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Abstract

Extra-axial tumors are lesions, neoplastic and not, which are external to the brain parenchyma and can originate in the skull, meninges, cranial nerves, and brain appendages such as the pituitary gland. Surgery provides a diagnosis and can be the first step in the treatment. When chosen as a treatment, we should consider the access and the approach to the lesion, the adequate operative technique, and related skills, minor or major complications. Because of the benign nature of these tumors, the evaluation of the risk/benefit in submitting a patient to a surgical treatment has to be considered. We would like to give an overview about benign extra-axial tumors and surgical operative techniques and tools that can be applied to improve patient’s outcome.

Keywords: benign extra-axial tumors, surgical techniques, meningiomas, schwannomas, surgical approaches

1. Introduction and background

1.1. Definition, pathophysiology, and epidemiology

Extra-axial tumors are lesions, neoplastic and not, which are external to the brain parenchyma and can originate in the skull, meninges, cranial nerves, and brain appendages such as the pituitary gland. From a surgical point of view, it is important to understand their relationship with the subarachnoid spaces because it is in this space that nerves and vessels travel to and from the brain; hence, avoiding injury to these structures rests on a clear understanding of their relationships with the tumor. Lesions that originate outside the dura such as chordomas, chondrosarcomas, and paragangliomas are easy to understand as they are usually separated from neurovascular structures by an intact arachnoidal membrane.
Pituitary adenomas are intradural but extra-arachnoidal lesions. Meningiomas and cranial nerve schwannomas are usually covered by an arachnoidal layer but from a surgical point of view are extra-arachnoidal lesions, while epidermoid, dermoid, and craniopharyngiomas are intra-arachnoidal and in the case of craniopharyngiomas occasionally intrapial lesions [1, 2].

They represent about one-third of all intracranial primary neoplasms in adults and about one-quarter of brain tumors in children [3].

They can be classified according to their site in supratentorial and infratentorial tumors.

The most common benign extra-axial lesions are meningiomas, pituitary adenomas, craniopharyngiomas, and cranial nerve schwannomas.

1.2. Clinical presentation

Because of their slow growth, the onset of symptoms can be insidious.

Supratentorial tumors can present with progressive focal deficits, mental status changes, or seizures. Infratentorial tumors can present with decreased hearing, gait disturbances, ataxia, vertigo, diplopia, multiple cranial nerves deficit, and long-tract abnormalities (if there is a brain stem involvement).

Common symptoms of both supratentorial and infratentorial masses are headache, nausea, and vomiting due to the increased intracranial pressure (ICP) [4, 5].

1.3. Diagnosis and imaging

Radiological imaging is of primary importance for a preoperative diagnosis.

Computerized tomography (CT) scan, without and with contrast, is usually the first diagnostic step and it can provide a better identification of tumors involving the bone and the presence of calcification.

Magnetic resonance imaging (MRI) is considered the gold standard because it provides a greater resolution for soft tissues and better identifies the margins and extent of the tumor, its relationship with nerves and vessels, and also affords optimal imaging of lesions about the skull base. Imaging features that are consistent with a benign tumor are usually homogeneous enhancement, smooth-rounded margins, no associated brain edema, and no satellite lesions.

Rising numbers of MRI studies performed during evaluations for different diseases caused a significant increase in the number of incidentally found brain tumors.

Conventional cerebral angiography is at times useful in the preoperative management of patients with meningiomas, occasionally for embolization purposes and more often to ascertain the patency of major sinuses and the alternative venous drainage when the lesion abuts or involves major dural sinuses [6].
1.4. Treatment options and alternatives

Different factors, patient and tumor related, are involved in the decision-making process. They can influence the possibility and extent of surgical resection or the choice of a nonsurgical treatment.

Factors can be classified as follows:

• Patient factors: neurologic conditions, comorbidities, age, and life expectancy;
• Tumor factors: location, size, vascular and neural involvement, and, in cases of recurrence, prior surgery or radiation therapy.

Conservative approach is based on monitoring the patient clinically and with serial MRI scans. It can be proposed for asymptomatic tumors (including incidental findings) with no evidence of growth or in elderly people with a high surgical risk [7, 8].

Age is becoming more and more of a relative concept with many papers demonstrating the safety of surgery—when indicated—in elderly people [9].

Surgery provides a diagnosis and can be the first step in the treatment.

