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Original Article

Microsurgical treatment of large and giant tympanojugular paragangliomas

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Abstract

Background: Tympanojugular paragangliomas (TJPs) are benign, highly vascularized lesions located in the jugular foramen with frequent invasion to the temporal bone, the upper neck, and the posterior fossa cavity. Their natural history, surgical treatment, and outcome have been well addressed in the recent literature; however, there is no consensus regarding the optimal management while minimizing treatment-related morbidity. In this study, we assessed the interdisciplinary microsurgical treatment and outcome of large TJP collected at a single center.

Methods: Out of 54 patients with skull base paraganglioma, 14 (25%) presented with large TJP (Fisch grade C and D). Posterior fossa involvement was present in 10 patients (Fisch D). Eleven patients presented with hearing loss, two patients with mild facial nerve palsy, and two patients with lower cranial nerve deficits. Two other patients with previous surgery presented with tumor regrowth.

Results: Preoperative embolization was performed in 13 cases. Radical tumor removal was possible in 10 patients. Hearing was preserved in four patients with normal preoperative audiogram. The facial nerve was preserved in all patients. Temporary facial nerve palsy occurred in two patients and resolved in long-term follow-up. In three patients, preexisting facial nerve palsy remained unchanged. Persistent vocal cord palsy was present in three patients and was treated with laryngoplasty. The global recovery based on the Karnofsky performance scale was 100% in 10 patients and 90% in 4 patients.

Conclusion: Preoperative embolization and interdisciplinary microsurgical resection are the preferred treatment for selected patients due to high tumor control rates and good long-term results.

Key Words: Embolization, glomus jugulare tumors, jugular foramen, microsurgery, tympanojugular paraganglioma

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INTRODUCTION

Paragangliomas have their origin in paraganglia of the chemoreceptor system. Tympanojugular paragangliomas (TJPs), also known as glomus jugulare tumors, arise from a small group of cells in the adventitia of the jugular bulb. Despite their benign origin, they represent locally aggressive, destructive neoplastic lesions, with frequent invasion of the middle ear, the temporal bone, the upper neck, and through the jugular foramen (JF) into the posterior cranial fossa. Based on their location, size, and extent, they have been classified by Fisch into four categories[1,8] [Table 1].

Treatment of TJP still remains controversial. Fractionated radiotherapy, stereotactic radiosurgery, gamma knife radiosurgery, and cyberknife radiosurgery as the primary treatment revealed high rates of tumor growth control and relatively low morbidity in recent series.[2,4,11,14-19,24,26,45] Surgery for large TJP is challenging due to their high vascularity and close relationship with delicate neural and vascular structures.[1,27,39] However, favorable long-term results can be achieved by combining surgical expertise from specialized neurosurgeons, ENT surgeons, and interventional neuroradiologists in the planning and execution of surgery. In our retrospective study, we present preoperative evaluation, surgical treatment, follow-up management, and long-term results for 14 patients with large TJP (Fisch Class C and D) treated at a single center.

Table 1: Adapted Fisch classification of tympanojugular paragangliomas[1,8]

Class A	Tumor limited to the middle ear cleft
Class B	Tumor limited to the tympanomastoid area with no infralabyrinthine compartment involvement
Class C	Tumor involving the infralabyrinthine compartment of the temporal bone and extending into the petrous apex
Subclass C1	Involvement of the vertical portion of the carotid canal
Subclass C2	Invasion of the vertical portion of the carotid canal
Subclass C3	Invasion of the horizontal portion of the carotid canal
Class D	Tumor with an intracranial extension
Subclass D1	Less than 2 cm in diameter
Subclass D2	Greater than 2 cm in diameter

PATIENTS AND METHODS

Patients

Between January 2003 and March 2014, 14 patients (13 female and 1 male) with TJP were treated in our department. Patient files and images were reviewed in the retrospective study [Table 2]. General medical and neurological condition was assessed preoperatively and several times during the follow-up. The mean age of the 14 patients was 54 years (range 16–78 years). Eleven patients had hearing loss as the presenting symptom. Progressive facial nerve palsy was also present in two patients. Two patients presented with dysphagia and dysarthrophonia because of lower cranial nerve involvement. Two patients who were initially treated surgically in other institutions demonstrated tumor regrowth. Both of them had facial nerve palsy [House–Brackmann (HB) grade V] and lower cranial nerve palsy. No patient presented with an incidence of pathologic catecholamine secretion. Malignant variants with lymph node metastasis were not present in our series.

