Symptomatology and therapy of middle and later cranial fossa meningiomas, in the period 2017-2019. Narrative review.

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ABSTRACT

Introduction: Meningiomas are the most common primary tumors, although most are benign, their location in the central nervous system can cause severe morbidity and mortality. Around the world this type of neoplasia has an incidence of 7.7 per 100,000 inhabitants and presenting a variable incidence in each region, being 3.8% in the middle fossa, 10% in the posterior fossa and in general 36% of all intracranial tumors. Their development will depend on several risk factors that are associated with both genetic to environmental causes.

Interpretation: Meningiomas are the most common primary intracranial tumors and both its size and location differs, causing symptoms by mass effect therefore, in the middle fossa, the affection is visual, while in posterior fossa vestibular symptoms, and even though the histological benign nature of this tumors, patients suffer from neurological symptoms and will require treatment; Being the surgery the primary treatment in all the cases which are accessible, on the other hand, radiation can be used as a primary treatment or, therefore, for recurrent or inaccessible lesions.

Keywords: Meningioma, Posterior Fossa, Neoplasm, Middle fossa.

INTRODUCTION

Meningiomas are the most common primary tumors representing one third of all intracranial tumors, of extra axial origin derived from meningothelial arachnoid cells in Pacchioni granulations; more common in women than in men even though most of them are benign, their morbidity and mortality risk increase, depending on their location. Also their incidence increase with age, appearing from the age of 65 (1) (3), with the exception of neurofibromatosis type 2 or a radiotherapy history that predisposes to early presentation. They are also present in 1.2 to 7.7 of 100000 people (2) (3), with variable incidence between each region being 17 - 25% in middle cranial fossa, 10 % in posterior cranial fossa and representing in general, a 36% of all the intracranial tumors (4) (5). Therefore, it is sought from this manuscript, to describe the different types and characteristics of meningiomas, both those in the middle fossa and in the posterior fossa and a therapeutic approach in each case.

MATERIALS AND METHODS

A bibliographic search of published articles, research, book extracts, repositories and clinical cases at the global level was conducted, from between the years 2017-2019 at UpToDate, Science Direct, PubMed and Clinical Key.

The keywords used were: meningiomas, middle fossa meningioma and posterior fossa meningioma.

In the same way, a search was started on the Google Scholar portal about articles, documents and cases published previously, in different journals of neurology, neuro oncology and neurosurgery.

Risk factors

Intrinsics:

- **Sex**: greater predominance in women than in men, with a 3:1 ratio, which may suggest a hormonal and genetic role in their development (4) (6) (3).

- **Hormonal factors**: higher incidence in posmenarcheal women; increases in reproductive years, progesterone and androgen receptors are found in 2/3 of the patients, but this represents a minimal risk (1).

- **Ethnic group**: the incidence varies from region to region being 7.7 (1) on average, in addition, can vary up to 8.8 per 100000 inhabitants in black population (6) and 4.3 in Asian, which could be due to genetics, nutrition or environment (3).
• **Genetic predisposition**: the presence of neurofibromatosis type 2 (3) caused by the mutation of the tumor suppressor gene on chromosome 22, significantly increases the risk for the development of multiple intracranial tumors, which is 75% higher for the development of meningioma.

Patients with multiple endocrine neoplasia type 1 (MEN1) also have a higher risk (6).

Extrinsics:

• **Ionizing radiation**: most important acquired factor due to radiation therapy or incidental exposure. Higher incidence of being multiple and atypical as opposed to sporadic (4) (5). Radiation damages tissue by breaking down and rearranging genes, which can result in the development of cancer (3).

A systematic study describes that the development of meningiomas occurs in a period of 22.9 years, presenting different WHO grades, being 68% grade I, 27% grade II and 5% grade II (7).

• **Others**: diseases in which hypertension or diabetes mellitus stand out, and in addition the use of telephone has been theorized as a predisposing factor due to electromagnetic fields (3); however, it has not been possible to demonstrate a direct relationship with the formation of tumors (4) (6).

**Classification**

WHO classifies the meningiomas into three types according to the histopathology, dividing into 9 benign (WHO grade I, 3 of the intermediate risk or atipic WHO II) and finally, 3 that are malignant WHO III (2) (8).

**WHO 1**: They are of benign type and do not present a major lesion, according to the morphological structure (1). Moreover, they lack criteria for atypical or anaplastic meningiomas (4).

