

THREE-YEAR COMPARATIVE ANALYSIS OF THE PRESENCE OF MENINGIOMAS AND SECONDARY DEPOSITS IN THE BRAIN

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About 16% of the world's population is covered by registration systems that provide cancer incidence statistics, while mortality data are available for about 29%. The percentage of metastatic changes in the brain, as secondary deposits, is also increasing. Meningiomas are most often slow-growing, benign, primary intracranial tumors in adults, middle-aged (45 to 55 years). Early detection, favorable localization in the brain and well-performed surgery bring good results to the patient in terms of improved outcome.

A retrospective study included patients with metastatic changes in the brain and meningiomas treated at the Clinic of Neurosurgery and the Clinic of Oncology of the University Clinical Center Niš in the period from the beginning of 2018 to the end of 2020.

By comparing the ratio of the presence of meningioma, as benign tumors in the brain, in relation to the percentage of secondary deposits present, we come to the conclusion that malignancy is on the rise. Early diagnosis and suspicion of this dissemination in primary metastasis enable surgical intervention followed by oncological treatment, which together prolong the patient's life.

Comparing the patients with meningioma who underwent surgery in the period from 2018 to 2020 according to gender, age structure, tumor localization, no statistically significant difference was observed. Females are ahead of males in terms of meningioma.

There has been an evident increase in malignancy in recent years in both genders. In meningioma, the treatment is surgical. In case of solitary changes after surgery, oncological treatment is performed. In the case of multiple changes in the brain, the treatment is oncological, which includes the use of radio and chemotherapy.

Acta Medica Medianae 2022;61(2):14-20.

Key words: meningioma, multiple metastases, solitary metastasis, oncological treatment

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Introduction

The presence of malignant patients is evidently increasing in recent years. About 16% of the world's population is covered by registration systems that provide cancer incidence statistics, while mortality data are available for about 29%. The incidence and mortality from breast cancer vary significantly depending on the world region (1). The American Cancer Society, the Centers for Disease Control and

Prevention, the National Cancer Institute, and the North American Association of Central Cancer Registry work together each year to update cancer rates and trends in the United States. This report updates statistics on lung, breast, prostate and colorectal cancer and highlights the use of selected surveillance data to help develop national cancer control plans (2).

The percentage of metastatic changes in the brain, as secondary deposits, is also increasing. Single or multiple changes in the brain are an increasingly common subject of treatment in neurosurgical institutions. The number of brain metastases is far higher than primary brain tumors. The most common sources of brain metastases are lung cancer, breast cancer and melanoma. While lung cancer and breast cancer are much more common, melanoma has the highest risk of spreading to the CNS among all common types of cancer. (3). Management of patients with brain metastases has become more important recently due to the increased incidence of these tumors and the prolonged survival time of the patient that accompanies the increased control of systemic carcinoma (4).

Fast lifestyle, irregular and improper diet, problems at work, numerous obligations, leave less and less time for an individual to take care of himself and dedicate time to his health. Antioxidants are important ingredients present in fruits and vegetables (FAV). With increased consumption of FAV in its raw and processed form, a predominantly plant-based diet rich in FAV could reduce the risk of developing malignant human diseases (5). There is ample evidence that FAV consumption is important for human health because it is rich in health-enhancing nutrients (6, 7).

All the unwanted symptoms are attributed to fatigue, a little time spent sleeping, and when things get more serious and when one dedicates time to oneself, one comes to the realization that it is a serious illness. Gavurova et al. state that environmental health is among the priority areas of public health and the current professional community is intensively dealing with it (8). Appeals for preventive examinations bear fruit and make one sets aside time for oneself and dedicates oneself to taking care of one's health. Asymptomatic metastases are increasingly being diagnosed through increased screening due to known risk factors, as well as mandatory imaging required during screening for many clinical trials of melanoma (9, 10). Symptoms caused by increased intracranial pressure, mass effect, impaired drainage of cerebrospinal fluid lead to focal deficit, weakness, numbness, imbalance, vision loss, behavioral changes, and often epileptic seizures (11). When the examinations start, it is understood that it is a serious health disorder. Sometimes frequent headaches, nervous insomnia lead the doctor to suspect that it is a change in the brain, so MSCT of the brain is indicated. In contrast to malignant diseases, the distribution of benign tumors, meningioma has been homeogenic for many years. Meningioma is characterized by slow growth, nonspecific symptoms related to the region in which they occur. Meningiomas are most often slow-growing, benign, primary intracranial tumors in adults, middle-aged, 45 to 55 years (12, 13). Early detection, favorable localization in the brain, and well-performed surgery bring good results per patient in terms of cure. Meningiomas are rare intra-