Tumor excision improves symptoms related to increased intracranial pressure or those related to brain parenchyma/cranial nerves compression. When choosing surgery as a treatment, we should consider the access and the approach to the lesion, involvement of major vessels or cranial nerves, and risks for potential postoperative minor or major complications. Because of the benign nature of these tumors, the evaluation of the risk/benefit of a total resection versus a subtotal resection will be guided by the basic principle of “do no harm”. Whenever a total resection presents a significant risk of morbidity (such as a neurological deficit or a fatal bleeding), part of the tumor can be left in situ and the patient can be submitted to clinical and radiological follow-up and eventually to surgery or focused beam radiation therapy in single or multiple fractions if tumors start re-growing or symptoms progress.

In cases where surgery is medically contraindicated, technically difficult, or high risk, primary radiation therapy may be considered as a definitive treatment option [10].

Radiation therapy for residual benign neoplasms is still somewhat controversial, although there is good evidence that subtotal excision plus radiotherapy produces local control and overall survival that is superior to subtotal removal alone. Timing of radiation therapy in cases of subtotal resection of a benign neoplasm is also somehow controversial with some authors using it only if and when there is evidence of tumor progression. The problem of arachnoid scarring created by radiotherapy makes reoperation for recurrence much more challenging. This concern needs to be balanced against the risk of earlier recurrence.

Finally, medical treatment can be considered for prolactinomas, who usually have a good response to dopamine agonist such as bromocriptine or cabergoline. For meningiomas, chemotherapies and hormonal therapies have been limited for the treatment of tumors that recur after surgery and when radiotherapy options are exhausted [11, 12]. They are considered generally ineffective, although somatostatin analogs may have therapeutic potential. There is
also increasing interest in targeted molecular therapies. Agents inhibiting platelet-derived growth factor receptors and epidermal growth factor receptors have shown little efficacy, but molecular agents inhibiting vascular endothelial growth factor receptors appear to have some promise [13].

Although interest in pharmacotherapies against vestibular schwannoma is increasing [14], none are Food and Drug Administration (FDA) approved [15].

1.5. Goal and advantages of selected surgical approaches

When choosing a surgical approach, several considerations come into play:

• Exposure of the tumor and its margins, of its main arterial feeders, of its venous drainage and of the adjacent neurovascular structures. Clearly in large tumors all of these goals are unattainable;

• Adequate operative space to comfortably perform surgical maneuvers;

• Exposure of the lesions from multiple angles so as to be able to use different surgical corridors as needed;

• Minimize violation/trauma of the normal cerebral parenchyma at the expense of bone or extra-cerebral tissues removal;

• Respect as much as possible patient’s aesthetics.

1.6. Indications

Indications for surgical treatment are as follows:

• Symptoms attributable to tumor compression of nearby structures;

• Demonstrated growth with sequential scans;

• Significant peritumoral edema;

• Need for diagnosis.

1.7. Contraindications

• High surgical risk related to the patient’s age, clinical status, and comorbidities;

• Small asymptomatic tumors with no evidence of growth.

2. Operative details and preparation

2.1. Preoperative planning and special equipment

Good surgical results are not just dependent on surgeon’s ability and skills but also on an accurate preoperative planning.
The side and site of the tumor and patient position has to be communicated to the operating room personnel in advance to properly position instruments and equipment before patient’s arrival. Thromboembolism of the lower limbs has to be prevented using elastic or pneumatic stockings. Intraoperative-evoked potential, electroencephalogram, or other specialized monitoring devices are required in selected surgeries.

Navigation systems are helpful in planning skin and bone flaps, and in showing the relationships of the tumor to the bone and neurovascular structures of the skull base. When using neuronavigation for microsurgery of skull base tumors, the hand-held pointer needs to be replaced by the microscope/navigation integration where the microscope focal point becomes the tip of the virtual pointer. Indeed, using hand-held pointers is cumbersome and is not conducive to a smooth flow of the operation.

In selected cases, when cranial nerves or eloquent areas are involved by the tumor, intraoperative stimulation in and around a tumor will identify the functional tissue, and its preservation will minimize the risk of permanent postoperative deficit. In that regard, facial nerve stimulation in vestibular schwannoma surgery is fundamental in maximizing the chances of facial nerve preservation and functional integrity. It is important to remember that cranial nerve monitoring is only as good and helpful as the person who is able to read their traces and to critically interpret their changes as not to have under- or over-readings.

The role of endoscopic-assisted microsurgery relies on the seminal work of Perneczky [16] and on the often-quoted sentence that “endoscopes allow visualization around the corners”. While it is possible to introduce the endoscope in a microneurosurgical environment at the present time, its use may be made more efficient by the development and refining of good-quality display of the endoscopic image in the microscope oculars.

2.2.1. Microsurgical instruments

- **Bipolar coagulation**: the coagulation is localized and causes no current spread or radiation of heat to the surrounding tissues. The size, shape, weight, and balance of the bipolar forceps are important features of their design. A bayonet shape allows a better field of vision avoiding the block of the surgeon’s hand. Bipolar forceps can also be used for dissection.

