

# PROPER THERAPEUTIC ATTITUDE IN CASE OF A GIANT MENINGIOMA ASSOCIATED TO MALIGNANT NON-HODGKIN'S LYMPHOMA (MNHL)

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**Keywords:**  
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**Abstract:** Meningiomas are a type of tumours that originate from the meninges, the membrane layers that contain the central nervous system (CNS). They represent the most frequent type of cerebral tumour, approximately 30%. Their starting point is the "cap" cells of the arachnoid granulations. This type of tumour is usually benign; although, a small percentage becomes malignant. Most of them are asymptomatic over the course of an individual's life and do not require other treatment than close observation.

**Cuvinte cheie:**  
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benign, asimptomatic

**Rezumat:** Meningioamele sunt un tip de tumori ce derivă din meninge, straturile membranoase ce înconjoară sistemul nervos central (SNC). Reprezintă cel mai frecvent tip de tumoră cerebrală (cca 30%). Au ca punct de plecare celulele "cap" cells ale granulațiilor arahnoidiei. Acest tip de tumori este de regulă benign; totuși un mic procent se malignizează. Majoritatea sunt asimptomatice pe parcursul întregii vieți a unui individ și nu necesită alt tratament decât monitorizarea periodică.

## INTRODUCTION

Meningioma is a benign tumour originating from the arachnoid, 90% are intracranial but there is the possibility of an intrarahidian development. It constitutes approximately 15% of all intracranial tumours and presents the most increased incidence in the seventh decade of age, being more common in women. Meningiomas may precede the installation of the neurological symptoms by 10-15 years of evolution, which shows their slow growth rate, sometimes reaching large sizes; they are discovered incidentally on plain skull radiographs or on cranial CT. Laboratory diagnosis is made by cranial CT or MRI, where they appear as a pathognomonic, round, well defined area, which may contain calcifications, compressing the adjacent brain parenchyma. They are directly related to the meninges or cranial vessels and on the administration of the contrast, they capture strongly and uniformly the "dural tail" sign, which is characteristic of these tumours.

## CASE REPORT

Patient, aged 58 years old, was brought to the emergency service with marked confusional syndrome and total motor deficit of the right limb, with unspecified onset.

The general examination revealed pathological elements (leukocytosis  $61,590/\text{mm}^3$  with lymphocytosis 55.9%) and the neurologic examination showed only the items already listed: considerable confusion, impossible gait and orthostatism, impossibility to perform the tests of coordination with the right limbs, much diminished osteotendinous reflexes in the right limbs, no sensitivity threshold, temporal-spatial, allo- and autopsychic oriented, self conscious, cooperative.

As a result of this situation and due to the absence of the risk factors for cerebrovascular events, a native CT scan was performed that revealed a tumour mass in the left fronto-parital side of 40/50 mm, with marked mass effect, midline shift and compression of the right lateral ventricle, accompanied by

edema adjacent to the tumour mass.

On 20.03.2013, a CT scan was performed with contrast agent, confirming the previously found (left frontoparietal mass, isodense, idophilic, with mass effect and midline deviation).

Figure no. 1. Left frontoparietal brain tumour. Sagittal sections

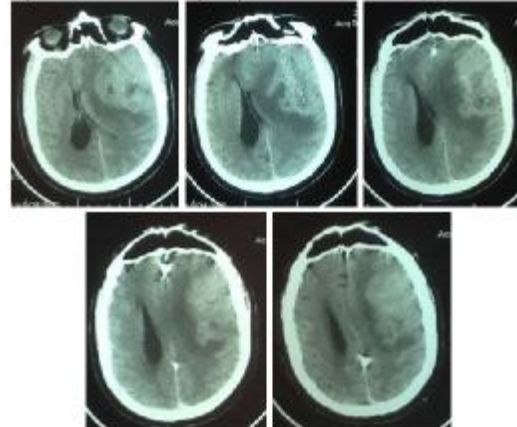
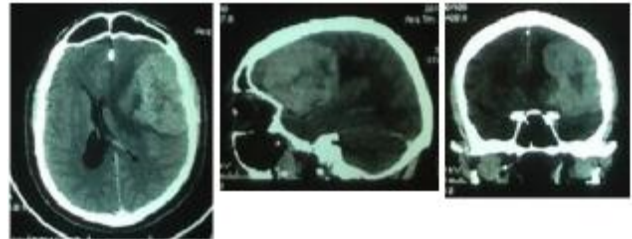


Figure no. 2. Left frontoparietal brain tumour. Sagittal, coronal sections



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## CLINICAL ASPECTS

As a result of this diagnosis and taking into account the patient's condition, surgery was decided. An arched scalp incision was practiced for the left fronto-parietal craniotomy. Scalping was performed and the flap bone was removed, noticing a highly vascularised mass in the left fronto-parietal region. Mass macroscopic excision was practiced. The dura mater was suspended, the flap bone was repositioned and the drainage tube was installed.

