Meningiomas of the skull base - a case series of microsurgically treated patients and our experience with recent European guidelines

Meningeomi baze lobanje - serija mikrohirurški tretiranih slučajeva i naša iskustva sa aktuelnim Evropskim vodičima

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ABSTRACT

Skull base meningiomas (SBM) represent 30% of all meningiomas, where majority of them are benign tumors. The World Health Organization (WHO) classified meningiomas in 3 grades: I-benign, II-atypical, III-malignant meningioma. Surgery of SBM is one of the biggest neurosurgical challenges due to deep location on the basis of skull and proximity of many intracranial anatomical structures. However, the total surgical resection is still the therapy of choice for SBM. In cases where the risk of total resection is beyond benefit, a partial resection is also an option. The remains after the partial meningioma resection or even recurrence can be treated with radiotherapy or radiosurgery. Such approach has been common practice for many years although new recommendations have introduced a little bit different approach. The meningiomas should be followed for a long term period given that they have a remarkable recurrence rate. This article presents a few illustrative cases of SBM at different locations, treated at our department in the recent years. Contemporary protocols for the treatment and follow up are also presented.

Key words: meningioma, skull base, Simpson Grade System, EANO guidelines

SAŽETAK

Meningeomi baze lobanje predstavljaju 30% svih meningeoma, a većina su beningni tumori. Svjetska zdravstvena organizacija je klasificirala meningeome u tri gradusa: I-benigni, II-atipični, III-maligni meningeom. Operacije meningeoma baze lobanje predstavljaju jedan od najvećih neurohirurških izazova, jer se nalaze duboko na bazi lobanje u blizini važnih intrakranijalnih anatomskih struktura. I pored kompleksnosti operativnog pristupa, totalna hirurška resekcija tumora predstavalja prvi terapijski izbor za meningeome. U slučajevima gdje je ukupni benefit od totalne resekcije menigeoma manji od operativnog rizika, tumor se parcijalno odstranjuje. Kod parcijalne resekcije meningeoma preostali dio može se tretirati radioterapijom ili radiohirurgijom. Ovakav pristup je uobičajena praksa, iako nove preporuke donose nešto drugačiju strategiju. Praćenje meningioma mora biti dugo, jer ovi tumori pokazuju veliku skolonost ka recividiranju. U ovom članku selektirali smo nekoliko ilustrativnih slučajeva mikrohirurški tretiranih meningeoma baze lobanje na različitim lokacijama, koji su operirani na našoj klinici unazad nekoliko godina. Također su prikazani savremeni protokoli za tretman i praćenje pacijenata sa meningeomima.

Ključne riječi: meningeomi, baza lobanje, Simpson gradusni sistem, EANO preporuke

INTRODUCTION

Neurosurgical treatment of skull base meningioma (SBM) is one of the most complex surgical interventions in neurosurgery. The incidence rate of meningioma in the United States is 1.8 for men and 4.2 for women per 100.000 population. From all brain tumors meningioma is the most common primary intracranial brain tumor and it represent 20% to 30 % of all brain tumors, with 30% of them located on the skull base (1-3). In a study of 276 patients treated for skull meningiomas the localization was as follows: sphenoid ridge (16%), convexity (14%), cerebellopontine angle (13%), parasellar (12%), parasagittal (11%), posterior fossa (8%), olfactory groove (8%), falx (7%), foramen magnum (3%), orbit (3%) and other (6%) (3,4).

Clinical features of meningioma include three big clinical signs: raised intracranial pressure, focal neurosurgical signs and epilepsy. In 2016 the World Health Organization (WHO) published a new classification of central nervous system tumors where meningeoma were classified in three grades: benign (grade I), atypical (grade II) and malignant meningioma (grade III) (5). For the majority of tumors gross total resection (GTR), known as Simpson grade I resection is the therapy of choice (6-9). Simpson grade I resection is a macroscopically complete removal of tumor, with excision of its dural attachment, and of any abnormal bone and includes resection of venous sinus if involved. Simpson Grading System is shown in Table I (10).