- **Retractors**: brain retraction has to be both minimized and properly used to prevent injuries. However, sometimes self-retaining retractors are useful to improve operative surgical angles or to reach deeper locations. Blades of different widths may be needed depending on the site and size of the lesion. One or more retractor blades are attached to a flexible arm near the resection site. Once the blade is on the desired position, the arm can be tightened. Retractor placement is a technical skill that needs to be mastered.

- **Suction**: the tip has to be smooth and atraumatic. The suction tube can also be used as a retractor or for a blunt dissection. Different diameters and lengths are available to better fit the depth and size of the surgical field.

- **Tumor knives and forceps**.
• Scissors: with fine blades on straight and bayonet handles are frequently used. Cutting should be done by the distal half of the blade. The blades can be straight or curved.

• Dissectors: divided in macro- and microdissector. Straight, rather than bayonet, dissectors are preferred for most intracranial operations because rotating the handles of the straight dissector does not alter the position of the tip. For transphenoidal surgery, dissectors with bayonet handles are preferred because the surgeon’s hand is prevented from blocking the view [17]. Different kinds of microdissector are as follows: round, spatula, flat, and micro-Penfield, nerve hook, angled and straight needle dissectors, microcurette, and teardrop dissectors.

Ultrasonic aspirators present the advantage to rapidly debulk tumors. Thanks to ultrasound waves, they fragment and aspirate tumor tissue. Care must be taken because they can quickly open through the surface of a tumor capsule and damage contiguous nerves and vessels.

Carbon dioxide laser produces energy that vaporizes tissues containing fluid. Because the beam cannot pass through fluid, its maximal effect is on the surface [17]. It is mainly used to debulk large tumors.

2.2.2. Microsurgical concepts: expert suggestions/comments

The key point in the removal of benign extra-axial neoplasm is the preservation of the arachnoidal plane that separate the tumor from the subarachnoid space and from the neurovascular structures contained in it. In the majority of cases, this plane may be preserved and at the end of the surgical procedures an intact layer of arachnoid where the tumor was may be recognized. To accomplish this key step, it is necessary to identify the tumor arachnoid interface. In large tumor, this may only be accomplished once the tumor size has been significantly decreased by internal (intracapsular) decompression (debulking) [1, 5].

Centripetal retraction of the tumor, away from the brain, rather than retract the brain parenchyma away from the tumor is considered another mainstay of microsurgical dissection.

The arachnoid must be grabbed with medium-size bayonet forceps and gently lifted off away from the tumor. The use of microbayonet, which are sharper than macrobayonet, will inevitably lead to violation of this interface. The use of curved tumor dissectors is helpful in further developing this plane even in areas that are not directly visualized, provided that the surgeon’s hand recognizes and properly interprets the proprioceptive feedbacks coming from the distal end of the instrument. Once separation has been accomplished, cottonoids of different sizes are introduced in the space created to maintain and identify it. Bipolar coagulation at this interface needs to be minimized because coagulation coalesces this interface and makes impossible atraumatic development of this plan. En bloc resection of large-size tumor is often impossible and dangerous; en bloc resection of medium-size tumor while tempting must be resisted for the sake of the principles discussed above. Annoying oozing from some area of the tumor may be controlled with topical hemostatic agents and gentle cottonoid applications while the attention of the surgeon goes to another area of the surgical field. Much has been made of early devascularization of large meningiomas; however, in many cases the main vascular pedicle is not accessible at the early stage of an intracranial procedure, and misguided
attempts at accomplishing it may result in undue brain damage, often due to retraction. Meticulous attention has to be paid to all veins and attempts need to be made to preserve them, no matter their size.

Gentle retraction of the brain is one of the decisive general factors in minimizing postoperative complications. Again, brain retraction is a skill that needs to be mastered and studied. In general, it is better to work in a channel that is kept open by a properly placed retractor than to use in-and-out suction retraction. Positioning, administration of diuretics, drainage of cerebrospinal fluid (CSF), and hyperventilation are commonly used techniques that can help in reducing brain retraction. When the brain has to be retracted continuously, the retractor should be moved every few minutes to another part of the cortical surface or released for a while.

For tumors with potential involvement of the venous sinuses and draining veins, a preoperative MR venography or angiography will help the surgeon decide whether total excision is possible and which vessels can be sacrificed.

Microvascular Doppler can be used to localize major arteries that clearly need to be spared.