Imaging

In all patients, pre- and post-operative cranial computed tomography (CT) and magnetic resonance imaging (MRI) with and without contrast media were performed [Figures 1-3]. Multisite high-resolution CT scans allow precise identification of bone destruction and tumor involvement of the mastoid air cells, JF, internal

Table 2: Patient characteristics

Sex	Age	Presenting symptom	Adapted classification according to Fisch	Outcome according to Karnofsky performance scale	Follow-up time
Female	58	Otalgia, hearing loss, facial nerve palsy, dysphagia	C3+D0	100	124
Female	72	Hearing loss	C2+D0	100	88
Female	44	Glossopharyngeal and hypoglossal nerve palsy	C3+D1	100	88
Female	51	Regrowth 17 years after primary surgery	C3+D2	90	85
Female	60	Otalgia, sudden hearing loss	C2+D1	90	78
Female	26	Hearing loss, residual Otitis media	C3+D1	90	72
Female	71	Hearing loss, tinnitus	C2+D1	100	69
Male	67	Regrowth 24 years after primary surgery	C3+D2	90	41
Female	49	Hearing loss	C3+D0	100	36
Female	74	Hearing loss	C3+D1	100	35
Female	67	Hearing loss, facial nerve palsy	C3+D1	90	34
Female	14	Hearing loss	C3+D1	100	28
Female	47	Hearing loss	C3+D0	100	12
Female	28	Hearing loss	C3+D1	100	8

auditory canal, and cochlea. In the case of intracranial extension, MRI is mandatory to assess the relationship of the tumor to the brainstem, cerebrovascular anatomy, and cranial nerves. All patients received cranial digital subtraction angiography (DSA) [Figures 1-3]. DSA is essential to assess feeding vessels and venous drainage of the tumor. Multistage preoperative embolization of the tumor was performed in all except one patient by WW, AR, and SR.

Surgical techniques

Surgery is performed generally with intraoperative electrophysiology including brainstem auditory-evoked potentials and facial nerve monitoring. The patients are placed in the lateral park bench position. The head is fixed a little forwardly flexed in the Mayfield clamp. The shoulders are retracted caudally with tapes to prevent obstruction of the surgical trajectory. Skin incision is made in the shape of a question mark, beginning postauricular to the lateral borders of the sternocleidomastoid muscle. After neck dissection, the internal carotid artery and the jugular vein are identified and ligatures are placed but not tightened. A lateral suboccipital craniotomy and a complete mastoidectomy with removal of bone anterior of the sigmoid sinus are performed. The jugular bulb is widely exposed by complete removal of the mastoid tip.

After opening the posterior and anterior walls of the external auditory canal and removal of the tympanic membrane, tumor within the ear and Eustachian tube and the mastoid cells are removed. In the next step, the facial nerve is skeletonized, but left in a Fallopian bridge [Figure 1d]. The digastric ridge is an important landmark for defining the exit of the facial nerve from the stylomastoid foramen. The Fallopian canal is usually located 12–15 mm deep from the outer cortical surface of the mastoid. We do not routinely transpose the facial nerve. Figure 4 demonstrates the surgical trajectory. Afterward, the sigmoid sinus is closed with suture ligation. The posterior fossa dura is opened and after retraction of the cerebellum, the cerebellomedullary cistern is opened and the intracranial portion of the JF is inspected. [Figure 1c] Often the tumor is partially devascularized by embolization and appropriate exposure. However, the tumor receives a residual supply from the posterior inferior cerebellar artery and other branches of the vertebral artery. Shrinking by bipolar coagulation is performed before debulking, sharp dissection, and tumor removal. The identification of cranial nerves may be difficult in the case of a large TJP compressing the brainstem. In these cases, step-by-step shrinkage and tumor removal permits the identification of the cranial nerves at the brainstem. Care has to be taken not to injure the facial, vestibulocochlear, and lower cranial nerves. We generally perform single-stage resection in the case of intracranial involvement. After wide exposure, the sigmoid sinus along the jugular bulb to the jugular vein is incised. If tumor invasion of the inner layer of the jugular bulb is assumed, it is elevated superiorly with care taken not to injure the lower cranial nerves. Removal of the tumor, infiltrated bone, and dura mater is attempted in all cases. Surgicel packing controls bleeding from the inferior petrosal sinus. After adequate hemostasis, a watertight dural closure should be the goal. If there is a large defect, as in the cases of larger tumors, an alloplastic graft (Tutopatch®) or pericranial flap followed by fibrin glue may be used. An autologous fat graft may be used to pack the mastoid defect. The muscle and skin are closed in several layers. In some cases, a lumbar drain is emplaced for 5–7 days.