Table I **Simpson Grading System for removal of meningiomas.**

Grade	Description
I	Macroscopically complete removal of tumor, with excision of its dural attachment, and of any abnormal bone. Includes resection of venous sinus if involved.
II	Macroscopically complete removal of tumor and its visible extensions with coagulation of its dural attachment.
III	Macroscopically complete removal of the intradural tumor, without resection or coagulation of its dural attachment or its extradural extensions.
IV	Partial removal, leaving intradural tumor in situ.
V	Simple decompression, with or without biopsy.

However the resection of SBM can be very difficult and challenging. The deep location and proximity of the skull base delicate structures specially blood vessels and cranial nerves involvement are factors which making these tumors a challenge to a neurosurgeon (11). Such features of SBM imply that in some cases the neurosurgeon cannot remove the complete meningioma, which leads to a higher resection grade (11-16). In such cases or in cases of recurrent tumor patients undergo radiotherapy or radiosurgery, depending of the grades of meningioma based on WHO classification, and on its location (17). Long term recurrence of the meningioma, especially of those partialy resected, is a big concern and need monitoring for up to 20 years (18).

This article presents a few typical SBM surgery cases, based on the corresponding author's personal series (7), and gives a brief review of European Association of Neuro-Oncology (EANO) guidelines protocol for treatment of meningiomas.

CASE 1

A 57-years-old female patient with a headache history, gait disturbance, left eye amblyopia and pituitary dysfunction was admitted to our department. She did not have any other neurological signs. A MRI showed a tumor mass located on sphenoid wing and optic sheath (Figure 1). The radiological features of the tumor indicated meningioma. A surgical resection of the tumor was performed (Simpson grade III), and meningeoma was confirmed pathologically. After the surgery the patient's symptoms improved. As shown on the 3 year follow up contrast MRI, there is a small part of residual tumor very close to the important neurovascular structures on the anterior cranial fossa and pituitary (Figure 2). No additional therapy except initial surgery has been needed so far. The patient is pretty good and tumor is followed up.

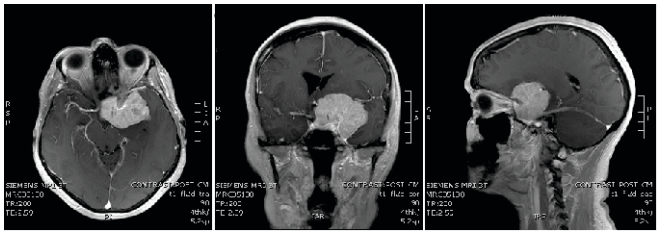

Figure 1 **Preoperative T1 MRI scan with contrast revealed meningioma on the optic sheath and sphenoid wing. *Left*: Axial T1-weighted scan. *Middle*: Coronal T1-weighted scan. *Right*: Sagittal T1-weighted scan. It is obvious that the both internal carotid artery and middle cerebral artery with its branches are involved in the tumor which makes it very difficult and even dangerous for complete resection.**

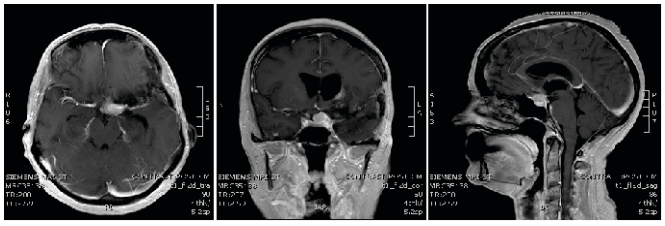

Figure 2 **Postoperative contrast MRI scan after 3-year follow up show a small rest of the tumor but there is no evidence of grow up compared to the previous follow up scans. Also this rest does not produce any obvious symptoms, so the "wait and see" strategy was chosen. *Left*: Axial T1-weighted scan. *Middle*: Coronal T1-weighted scan. Right: Sagittal T1-weighted scan.**