cranial tumors in childhood and adolescence and account for 0.4-4.1% of all tumors in children (14). Data from the literature indicate that the highest incidence of meningioma is from the age of 45 to 55, and that it increases until the age of seventy (15). If the MSCT of the brain shows the presence of multiple mentions, the presence of secondary deposits is suspected. The incidence of multiple meningiomas ranges from 1-2% to 8% (16).

Brain MRI is a diagnostic procedure that determines the further course of treatment. Based on it, a further plan of neurosurgical treatment is performed, which is supplemented by the use of radiotherapy for multiple metastases.

Methods

A retrospective study was performed at the Clinic of Neurosurgery of the UCC Niš and the Clinic of Oncology of the UCC Niš in the period from the beginning of 2018 to the end of 2020. The following groups were monitored: a group of patients with malignant diseases and secondary metastases, and a group with a benign brain tumor, meningioma in the mentioned period.

Results

In the examined group, in the three-year period, there were 86 patients who underwent meningioma, among which there were 32 (37.2%) men and 54 (62.8%) women. There was no significant difference in age structure by sex ($p = 0.572$).

There was no significant difference in the distribution of patients who underwent meningioma surgery by sex according to the examined years ($p = 0.667$), or by age structure ($p = 0.448$). In relation to the distribution of meningioma localization, there was no statistically significant difference in the three examined years ($p = 0.882$). The number of deceased patients by age was uniform without significant difference ($p = 0.503$) (Table 1).

It was found that a significantly higher number of deceased patients had basal localization of meningioma ($p = 0.021$) (Table 2).

Table 1. Data by years of testing

		2018.	2019.	2020.	p
Gender	<i>m</i>	13 (43.3)	12 (35.3)	7 (31.8)	0.667
	<i>f</i>	17 (56.7)	22 (64.7)	15 (68.2)	
Age		66.07 ± 11.86	63.76 ± 8.27	67.00 ± 9.48	0.448
Region of brain	<i>Temporally</i>	10 (33.3)	6 (17.6)	5 (22.7)	0.882
	<i>Parietal</i>	9 (30.0)	13 (38.2)	8 (36.4)	
	<i>Basal</i>	3 (10.0)	3 (8.8)	2 (9.1)	
	<i>Frontally</i>	8 (26.7)	12 (35.3)	7 (31.8)	
Death		1 (3.3)	2 (5.9)	0 (0.0)	0.503

Table 2. Distribution of meningioma by localization and lethal outcome

Region of brain	Death		p*
	No	Yes	
<i>Temporally</i>	21 (25.3)	0 (0.0)	0.021
<i>Parietal</i>	29 (34.9)	1 (33.3)	
<i>Basal</i>	6 (7.2)	2 (66.7)	
<i>Frontally</i>	27 (32.5)	0 (0.0)	

* Fisher's test

In the three-year period (2018-2020), there were 319 patients in the examined population, including 111 (34.8%) patients with individual metastases, 122 (38.2%) patients with multiple metastases and 86 (27.0%) patients with meningiomas.

A significant difference in the distribution of tumor changes in the three-year period was found ($\chi^2 = 11,768$; $p = 0.019$). Metastases were more prevalent in 2020, while in 2018 multiple metastases were the most prevalent. The distribution of meningioma is homogeneous over a three-year

period (Table 3).

A significant difference in gender distribution was found among the examined groups ($\chi^2 = 13.487$; $p = 0.001$). Single metastases were more common in men, while meningiomas were more common in women. Multiple metastases were equally present in both genders. There was no significant difference in age distribution ($p = 0.513$).

Mortality is highest in multiple metastases ($\chi^2 = 47,485$; $p < 0.001$) (Table 4).