**WHO 2**: Atypical, clear cell and choroid meningiomas, brain invasion and criteria such as increased cellularity, small cells with a high nuclear-cytoplasmic ratio, prominent nucleoli, without uninterrupted pattern or lamina similar growth or spontaneous necrosis foci (1) (4). It also has a mitotic index greater than or equal to 4 (8).

**WHO 3**: Malignant with anaplastic, papillary and rhabdoid types. These have malignant characteristics that resemble carcinomas, sarcomas or melanomas, there is infiltration of the underlying brain, abundant mitosis with atypical forms and multifocal microscopic foci of necrosis (1), they have a mitotic index greater than or equal to 20 (8) (4).

**DIAGNOSTIC**

Neuroimaging diagnosis is simple because it has a characteristic appearance and is noticeable in both resonance and tomography (1). In MRI this is hard, isointense or hypointense base in T1; while in T2 it is presented as hyperintense and in both, the displacement of the brain is noticeable (1).

Diagnosing a malignant meningioma of a benign is a challenge when using neuroimaging alone, but some features that differentiate a high-grade meningioma from a low-grade meningioma can be observed, such as:

- Intratumoral cystic change
- Hyperostosis of the destruction of the skull and/or adjacent bone
- Extension of the tumor through the base of the skull
- Peritumoral brain edema
- Low values of the apparent diffusion coefficient
- Cerebral blood volume elevated.

**Treatment**:

It is advisable to treat symptomatic, fast-growing, large tumors and if an aggressive variant is suspected; however, some of these tumors may have no symptoms and may be small. In case of being in inaccessible areas, its resection is ideal. The Simpson classification can be used to analyze the degree of tumor resection (7) (9).

In general, the primary treatment is surgical, with an individual approach for each tumor depending on its location.

Surgical techniques for each meningioma represent a challenge, in each case are exposed in a simplified way; however, it does not represent the reality of these that have to be studied in depth to understand them. In some cases, that the surgical area is inaccessible, therapies such as radiation may be used.

It is important to mention that despite the available
treatments, there is a recurrence rate of this type of tumor, which ranges from 0.00 to 2.36 per 100 person-years for WHO grade I meningiomas, and from 7.35 to 11.46 per 100 person-years for WHO grade II (10).

**Craniotomy**

**Resection:** The approach will depend on the tumor location, having as options a total resection, which has a lower probability of recurrence and is used in accessible areas. Consist in the remotion of all the tumor, the associated dural adherences and the affected bone; however, in 30 % of the cases is impossible to carry out a complete exeresis due to the location and the proximity with neurological and vascular structures, as happen with posterior fossa meningiomas (9) (11) or those located on the back of the sagittal sinus, petroclival region or in the internal wing sphenoids (4). In order to avoid a greater morbidity in patients, in these cases a subtotal approach will be chosen in which only a part of the tumor is extracted, this means a higher rate of recurrence.

**Radiotherapy:** In surgically inaccessible areas, or medically inoperable patients or who do not want surgery. In addition, it also uses as adjuvant treatment, after the total or partial surgical remotion, in recurrence cases. Its use is recommended especially in young patients with tumor locations that are likely to become symptomatic (11) and difficult to access, or patients to whom a partial tumor resection was performed/carry out and there is still a tumor remnant.

**Radiosurgery** (Proton beam therapy): In critical anatomical areas as the base of the skull; its use is restricted to patients who are not suitable for surgery or incomplete surgical resection. Its main advantage is the low risk to adverse events (12).

Consist of the administration of multiples beams of radiation to the tumoral tissue in different directions, that is to say, sending one or several dosis of radiation to a small defined area by the use of these rays that converge at a single point. These doses range from 7 Gy to 70 Gy, depending on the pathology.

To avoid damage to the surrounding healthy tissue a progressive decrease in dose is made (13). Therefore, this medium can be used; for that, it is very important to have previous images that will serve as guide and accurate marking, knowledge of the neuroanatomy that surrounds the lesion and thus, administer the treatment reliably (13).