CASE 2

A 36-years-old female patient with partial paresis of the III, IV and VI cranial nerve (after the first surgery) and right eye mydriasis was admitted to our department. She had a meningioma surgery 6 years ago at other institution, with a gross total resection. A part of the tumor was left in the right cavernous sinus (CC), and followed up. After 6 years her condition deteriorated in hearing and gait disturbance. MRI showed a recurred tumor mass located in the right pontocerebellar angle (PCA) (Figure 3). The radiological features of the tumor indicated that it was meningioma, which was macroscopically and pathologically confirmed. A micro surgical total resection of the tumor in the PCA was performed (Simpson grade II resection). At the 6-month postoperative outpatient clinical follow-up, the patient's symptoms improved. MRI was performed 2-year postoperatively, showing no recurrence of the meningeoma in PCA (Figure 4), but with minimal growth of the CC part. Patient underwent a Gamma Knife surgery of the cavernous sinus meningioma.

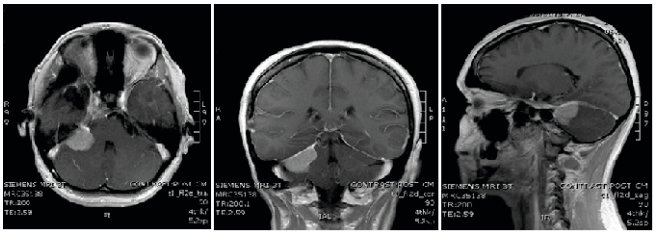

Figure 3 **Preoperative contrast MRI scan revealed meningioma in the posterior cranial fossa - PCA. *Left*: Axial T1-weighted scan**

with contrast. *Middle*: Coronal T1-weighted scan. Right: Sagittal T1-weighted scan.

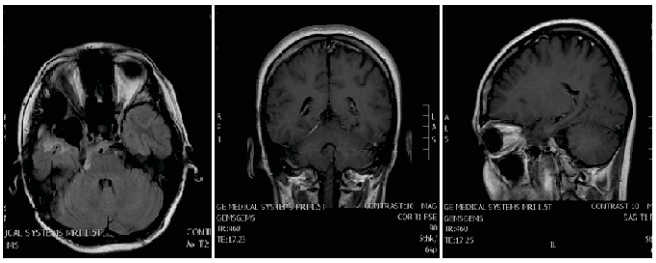

Figure 4 Postoperative 6-months follow up contrast enhanced MRI scans. *Left*: Axial T2 FLAIR- scan. *Middle*: Coronal T1-weighted scan. Right: Sagittal T1-weighted scan. No signs of recurrence in the middle fossa and CPA, but with small rest in CC.

CASE 3

A 62-years-old female patient with history of anosmia, gait disturbance, cognitive changes, visual deterioration, especially of the left eye, and pituitary dysfunction was admitted to our department. A MRI showed a tumor mass located suprasellar (Figure 5). Complete (Simpson grade I) resection was performed, and the pathology confirmed meningioma. After the surgery the patient's symptoms improved. After 15 months follow up MRI showed no recurrence of the meningioma. The patient is completely asymptomatic with no neurological deficit.

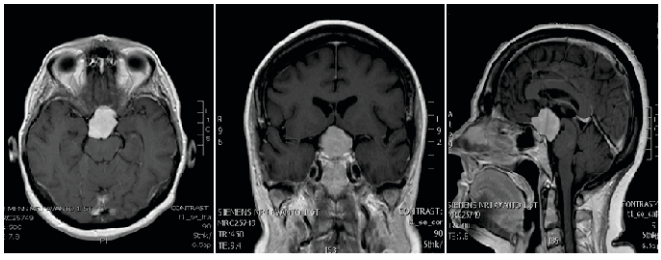

Figure 5 Preoperative contrast MRI scan revealed suprasellar (diaphragma sellae) meningioma. *Left*: Axial T1-weighted scan. *Middle*: Coronal T1-weighted scan. Right: Sagittal T1-weighted scan.

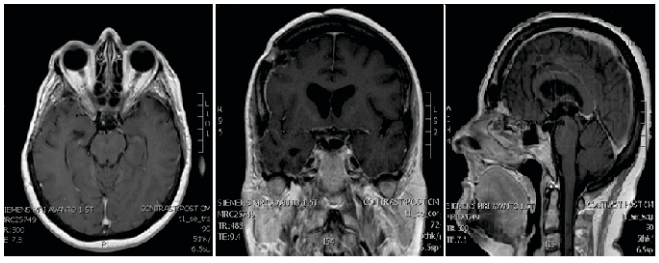

Figure 6 Postoperative 5-year follow up contrast enhanced MRI scan show no recurrence. *Left*: Axial T1-weighted scan. *Middle*: Coronal T1-weighted scan. Right: Sagittal T1-weighted scan.

