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Abstract

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PECULIARITIES OF TREATMENT OF CERVICAL SPINAL NERVE TUMORS WITH PARAVERTEBRAL EXTENSION

Introduction. To evaluate the results of surgical treatment of patients with malignant peripheral nerve sheath tumors (MNST) with specification of the peculiarities of their structure and extension pattern, and to determine prognostically unfavorable morphological features in malignant tumors of peripheral nerves.

Materials and methods. The study is based on a retrospective analysis of the medical records of 48 patients. The indication for the operation was worsening neurological symptoms as a result of the tumor process in the cervical spine, verified by methods of neuroimaging (spondylography, CT, SCT, MRI).

Results. he expected response to surgical treatment in patients with MPNST depends on many factors: localization, directions of neoplasm extension, radical nature of the treatment and the histological variant of the tumor. In most cases, MNST is diagnosed in patients aged 27 to 56 years. The time from the onset of neurological symptoms to diagnosis varies from several weeks to one year.

Conclusions. Determining the tactics of surgery and the choice of surgical access is an important component for achieving long remission. The choice of an adequate approach makes it possible to totally remove the tumor, reduces the time of intervention, blood loss, injuries to the nervous structures during removal of the tumor.

Keywords: malignant tumors of the spinal nerves; peculiarities of surgical treatment; cervical spine.

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Резюме

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ОСОБЛИВОСТІ ЛІКУВАННЯ ЗЛОЯКІСНИХ ПУХЛИН СПИННОМОЗКОВИХ НЕРВІВ ШИЙНОГО ВІДДІЛУ ХРЕБТА З ПАРАВЕРТЕБРАЛЬНИМ ПОШИРЕННЯМ

Мета: оцінити результати хірургічного лікування пацієнтів із злоякісними пухлинами оболонок периферичних нервових стовбурів (ЗОПНС) з уточненням особливостей їх структури та характеру поширення, визначення прогностично несприятливих морфологічних ознак у злоякісних пухлинах периферичних нервових стовбурів.

Матеріали та методи. Дослідження базується на ретроспективному аналізі історій хвороб 48 пацієнтів. Показаннями до операції була наявність прогресуючої неврологічної симптоматики, в результаті пухлинного процесу на рівні шийного відділу хребта, верифікованого методами нейровізуалізації (спондилографія, КТ, СКТ, МРТ).

Результати. Прогноз хірургічного лікування у хворих із ЗОПНС залежить від багатьох факторів: гістологічного варіанту пухлини,

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особливостей локалізації та напрямків поширення новоутворення і радикальності проведеного лікування. ЗОПНС в більшості випадків діагностовано у пацієнтів у віці від 27 до 56 років. Час від появи неврологічної симптоматики до встановлення діагнозу варіює від декількох тижнів до одного року.

Висновки. Визначення тактики операції і вибору хірургічного доступу є важливою складовою для досягнення тривалої ремісії. Вибір адекватного підходу дозволяє тотально видалити пухлину, зменшує час втручання, крововтрату, травматизацію нервових структур при видаленні новоутворення.

Ключові слова: злоякісні пухлини спинномозкових нервів, особливості хірургічного лікування, шийний відділ хребта.

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ОСОБЕННОСТИ ЛЕЧЕНИЯ ЗЛОКАЧЕСТВЕННЫХ ОПУХОЛЕЙ СПИННОМОЗГОВЫХ НЕРВОВ ШЕЙНОГО ОТДЕЛА ПОЗВОНОЧНИКА С ПАРАВЕРТЕБРАЛЬНЫМ РАСПРОСТРАНЕНИЕМ

Цель: оценить результаты хирургического лечения пациентов со злокачественными опухолями оболочек периферических нервных стволов (ЗОПНС) с уточнением особенностей их структуры и характера распространения, определение прогностически неблагоприятных морфологических признаков в злокачественных опухолях периферических нервных стволов.