Table 3. Distribution of primary cancers and metastases by age

	2018.	2019.	2020.	p
Solitary metastases	35 (37.8)	40 (35.1)	36 (45.6)	0.019
Multiple metastases	61 (48.4)	40 (35.1)	21 (26.6)	
Meningioma	30 (23.8)	34 (29.8)	22 (27.8)	

Table 4. Gender and age distribution by groups

		Solitary metastases	Multiple metastases	Meningioma	p
Gender	<i>m</i>	70 (63.1)	68 (55.7)	32 (37.2)	0.001
	<i>f</i>	41 (36.9)	54 (44.3)	54 (62.8)	
Age		64.24 ± 10.41	63.63 ± 11.84	65.39 ± 9.93	0.513
Death		9 (8.1)	44 (36.1)	3 (3.5)	< 0.001

Discussion

The existence of malignancies in the world, as well as in our country, has been a current topic in recent years. Each year, the American Cancer Society estimates the number of new cancers and deaths expected in the United States in the current year and compiles the latest data on cancer incidence, mortality and survival based on incidence data from the National Cancer Institute, Centers for Control and Prevention (17). The fact is that the rate of benign changes in the brain, in stagnation, is homogeneous. By comparing the ratio of the pres-

ence of meningitis, as benign tumors in the brain, in relation to the percentage of secondary deposits present, we come to the conclusion that malignancy is on the rise.

Comparing the operated patients with meningioma, in the period from 2018 to 2020, according to gender, age structure, tumor localization, no statistically significant difference was observed in the examined three-year period. Following other literature, it has been noticed that females are ahead of males in terms of meningioma. Meningiomas are twice as common in women as in men (18). The annual incidence of meningioma is 2 to 7 per

100,000 women and 1 to 5 per 100,000 men (M: F = 1.8: 2.1) (19). Maja G. Et al. indicate that 85.4% of subjects had meningiomas localized in the anterior cranial fossa, while 14.6% of subjects had meningiomas in the posterior cranial fossa (20). A higher presence of meningiomas in the anterior cranial fossa was noted and in the study of Milenković and associates (21). According to data from the literature, most meningiomas are located on the convexity (35%), most often parasagittal, along the upper sagittal sinus (20%) (22). Regarding the localization of the meningioma in our series, the most common presentation of the tumor was in the parietal lobe (Table 2). The results of Bassiouni et al. show that meningiomas of the frontal (42%), temporal (54.5%) and parietal localization (70%) are more often found on the left side. The frequency of meningiomas on the right and left sides of the occipital region and cerebellum is equal (50%). Of the total number of subjects, 4.38% have meningiomas localized in sella turcica (23).

The number of deceased patients in regard to age was uniform (Table 1). Monitoring and comparing meningiomas according to localization showed that a significantly higher number of deceased patients had a basal presentation of the tumor (Table 2). This is explained by the fact that in this localization of the tumor, the operative approach itself is much more complicated, with a major disruption of important brain structures. Surgical treatment of skull-based meningiomas has changed radically in the last two decades. Extensive surgery for patients with basal meningioma is the main treatment; however, this is often challenging due to narrow surgical corridors and the proximity of critical neurovascular structures.

New surgical technologies, including three-dimensional (3D) preoperative imaging, neuromonitoring, and surgical instruments, have gradually facilitated the surgical resectability of these meningiomas, reducing postoperative morbidity (24). Also, basal meningiomas often develop local recurrences after surgical resection. Complete removal is difficult because these deep-rooted tumors involve critical neurovascular structures. Therefore, the treatment strategy for recurrent basal meningiomas remains controversial (25). With recent advances in surgical technology such as preoperative imaging, neuromonitoring, and surgical instruments, surgical resectability of intracranial meningiomas has increased in the last two decades (26).

Regarding secondary deposits, a significant difference was found by years in terms of the presence of one or more metastases. Namely, in 2020, there was a higher number of detected mono metastases than in 2018, when a higher number of multiple changes in the brain was recorded (Table 3). About 80% of brain metastases are supratentorial, while 15% are infratentorial or leptomeningeal, and 5% affect the brainstem itself. CT scans of the brain with and without contrast can detect most metastases ≥ 10 mm in the supratentorial region and most hemorrhagic lesions (27). However, magnetic resonance imaging (MRI) with and without gadolinium is far more sensitive, especially for

smaller lesions, posterior fossa lesions, and leptomeningeal disease (28).