**Middle Fossa Meningiomas:** They are divided according to the area they occupy. In sphenoids they are presented in 2%, dividing in turn in the minor wing of the sphenoid with proposed subdivision, initially by Cushing and Eisenhardt in meningioma of the lateral or pterional third, of the middle third or wing, and of the medial third or dinoideum (5); the major wing of the sphenoid, the cavernous sinus incidence of 12%, the optical channel and the optic nerve sheath, Meckel fossa and the upper portion of the clivus (4) (5).

**Symptoms:**

They are slow-growing and usually present asymptomatically for a long time and are discovered by accident (1), but the onset of symptoms is often insidious (4). In 30% of cases, there are seizures, but commonly when the location is not in skull base (1).

**Treatment:**

It consists of giving a definitive resolution and the prevention of neurological damage thereof, it should be taken into account both the age of the patient and the location and relationship with the critical structures and histopathological characteristics of the tumor, so it is that, grade WHO (2) (4).

In small tumors, up to 2 cm in diameter, which are discovered by accident and have no symptoms, more observation is done unless it grows and is accompanied by symptoms, so the patient should be evaluated with MRI or CT from 3 to 5 months; if the person continues asymptomatic and there is no tumor growth, should be monitored with images annually from 3 to 5 years and then from 2 to 3 years. This approach of observing and waiting is appropriate for older patients with more comorbidity.

In large tumors with symptoms, which expand, infiltrate and have surrounding edema, resection is best, as long as it is feasible, since in the case of tumors of the middle fossa that involve the medial sphenoid wing or cavernous sinus, they are often inaccessible, so radiation therapy is the choice, because it can be very effective in providing excellent tumor control and in a profitable way, the risks of surgery are avoided. However, the size of the tumor should be taken into account, since it can cause reactive postRT edema, which ends with seizures and neurological deficit.

**Craniotomy:** It consists of the opening of the skull and its covers extensively to reach the brain and resolve the lesion, allowing the visualization of the entire tumor together with its limits, thus, it is a much more invasive technique and involves several treatments to perform it.
In general, they are classified in different forms, such as osteoplastic and osteoclastic craniotomy; the first retains the bone flap and restores it at the end of the surgery, while in the second, the opening is left open.

Depending on their location, they can be supratentorial or infratentorial, and in turn, they can be uni or bilateral, in addition, they can be given by their basal height, high or intermediate; the first are used in anterior, middle or posterior fossa bone.

**Supratentorial Craneotomy:** for lesions in the sellar and suprasellar region, anterior and anterolateral accesses may be used, through frontal and sphenoids bones, or temporal and parietal, allowing access to the anterior part of the middle fossa, in case of meningiomas of the lesser wing of the sphenoid.

**Sinus Cavernosus Meningioma:** less than 3 cm and if born within the sinus, may decrease the caliber of the carotid artery and even extend to a preopticine cistern (6) (14).

Most patients present with affection of the cranial pairs: III and VI (6).

**Treatment:**

Radiation therapy, observation, and surgery may be used; the latter requires greater complexity, both in terms of location and techniques to perform them due to before carrying it out the internal carotid artery and the collateral system must be studied to evaluate blood flow, using different techniques, be it resonance angiography or conventional. The approach is performed at the zygomatic cranium – orbital level, maintaining control over the internal carotid artery both proximally and distally; the tumor is removed from inside the cavernous sinus space by suction, bipolar coagulation and micro dissection (15). Since there may be an alteration in the oculomotor nerves after surgery, it has been decided to start with radiosurgery and also this therapy is of choice in small tumors with symptoms and intracavernoses (15) (16).

**Meckel Meningioma:** Meckel Cavum is located in the Gasser ganglion, neoplasms of this region are very rare, but when it present, it mainly occurs with facial pain, by alteration to the trigeminal nerve branches V1 and V2 (6).

**Treatment:**

They are very rare so there is not consensus of its treatment; however, a frontotemporal approach with extradural or intradural clineidectomy may be used.

**Lateral third or pterional Meningioma**

By being in the external sphenoid wing these can affect frontal and temporal lobes and basically, may present with symptoms such as headache, visual disturbances (diplopia or changes in visual acuity), nausea, vomiting, seizures, hemiparesis, mood swings and confusion (17).

**Wing Meningioma:** It is originated in the minor wing and can compress the frontal and temporal lobes. It is presented to a greater extent, as asymptomatic and can present headache, altered mental state, epileptic seizures or even hemiparesis (5).

