



INTRAMEDULLARY EPENDYMOMAS: LONG-TERM OUTCOMES OF SURGICAL TREATMENT*

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Objective. The study was aimed at assessing the long-term outcomes of surgical treatment of intramedullary ependymomas. **Material and Methods.** Spinal ependymomas were detected in 91 (20.2 %) of 450 operated patients. Intramedullary location of the tumor was diagnosed in 41 (45.0 %) patients. Ependymoma was benign in 78.1 % of cases and anaplastic in 9 (21.9 %) cases. Radical removal of the tumor was achieved in 36 (87.8 %) patients, and subtotal resection was performed in 5 cases (12.2 %).

Results. Long-term persistence of severe neurological symptoms was observed in 6 (24.0 %) patients. Structural changes in the spine associated with surgical intervention were detected only in 12.0 % of cases; relapses and continued tumor growth was observed in 16.1 % of cases. Early postoperative mortality was 4.8 % (2 patients out of 41 died). Four more patients died in the late postoperative period, so that the overall mortality was 14.6 %. Five-year survival rate of patients was 80.6 %.

Conclusion. Radical surgery is an effective treatment for intramedullary ependymomas. The prognosis of intramedullary ependymoma may be considered favorable in the case of radical removal of the tumor, its benign nature, and good functional outcome of surgical treatment.

Key Words: long-term period, intramedullary tumors, ependymoma, spinal cord, radical removal, functional outcomes of surgery, independence, adaptation level.

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Intramedullary tumors account for 10–20 % of primary tumors of the central nervous system [2, 6, 15, 16]. In children and young patients, this value is up to 35 % [8]. The sources of spinal ependymoma growth include ependymal cell lining of the central canal of the spinal cord and ependymal cell cluster in the terminal filament of the spinal cord [13, 14, 17]. Ependymomas are the encapsulated neoplasms and usually have well-defined margins. They account for 4–6 % of primary tumors of the central nervous system and one third of them are intramedullary. According to the WHO pathological classification (1999), typical perivascular pseudorosettes are the histopathological markers of these tumors. Ependymomas have specific histopathological characteristic features, which lie in the fact that necroses and hemorrhages, which often occur in this tumor, are not malignancy signs. Only the presence of frequent mitoses and vascular prolifer-

ation is indicative of anaplastic (or grade 3) ependymoma.

The vast majority of these neoplasms are demarcated tumors that can be removed radically [3]. According to contemporary authors [1, 4], the choice of expectant management and non-radical surgical interventions are inadequate treatments for spinal cord ependymomas. At the moment, only radical removal of these tumors with maximum preservation of spinal cord function makes it possible to achieve actual cure of a patient.

The objective of the study is to assess the long-term outcomes of surgical treatment of intramedullary ependymomas.

Material and Methods

The study was carried out based on clinical data obtained at the neurosurgical department of the Novosibirsk Research Institute of Traumatology and Orthopedics (NRITO). In 1999–2013, 450 patients with various primary spi-

nal tumors underwent surgical treatment. Patient setting was carried out according to the results of histopathological examination, which was conducted in all cases when biopate was obtained during the surgery.

The study involved the analysis of medical records, evaluation of neurological and orthopedic status, results of neuroimaging (MRI, MSCT), and pathomorphological studies. We performed standardized assessment of the functional state according to McCormick scale based on the severity of neurological deficit. Furthermore, the functional outcomes of surgeries were evaluated by studying adaptation level of operated patients using SCIM scale and its self-administered questionnaire (SCIM-SR) [9, 10, 12]. In connection with the common complaints of operated patients on dysesthesia and pain during the study, DN4 scale was used [7] to detect and confirm neuropathic pain or neuropathic pain component. In order to assess the out-

comes of surgical treatment and quality of life in the preoperative and postoperative periods, we used the classification of patient's functional status as revised by G.Yu. Evzikov [2].

Based this scale, the following evaluation of surgical treatment outcomes was adopted: 1 – good results (improvement to higher functional class level or improvement within this class); 2 – satisfactory (improvement within one functional class or absence of deterioration); 3 – unsatisfactory (deterioration or lack of improvement).