The lungs, breasts, and skin (melanoma) are the most common sources of brain metastases, and up to 15% of patients' primary sites remain unknown (29). Early diagnosis and suspicion of this dissemination in primary metastasis enable surgical intervention followed by oncological treatment, which together prolong the patient's life. The average survival time with brain metastases is usually less than a year, but when only isolated metastases (oligometastases) are found and can be treated, over 60 percent of people can survive two years or longer (30). Commonly prescribed treatments for brain metastases are surgery and/or radiation therapy. Optimal management of brain metastases remains controversial. Both whole-brain radiotherapy (WBRT) and local treatment or surgery (S) or radiosurgery (RS) are the cornerstones of treatment. Combination therapy can improve both overall survival and local control in patients with a single metastasis, but also leads to the benefit of local control in patients with two to four lesions (31).

Comparing the sex distribution, it was noticed that individual metastases are more present in males, while meningiomas are more common in females. Matthew et al. note that meningiomas are twice as common in women as in men (18). Kleihues et al. state that the annual incidence of meningioma is 2 to 7 per 100,000 women and 1 to 5 per 100,000 men. (19).

Multiple metastases are equally present in both sexes. There was no significant difference in age structure, while mortality was highest in multiple metastases (Table 4). Risk factors associated with melanoma metastases to the brain include male, mucosal or primary head and neck tumors, thick or ulcerated neoplasms, acral lentiginous or nodal lesions, and stage IV disease.

Current treatment strategies are unsatisfactory and brain metastases contribute to death in almost 95% of patients, with a median survival of less than 1 year despite treatment (32).

Certainly, improvements in imaging technologies during this period have led to increased detection of metastatic lesions; powerful neuroimaging modalities have become widely available and used to detect brain metastases, especially MRI, which is currently used to assess approximately 64% of cancer patients compared to 2% 20 years ago (33).

Conclusion

Females predominate in the percentage of meningioma in relation to males.

There has been an evident increase in malignancy in recent years in both genders.

MRI enables much better and more accurate diagnosis of the presence of secondary deposits in the brain.

In meningioma, the treatment is surgical.

In case of solitary changes after surgery, oncological treatment is performed.

In case of multiple changes in the brain, the treatment is oncological, which includes the use of radio and chemotherapy.

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Originalni rad

UDC: 616.831:616-006
doi:10.5633/amm.2022.0202

TROGODIŠNJA UPOREDNA ANALIZA PRISUSTVA MENINGIOMA I SEKUNDARNIH DEPOZITA NA MOZGU

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Oko 16% svetske populacije pokriveno je sistemima registracije, koji pružaju statistiku incidencije raka, dok su podaci o smrtnosti dostupni za oko 29% populacije. Povećava se i procenat metastatskih promena u mozgu, kao sekundarnih naslaga. Meningiomi su najčešće spororastući, benigni, primarni intrakranijalni tumori kod odraslih, srednjih godina, od 45 do 55 godina. Rano otkrivanje, povoljna lokalizacija mozga i dobro izvedena operacija donose dobre rezultate po bolesnika, u smislu izlječenja.

Retrospektivnom studijom, u periodu od početka 2018. do kraja 2020. godine, obuhvaćeni su bolesnici lečeni na Klinici za neurohirurgiju i Klinici za onkologiju Univerzitetskog kliničkog centra Niš, sa metastatskim promenama na mozgu i meningiomima.

Upoređivanjem odnosa prisustva meningitisa, kao benignih tumora u mozgu, u odnosu na procenat prisutnih sekundarnih naslaga, dolazi se do zaključka da je malignitet u porastu. Rana dijagnoza i sumnja na ovu diseminaciju u primarnim metastazama omogućavaju hiruršku intervenciju praćenu onkološkim lečenjem, što, zajedno, produžava život bolesnika.

Poređenjem operisanih bolesnika sa meningiomom, u periodu od 2018. do 2020. godine, prema polu, starosnoj strukturi i lokalizaciji tumora, nije uočena statistički značajna razlika u ispitivanom trogodišnjem periodu. Žene su ispred muškaraca, u pogledu meningioma.

Poslednjih godina, evidentan je porast maligniteta kod oba pola. Meningiom se leči hirurški. U slučaju solitarnih promena posle operacije, radi se onkološko lečenje. U slučaju višestrukih promena na mozgu, lečenje je onkološko, što podrazumeva primenu radioterapije i hemoterapije.

Acta Medica Medianae 2022;61(2):14-20.

Ključne reči: meningiom, multiple metastaze, solitarne metastaze, onkološki tretman