Chapter

Jugular Foramen Paragangliomas

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Abstract

Jugular foramen paragangliomas are rare neoplasms occurring with a myriad of symptoms originating from paraganglionic tissue derived from the neural crest, comprising about 0.03% of all human tumors. Patients usually present with symptoms of dysfunction of VI, VII, VIII, IX, X, XI, XII nerves and sympathetic trunk. Depending on the tumor's topography, various approaches might be used to obtain its gross total resection. Jugular Foramen's paraganglioma classification, nuances of the approaches, pathology, postoperative complications, and outcomes are revised as follows. In conclusion, anatomical knowledge and the disease's comprehension are essential when dealing with such tumors, and despite their rarity, we must be obstinately committed to the surgical technique and devoted to the patient's functional postoperative outcome.

Keywords: paraganglioma, brain neoplasms

1. Introduction

Tumors located in the jugular foramen are rare, being one of the significant challenges in the surgical practice for cranial base neurosurgeons. Several tumors can affect this region, among them schwannomas, paragangliomas, and meningiomas representing the most common. Head and neck paragangliomas are rare neoplasms comprising about 0.03% of all human tumors. The yearly incidence is estimated to be at around 0.001% [1, 2]. Rarely, tumors located in the jugular foramen show intracranial and extracranial extension and, thus, present a myriad of symptoms, with several clinical syndromes described in the literature (see clinical presentation). The term "glomus tumor" has been used to describe the most common tumor related to this region, representing a tumor originating from paraganglionic tissue derived from the neural crest whose cells have the capacity to reserve and release catecholamines and may have clinical implications (see preoperative preparation) [3, 4].

Malignant tumors can also affect the jugular foramen, including metastatic tumors (carcinomas), chondrosarcomas and chordomas, as part of the differential diagnosis of these lesions [3]. The detailed discussion of the differential diagnosis of these lesions is not part of the scope of this chapter and can be seen in other references [3-5].

Advances in diagnostic imaging and surgical technique have allowed the understanding of these tumors and their exeresis with lower morbidity and mortality. A brief review of the clinical, diagnostic, imaging, histopathological and surgical aspects related to the glomus tumors of the jugular foramen is given below.

2. Clinical presentation

Glomus tumors of the jugular foramen present with slow growth and with early signs and clinical symptoms, being diagnosed on average after 5 years of onset of symptoms. These tumors have an average growth rate of approximately 1 mm per year [6]. The symptoms are directly related to the site of involvement and infiltration. Tumors of glomus jugulare represent neoplastic lesions that originate in the adventitia of the jugular vein and most commonly present with symptoms related to the involvement of lower cranial nerves, such as vagus (X), accessory (XI) and hypoglossus (XII). In the variant of glomus tympanicum, which are tumors related to the Jacobson's nerve, the most common initial clinical presentation is the presence of tinnitus, followed by conductive deafness and vertigo. Jacobson's nerve represents a tympanic branch of the glossopharyngeal nerve, which conveys the sensitivity of the tympanic membrane, auditory tube, and mastoid region. In the third anatomotopographic variety of this tumor we have the glomus vagale, originating from Arnold's nerve. Arnold's nerve emerges between the superior and inferior ganglia of the vagus nerve (auricular branch of the vagus nerve) and