Материалы и методы. Исследование базируется на ретроспективном анализе историй болезней 48 пациентов. Показаниями к операции было наличие прогрессирующей неврологической симптоматики, в результате опухолевого процесса на уровне шейного отдела позвоночника, верифицированного методами нейровизуализации (спондилография, КТ, СКТ, МРТ).

Результаты. Прогноз хирургического лечения у больных с ЗОПНС зависит от многих факторов: гистологического варианта опухоли, особенностей локализации и направлений распространения новообразования и радикальности проведенного лечения. ЗОПНС в большинстве случаев диагностирован у пациентов в возрасте от 27 до 56 лет. Время от появления неврологической симптоматики до установления диагноза варьирует от нескольких недель до одного года.

Выводы. Определение тактики операции и выбора хирургического доступа является важной составляющей для достижения длительной ремиссии. Выбор адекватного подхода позволяет тотально удалить опухоль, уменьшает время вмешательства, кровопотерю, травматизацию нервных структур при удалении новообразования.

Ключевые слова: злокачественные опухоли спинномозговых нервов, особенности хирургического лечения, шейный отдел позвоночника.

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Вступ

When studying the peculiarities of the structure of spinal nerve malignant tumors, peculiar features indicating their low degree of differentiation (malignancy) were found; that is why the 1999 edition of nervous system tumor classification they were singled out as a distinct disease – malignant peripheral nerve sheath tumor (MPNST) [1]. According to

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the latest edition of WHO nervous system tumor classification (developed by the International Agency for Research on Cancer, IARC), Leon, 2016 [2], the spinal nerve tumors are divided into: schwannomas, neurofibromas, perineuromas, malignant peripheral nerve sheath tumors (of various variants and degrees of malignancy) [2]. Given the heterogeneity of their morphological structure, differential diagnosis of these tumors is complicated (in terms of their variant and grade objectification), as well as prognosis of further course and possibility of relapses of MPNST, which necessitates the need for clinico-morphological comparisons and improvement of certain structural criteria for optimization of treatment.

A special topographic variation of spinal nerve tumors is presented by hourglass tumors, also referred to as dumb-bell tumor or sand-glass tumor. This term is used to denote a group of tumors, which are conventionally divided into two parts: intracanal and paravertebral, connected by an isthmus [3].

One of the most difficult tasks for neurosurgeons is treatment of malignant peripheral nerve sheath tumors. The treatment of patients with tumors of this histological type is characterized by a high level of postoperative disability, a significant number of postoperative complications, relapses and unfavorable course of the disease, which are expressed via severe and in most cases irreversible neurological disorders [4]; due to this, a detailed analysis of the tumors is required.

The purpose: to evaluate the outcomes of surgical treatment of the patients with MPNST and clarify the peculiarities of tumor structure and extension; to determine prognostically unfavorable morphological features in malignant tumors of peripheral nerves.

Materials and methods.

The study is based on a retrospective analysis of the treatment outcomes according to the case histories of 48 patients (1998 to 2016) operated on spinal nerve tumors with hourglass-type intra-extravertebral extension at the department of spinal neurosurgery, Institute of Neurosurgery named after Academician A. P. Romodanov.

The indication for the operation was worsening neurological symptoms as a result of the tumor process in the cervical spine, verified by methods of neuroimaging (spondylography, CT, SCT, MRI). The data were used from handwritten and computerized electronic patient records covering a wide range of clinical and instrumental diagnostic methods with description of surgical treatment options and pathological findings with profound retrospective evaluation. Among the patients studied, 18 (27.1 %) were men and 30 (72.9 %) were women. Patients' age ranged 15 to 70. The mean age equaled 41 ± 4.4. Prospective follow-up terms ranged 1 to 40 years.

Of 48 patients with cervical spinal nerve tumors, schwannomas (neurinomas) were diagnosed in 26 (54.2 %), neurofibromas – in 9 (18.8 %), malignant peripheral nerve sheath tumors – in 13 (27 %).