Contrast-enhanced MRI should be used in all cases in order to diagnose intramedullary tumors, the degree of radicality of the operation, relapses or continued growth. To this end, we used the device with a magnetic field strength of 1.5 T. The study was performed preoperatively and postoperatively in 100 % of patients. According to the results of MRI, neoplasms were diagnosed within one spinal segment in 5 (12.2 %) patients, within two segments in 12 (29.3 %) patients, three – 10 (24.4 %), four – 3 (7.3 %), and five – 2 (4.9 %). In 46.3 % of cases (n = 19), MRI detected tumorous cysts. There were intratumoral cysts in 6 (31.6 %) of 19 patients and peritumoral cysts at the poles of a solid tumor component in 13 (68.4 %) cases. In 87.8 % of cases, ependymoma was located strictly in the center of the spinal cord and only in 5 (12.2 %) patients axial images revealed asymmetric growth of tumors, mostly right-sided one.

Tomographic control in the early postoperative period (1–2 days from the time of operation) provides the evidence of the radicality of surgical intervention and shows the dynamics of post-operative changes of the spinal cord. Tomographic control is especially valuable for diagnosis in the cases when additional neurological deficit arises, since it enables detecting signs of complicated postoperative course, such as progressive spinal cord edema and bleeding in the resected tumor bed. When there were clinical signs that could be accompanied by structural changes in the spine, patients underwent radiological examination, such as spondylography in two

projections with functional tests and MSCT of the spine.

Radicality of tumor resection was assessed based on the analysis of surgical records (information about tumor resection within visible boundaries) and postoperative results of the contrast-enhanced MRI. Diagnosis of relapses or continued tumor growth was always supported by contrast-enhanced MRI with assessment of the dynamics of changes in the tomographic picture compared to the tomographic images obtained in the early postoperative period. Non-contrast-enhanced study was allowed no earlier than 5–7 years after tumor resection, providing that it was conducted on the tomographic scanner with magnetic field strength of at least 1.5 T.

Pathomorphological tumor structure corresponded to ependymoma in 91 (20.2 %) patients. In these patients, intramedullary location of the tumor was detected in 41 (45.0 %) cases. In 38 (92.7 %) of 41 these patients, there were newly detected tumors. In 3 (7.3 %) cases, the operations were carried out for continued growth and recurrences of previously operated intramedullary ependymomas.

The number of males and females was 24 (58.5 %) and 17 (41.5 %), respectively. The following location of intramedullary ependymomas was observed: 25 (61.0 %) patients had tumor at the cervical level and 16 (39.0 %) patients had tumor at thoracic level.

The results of pathohistological examination confirmed benign nature of ependymomas in 32 (78.1 %) cases, signs of malignancy were observed only in 9 (21.9 %) cases.

The follow-up period averaged 6.5 ± 2.9 years. Long-term outcomes of treatment were evaluated in 31 (75.6 %) of the operated patients, in 10 (24.4 %) cases they were not available because the contact with the patient was lost.

Neurological symptoms depends on the level, where the tumor is located with respect to the length of the spinal cord and sagittal plane, the dimensions of tumors and development of secondary compression and ischemic disorders. Only 4 (9.8 %) of patients had no neuro-

logical deficit. In this group of patients, the tumor was identified during the MRI study for existing vertebrogenous pain syndrome.

Most often, the disease manifest as segmental and segmental-conductive sensory disorders. They were detected in 33 (80.5 %) cases. Only 8 (19.5 %) patients had no sensory disorders.

Somatosensory evoked potentials (SSEP) generated in response to nerve stimulation of the upper or lower extremities (depending on tumor location in the cervical or thoracic region) were recorded during preoperative examination in order to obtain an objective instrumental assessment of the severity of sensory disorders, including lateral differences arising from the characteristics of tumor localization. All patients demonstrated reduced magnitude of SSEP during preoperative examination and there were varying degrees of differences in SSEP magnitudes in response to stimulation of the left and right limbs. The degree of reduction in general correlated with tumor length. Delay, broadening, and desynchronization of the main components of SSEP (N20 for median nerve stimulation and P39 for tibial nerve stimulation) also correlated with tumor length. The lowest modified SSEPs were recorded during stimulation of lower extremity nerves in patients with large thoracic tumors. In 7 (17.0 %) patients, they were almost completely absent.