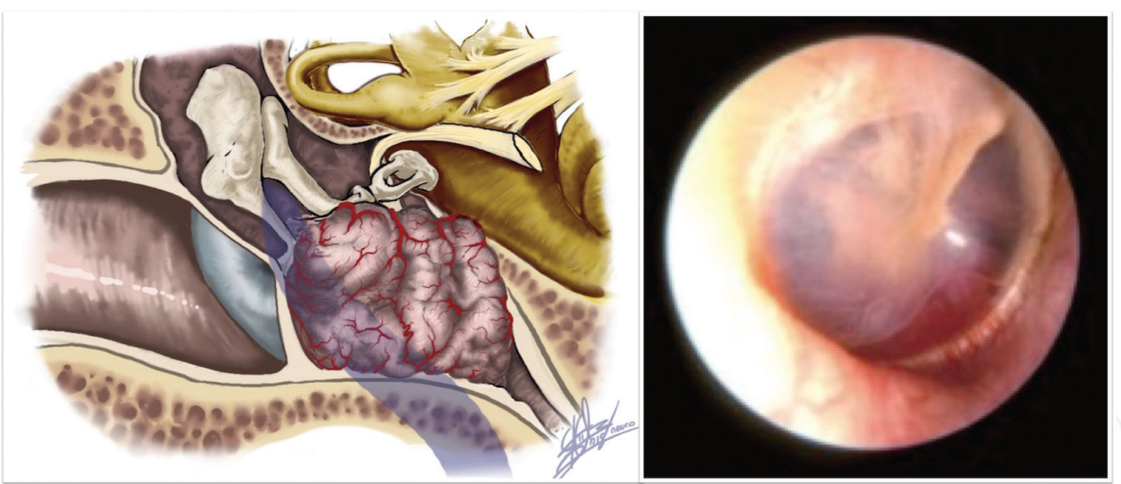

Figure 1.
On the left, anatomical relationships of the glomus tumor of the jugular foramen; on the right, otoscopy revealing the presence of a tumor in the lower right field.

Jugular foramen syndromes and respective affected nerves	Vernet	Collet-Sicard	Vilaret	Tapia	Jackson	Schmidt
IX	+	+	+			
X	+	+	+	+	+	+
XI	+	+	+	+/−	+	+
XII	—	+	+	+	+	—
Sympathetic fibers	—	—	+	+/−	—	+

Table 1.
Syndromes related to the jugular foramen.

is responsible for the sensitive innervation of the skin over the outer ear's shell. Detailed examination through otoscopy may reveal the presence of tympanic membrane invasion, and otorhinolaryngology may be evidenced in some cases (**Figure 1**). Classical syndromes related to this type of tumor and their respective locations are described in **Table 1**.

3. Pre-operative diagnosis and image classification

Detailed clinical examination is essential for accurate lesion location and scheduling of resection of the intra- and extracranial portions of the tumor. Detailed examinations of the functions of VI, VII, VIII, IX, X, XI, XII and sympathetic trunk should be performed, seeking to predict the intraoperative relations of the tumor with the cranial nerves. Prior to the decision to resect the lesion, evaluation of lesion growth pattern through serial imaging is not considered bad practice. Computed tomography (CT) scans and fine sections (1.0 mm) with reconstruction in the coronal and sagittal planes are essential to delineate the bone relations of the tumor during the chosen surgical approach, as well as the study by the magnetic resonance imaging (MRI) with gadolinium is essential for the evaluation of the neurovascular relationships of the lesion. Tomography can show a smoother surface and have associated bone erosion in cases of schwannoma of the jugular foramen, in contrast to paragangliomas of this region, which demonstrate a more irregular