2.3. Key steps of the procedure

2.3.1. Patient positioning

When choosing the patient position, the following criteria have to be considered:

- Safety: the patient has to be secured and prevented from falling if the operating table needs to be moved during the surgery;
- Body compression sites have to be carefully inspected and protected with soft materials;
- Venous drainage has to be guaranteed: always place the head on higher level than the heart and avoid neck flexing that compresses jugular veins;
- Skin incision has to be completely visible and accessible;
- Gravity helps in brain relaxation.

2.3.2. Skin incision

When choosing the skin incision, the following criteria have to be considered:

- Maximal tumor exposure in the center of the surgical field minimizing the risk of injury to the surrounding neurovascular structures. Best results can be achieved with the use of neuronavigation.
- Vascular supply to the skin flap: in a wide flap, the base of the skin incision has to be proportional to its height. Careful evaluation of previous skin incision that can alter the normal vascularization of the skin flap is required.
- Avoidance of visible cosmetic defects.
2.3.3. Tumor excision

- To decide the craniotomy and the dural opening, neuronavigation can be used. The tumor has to be exposed as much as possible, minimizing normal brain parenchyma exposure. If there is cerebral edema, a wide bone and dural opening prevent cerebral compression and damage.

- Tumor devascularization has to be performed in the first stages whenever possible. It helps in reducing the blood loss and guarantees an easier tumor removal.

- General microneurosurgical concepts (already discussed) have to be followed.

2.3.4. Hemostasis

When the tumor excision has ended, the hemostasis of the surgical field has to be very accurate to prevent postoperative bleeding.

The following steps need to be followed:

- Generous washing of the surgical cavity to remove all blood clots;

- Bipolar coagulation of all the active bleeding points;

- Avetin is microfibrillar bovine collagen that favors the platelet aggregation at the site of oozing. It is helpful in control oozing from raw brain parenchyma. Flowseal, Gelfoam, and Surgicel may also be used;

- Once hemostasis has been achieved, perform a Valsalva maneuver to make sure there is no occult bleeding;

- Dural suspensions to control epidural bleeding.

2.3.5. Closure

The dura has to be closed to avoid CSF leaks. If the patient dura is not available, galea or synthetic dural substitutes can be used.

A 4-0-silk stitches can be used to perform a continuous suture. At the end, fibrin glue can be spread all over the dura to increase the sealing. An onlay Duragen or a similar material may be used to reinforce the dural closure.

The bone can be fixed with titanium screws and plates. If the patient’s bone is not available, bone substitutes can be used.

Muscle reconstruction is very important. In frontotemporal approaches, the temporal muscle has to be reconstructed properly to avoid mastication problems and cosmetic defects. In posterior fossa muscle layers reconstruction represents a further barrier for CSF leaks.

Management of intracranial air containing spaces: if the frontal sinus mucosa is violated, then complete exenterating of the frontal sinus and its mucosa is usually recommended. The nasofrontal ducts are plugged with fat and fibrin glue. A more generous fat graft may be
needed if a large dead space is present or to supplement the dural closure when needed. Entered mastoid cells are plugged with bone wax, fat, and fibrin glue.

Skin flap has to be properly closed to avoid subcutaneous haemorrhages, CSF leaks, and cosmetic defects.

2.4. Surgical approaches

For supratentorial tumors, the most common approaches are as follows:

- Monolateral or bilateral subfrontal approaches: for the access to the anterior cranial fossa and anterior midline structures, posterior orbit and apex [18], the bifrontal approach is preferred when treating larger or purely midline lesions because of its better angle of view. When dealing with tumors such as olfactory groove meningiomas, a direct access to anterior ethmoid arteries is possible. Their coagulation reduces the dural blood supply to these lesions. Moreover, the position of the head in the subfrontal approaches reduces the intraoperative brain retraction taking advantage of gravity. The use of lumbar drain is often helpful when dealing with large lesions that preclude early access to CSF spaces.

- Frontotemporal/pterional approach: for tumors located in the anterior and middle cranial fossa, in the sphenoid, parasellar, and cavernous sinus regions, this approach forms a pyramidal-shaped working space whose apex is directed toward the limen insulae [1]. Splitting the Sylvian fissure allows the frontal lobe to fall away from the temporal lobe with minimal or no retraction. Early brain relaxation can be achieved opening the basal cisterns. The pterional approach allows the access and control of vital structures such as carotid artery and its main branches, cranial nerves, and the cavernous sinus region.

- Fronto-orbito-zygomatic approach: it offers a wide angle of exposure and a greater rostral trajectory for the management of lesions involving the cavernous sinus, parasellar region, upper clivus, and adjacent neurovascular structures. Removing the zygomatic arch enables the temporalis muscle to be displaced inferiorly, allowing a better subtemporal visualization. However, one should keep in mind that the periorbita is an unyielding structure that should not be unduly compressed. Hence, the advantage of removing the orbital roof is marginal.

