al. (2009) believes that surgical resection is the main and most effective treatment option. In most cases, radical resection of tumor is possible, providing the patient's recovery. However, Pozdnyak et al. (2006) observed that radical resection is not always impossible in some patients because of location of tumors, place of their initial growth, complex relationships with surrounding functionally important brain structures, as well as features of histobiology. According to Stupak et al., (2004), one of the factors that limit the volume of surgical intervention is the close connection of tumor with brain magisterial vessels.

Last decades, there are great advantages in the surgical treatment of extracerebral tumors. However, an issue of treatment of patients with tumor recidives still is not well studied, and the results are not very satisfactory (Sambor, Kvasha, and Borisova, 2008). Survival terms for atypical meningiomas are defined to range from 1 to 6 years (Stupak and Kalinowski, 2008). Tigliev (2002) observed that despite the radical resection approximately 10% of patients develop recidives of benign meningiomas in up to 15 years; and the frequency of continued growth and recidives depended on the degree of malignancy (Tastanbekov et al., 2002). For example, according to Frayerman, and Medyanik (2006),
meningiomas with typical structure recur in 7-20% of patients, with atypical one in 29-38%, with anaplastic structure in 50-78% patients, accordingly. In this case, issues of medical approaches for continued growth of brain meningiomas concluded by Shamkalovich et al. (2007) to be most problematic in neurooncology. Regardless of the effectiveness of comprehensive treatment which conducted previously, as well as histological structure, meningiomas trend to grow progressively (Shmyryov et al, 2007). Continued growth of malignant meningiomas replaces brain tissue by tumor tissue with subsequent proliferation and increasing of malignancy (Shugol et al., 2002). Tumor often extends beyond the zone of initial localization. Sometimes multifocal growth is possible. In the depth localization tumor grows beyond the midline to the opposite hemisphere (Shamkalovich et al., 2006). Khamashta (2002) believed that the use of modern technical equipment and tools leads to a decrease in recurrence and continued growth of tumors to 30%. Alliez et al. (2006) established that the possibility of recidives of meningiomas depends on the following four factors: primacy of operation, its radicalism, histological malignancy of meningeoma, and radiotherapy.

Hypertensive syndrome is a clinical sign of continued growth of meningiomas in the initial stages, whereas focal neurological deficit develops when the adjacent functionally important areas are involved. The increase in the volume effects on brain requires surgical intervention, when priority is to optimize the “radicalism” of operation depending on the topographic features of tumor localization and its degree of malignancy (Le Garlantezec et al., 2005). Pre-operative and instrumental examination conducted in modern level provides insight into the anatomical relationships of tumor and adjacent brain structures, as well as features of blood supply and the possibility of increasing of malignancy degree. An integrated approach to treating fast growing meningiomas with compulsory use of radiotherapy believed by Le Garlantezec et al. (2005) to be possible prolong the life duration of patients and improve the disease outcomes.

Therefore, an analysis of techniques and methods of treatment, described in the literature, indicates that so far a unified opinion about the necessity of combined treatment for all types of atypical meningiomas, as well as the timing of treatment, the sequence of chemotherapy and radiation, and also proton therapy has not developed. Carrying out routine irradiation for atypical meningiomas prolongs the life of patient, stops tumor growth, substantially does not deteriorate the quality of life.

The purpose of this study was to improve the results of surgical treatment with subsequent radiotherapy in patients with brain meningiomas and their recidives.

Materials and methods

375 patients, who had operated in the Republican Scientific Center of Neurosurgery of Tashkent city with using standard treatments and new technologies between 2000 and 2010, were a basis for this analysis. 63 (16.8%) of patients were re-operated. Radicality of surgical treatment was estimated on Simpson’s scale. Neurological deficit symptoms and the quality of life of patients were assessed before surgery, at discharge from the hospital and at 6 months after operation. In addition, we studied the percentage of recurrence and continued growth of meningiomas, as well as inter-recidives period and the time of continued growth.

Results and discussion

Therapy results after primary surgery were studied in 230 (61.4%) patients. Women dominated in both groups: at the time of primary surgery (I group) they were 143 (62.2%), at recidives and continued growth of tumors (II group) - 36 (57.2%), whereas men were 87 (37.8%) and 27 (42.8%), respectively. The age of patients at primary surgery, recidives and continued growth of tumor varied from 45 to 59 years. Minimum period of monitoring in both groups was 6 months, maximum - 10 years. The average follow-up was 8 years old. Meningioma of cerebral hemispheres occurred in 331 (88.2%) cases, in
posterior fossa in 44 (11.7%) cases. The radicality degree of resection of meningiomas was analyzed in both groups. At primary surgery, I degree of radicalism (by D. Simpson) was achieved in 34 (14.8%), II degree in 58 (25.2%), III degree in 74 (32.2%), and IV degree in 64 (27.8%) patients, respectively. At recidives and continued growth of tumors, I degree of radicality was achieved in 9 (14.2%), II degree in 17 (26.9%), III degree in 24 (38.1%), and IV degree in 13 (20.1%) patients, respectively. According to the histological studies of meningioma that removed during surgical re-intervention for continued growth of tumor, the degree of malignancy trended to increase.