For all patients, a standard clinical examination was performed, which included an examination of neuropathologist and neurosurgeon. Primary diagnostic measures included spondylography, CT, MRI, and a number of angiographic studies. X-rays were performed in standard (anteroposterior and lateral) view. The examination was performed in all patients. CT (SCT) examination, bi-plane CT was performed in case of spine deformation at the tumor location level. In this case, the study allowed visualizing the extent to which the paravertebral nodes of the tumor cause damage to the back support complex, in particular – the deformation with the excavation of the vertebral bodies and the destruction of the arches of vertebra and intervertebral joints were determined. MRI was performed in all patients (in 100% of cases) in sagittal, axial, and frontal planes in standard T1 and T2-weighted regimes using contrast agents.

As an additional diagnostic method angiographic examination was used. Vertebral and carotid angiography was performed, which allowed to spot dystopia and permeability of vertebral and carotid arteries in all segments. In some cases, we managed to identify the features of the tumor angioarchitecture, to find prognostically significant sources of blood supply or to confirm the absence of such in the pathological process.

The evaluation of neurological disorders before and after surgical intervention was performed using Frankel scale.

All cases were diagnosed with morphological methods. For light microscopy, after the tumor removal the tissue was immediately fixed in a 10% neutral formalin solution for no more than 24 hours and embedded in paraffin using a standard procedure. Histological sections of 5-10 μm were made on NM 430 sledge microtome (CarlZeiss Jena GmbH, Germany) and stained with observational and special techniques. The study of microslides was performed using Leica binocular microscope

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(Germany) with x10 eyepiece and x10-80 lens. Histoarchitecture, pattern and intensity of cell staining (nucleus, cytoplasm, membrane) were evaluated. Microphotorecording was carried out using Leica DM1000 digital camera.

Results and discussion

The expected response to surgical treatment in patients with MPNST depends on many factors: localization, directions of neoplasm extension, radical nature of the treatment and the histological variant of the tumor.

We paid special attention to the tumors of the spinal nerves showing signs of aggressive and invasive extension, which after the operation were verified as malignant peripheral nerve sheath tumor (MPNST).

The neurological status according to Frankel classification is presented in Table 1 before surgery and in Table 2 – after surgery.

Table 1 – Preoperative neurological status

Neurological deficit by Frankel classification in patients with tumors	A	B	C	D	E
Number of observations	2	5	25	16	5

The average size of the cervical spinal canal in the anterior-posterior direction in our observations varied as follows: at C1 level: 23 mm, C2 level: 20 mm, C3-C6 level: 17 mm, C7 level: 15 mm.

Localization data from all observations are provided in Table 3. In dependence to the direction of extension, the predominance of extravertebral or intracanal component, the topical ratio, and the degree of tumor involvement into the great vessels of the neck, we used different approaches that are presented in Table 3.

Table 2 – Postoperative neurological status

Neurological deficit by Frankel classification in patients with tumors	A	B	C	D	E
Number of observations	2	3	14	12	21

Taking into account the unique experience of the clinic, we consider necessary to emphasize the prognostic significance of a detailed pre-operative assessment of tumor-to-vertebral artery ratio. Spinal nerve tumors are formed and grow at different speed as was demonstrated by dynamic neuroimaging studies. MPNST grow rapidly, while benign tumors may develop slowly, sometimes existing for a long time before revealing some objective clinical signs. According to our data, the average growth rate = progression of neurinomas reached 2.4 mm per 1 year (range 1.8–3 mm) and was relatively stable. The growth rates of the neurofibromas ranged 1.8 mm to 37 mm per 1 year, making an average of 16 mm per year, and were unstable. During observation, the growth rates were variable (certain periodicity of active progression). The growth rate of MPNST was significantly faster and unstable; however, it was difficult to systematize.

MPNST with mesenchymal differentiation were diagnosed in 8 cases, with neuronal differentiation – in 3 cases, with epithelioid differentiation – in 2 cases. Evaluating the cases of prolonged tumors growth, signs of pathomorphosis were detected by complex clinical and morphological comparisons in 3 observations (at the time of addressing SE Institute of Neurosurgery, more than 3 operations were performed).