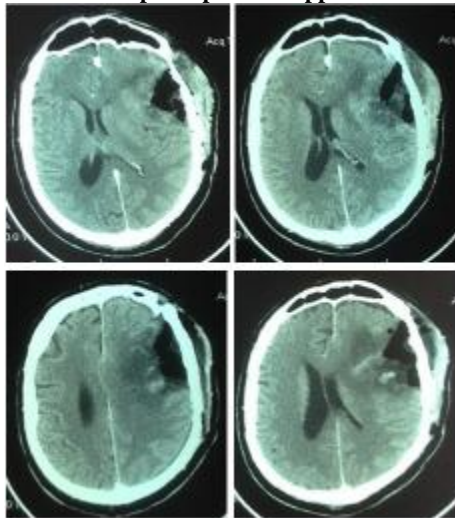
Postoperatively, the patient's evolution was favourable, afebrile, with the smooth healing of the operative wound and with the neurological deficit recovery.

Histopathological examination showed that the tumour was benign, that is meningothelial meningioma.

Following significant leukocytosis with lymphocytosis, haematological consultation was requested. In the first instance, the routine analyses did not reveal any unusual aspect. Therefore, marrow puncture was practiced and the myelogram showed a rich cellularity, monomorphic, with medullary appearance of chronic lymphoproliferative syndrome, with phenotypic and biopsy recommendation. There was raised the suspicion of lymphoid leukemia and therefore, chemotherapy was initiated (8 courses of chemotherapy until October 2013), with the total remission of the disease.

A check-up CT scan was performed on 03/06/2013, showing a mixed fluid and air collection at the site of excision, with a corresponding epicranial hematoma, also with air content; the disappearance of the mass effect and the significant improvement of the edema.

**Figure no. 2. Normal post-operative appearance**



Later on, on 20.12.2013, a PET-CT scan was performed showing a porencephalic area of 25/20 mm in the left fronto-parietal region with FDG capitation deficit, explicable due to the surgical background; no other FDG morphological or functional changes detectable at crano-cerebral level or at neck level; with no latero-cervical or supraclavicular lymph nodes, axillary and mediastinally and without FDG functional or morphological changes detected in the parenchymal abdominal-pelvic organs or at the level of the digestive tract; without retroperitoneal pelvic or inguinal lymph nodes.

The patient returns for haematological check-up during the month of May 2014, when a bone marrow harvest was performed, which, on the histopathological examination showed a cellularity of about 60% with modified architecture, with nodular interstitial infiltration and with diffuse areas with a population of atypical small lymphocytes with round, slightly irregular nuclei, angulated, incised, chromatic, some of them

representing 75% of the mature cells population; precursor elements of erythroid and myeloid series appear disorganized with reduced cell maturation; reticulin fibrosis areas with fine fibres network, low iron deposits. It was concluded that the microscopic and the immunohistochemical appearance advocates for marrow infiltration with nodular appearances and diffuse areas within a mantle B-cell NHL.

## DISCUSSIONS

Meningiomas bring about the symptomatology through several mechanisms, namely by the irritation of the cerebral cortex, brain mass compression, hyperostosis and soft tissue invasion or by producing various vascular lesions. The symptoms can aggravate due to pregnancy, but they usually resolve or improve post-partum. Cortex irritation can cause seizures; de novo crises justify the imagining exploration for the differential diagnosis with a brain tumor mass. Symptomatic meningiomas are approached either through radiosurgery or through the conventional surgical method, apparently addressed early in the nineteenth century with modest results.(1,2,3) Most often, compression can lead to headache, and focal weakness, dysphasia, apathy, somnolence. Vascular damage can lead to cerebral artery occlusion leading to phenomena such as, transient ischemic attack or stroke. Other symptoms may include obstructive hydrocephalus, panhipopituitarism, visual disorders, blood disorders (Castleman syndrome).(4,5,6).

Meningiomas classification is done as follows: a) benign (meningothelial, fibrous, mixed, angiomatos, microcystic, secretory, metaplastic), b) atypical (choroid, with clear cells atypical) that show cellular and tissue abnormalities and grow faster; they can invade the brain tissue and have an increased relapse rate and c) malignant (papillary, rhabdoid, anaplastic) with the highest rate of growth, invasion and metastasis. In their case, tumor markers (MIB-1 and Ki-67) can help, present in tumors with increased chances of recurrence.

**Risk Factors.** The most predisposed population are those between 30 and 70 years old, the sex ratio is of 2 to 1 with a higher frequency in women but with malignant forms, 3 times more common in men.

In the general population, those who are exposed to ionizing radiation are more likely to develop brain tumors, especially meningiomas. The most famous case is the Israeli children irradiated during 1948-1960 for various dermatophytosis. It is expected that repeated dental radiographs can represent an increased risk.