Dissatisfaction with the treatment outcomes for extracerebral and intracerebral tumors, frequent recidives, poor quality of life, high morbidity and mortality are the basis to search new, more effective methods of their surgical treatment. In neurological status of patients before the operation, the leading focal symptoms were movement disorders in 86 (22.9%) patients, including paresis in 72 (83.7%), plegia in 14 (16.2%) patients, and various forms of speech disorders in 57 (15.2%) patients. In 48 (12.8%) patients, aphasia is associated with movement disorders: from moderate hemiparesis to hemiplegia. Epileptiform seizures were observed in 273 (72.8%) patients. Regression of motor deficit was observed in 156 (41.6%) patients for 2-3 days after surgery, aggravation of existing symptoms developed in 63 (16.8%) persons. 18 (4.8%) patients developed new neurological symptoms because of the location of tumor in functionally significant speech-motor areas of brain. Mortality of patients in both groups was not significantly different, 18 (4.8%) patients died after primary surgery, 9 (2.4%) patients died after recidives and continued growth of tumors.

Radiotherapy (X-ray therapy) was performed in 96 (25.6%) patients. After radiotherapy the incidence of postoperative recidives of brain meningiomas decreased in 1.8 times, compared with those in 279 (74.4%) patients who had not received it. However, radiotherapy was not equally effective in all patients. When analyzing the clinical course of brain meningiomas depending on the degree of malignancy, we confirmed that the degree of malignancy increases, the treatment efficacy reduces in both groups. Thus, if at typical forms of brain meningiomas five-year survival reached 100%, then at atypical and anaplastic forms it is significantly decreased (16.8%) and depended on the treatment option. 56 (58.3%) of patients with atypical brain meningiomas, whose complex treatment included radiotherapy, lived 5 years, while at the same time, the five-year survival achieved in 40 (41.6%) of patients with atypical brain meningiomas, who had not received radiotherapy. Radiotherapy for atypical meningiomas has increased the five-year survival rate to 90%. As a rule, all patients were noted uncomplicated postoperative course. Only patients with giant brain meningiomas had severe postoperative period. Postoperative mortality was in 27 (7.2%) of all patients, who had large and giant tumors with gross compression of brainstem. Mortality causes were hemodynamic abnormalities in brainstem that developed after tumor resection and its decompression. Thus, the inclusion of radiotherapy into the comprehensive treatment of patients with brain meningiomas allowed to increase the effectiveness of therapy and to increase the five-year survival rate in patients with atypical meningiomas almost 1.5 times, and 2 times in case of anaplastic tumors. Despite the relatively small number of observed cases, the data of the average timing of recidives-free survival indicate the efficacy of radiotherapy, as it increased from 34.5 to 66 months (i.e. 1.9 times). The use of radiotherapy in the treatment of patients with brain meningiomas is proved and can improve the effectiveness of treatment, recidives-free survival in atypical and anaplastic structures. The patients observed who received radiotherapy for continued growth of brain meningiomas are noteworthy. Due to tumor topography, connections with brain vital structures, only in 43 (11.4%) patients we performed partial resection of meningioma with subsequent appointment of radiotherapy; However, since its effectiveness was low, there was a need of re-operation for continued growth of brain meningiomas. Histological examination of the materials after re-operations in patients of this group identified changes which were characterized by the sharp degree of malignancy. Our clinical studies showed that the use of radiotherapy was effective in 50% of patients. The results obtained proved the expediency of including of
radiotherapy into the complex therapy for brain meningiomas to achieve a stable remission. A key of success of radiotherapy in patients with brain meningiomas is the rational application, which reduces the degree of disability and, thus, improves the quality of life of patients.

**Summary**

At present time, despite significant advances in surgery of recidives of brain tumors, issues of resection of meningiomas, especially of giant ones and with inaccessible location, are one of the most difficult and far from being resolved. The basic principle in achieving favorable treatment outcomes for atypical brain meningiomas is the use of microsurgical techniques, neurosonography, which increases the level of radical resection of tumors, reduces the amount of blood loss and traumatization of brain structures, preserves functionally important veins, as well as reduces the frequency of recidives and mortality. Hence, it is necessary to search new methods of treatment with use of radiotherapy and chemotherapy to avoid the continued growth of atypical meningiomas.

The results obtained are evidence of the use of microsurgical technique which can significantly increase the radical surgical intervention for brain meningiomas, resulting in lower frequency of recidives and reducing number of complications. Thus, the use of microsurgical technique at the stages of resection of meningiomas with the consequent coagulation of the matrix increases the radicality of surgical treatment, reduces the risk of recidives and continued tumor growth. At the same time, it does not worsen the quality of life in the early and late postoperative periods, does not lead to additional traumatization of cranial nerves as compared with conventional methods of surgical treatment. So, the use of radiotherapy (X-ray therapy) after partial and subtotal resection of tumor should be as soon as possible, for reduction of meningiomas malignancy after the first operation.

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