Limb movement disorders is one of the most specific symptoms. This symptomatology was diagnosed in 26 (63.4 %) of 41 patients. Among them, tetraparesis prevailed in 8 (30.8 %) patients, hemiparesis prevailed in 2 (7.7 %) patients, upper monoparesis prevailed in 6 (23.0 %) patients, lower paraparesis prevailed in 7 (23.0 %), and upper paraparesis prevailed in 3 (11.5 %) patients.

Pelvic organ dysfunctions were observed in 8 (19.5 %) patients, all of them were diagnosed with central (obstructive) disturbances. Pain syndrome was diagnosed in 7 (17.0 %) patients and it was not a specific manifestation of intramedullary ependymomas.

Functional state of operated patients was assessed based on studying the sever-

ity of the initial neurological symptoms according to McCormic scale (1999). Neurological symptoms of 11 (26.8 %) patients corresponded to functional class I, 13 (31.7 %) patients – class II, 15 (36.6 %) patients – class III, and 2 (4.9 %) patients – class IV.

Radical resection of neoplasms was performed in 36 (87.8 %) cases, subtotal resection – in 5 (12.2 %) cases, including 4 (9.7 %) patients, who were operated for the first time and 1 (2.5 %) patient with recurrent tumor.

Removal of the spinal cord ependymomas was always performed from the posterior medial approach. Based on the tomography results, posterior vertebral structures were resected at the level of the tumor so as to be able to remove not only the solid component of the tumor, but also dissect and drain tumor cysts. Laminectomy was performed in 30 (73.3 %) cases. In 5 (12.0 %) cases, surgical approach was carried out through the hemilaminectomy. Osteoplastic laminectomy was conducted in 6 (14.7 %) patients using high-speed drill. Surgical approach within one vertebra was carried out in 5 (12.2 %) patients, two – in 12 (29.3 %) patients, three – in 10 (24.4 %) patients, four – in 3 (7.3 %) patients, and five – in 2 (4.9 %) patients.

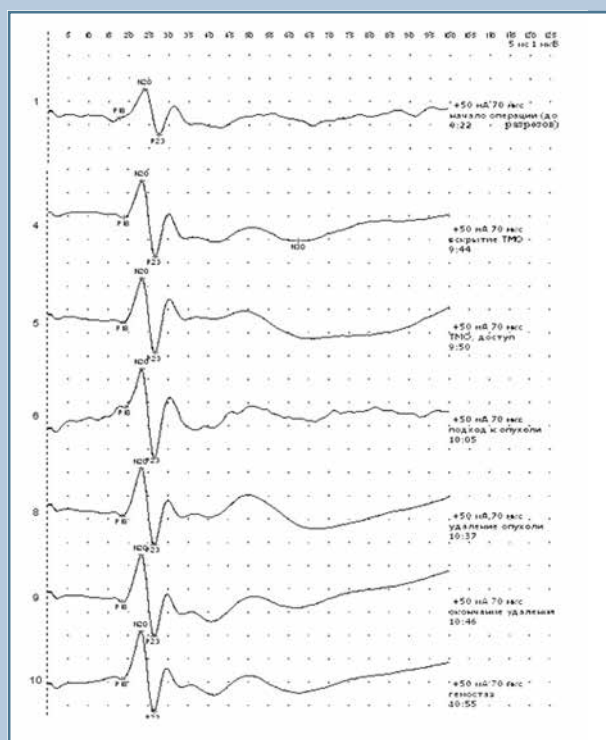


Fig.