**Medial or Clinoid Meningioma:** Benings and are located surrounding the anterior clinoid. Due to its proximity to the optic nerve its main sign is the decrease of visual acuity accompanied by headache and in very low proportion, abnormality of the oculomotor nerves with visual field defects. (18).

**Treatment**

Frontotemporal craniotomy approach with orbitotomy, in the case of meningiomas of the lesser wing of the sphenoid (18) (16) or extradural clinoidectomy, since it allows an early devascularization of the tumor (19), besides, it presents less complications and is easier to use, unlike the intradural technique; however, the latter facilitates the visualization of structures. In both, the decompression of the optic nerve must be complete (19) (16).

Total resection of this tumor is impossible by adjacent structures, however, extradural clinidectomy allows to preserve the dura mater and prevent bone particles from depositing and subsequent repair with dural graft (19).

In the case of pterional meningiomas, a craniotomy with temporal extension may be used, in this method, the sphenoid wing is perforated from lateral to medial until clinoid processes are observed where the meningo-orbital artery is located. The posterior third of the lateral and upper orbital wall will be removed (20).

**Clival Meningioma:** They have similar characteristics to the petroclival meningiomas, but sphenoid forms have a more extensive and invasive involvement of the cavernous sinus and clival bone (15). Patients present instable gait, extremities weakness, dysphagia, hearing and and vision loss, headache, papiledema and facial numbness due to nearness to V CN (20).
Treatment:

Similar to petroclival ones.

Greater Wing of Sphenoid Meningioma: decreased visual acuity, limitation to eye movements (cranial pair VI) and decreased hearing. These meningiomas can affect soft tissue. Besides, is associated with sphenoid hyperostosis. This lesion extends into the intra- and extra-conal left space, conditioning proptosis, as well as, medial displacement of the optic nerve (21).

Posterior Fossa Meningiomas: 10% of all intracranial meningiomas arise in the posterior fossa. Almost half of this meningiomas are located in cerebellopontine angle, 40% are tentorials or are in convexity of the cerebellum, 9% are clival, and 6% in magnum foramen.

The audio-vestibular symptoms are the first to appear.

Surgical treatment is chosen, in which the approach will depend on the location of the tumor and its relationship with adjacent structures. In certain tumors with difficult surgical access, an endonasal endoscopic approach may be applied.

Transclival endonasal endoscopic approach: This type of procedure prevents the retraction of the brain and brain stem, early vascularization, and achievement of grade 1 Simpson resection. Therefore, posterior fossa meningiomas, ideal for an EEA, are those rare tumors that arise from the medial to cranial nerves III, VI, and XII. However, these lesions when are treated through an EEA, pose technical challenges in tumor resection and skull base reconstruction, so the expertise of the surgical team and the resources available are critical (22).

The choice of this type of approach depends more on the experience of the surgeon and knowledge of the anatomy than on experience with a particular type of tumor.

Petroclival meningiomas have a particular pattern of displacement of surrounding structures, usually dislocating the cranial nerves (CN) V, VII, VIII, IX, X, XI subsequently. The approach of these tumors, through an earlier route, offers a clear advantage in the subsequent displacement of the cranial nerves (22). If the tumor is in a higher position and CN VI is pushed down, an EEE would be a safe option. Similarly, when the tumor has a lower origin, VI CN can be pushed up, allowing a safe EEA to be performed again (22).

In cases where the abducens nerve travels through the tumor, a combined approach is the treatment of choice to preserve nerve function. In addition, the midline component of these tumors can be safely resected through an EEA, and the lateral component is best conducted with a retrosigmoid, presyringed, or anterior petrosectomy approach. These are highly challenging cases and achieving a good result with normal neurological function is difficult by any means (15) (22).

For lesion of the foramen magnum, displacement of the lower cranial nerves should guide the selection of the approach. When originating from the anterior edge of the foramen magnum, meningiomas are suitable for an EEA, as they arise medially to hypoglossal and jugular foramen, and displace CN IX, X, XI, and XII, posterior and laterally. When nerves move earlier, a posterolateral or open lateral surgical corridor with open craniotomy should be used (22).

Cerebellopontine angle meningiomas: The symptoms are associated with CN affection such as: IV, V, VI, VII, VIII, IX and XI are common. These symptoms may include hearing loss, facial pain or numbness, and facial weakness or spasm, as well as headache and cerebellar hemispherical signs.