The majority of cases of MPNST have been diagnosed in patients aged 27 to 56 years. The time from the onset of neurological symptoms to the diagnosis ranges from several weeks to one year. The main complaint is an expressed pain syndrome in the dermatome along the root. Later segmental abnormality adds to the conduction abnormalities. Along with the tumor growth to a large or gigantic size, complete conduction impairment develops and, when the tumor is located in the upper cervical spine, respiratory disturbance appears.

When comparing between the groups of benign tumors of peripheral nerves and MPNST, the latter do not reach significant size; in our opinion, this is due to the growth rate and invasive extension of the tumor and worse compensatory ability of the spinal cord against its fast compression and destructive changes.

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Table 3 – Distribution of observations of cervical spinal nerve tumors by topographic characteristics

Tumor topographic variations	Optimal approach used for the indicated tumor localization	Lesion grade (number of observations)	Histologic variation of the tumor (number of observations)
Tumors originating from the ventral root (n = 1)	anteriolateral approach	C4 – C5 -1	neurinoma-1
Tumors originating from the dorsal root (n=2)	posterior approach, lateral approach	C1 – C2 -1 C3 – C4 -1	neurofibroma-1 neurinoma-1
Tumors originating from the ganglionic area of a peripheral nerve (n = 5)	posterior approach, posterolateral approach, far lateral approach	C2 – C3 -2 C4 – C5 -2 C5 – C6 -1	neurinoma-4 MPNST-1
Tumors originating from the postganglionic area of a peripheral nerve (n = 3)	posterolateral approach, far lateral approach	C1 – C2 -1 C5 – C6 -2	neurinoma-2 MPNST-1
Tumors originating from the ventral root of a peripheral nerve division (n = 3)	anteriolateral approach	C4 – C5 -1 C5 – C6 -2	neurofibroma-1 neurinoma-2
Tumors originating from the dorsal root of a peripheral nerve division (n = 4)	posterior approach, posterolateral approach, lateral approach	C3 – C4 -2 C7 – Тн1 -2	neurinoma-2 MPNST-2
Tumors originating from the anterior root with paravertebral extension (n = 3)	anteriolateral approach	C3 – C4 - 2 C4 – C5 -1	neurofibroma-1 neurinoma-1 MPNST-1
tumors of spinal nerves originating from the dorsal root with paravertebral extension (n = 3)	posterior approach, lateral approach	C6 – C7 - 2 C7 – Тн1 -1	neurofibroma-1 neurinoma-1 MPNST-1
Tumors originating from the ganglionic area of a peripheral nerve with predominant paravertebral extension (n = 8)	extreme lateral approach lateral approach, anteriolateral approach	C1 – C2-2 C2 – C3-1 C4 – C5-2 C5 – C6-1 C6 – Тн1-2	neurofibroma-1 neurinoma-4 MPNST-3
Tumors originating from the ganglionic area of a peripheral nerve with predominant intracanal extension (n = 2)	lateral approach, anteriolateral approach	C4 – C5 -1 C5 – C6 -1	neurofibroma-1 neurinoma-1
Tumors originating from the ganglionic area of a peripheral nerve with concurrent paravertebral and intracanal extension (n = 2)	lateral approach, anteriolateral approach	C3 – C4 -1 C4 – C5 -1	neurinoma-1 MPNST-1
Tumors originating from the postganglionic area of a nerve with predominant paravertebral extension (n = 5)	lateral approach, anteriolateral approach	C3 – C4 -1 C4 – C5 -1 C5 – C6 -1 C6 – C7 -2	neurofibroma-1 neurinoma-3 MPNST-1
Tumors originating from the postganglionic area of a peripheral nerve with paravertebral and intracanal growth (n = 4)	lateral approach, anteriolateral approach	C2-C3 -2 C3-C4 - 1 C5 – C6 -1	neurofibroma-1 neurinoma-2 MPNST-1
Tumors originating from a peripheral nerve with paravertebral and intracanal growth (n = 3)	lateral approach, anteriolateral approach	C3- C4 - 1 C5 – C6 -1 C6 – Тн1 -1	neurofibroma-1 neurinoma-1 MPNST-1

During the operation, we have identified visual criteria that are characteristic for MPNST, namely: characteristic impairment or absence of a fibrous capsule and signs of local invasive extension into surrounding tissues, excessive bleeding and areas of significant induration of tumor tissues. Taking into

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account the prevalence of the soft consistency of these tumors, they pass through the intervertebral foramen and reach significant sizes in extravertebral area, with signs of varying degrees of invasive severity.