It is also considered that the presence of neurofibromatosis of type 2 is an increased risk of disease occurrence, even with the development of multiple meningiomas.(7) The association with Gorlin, Rubinstein-Taybi syndromes is mentioned in the literature.(8,9) The question is raised in terms of the link between the meningioma risk and hormones (due to the presence of progesterone, estrogen receptors on some meningiomas), as well as breast cancer, oral contraceptives or hormone replacement therapy.(10,11,12)

Meningiomas diagnosis can be very difficult because most of them are slow-growing tumours and mainly affects adults and the symptoms can be so subtle that they can be attributed to aging. The symptoms can also be attributed to other comorbidities. Under these conditions, it can reach up to several years to establish a correct diagnosis. Therefore, if a patient with de novo seizures, persistent headache or signs of increased intracranial pressure (vomiting, papilledema) needs a neurological exam and imaging investigations.

Drug treatment is limited to pre and post-operative medication in order to reduce mortality and morbidity

## CLINICAL ASPECTS

(corticosteroid medication), antiepileptic administered pre-operatively and at least 3 months after the surgery.

Chemotherapy is reserved for the cases in which surgical approach and radiotherapy have failed. In this sense, temozolomide, RU-486 and interferon alpha have been used. However, even in these cases, the results are disappointing.(13) Radiation therapy can be considered a valid option in case surgical option may not be taken into account. In many such cases, there was a tumour regression or stasis after radiotherapy. It is mainly indicated in incomplete resected tumours, relapse, or atypical or malignant meningiomas, as well as in the case of accessible tumours (optic nerve meningioma).(14)

Stereotactic radiosurgery can be used for an excellent local tumour control with minimal toxicity. It is used especially for residual or recurrent lesions less than 3 cm for which the surgical approach would be a risk, but also for small meningiomas and those located at the base of the skull and of those of the cavernous sinus.(15)

Considering that meningiomas are benign, well-defined tumours, the surgical treatment is the most indicated. The therapeutic approach consists in the microscopic total resection (Kobayashi) in order to prevent recurrences. The adjacent, infiltrated dura is also resected, also removing the infiltrated bone portions followed by dural and marrow plasty.(16) The main goal is the complete excision of the tumor, while also taking into account the risks, such as cellular invasions or vascular inclusions. Although the goal of the surgery is excision, the priority is to preserve the neurological functions. If total excision involves such risks, partial excision is practiced and the remaining tumour is monitored imagistically, possibly performing radiotherapy.

A measure that is more and more applied is the endovascular embolization to decrease the intraoperative risk. It is a procedure similar to cerebral angiography with the exception that adhesive substances are used to prevent the blood supply to the tumour.(17)

One can choose the expectation in case the patient is a) oligosymptomatic without cerebral edema, b) with moderate symptoms and a tumour history without negative effects on the patient c) elderly patients with slow tumour development d) patients at high risk regarding the treatment e) patients who refuse surgery.

The prognosis is directly related to the patient's age (young people have a better prognosis). The complete excision also favorably influences the patient outcomes (5-year survival rate is of 80%).(18) Unfortunately, this is not always possible. Atypical and malignant meningiomas, although rarely metastasize, have a worse prognosis, with a 5-year survival rate of only 60%.

The peculiarity of the case presented is the association of the neurosurgical pathology to the hematological one, situation that could darken even more the patient's prognosis.

Mantle cell lymphoma is a B-cell lymphoma that develops from an acquired and not inherited alteration of the DNA occurring within the zygote. Thus, the error is perpetuated with every new replication, thus providing an advantage and a survival rate increasingly higher in the detriment of normal lymphocytes. Moreover, cellular balance is not accomplished by the cell death, so that tumour cells accumulate and form tumours, most often in lymph nodes. The average age of diagnosis is the sixth decade of life, men being more affected (75-80%).

Disease prevalence is low (7% of non-Hodgkin's lymphoma). At the time of diagnosis, the disease is usually spread systemically (stage III / IV disease – with the spread of tumour formations outside the lymphatic system).

## CONCLUSIONS

Meningiomas are usually benign, slow-growing tumours that generally have a good prognosis. Both radiosurgery and classical surgery are considered worthy options to take into consideration in the case of the tumour formations that have to be excised. Although in the past, the classic surgery was the preferred technique in total tumour excision and it is still used for convexital very reachable meningiomas, the increasing availability of radiosurgery made possible to rethink the meningiomas approach, especially of those with high difficulty. There is already a history of long-term tumour control associated with low morbidity through radiosurgery.

There is though the question whether the risk for choosing the more aggressive classical surgery is justified, especially in higher difficulty meningiomas (skull base) having radiosurgery at hand. Starting to use radiosurgery as a first treatment choice for small meningiomas and its association with surgical decompression or subtotal excision (to avoid neurological deficits that may arise from radical excision), in large tumors, it becomes slowly but surely, the option of choice.

In the case presented, the total removal of the giant meningioma was performed under permanent control and continuous monitoring of the multidisciplinary team consisting of a neurosurgeon, hematologist, anesthesiologist, the ultimate goal is the complete treatment and the patient's professional reinserion.

Meningioma is the neurosurgeon's "friend" and often, the most formidable challenge. Both for the physician and for the patient, it is a profoundly benign condition that offers the chance of healing in about 80% of cases. However, the long-term prognosis for a patient with such a tumour is directly related to the skill, talent and perseverance of the surgeon who approaches it.

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