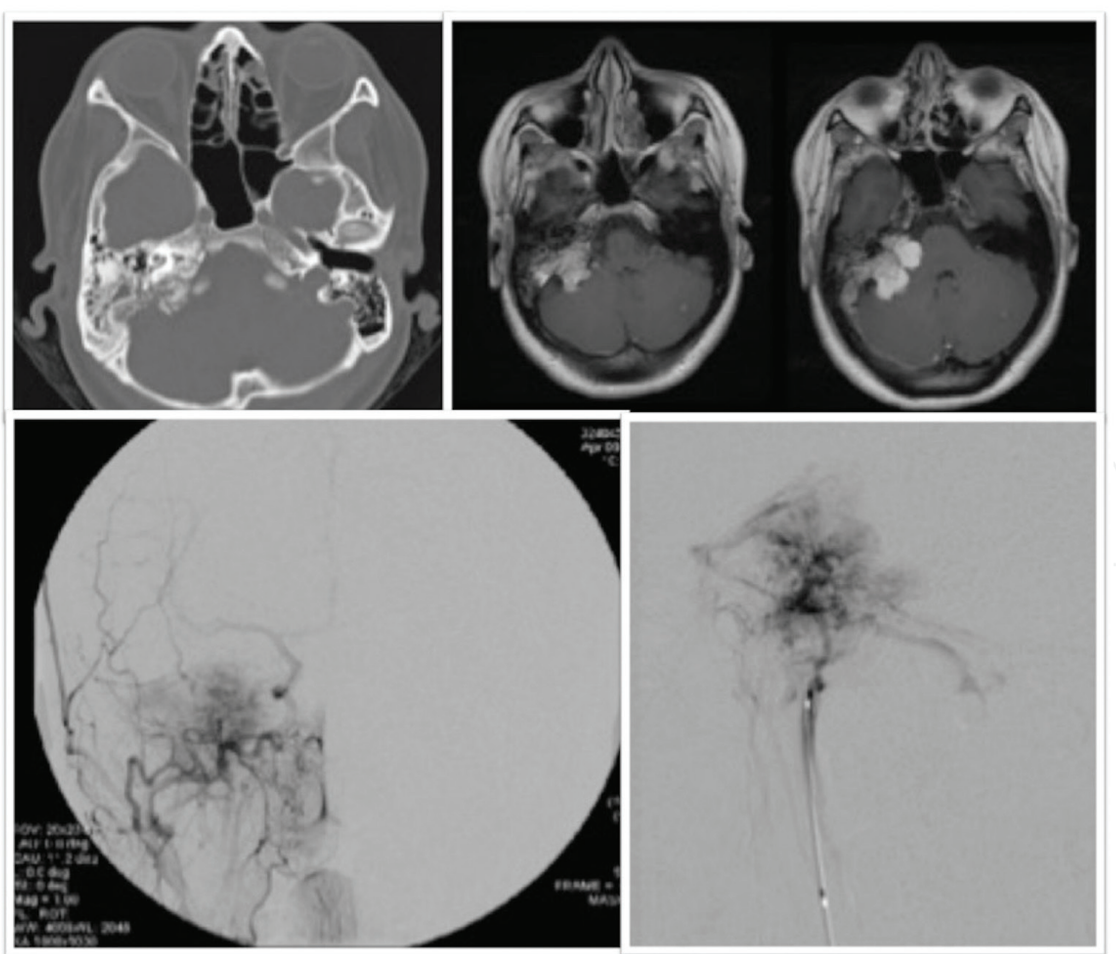

Figure 2.
On the superior left, glomus tumor of the right jugular foramen seen on the tomography (moth-eaten pattern); on the superior right, magnetic nuclear resonance with "salt and pepper" appearance; below, angiography evidencing irrigation of a glomus tumor of the head predominantly by the right ascending pharyngeal artery.

tumoral surface with adjacent bone destruction (**Figure 1**). Neurovascular relationships with the internal carotid artery, cephalic trunk, as well as its intra and extracranial extension are better visualized through the MRI. In T1 weighted images, the glomus tumor is hypo/isointense to the brainstem, and gadolinium injection presents the classic salt and pepper enhancement pattern (**Figure 1**).

Pepper's image represents the hypointense void sign, and the "salt" image represents the hyperintense signal caused by low vascular flow or intratumoral subacute hemorrhage. These tumors typically have a distinct pattern of infiltration, generally following pathways of lower resistance, such as air mastoid cells, vascular channels, Eustachian tube and neural foramina [7, 8].

Angioresonance, angiotomography, or venography may help to demonstrate the type of vascularization of the tumor and its local venous circulation (**Figure 2**). Digital angiography is a prerequisite in patients with extremely vascular lesions, for whom preoperative embolization is necessary to reduce bleeding during surgery. **Table 2** shows the imaging modalities and the peculiar characteristics of the tumors of this region during the preoperative study, aiming to differentiate the three most common lesions of this region. A balloon occlusion test should be performed in case of involvement of the internal carotid artery.

The most relevant laboratory exams prior to surgery are serum and urinary catecholamines, as well as urinary levels of vanilmandelic acid and urinary metanephrines, to determine the possibility of neuroendocrine secretion of the tumor. Five percent of glomus tumors of the jugular foramen (JF) are secretory, and in

Tumor type and radiological features by imaging studies	Computed tomography	Nuclear magnetic resonance	Digital angiography
Glomus tumors	• "Moth-eaten" pattern of temporal bone • Dehiscence of the floor of the tympanic cavity • Erosion of the ossicular chain	• T1 weighted images heterogeneously enhanced with gadolinium "salt and pepper" pattern	• Irrigation of the inferomedial portion of the tumor by the ascending pharyngeal artery • Posterior auricular, stylomastoid and • occipital arteries irrigate the posterolateral portion of the tumor • Internal maxillary artery and ACI may contribute to larger tumors
Schwannoma	• Isodense tumors • Enlargement of the jugular foramen without destruction	• T1 hypointense, T2 hyperintense and moderate enhancement with gadolinium	• Absence of significant irrigation or compression of the jugular vein
Meningioma	• Isodense with intense and homogeneous contrast enhancement • Hyperostosis, intralesional calcifications	• Characteristic and homogeneous enhancement • Presence of dural tail	• Early enhancement with slow emptying

Table 2.
Differential diagnoses by imaging of the main lesions affecting the jugular foramen.

