The treatment of jugular foramen tumors has always been a challenge to skull base surgeons. These lesions are relatively rare, located near cranial nerves and important neurovascular structures and are very often highly vascularized. These tumors may involve adjacent structures, such as the jugular bulb, carotid artery, the middle ear, petrous apex, clivus, infratemporal fossa, and posterior fossa. Along the years, several studies were conducted including advances in neuroimaging, techniques of endovascular embolization, neuromonitorization, and surgical techniques to achieve safe resection of these tumors with lower rates of morbidity and mortality, which were quite expressive in the past.

Such improvements, once reached, provided a better outcome. Initially it was restricted to the preservation of patient’s life, and further it was changed to a better control of bleeding, preservation of cranial nerves function, reduction of the number of surgical approaches needed for a complete resection of the tumor, and better postoperative cosmetic results.

**First Descriptions**

Valentin (1840) [1] described a small structure resembling a ganglion, in the initial part of the tympanic nerve, suggesting calling it as “Gangliolum Tympanicum” or intumescentia gangliosa.

Krause (1878) [2] demonstrated that this structure was not a ganglion, but a vascular tissue resembling the carotid body and called it “die Glandula tympanica” [3]. It was located between the perineurium and the periosteum in the initial part of the upper tympanic canal. This structure resembled the “carotid gland” (Glomus caroticum), which led Krause to propose the name of “tympanic gland,” as reported by Von Lushka (1862) [4].
Zettergren and Lindstrom (1951) described the findings of Krause in their study as [5]:

On opening up the canaliculus tympanicum of a human petrous bone, it will be observed that there is a fusiform swelling of the tympanic nerve where it has entered the canal after leaving the petrous ganglion. This swelling is about 4 mm long with a thickness not exceeding 1 mm. When the veins are well filled with blood, its reddish colour makes it resemble a small ganglion (the glangliolum tympanicum); when empty of blood it will have a whitish colour and look like a thickening of the periosteum. – Actually, it is neither the one nor the other. – The substance in question is highly vascularized consisting of a basic framework of connective tissue with elastic fibres. It contains a network of arteries, veins and capillaries. The arteries are branches of the 0.12 mm thick ramulus tympanicus of the ascending pharyngeal artery, which accompanies the tympanic nerve. This highly vascular tissue is characterized by triangular pyramidal or star-shaped perithelial cells of a diameter of 0.007-0.015 mm, varying in number. The nuclei of these cells are about 0.004 mm. Occasionally, such cells may be clustered round winding vessels in tubular formations suggesting the structure of the carotid body. Like the latter and the pineal body, the gland-like organ represents a relic of the history of evolution. To distinguish the tympanic gland formation from the so-called lymph node of the cavum tympani, it may be termed the glandula tympanica branchialis.

These studies have been widely referenced and followed in old handbooks. But, in 1932, the descriptive study of Watzka [6], using four human fetuses, two neonates, two adult guinea pigs, and a 57-year-old woman, categorically denied the existence of these structures. Therefore, the references work of Valentin and Krause disappeared almost completely from the literature.

**First Definitions**

In 1941, during the American Association of Anatomists meeting in Chicago, Guild SR [7, 8] (Fig. 2.1) had rediscovered the nonchromaffin paraganglioma of the jugular bulb and described the glomus tissue as an ovoid body flattened in the adventitia.
of the dome of the jugular bulb, and called these bodies of glomus jugulare. This paraganglionic structure was comprised of capillaries or pre-capillaries interspersed with a number of epithelial cells found along the jugular bulb. In a process of sectioning human temporal bones, Guild reported 50% of this tissue in the jugular bulb. Approximately 25% was found over the course of the tympanic branch of the glossopharyngeal nerve (Jacobson’s nerve) and 25% was found throughout the auricular branch of the vagus nerve (Arnold’s nerve). This aspect explains the existence of “glomus tumors” that occurred both in middle ear (glomus tympanicus tumors) and in the region of the jugular bulb (glomus jugular tumors).