- Basal interhemispheric approach: for tumors of the sagittal midline arising deep to the flax.

- Transsphenoidal approach: for pathologies involving the sella, suprasellar space, and sphenoid bone. It provides excellent visualization of the pituitary and is minimally traumatic to the brain, and avoids brain retraction and visible scars. It can be performed by the use of an operative microscope (with the advantage of a three-dimensional (3D) viewing) or by an endoscope (who enlarges the surgeon’s field of view).

For infratentorial tumors, the most common approaches are as follows:

- Suboccipital median/paramedian/lateral approach: for tumors located in the posterior fossa and cerebello-pontine angle (CPA). The suboccipital lateral approach gives access to the CPA and allows early identification of various neurovascular structures. The surgical
exposure extends from the trigeminal nerve and tentorium superiorly to the foramen magnum and jugular foramen inferiorly [19].

- Far lateral approach: for tumors located in the vertebro-basilar junction. Adding a C1 laminectomy to the standard suboccipital craniectomy provides adequate visualization of approximately 270° of the circumference around the medulla.

- Subtemporal and Kawase’s approach: for tumors located in the middle fossa and in the petroclival region. It provides a lower manipulation of cranial nerves. Adding the anterior petrosectomy gives access to the internal acoustic meatus and both middle and posterior fossa. Surgical adjuncts such as division of the tentorium and zygomatic osteotomy can provide additional working space and versatility.

- Translabyrinthine or transcochlear petrosal approach: for tumors located in the CPA, when hearing is already compromised. It gives a wide exposure and surgical space, avoiding cerebellar retraction.

2.5. Avoidances/hazards/risks

When choosing a surgical treatment, we should consider its indications and the balance of associated risks and reasonable goals. When considering hazards and risks, patient factors such as age, life expectancy, neurologic condition, and general medical conditions should be taken into account. In addition, tumor factors should be considered. Higher risks include the following:

- Location: tumor located close to eloquent areas;
- Infiltration of dural sinuses;
- Infiltration of major arteries;
- Cranial nerve involvement.

2.6. Salvage and rescue

It is important to have a clear preoperative plan. However, more important is the ability to modify the preoperative plan based on the operative findings. Indeed, it is impossible to know preoperatively what is the tumor consistency, which is a major determinant, everything else being equal, of the challenges associated with its removal. It is important to keep in mind that the majority, the overwhelming majority of extra-axial tumors, have a benign clinical course and that most of them respond to focused radiotherapy, in single or multiple fractions.

3. Outcomes and postoperative course

3.1. Complications

Postoperative fastidious patient monitoring can detect early complications.
In general, increasing headache in the postoperative period should not be treated symptomatically unless and until a postoperative complication has been ruled out by a CT/MRI.

These are the most common complications and their management:

- **Bleeding:**
  - in the tumor bed;
  - Subdural;
  - Epidural;
  - Subcutaneous.

  The management strictly depends on the entity of the bleeding and on the compression on the brain parenchyma or neurovascular structures. The patient can be clinically or radiologically monitored or may need a surgical evacuation of the hematoma.

- **CSF leaks:** more common in posterior fossa approaches. A conservative management consists of wound medication and a spinal CSF drainage placement. If the leak still persists, there is a higher risk of infection and surgery with a wound revision has to be performed.

- **Infections:** patients with CSF leaks, or comorbidities, present a higher risk. The infection can involve just the superficial layers and in these cases it can be managed by an antibiotic therapy. If the bone, dura, or the surgical field is involved, a surgical wound revision is needed.

- **Neurological deficits:** they can be caused by brain parenchyma injury, edema or ischemia (for a vessel occlusion), or by cranial nerves damage. The management is conservative in most of the case with anti-edema therapy and brain protection. The neurological deficit can be temporary and the patient can recover in few months. If there is a persistent damage to the facial nerve, a hypoglossofacial nerve anastomosis can be indicated.

- **Deep vein thrombosis (DVT) and pulmonary embolism:** higher risk for patients who develop neurological deficit or present a complicated postoperative course. Treatment is based on anticoagulant therapy. In cases of a massive pulmonary embolism, an endovascular treatment can be indicated.

### 3.2. Outcomes and prognosis

Outcomes depend on the kind of tumor and its location, on the kind of removal (if total or subtotal), and on the presence of intraoperative or postoperative complications.

Since these are benign tumors, prognosis is good in most of the cases and can be little modified by the amount of surgical excision.
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