A	Tumors limited to the space of the middle ear
B	Tumors limited to the middle ear or mastoid, without involvement of the infralabirintic space of the temporal bone
C	Tumor involving the infralabirintic space and apical spaces of the temporal bone, with extension to the petrous apex
C1	Tumor with little involvement of the vertical portion of the carotid canal
C2	Tumor invading the vertical portion of the carotid canal
C3	Tumor invading the horizontal portion of the carotid canal
D1	Tumor invading the horizontal portion of the carotid canal
D2	Tumor with intracranial extension >2 cm in diameter

Table 3.
Fisch classification for glomus tumors of temporal region.

I	Tumor involving jugular bulb, middle ear and mastoid
II	Tumor extending below the internal acoustic meatus; may present intracranial extension
III	Tumor extending to the petrous apex; may present intracranial extension
IV	Tumor extending beyond the petrous apex to the infratemporal clivus or infratemporal fossa; may present intracranial extension

Table 4.
Glasscock-Jackson classification for glomus tumors of jugular foramen.

these cases, the preoperative use of alpha and beta-blockers are essential to avoid complications. The most commonly used radiological classification in the preoperative evaluation of patients with glomus tumors of the jugular foramen are Fisch [9] (**Table 3**) and Glasscock-Jackson [10] (**Table 4**). The most used classification of schwannomas of the jugular foramen is Samii's classification, who divided the schwannomas of the jugular foramen into four groups: type A which represents the primary tumors of the cerebellar angle with minimal enlargement of the JF; type B that are the primary tumors of the JF with intracranial extension; type C which have extracranial tumors with extension to the jugular foramen (with clinical signs of involvement of the XII nerve); and type D being the "hourglass" tumors with intra and extracranial involvement [11].

4. Histopathological characteristics

Glomus tumors of the jugular foramen present polygonal epithelioid cells with clear and abundant cytoplasm arranged in small lobes (alveolar arrangement). These cellular clusters were given the name Zellballen, which means "cellular balls" in German. Numerous capillaries can also be observed in the proximity of tumor cells that perform tumor irrigation (**Figure 3**).

5. Surgical approaches

Patients should be routinely monitored, and preoperative antibiotic (30 min before incision) should be administered. The ideal approach for each patient should be chosen after a meticulous preoperative study of lesion's location. Tumors that

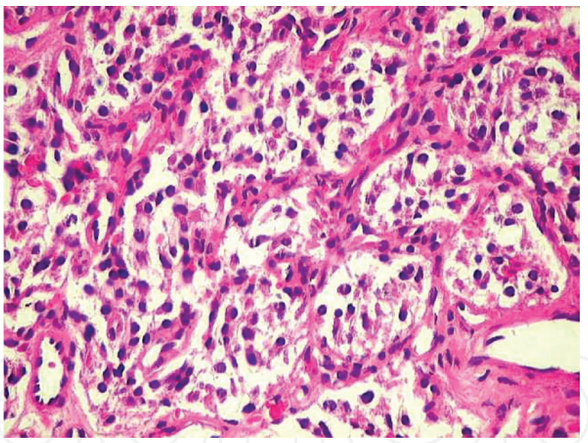

Figure 3.
Typical alveolar pattern with presence of Zellballen, which are classic epithelioid clusters of these tumors.