CASE 4

A 60-years-old male patient with a history of dysphasia, gait, cognitive changes and left sided hemiparesis was admitted to our department. A MRI showed a tumor mass located on the sphenoid wing, with radiological features of meningioma (Figure 7). A total surgical resection (Simpson grade I) was performed, which was pathologically confirmed as meningioma. After the surgery the patient's symptoms improved. After 2 years of follow up MRI was performed (Figure 8). As shown on the MRI there was no recurrence of the meningioma. The patient has neurologically improved.

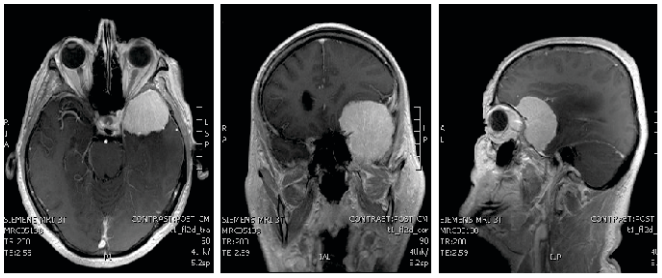

Figure 7 Preoperative contrast MRI scan revealed large meningioma on the sphenoid wing on the left side. *Left*: Axial T1-weighted scan. *Middle*: Coronal T1-weighted scan. Right: Sagittal T1-weighted scan with contrast.

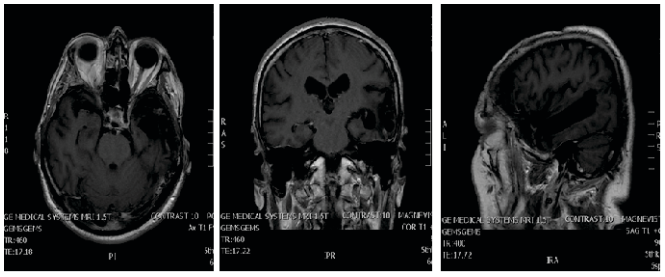

Figure 8 Postoperative contrast MRI scan after 2 years of follow up. There is no recurrence of the tumor. *Left*: Axial T1-weighted scan. *Middle*: Coronal T1-weighted scan. Right: Sagittal T1-weighted scan.

CASE 5

A 59-years-old female patient with a history of hearing problems, gait disturbance, facial nerve symptoms, and mild right hemiparesis was scheduled for surgery after the contrast enhanced brain MRI revealed large petroclival meningioma of the left side (Figure 9). Complete surgical resection (Simpson grade I) was achieved after extended left retrosigmoid approach was performed. Postoperative MRI showed that the tumor was completely removed (Figure 10).

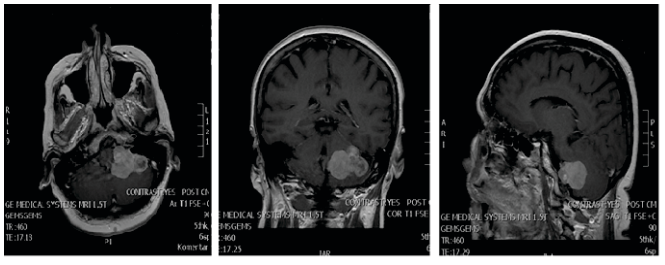

Figure 9 Preoperative contrast MRI scan revealed left petroclival meningioma. *Left*: Axial T1-weighted scan. *Middle*: Coronal T1-weighted scan. Right: Sagittal T1-weighted scan.