Rosenwasser H (1952) (Fig. 2.2) [9] described the removal of a tumor with severe bleeding from the middle ear, which protruded to the external ear. The histological analysis of tumor proved to be a lesion similar to those found in benign tumors of carotid bodies. In 1945, he published the first description of a paraganglioma of the middle ear and associated these tumors with the glomus jugulare bodies.

Rosenwasser (1952) [10] was the first to suggest a possible relationship between the glomus jugulare and tumors of carotid bodies in the temporal bone. The designation “glomus jugulare tumors” was firstly mentioned by Lattes and Waltner (1949) [11].

The treatment of the jugular foramen tumors has evolved over the years. The inaccessibility of the jugular foramen due to its deep location, and the proximity of cranial nerves and vital vascular structures turn tumors arising in this region extremely challenging, and surgery was often associated with a poor outcome.

Surgery in the 1930s was primarily conducted through a suboccipital approach with removal of bone around the jugular foramen to avoid excessive bleeding [12]. Subtotal resection followed by radiation therapy was generally performed [13, 14]. In the postoperative period the majority of patients had paralysis of lower cranial nerves.
The mobilization of the facial nerve in order to offer a better access to the jugular foramen was first described by Capps (1952) [15] combined with proximal and distal control of sigmoid sinus and jugular vein. However, the attempts to remove the jugular bulb ended with excessive bleeding and poor results.

Chemoreceptor Function

De Castro (1926) [16] was the first to suggest that the carotid body had a chemoreceptor function. Later works of Heymans and Bouckaert (1939) [17], Schmidt and Comroe (1940) [18], and Dripps and Comroe (1944) [19] verified and confirmed the suggestion of de Castro, not only regarding to the chemoreceptor function of carotid paraganglioma, but also certified the existence of this function in paraganglion aortic. These structures are sensitive to changes in pH and in oxygen and carbon dioxide tensions in circulating blood. Under certain conditions they may be of greater importance in the regulation of breathing. It is also interesting to note that Christie, in 1933 [20], showed that the carotid paraganglioma does not contain epinephrine.

Diagnostic and Treatment Refinement

In the 1960s and 1970s, the advent of a better surgical technology has resulted into most accurate diagnosis and better surgical results. These innovations included the surgical microscope, techniques of tumor dissection with microsurgery, bipolar electric cautery, safer neuroanesthesia, arteriography and embolization [21, 22], retrograde venography of the jugular vein [23], computed tomography (CT) [24], and magnetic resonance imaging [25].

Classifications

Surgical removal of glomus tympanicum tumors, with hearing preservation, was first proposed by House and Glasscock [26]. In 1969, McCabe and Fletcher [27] proposed that the size and extent of the tumor would be the determining factors for the choice of a more appropriate surgical approach. Soon after, new classification schemes have been proposed by Fisch [28] and by Jackson et al. [29] based on the size of the tumor, intracranial extension, and surgical viability.

Various classifications for paragangliomas were proposed. The most used were those described by Jackson and Glasscock (1982) [29] and by Fisch (1978) [28]. The Fisch classification was changed in 1981 to include tumors with intracranial extensions.
Ramina et al. (1988) [30] have formulated the Classification of Curitiba with the advantage, over the other classifications, of anticipating surgical difficulties that would be encountered, in addition to being easy to remember, based on the location and extent of the lesion, according to the authors conception.

Evolution of Surgical Technique

During the 1950s, several authors made efforts to treat glomus jugulare tumors, ending in disappointing results in the majority of cases [13, 31]. The complex anatomy of the region of the jugular bulb and the risk of hemorrhage during tumor dissection, in combination with the lack of studies of high definition images to elucidate tumor margins, were significant limitations at that time. In 1951, Weille and Lane [12] suggested the removal of the bone which surrounds the tumor to reduce intraoperative bleeding. Their approach did not take into account that the removal of the jugular bulb was an important risk of hemorrhage from the inferior petrosal sinus.