are primarily intracranial located (Samii type A schwannomas) or tumors with a more significant intracranial extension may be approached by the classic lateral suboccipital retrosigmoid approach. The patient should be ideally positioned in a semi-sited position, since the presence of tumor bleeding gravitates downward, maintaining the surgical field with better visibility throughout the resection. Ideally, central venous access and pre-cordial Doppler should be used to prevent and treat air embolism. Pneumatic compression boots should be used to facilitate venous return. The head should be rotated about 30° to the same side of the lesion, aiming a straight direction in relation to the jugular foramen, as well as a smaller cerebellar retraction, and be fixed in a Mayfield head holder. Discrete flexion helps to expose the suboccipital region, facilitating the positioning of the surgeon during the approach. Vigorous rotation and flexion should be avoided as they may compromise jugular venous return; so a space of two fingers should separate the chin from the ipsilateral clavicle for this purpose. A cutaneous incision should be made with an upper limit on the pinna to the posterior musculature of the neck, maintaining a distance of about 3 cm from the mastoid. After incision of the muscular plane, suboccipital craniectomy is performed, ideally exposing the inferior portion of the transverse sinus and medial portion of the sigmoid sinus. The most crucial step of the craniectomy is its inferior extension to the posterior border of the magnum foramen. The dura mater should be cut in a "C" fashion with its convex portion of the cut close to the transverse and sigmoid sinuses. The dura mater, when cut in this way, not only protects the cerebellar hemisphere from contusions but also prevents dural redundancy in the visual field of the surgeon, also allowing more adequate closure at the end of the procedure.

Next, the arachnoid trabeculae of the Magna cistern of the pontocerebellar angle (PCA) should be cut, and careful aspiration of cerebrospinal fluid should follow, allowing relaxation of the neurovascular structures. Then, the anterior and medial portion of the cerebellum must be carefully covered with cottonoids and retracted medially and superiorly with a spatula, and then fixed in a static position. Dialogue with neurophysiologists is essential during this time of surgery, and repositioning of the spatula may be necessary in case of disturbed auditory brainstem evoked potential. It is essential to determine the exact position of the tumor in relation to the sigmoid sinus and bulb of the jugular vein, because in larger tumors of this region the wall of these vessels may be compromised, with catastrophic bleeding that is difficult to control. Extradural drilling of the jugular foramen helps to define the margins of the tumor, and after this maneuver follows the careful debulking of the tumor.

We carefully proceed with the dissection between the tumor and the lower cranial nerves, as well as its separation of the sigmoid sinus and bulb of the jugular vein when they are involved. The use of ultrasonic aspiration helps significantly during

the resection of these tumors. As the tumor resection is performed, we maintain an incessant dialogue with the neurophysiologist observing the changes during the monitoring of the lower cranial nerves (IX, X, XI, XII). At the end of resection, hemostasis is followed, and defects in the skull base and mastoid should be covered with autologous fat and fibrin glue. The closure in subsequent layers is done, and extubation is monitored by an anesthesiologist in the operating room when there is no cranial nerve injury. Larger tumors (schwannomas B, C, and D of Samii) or glomus tumors involving the infralabirintic space, auditory meatus, jugular bulb, and mastoid need an exposition that allows a more adequate vascular control and more significant bone resection to allow complete or near-total resection of the lesions.

The patient should be ideally placed in the supine position, and his/her head should be rotated about 60–70 degrees contralaterally and fixed with the Mayfield head holder. Due to the need for a more considerable amount of autologous fat graft to later wound closure, we suggest the abdominal preparation for its eventual use. The incision follows from the anterior sternocleidomastoid (ECM) muscle to the retroauricular region, taking care to preserve the larger auricular nerve, since it may be a neural graft donor source for an eventual injury of intracranial nerves. Dissection of the neck allows adequate identification of the lower cranial nerves after their emergence of the skull, as well as carotid artery and internal jugular vein. Suboccipital craniectomy prior to mastoidectomy greatly facilitates control over the sigmoid sinus and jugular bulb, since the dura of the posterior fossa is less adhered to the sigmoid sinus and craniectomy facilitates its identification, reducing the possibility of injury to the sigmoid sinus even during mastoid air cells drilling. The cortical portion of the mastoid can be removed and used for the reconstruction of that region at the end of the procedure, and the mastoid air cells are drilled until a thin layer of bone remains over the sigmoid sinus/jugular vein's bulb. The venous structures are carefully separated, and the retrolabyrinthine bony portion resected until exposure of the posterior fossa dura. Care should be taken when drilling the anterior portion of this approach, avoiding entering the labyrinth and injuring the facial nerve. By drilling the intralabyrinthine portion, the extracranial portion of the tumor can be adequately resected. If there is an intracranial lesion, the opening of the dura mater in the presigmoid retrolabyrinthine region is followed, and the intradural resection is completed. In the case of preoperative anacusis (diagnosed by audiometry), presigmoid translabyrinthine approach, transcochlear approach and even posterior or total petrosectomy can be performed to maximize resection (**Figures 4–9**).