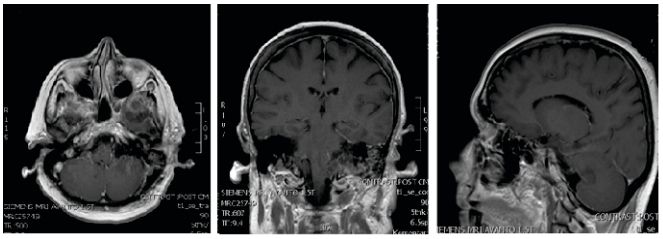

Figure 10 **Postoperative contrast MRI scan. Extended left retrosigmoid approach was used. There is no evidence of tumor residual. *Left*: Axial T1-weighted scan. *Middle*: Coronal T1-weighted scan. Right: Sagittal T1-weighted scan.**

CASE 6

A 48-years-old female patient with a history of gait disturbance and headache was scheduled for surgery after the contrast enhanced brain MRI revealed foramen magnum meningioma (Figure 11). The MRI showed that the tumor involved vertebral arteries and was compressing the brainstem. Complete surgical resection (Simpson grade I resection) was achieved. Postoperative MRI showed that the tumor was completely removed with a subacute epidural hematoma on the side where it was resected (Figure 12). Postoperatively, conservative treatment by Colistin was performed due to meningitis (Acinetobacter).

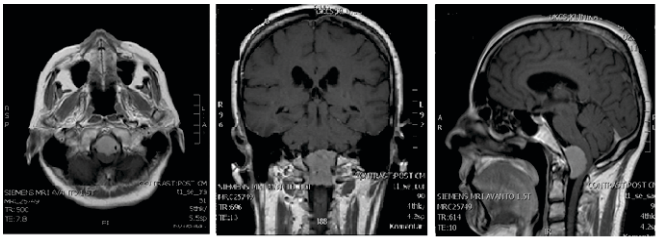

Figure 11 **Preoperative contrast MRI scan revealed foramen magnum meningioma. *Left*: Axial T1-weighted scan. *Middle*: Coronal T1-weighted scan. Right: Sagittal T1-weighted scan**

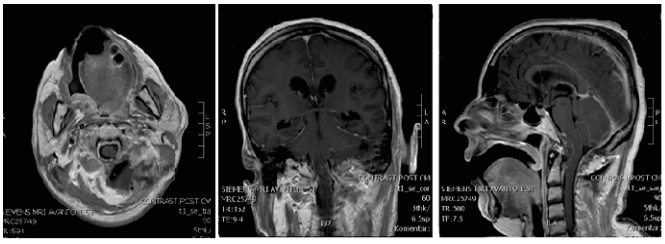

Figure 12 **Postoperative contrast MRI scan. There is no evidence of rest tumor. Subacute epidural hematoma is seen on the ventral side of brain stem, where the tumor was resected. *Left*: Axial T1-weighted scan. *Middle*: Coronal T1-weighted scan. Right: Sagittal T1-weighted scan.**

DISCUSSION

Most meningiomas are benign tumors WHO grade I, which can and should be successfully treated with surgery alone. Minorities of meningiomas are WHO grade II or III, which besides surgery also require radiotherapy, radiosurgery, chemotherapy or some other pharmacotherapy (10-13,19). In 2016 the European Association of Neuro-Oncology published guidelines for diagnosing and treatment of meningiomas (6). Prior to the guidelines the treatment of meningioma mostly depended on neurosurgeon's decision. These guidelines are standardizing management of meningioma across the world, with clear protocol showed in Figure 13 (6).

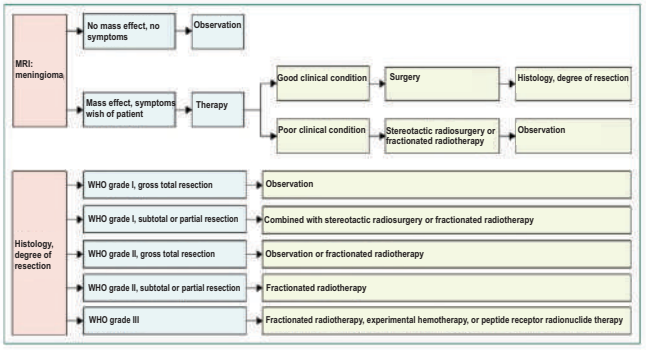

Figure 13 **Recommendations for the therapeutic management of meningiomas of WHO grades I–III concerning EANO guidelines.**