Monitoring of the brainstem somatosensory evoked potentials in response to stimulation of the left median nerve during surgery for resection of cervical ependymoma. Relatively low amplitude of evoked potentials at the beginning of the operation was caused by induction of anesthesia

Tumor was resected using microsurgical techniques with intraoperative SSEP monitoring. In the cases when baseline electrophysiological parameters of the sensory conduction were sufficiently preserved, we monitored the side with the greatest deviation from the norm. In the case of more significant disorders and supposed higher invasiveness of the surgery, we monitored better preserved SSEPs. Intraoperative SSEP monitoring provides more reliable approach to the total resection of tumors (Fig.).

All patients were operated on using microsurgical instruments and a microscope. We used magnification from 10 to 20. During resection, we used ultrasonic disintegrator, which enables internal decompression of the tumor with a view to its further mobilization and minimization of the impact on the adjacent structures of the spinal cord. All manipulations following the opening of the dura mater were carried out using surgical optics. The approach to the tumor was performed at the midline through the myelotomy. Its length in all cases corresponded to the length of solid tumor component. Along with this, we performed coagulation of small vessels accompanied by continuous irrigation of coagulated surface with warm saline, since application of cotton balls in order to achieve hemostasis leads to compression effect on the posterior columns of the spinal cord followed by the development of more severe local hemic disorders. In 5 patients with lateralized position of the tumor with respect to the central canal of the spinal cord, the approach was carried out through DREZ-zone in order to reduce the traumatic effects of the surgery. In the case of large tumors, we first performed internal decompression of the tumor using an ultrasonic aspirator, bipolar coagulation, and vacuum micro-suction unit. Excision of the tumor was carried out from the inside and sometimes emptying of the intramedullary cyst or hematoma provided favorable conditions for this. Resection of ependymomas proceeded on the sides, starting from the side where well-defined boundary with the spinal cord was observed. When there were peritumoral cysts, we always tried only to dissect and empty them. Small tumors were removed en bloc after separation along the border with the normal spinal cord. Radicality depended on the nature of its growth (focal or infiltrative). Hemostasis at the area of the removed tumor was achieved using hemostatic material (Sergesell) or, rarely, bipolar coagulation.

Statistical data processing was performed using non-parametric methods of Statistica 6.0 software (StatSoft). Fisher's exact test for discrete variable was used to assess the significance of differences between groups. The differences are significant at the significance level of $PFET \leq 0.05$.

Results

In most cases, microsurgical interventions did not cause pronounced deterioration of patient's state and increase in severity of existing focal symptoms. In the early postoperative period, good clinical outcome with symptoms on the preoperative level was observed in 25 (61 %) of 41 patients compared to the baseline condition of patients. Moreover, there was significant regression of neurology in 4 of them. Along with this, 12 (29.2 %)

of the operated patients demonstrated significant worsening of neurological disorders compared to preoperative level. This is evidenced by the functional outcomes of operated patients. For example, McCormic's (1999) functional class I was observed in 4 (9.7 %) patients (PFET = 0.042), II – 5 patients (12.2 %, PFET = 0.03), III – 22 patients (53.7 %, PFET = 0.0913), IV – 10 patients (24.4 %, PFET = 0.0128).

Positive dynamics of pelvic organ dysfunction was observed in 13 (52.0 %) patients.

In the postoperative examinations, positive dynamics of SSEP parameters was observed in 14.0 % of patients, no significant changes were observed in 58.5 % of patients, and worsening of conduction, including conduction from one of the limbs, was observed in 27.5 % of patients. The improvement or no change in SSEP parameters indicates that compressing effect of the tumor with respect to pathways was the main factor of impulse conduction disorder, which can be eliminated by removing the tumor, and that the surgical technique used results in minimum traumatization of spinal cord, i.e. reflects the positive results of surgical treatment.

Reoperations expectedly led to worsening of focal symptoms. Thus, tumors in the group of re-operated patients ($n = 3$) are in equal proportions represented by II, III and IV functional classes of neurological symptom severity. The total SCIM score was 65, indicating relatively high degree of dependence of these patients.