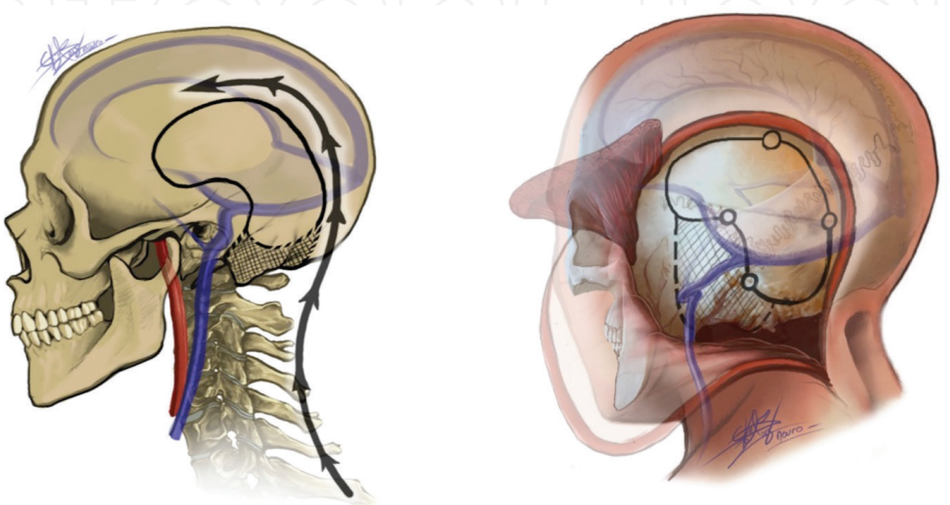

Figure 4.
Skin incision (arrows on the left), muscle dissection and bur hole demarcations (on the right) for a posterior petrosal approach.

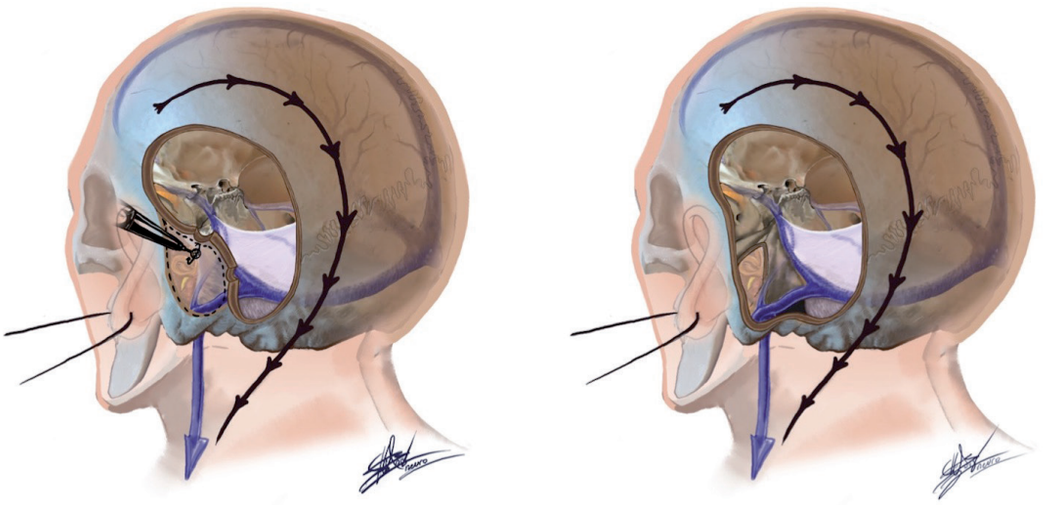

Figure 5.
Skin incision and bur hole demarcations for a posterior petrosal approach after the craniotomy (left side) and after mastoid drilling (right side).