Histologically, MPNST is a heterogeneous tumor in different zones and cell ratios, with polymorphic spindle-like cells, dense growth plates, hyperchromic cell nuclei, numerous mitoses, including pathological ones. Sometimes the distorted giant "monster cells" are visualized. Depending on the degree of aplasia, the number and prevalence of hemorrhages and necrosis foci are variable. The index of proliferation (Ki - 67) in MPNST tissue significantly fluctuated and ranged 7 to 44% in different observations, requiring a quantitative evaluation for Grade determination. The severity and density of stroma in different areas is different (numerous foci of myxomatosis and hyalinosis). Specific structural features of this tumor group include the features of the stromal component, which potentially affect the tissue differentiation of neuronal pool of tumor proliferating tissue (peculiarities of microenvironment). MPNST with the mesenchymal differentiation demonstrated the most malignant course. The peculiarities of the stromal-parenchymal relations in the tumor require the evaluation of three different sites of the tumor node and determination of proliferation index and its mean values. MPNST with neuronal differentiation should be differentiated from peripheral ganglioneuromas, neuroblastomas and a group of peripheral primitive neuroectodermal tumors.

Thus, MPNST is a complex pathology that requires clinico-morphological comparisons, a team approach invloving oncologists, and further in-depth study.

Regression of neurological deficit correlated with the histological variant of a tumor. MPNST presented with a faster and more expressed neurological symptoms and signs. The prognosis for further recovery is more favorable for benign forms.

Discussion. All tumors are subject to operative treatment from the surgical point of view. The main purpose of such operations is the total removal of the tumor. Surgical approaches vary significantly, depending on the peculiarities of localization in relation to the diameter of the spinal cord at certain levels of cervical spine [5].

Whereas surgical removal of tumors located on the dorsal or dorsolateral surface of the spinal cord is usually carried out using cervical midline approach and does not cause any special complexity, for the tumors that cause compression of the ventrolateral or ventral surface of the spinal cord surgical intervention becomes considerably more complicated and requires experience and special training.

At the preoperative stage it is necessary to substantiate the choice of surgical approaches, which should provide optimal visual control of tumor removal and the state of nervous structures, providing a personified treatment strategy.

Diagnosis of MPNST requires further consultations with the neuro-oncologist including planning of combined treatment (radiotherapy/chemotherapy). In 70% of cases, this group of tumors shows a rapid prolonged growth. In our paper we noted that the rate of tumor relapses depends on the size of the tumor, the presence and prevalence of tumor invasive growth, the correctness of the ongoing adjuvant therapy. With MPNST having significant size at the initial admission, re-operation was performed on average after six months. Combined treatment along with oncologists led to prolongation of the time from the first operation to re-operation for up to one year. Taking into account the above, further treatment strategy aimed at the local irradiation of the tumor burden after surgery must necessarily be carried out in a short time.

Conclusions

- Determination of the operation tactics and the choice of surgical approach is an important component for achieving long remission. The choice of an adequate approach makes it possible to remove the tumor totally and reduce the time of intervention, blood loss, injuries to the nervous structures during tumor removal.
- Corrected patient pathway and diagnostic measures over time allow to detail localization, prevalence, degree of compression of the spinal cord before operation and to optimize the stage of planning and extent of surgery.
- A factor that limits the possibility of MPNST eradication is its wide invasion with paravertebral extension and high rates of proliferative activity.
- Quality of life of patients and postoperative complications correlate not only with tumor size and radical nature of intervention, but also with histological variants of tumors.

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