In the same year, Semmes [32] operated on a patient with a glomus jugulare tumor through the suboccipital approach and reported this case in 1953. Even resecting all the tumor of the posterior fossa, no attempt was made to remove the lesion extension in the mastoid or in middle ear. A year later, in a series of five cases of glomus jugulare tumor reported by Capps [15] one of these patients (the first one) was subjected to an extensive surgical resection. It consisted on the mobilization of the facial nerve (this maneuver had not been described previously), gaining proximal and distal control of the sigmoid sinus and jugular vein, followed by an unsuccessful attempt to remove the jugular bulb. The postoperative complications observed with this patient made Capps to treat the other four patients with radiation therapy alone.

Albernaz and Bucy (1953) [31] reported on the case of a patient with compression of the jugular foramen and hearing loss. The case drew attention to the non-visualization of the tumor at the opening of the dura mater, with abnormalities in the lower cranial nerves and after the local manipulation the patient suffered a cardiac arrest during closure. Only the autopsy revealed a glomus jugulare tumor of 1.0 x 2.0 cm.

Shapiro and Neues (1964) [33] reported their experience with a patient showing recurrent glomus jugulare tumor. They performed a complete resection of the tumor, with the removal of the jugular bulb and translocation of the facial nerve. Unlike previous reports, there was minimal loss of blood with good neurological outcome. Gejrot [23] described a similar procedure performed in 1965 in a series of four patients.

These reports were from established baselines to contemporary surgical techniques. They showed that the extirpation of the tumor, along with the preservation of neuronal function, could be possible. Gejrot [23] gave a fundamental contribution which persists until now as a crucial component of modern surgical treatment of glomus jugulare tumor, stressing the importance of maintenance of the sigmoid sinus medial wall at the jugular bulb, in an effort to protect the cranial nerves running under this wall.
The techniques of preservation of hearing were introduced, mainly by House and Farrior, at the end of the 1960s. House [34] described the removal of the glomus jugulare tumor preserving the bone portion of the auditory canal. This approach does not perform translocation of the facial nerve, exposes the facial recess and the hypotympanum for resection of the tumor. The technique described by Farrior [35], modifying the technique of Shambaugh [36], was very effective for small glomus tumors with medial extension, but was not effective in tumors involving the anterior surfaces and the internal carotid artery.

In the 1970s multidisciplinary approaches of skull base have emerged [29], combining approaches of the lateral skull base with suboccipital craniectomy and mastoidectomy. In 1971, Kempe et al. [37] published a report using suboccipital craniectomy with standard mastoidectomy to remove a tumor that involved both the temporal bone and the posterior fossa. Hilding and Greenberg [38] reported a similar case in the same year including the exposure of the internal carotid artery through the glenoid fossa. Glasscock et al. [39] published their approach using a combination of Shapiro’s technique with a wide exposure of the cranial base and the technique of House using the extended facial recess. Gardner et al. [40] detailed a surgical technique in which the combined approach of the lateral base of the skull was used by a multidisciplinary team. Their approach consisted of the following three phases: (1) exposure of the base of the skull through the neck; (2) removal of the bone within the temporal bone and jugular fossa; and (3) removal of the tumor, followed by the reconstruction of the wound.

In 1977, Fisch [28] introduced the infratemporal approach to obtain access to the Internal Carotid Artery in the temporal bone, which was one of the main limitations of previous approaches, bringing more safety in the treatment of larger glomus tumors by controlling the carotid artery. Al-Mefty et al. (1987) [41] described a lateral infratemporal approach combined with a posterior fossa craniectomy to the removal of giant glomus tumors with large intracranial component. This approach allowed to access tumors thought to be inoperable avoiding the need for multiple surgical stages. Al-Mefty and Teixeira (2002) [42] reported the experience treating glomus jugulare tumors and classified them as tumors of complex type that meet one or more of the following criteria: giant size, multiple paragangliomas, malignancy, evidence of secretion of catecholamines, association with other injuries, previous treatment with adverse outcome, radiotherapy, or the adverse effects of embolization. Other modifications to access the jugular foramen using approaches to the skull base were subsequently defended by Bordi et al. [43], Patel et al. [44], and Liu et al. [45].