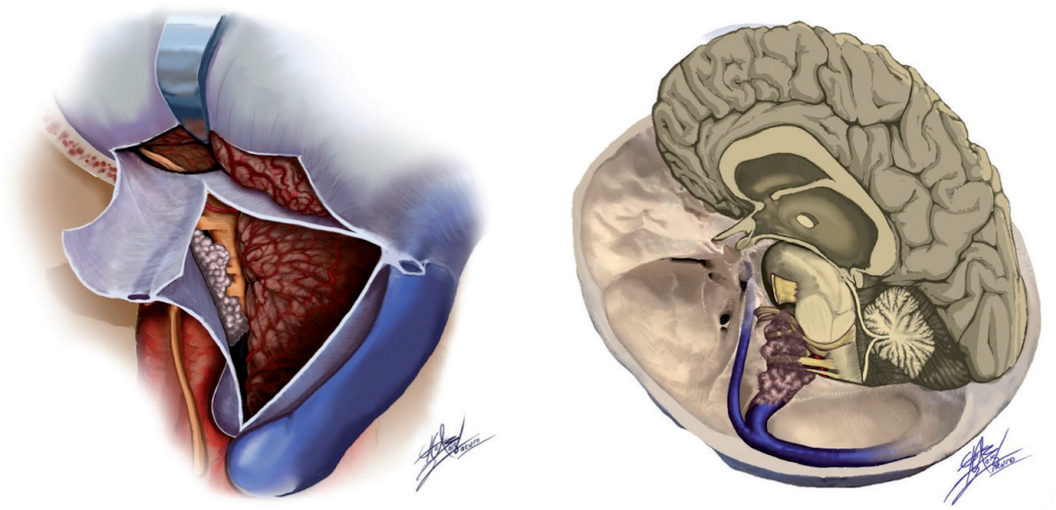

Figure 6.
Presigmoid approach and tentorial incision (on the left). Three-dimensional perspective of the tumor and its relationship with neural, vascular and skull base structures (right side).

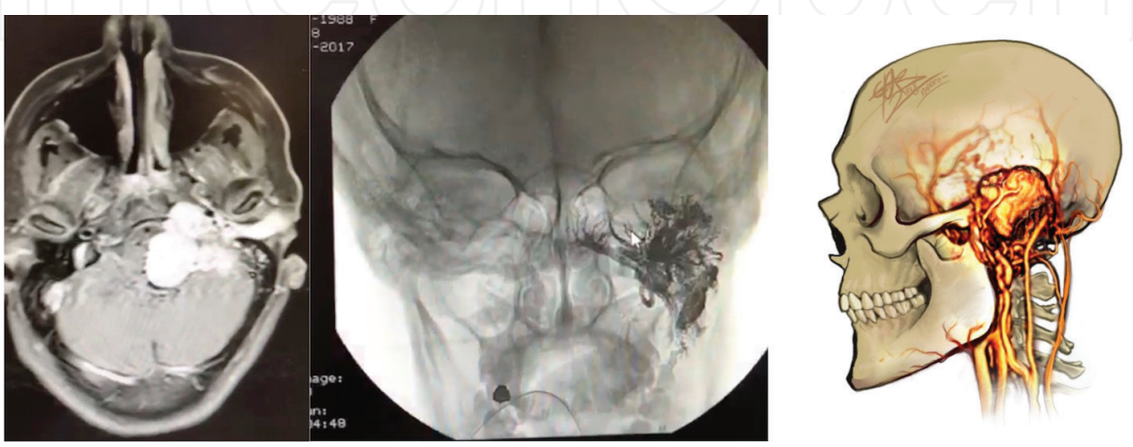

Figure 7.
On the left side, preoperative T1 weighted MRI with gadolinium from a patient operated in our institution; in the middle, preoperative embolization, 1 day before surgery. On the right side, artist's depiction of the tumor and its vascularity.