Five presented cases involved the first surgery of the meningioma, and one case is related to the second surgery for recurrent meningioma. We have shown different locations of SBM and different grades of SBM resection. Five patients were treated before EANO guidelines, and only the sixth patient was treated following the EANO guidelines publication. In Case 1 Simpson Grade III resection was performed due to neurovascular structures involved in the meningioma mass, internal carotid and middle cerebral artery. The rest tumor was monitored and it did not show any symptoms nor did it increase in size. Due to the rest tumor features we decided to monitor it on annual basis, with no additional therapy. This strategy was not in accordance with the EANO guidelines for WHO grade I meningioma where the rest tumor should be treated with radiosurgery or fractionated radio therapy (6). If the rest tumor started to show any symptoms or increases in size we would treat it with radio therapy or radio-surgery. In our Institution we used Linac SRS. In Case 2 we presented a patient with recurrent meningioma 6 years after the surgery. The recurrence of meningioma is one of the biggest concerns in the postoperative follow up, as shown in this particular case. After Simpson Grade II resection the patient underwent Gamma knife surgery for the little tumor rest in the CC. The risk of injuring neurovascular structures of cavernous sinus was much higher than the benefit of a total surgical resection. This was in line with the EANO protocol for subtotal resection of meningioma (6). In all other cases we presented GTR and Simpson I resection of differently located SBM.

Meningiomas have a slow growth pattern and are minimal or almost never involve brain parenchyma (18). The total surgical resection of the tumor for majority meningioma is the best therapy choice, especially for those with WHO grade I (4,16). But in the case of SBM the surgical approach and the resection of the meningioma can be very difficult due to deep location and anatomic structures nearby. In these cases a combined surgical and radio therapy approach can give better results than the surgery alone (15,16). With this approach the risk of total surgical resection can be minimized. After complete excision of benign meningiomas, the 5-year control rate is 72 to 100%. The 5-year control rate after subtotal surgical resection is 31 to 70%. With the addition of postoperative radiotherapy/radiosurgery, the control rate at 5 years has been reported to be 80 to 98% (20-23). Radiological diagnosis of

meningioma should be made by MRI. When MRI shows a clear radiological image of meningioma the pathological confirmation is even not mandatory (20). Preoperative embolization of the meningioma is not recommended, only in selected cases such as petroclival meningioma (7,15,20). In comparison to non-skull meningioma, skull meningioma requires surgical intervention at younger ages, and they have a lower MIB-1 index and majority of them are WHO grade I. Recurrence of skull meningioma has more than 100 months non-recurrence time than non-skull meningioma. These findings can have implications on surgical decision, long term follow up, and can predict the possibility of the need for the second intervention (18). Regarding the EANO recommendations of the WHO grade I meningioma should be followed up annually, and then every 2 and 5 years respectively, for WHO grade II the follow up is required every 6 months, and then annually after 5 years, and for WHO grade III the follow up is required every 3-6 months (7,13,20).

Nowadays good results in the SBM surgery can be linked not only with the well skilled and meticulously trained neurosurgeons but maybe even more to a few other points (24-29). They are primarily:

- well collected, published and wide accessible knowledge about SBM
- routine availability of highly sophisticated preoperative imaging
- clear understanding of skull base neuroanatomy
- routine but critically use of complex skull base approaches and avoidance of complications connected with those approaches
- better understanding of natural history and biology of those tumors especially with remnant application of intraoperative neuromonitoring
- availability of adjuvant and alternative modalities of treatment (30-33).

CONCLUSION

Total surgical resection is recommended and for the majority of meningioma the first option therapy. Each patient with meningioma needs a long term follows up. Radio therapy and radio surgery should be taken into consideration in patients with partially resected and small recurrent meningioma. Through a group of patients with postoperative results we have shown that at our institution, Clinical Center University of Sarajevo, the most complex pathology is successfully treated according to cotemporary guidelines and up to date knowledge, but also according to the *state of the art* surgical technique and world standards comparable postoperative results.

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