**The Contribution of Tumor Embolization**

Despite the improvements in surgical exposure, extreme vascularization of the tumor was still a major challenge during the surgery. The advent of superselective arterial embolization of the jugular foramen tumors published by Hilal et al. (1975) [46]
significantly reduced the tumor vascularization, making surgery safer despite of intraoperative massive bleeding. Murphy and Brackmann (1989) [47] based on the use of preoperative embolization reported a series of 35 patients. They concluded that there was a significant reduction in blood loss and intraoperative time. In addition, the embolization has led to a higher rate of total tumor resection. However, a reduced risk of injury to the cranial nerves was not reached. The morbidity associated with the embolization procedure, the current state of endovascular technology, and experience in interventional radiology have significantly reduced the incidence of stroke and injuries of cranial nerves more seen in the first years of their usage.

The technique for reconstruction of the skull base published by Ramina et al. [48] with rotation of the temporal muscle besides an excellent aesthetic result, also presented a considerable reduction of meningitis and postoperative CSF fistula, avoiding the need for the use of lumbar drain and consequently a shorter hospital stays. The technique was published in 2005 in spite of being used by the authors since 1987.

Radiotherapy and Radiosurgery

The first reports were made in 1973 by Spector et al. [49], who showed that the radiation therapy had relatively little effect on the tumor cells, with the more drastic changes consisting of a marked increase in the connective tissue of the fibrous stroma.

Several other authors have reported that the main effect of radiation therapy is a vascular injury secondary to irradiation [50, 51]. In addition, it has been shown in these studies that the catecholamine secretion is not affected by the radiation application [52].

However, in other studies with preferential radiotherapy an excellent control of the tumor was reached only in rare cases of progression of tumor [3, 53–55].

Two important considerations and worthy of note must be made on the findings of these studies. First, an overwhelming number of patients were followed up for less than five years, and is a well-known fact that recurrent tumors may arise until 25 years after the initial treatment [56]. The second point is that the majority of patients treated with radiation did not present any change in the size of your tumor. Regardless of the limitations of radiation therapy, surgical treatment involves the risks related to the anesthesia and carries the potential risk of injury of cranial nerves. Fractionated irradiation may reduce the risks of actinic complications.

Other irradiation treatment modality that has been currently used is radiosurgery (gamma knife, LINAC and Cyberknife) gamma knife. Foote et al. (1997) [57] published the first report as a preliminary study evaluating the immediate, acute, and chronic toxicity, and the effectiveness of stereotactic radiosurgery in patients with unresectable or partially resected glomus tumors. No acute or chronic toxicity was demonstrated, and eight of nine tumors remained stable in size with mean follow-up of 20 months. Two years later, Eustacchio et al. [58] showed in a series of 10 patients that 40% of patients presented a reduction of the lesion and the rest remained
unchanged at 36 months of follow-up. In a series published by Jordan et al. [59], in 2000, eight patients had no indication for the surgery and were treated with stereotactic radiosurgery. None of them had an increase of the lesion in 27 months of follow-up and one patient had untreatable vertigo requiring hospitalization. Several other studies have been repeating the same results, i.e., controlling the growth and a minority, with regress of the lesion.

The historical developments in the treatment of the jugular foramen tumors can show us that surgery is the first choice of treatment. The treatment with radiotherapy or radiosurgery remains controversial. So far, there is no conclusive data establishing radiation as the ideal primary treatment for all the jugular foramen tumors. We conclude that radiotherapy can have a significant benefit if the patient is unfit for surgery due to advanced age, clinical condition or has significant risk of injury of cranial nerves. Inoperable or partially resectable lesions may be candidates for treatment with radiosurgery.

The knowledge of the historical evolution of anatomical concepts, diagnosis and management is fundamental to understand the current treatment possibilities of these challenging lesions.

References

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Tumors of the Jugular Foramen
Ramina, R.; Tatagiba, M.
2017, XXII, 182 p. 165 illus., 121 illus. in color. With online files/update., Hardcover
ISBN: 978-3-319-43366-0