Treatment:

A retrosigmoid approach is preferred, which allows sufficient exposure for the removal of these tumors. The dural junction of meningioma is to the posterior pyramid that progressively coagulates and divides to devascularize the tumor; this should be done with care to avoid lesions to the cranial nerves that come out (15).

If the size of the tumor excludes its safe removal, the tumor capsule must be opened and the tumor must be shredded and devascularized. The capsule is carefully dissected from the surrounding cranial nerves, the brain stem, the upper cerebellar artery, the anterior lower cerebellar artery, and the posterior lower cerebellar artery. After the tumor is removed, the dural junction should be removed or clotted, and any hyperostotic bones removed, taking into account the location of nearby inner ear structures (15).

Petroclival Meningiomas

They present headache, cerebellar compression ataxia, spastic paresis and cranial neuropathies.

They involve the supratentorial and infratentorial compartments.

The differentiation between clival, petroclival and sphenopetroclival meningiomas is based on the surgical anatomy of the lesion. Tumors that arise from the upper two thirds of the
clivus and displace the brain stem are subsequently considered clival meningiomas. Petroclival meningiomas also involve the upper two thirds of the clivus and are located on the medial V nerve to the cranial, with most of the tumor more lateral, along the spheno-occipital syncondrosis. Likewise, Sphenopetroclival meningiomas have similar characteristics to petroclival meningiomas, but sphenoid forms have a more extensive and invasive involvement of the cavernous sinus and clival bone. These characteristics often make the achievement of a Simpson I grade resection of the sphenopetroclival variety unattainable (15) (9).

Treatment:
The difficulty of the surgical procedure, complications and risk of cranial nerve deficits may have a negative influence on the quality of life of the patients, so radiation therapy or radiosurgery has been preferred (15) (22).

In these tumors are preferred to perform a lateral approach of the skull base, to avoid brain retraction. The main considered approaches to these lesions are posterior petrous approach, anterior petrous approach to middle fossa by petrosectomy, or a combination of both. Currently, the transclival endonasal endoscopic approach is performed.

Jugular foramen meningiomas: This type of tumor is very rare and it can compress the inferior cranial nerves, invade the temporal bone, in addition to, invade, compress, narrow or obstruct, the jugular bulb. Generally, they are heralded by inferior cranial nerve deficit symptoms.

Treatment:
A surgical approach with skull base focusing is performed. The approach can be tranjugular, suprajugular or retrojugular, depending on the tumor extension.

Foramen Magnum Meningiomas: They are present with unusual symptoms, leading to incorrect diagnosis. Symptoms can be cervical pain, usually unilateral, motor and sensory deficiencies, especially in the upper limbs and later stages, progressing to spastic quadriplegia. Triad: cold, clumsy hands with intrinsic hand atrophy; it is helpful (15).

Treatment:
Lateral or posterior foramen magnum meningiomas can be resected using a standard inferior suboccipital approach; however, meningiomas of the foramen magnum ventral are difficult to access due to the involvement of the lower cranial nerves and the complex of vertebral-basilar artery and the significant compression of the brain stem, so a transcondilar approach is preferred (15).

DISCUSSION
The location of the meningiomas influences how people present their clinic; but, as the location is a key factor, it is also the size, since it will not only increase the intensity of symptoms, but will also have repercussions on what kind of therapeutic approach the patient will require. Data and collected information in this research demonstrated obvious symptomatological differences between each meningioma of the cranial base, the medial fossa have a predominance in visual symptoms due to their closest relationship with the optic nerve, while in the posterior fossa, what predominates are the audiostreams due to their proximity to the lower cranial pairs. The surgical approach must be individualized depending on the location and adjacent structures.

Knowing well the clinic of each patient is the first diagnostic step complemented with imaging techniques to obtain a better visualization of which structures are involved and to what degree and finally to be able to make the therapeutic decision that gives us a better resolution to provide patients with a good quality of life.

CONCLUSION
The meningiomas are the most common based brain tumors and are subdivided according to the space they occupy within the same base, whether middle or posterior fossa. Both should be diagnosed through their clinic, which despite having certain similar features, differs in several cases by the adjacent structures involved; thus, the choice of treatment should be individualized.

The main pillar of treatment continues to be surgery; however, the surgical approach will be individualized for each patient, taking into account the location of the tumor and its relationship to adjacent structures.

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