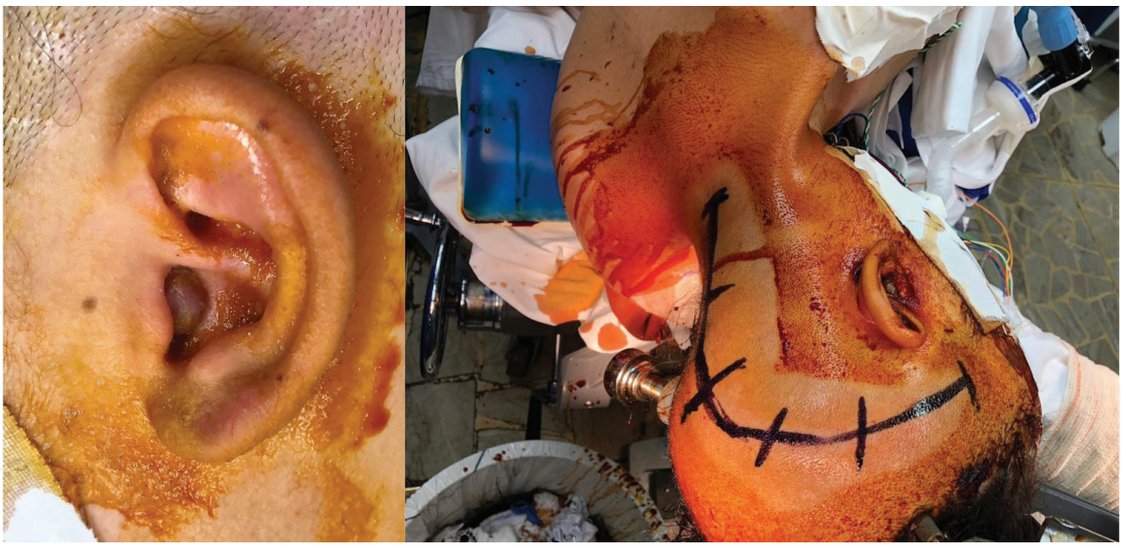

Figure 8.
External auditory meatus invasion by the tumor on the left side and skin incision on the right side.

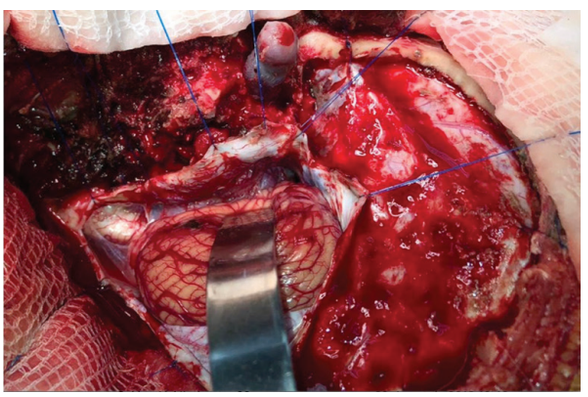

Figure 9.
Approaches' visualization after craniotomy, partial incision of the tentorium.

In cases of infiltration or occlusion of the sigmoid sinus by the tumor, its proximal and distal ligation can be performed, generally without the addition of deficits since the collateral venous drainage is developed by slow tumor growth. After hemostasis and verification of cranial nerve function by neurophysiologists, hemostasis follows. The retroauricular space with the mastoid should be filled with autologous fat graft and fibrin glue. Closure should than be performed.

6. Treatment with radiotherapy

Increasing evidence demonstrates that stereotactic radiosurgery, particularly Gamma-Knife (GK) surgery may play a relevant role in the treatment of these tumors. Results show no change in neurological signs and symptoms in up to 65% of patients [12]. Due to the best results with microsurgery, we prefer microsurgical resection with the use of radiosurgery in residual or recurrent tumor.

7. Postoperative complications and results

Possible complications include facial nerve damage, injury to the lower cranial nerves, injury to the internal carotid artery, excessive bleeding due to lesions of the

venous structures (sigmoid sinus and internal jugular vein), and other complications such as cerebrospinal fluid fistula and infection. Larger tumors (C and D of Fisch) represent a greater surgical challenge, and cranial nerve deficits can be seen postoperatively and in around 6% of cases [13]. Facial paralysis can be seen in around 6% of cases, and cerebrospinal fluid fistula occurs in about 5% of cases [13]. Giant tumors with invasion of multiple structures have a more difficult but feasible resection, and malignant tumors have a reserved prognosis [14].

8. Conclusion

Resection of paragangliomas is possible as long as accurate clinical evaluation and preoperative examinations are rigorously performed. Complications can occur during and after the surgery, and we must be adequately prepared for its treatment. The use of embolization in the preoperative period may considerably reduce bleeding during surgery, but it is not considered an innocuous procedure and may present cranial nerve paralysis due to vasa nervorum obstruction culminating with nerve ischemia. Once again we consider that experience is essential for its effective treatment.

Conflict of interest

Authors declare no conflict of interest.

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