Long-term outcomes of surgical treatment were studied in 31 patients. The severity of neurological symptoms (except of 6 patients, who died) was studied in 25 patients. By this time, statistically significant favorable clinical outcomes compared to the postoperative period were observed in 76 % ($n = 19$) of studied patients, and 23 % patients retained mostly mild neurological disorders. According to McCormick scale, 11 (44.0 %) patients were assigned to functional class I (PFET = 0.019); 8 patients – II (32.0 %; PFET = 0.0516), 4 patients – III (16.0 %; PFET = 0.022), and 2 patients – IV (8.0 %; PFET = 0.086).

Pain syndrome without structural changes in the spine (mostly muscle-reflex one) was observed in 12 (48.0 %)

patients. Neuropathic pain or neuropathic pain component according to the criteria of DN4 scale was detected in 7 (28.0 %) cases and corresponded to segmental-conduction disorders of pain and tactile sensitivity. The need for continuous bladder drainage preserved in 2 (8.0 %) patients.

Independence of operated patients was assessed in the late postoperative period according to SCIM III (2011) scale. According to this classification, the final total score for completely independent patient is 100. In our patients, the average self-care score was 14.95 (maximum 20), respiratory function and sphincter control – 33.7 (maximum 40), movement – 26.8 (maximum 40). As a result, the average total score was 75.45. At the same time, patients with monoparesis, despite the symptoms, have higher independence rates (the average total score of 97.5). Limitations in functional independence of patients with mild tetrapareses were mainly associated with impaired joint and muscular sensitivity and the need to use supporting equipment for self-care and mobility (total mean score of 86.3). Patients with paraparesis of 3 points and below are expectedly more dependent, since they use wheelchair for movement (the average total score was 66.9). The patients with deep tetrapareses are the most dependent ones (average score of 40.6).

The number of relapses and continued tumor growth was 16.1 % (5 of 31 patients, whose long-term outcomes are known). The analysis of tumor recurrences has shown that in the case of total resection in the group of primarily operated patients it amounted to 7.7 % (2 cases out of 36). In this cases, relapses occurred in re-operated patients in 2 and 13 years.

Clinical and tomographic data indicating continued growth of ependymomas were detected in 12.0 % of cases (3 of 4 patients after non-radical removal of ependymomas in 3 to 9 years). In this regard, three patients underwent re-operations with total removal of tumors. Another 1 patient had no signs of continued growth for 14 years from the date of the operation.

Orthopedic consistency of the spine in the late postoperative period is an important aspect of the functional activity of

operated patients. Severe kyphotic spinal deformity is the most common complication in the late period after extensive surgery involving multi-level resection of the posterior spinal structures [5, 11]. Only in 12.0 % of cases (two of three patients) with severe neurological symptoms in the form of deep tetraparesis and extremely low levels of adaptation and functional activity, paralytic scoliosis of thoracolumbar spine developed. Severe kyphosis of the cervical spine arose in one patient who underwent extensive resection of the posterior spinal structures).

Early postoperative mortality amounted to 4.8 % (two of 41 patients died). In one case, the death was caused by ascending edema of the spine and medulla oblongata after reoperation for relapse of ependymoma, which occurred in 13 years since the first operation, in the second case, it was caused by pulmonary embolism.

In the late postoperative period (within 5 years from the date of the operation), 4 more patients died. Overall mortality in the series was 14.6 %. In three cases, the death was caused by the underlying disease and development of somatic complications with underlying severe neurological symptoms in patients with continued growth of the tumor located at the cervical spine. In one case, the patient died due to progression of renal malignancy. Five-year survival of patients was 80.6 % (25 of 31).

Conclusions

1. Radical surgical removal of intramedullary ependymomas is an effective treatment method. It was used in 87.8 % of cases of intramedullary tumors, while subtotal removal was performed in 12.2 % of cases.

2. Prognosis of intramedullary ependymomas can be considered favorable in case of radical removal, benign nature of the tumor, and favorable functional outcome of surgical treatment.

3. The five-year survival rate was 80.6 %.

4. The total number of relapses and continued tumor growth was 16.1 %, while the number of relapses in the group of primarily operated patients who underwent total resection of ependymomas was 7.7 %.

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