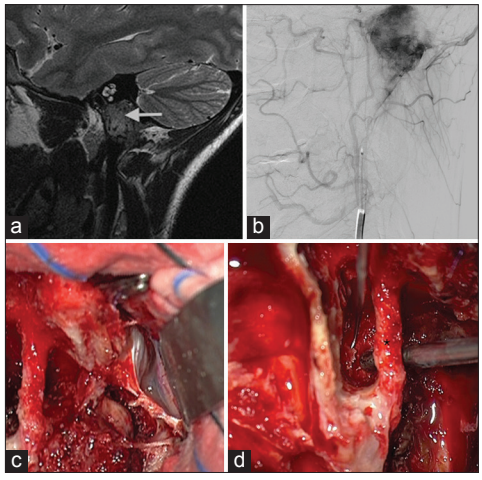

Figure 1: (a) T2-weighted sagittal MRI demonstrating the tumor (arrow) in relation to the labyrinth, cochlea, and the posterior fossa in patient 14. (b) Superselective DSA of the external carotid artery. (c) Intraoperative image of the intra- and extradural jugular foramen. The sigmoid sinus is ligated proximally with hemoclips and removed together with the jugular bulb. (d) Intraoperative image of the facial nerve within the Fallopian bridge. The tumor is removed from the temporal bone without transposition of the facial nerve

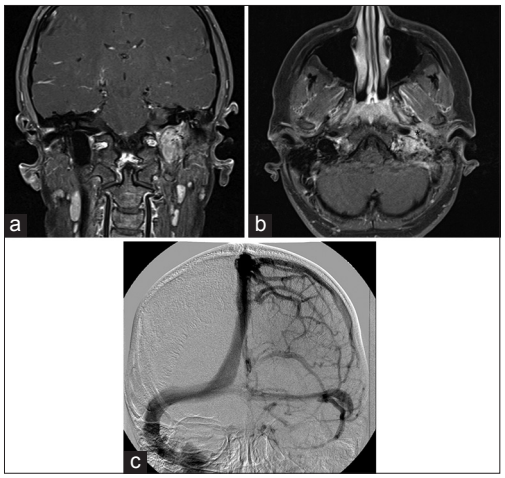

Figure 2: (a) T1-weighted contrast-enhanced coronar MRI demonstrating the tumor in relation to the jugular foramen (patient 12). (b) T1-weighted contrast-enhanced sagittal MRI showing invasion of the horizontal portion of the carotid canal. (c) DSA reveals reduced flow through the left transverse and sigmoid sinus

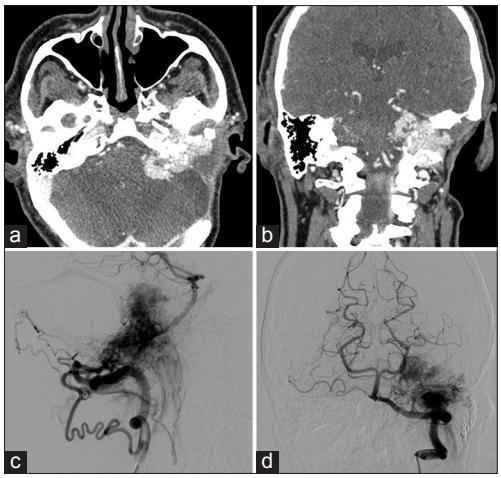

Figure 3: (a, b) Contrast-enhanced CT scan shows regrowing intra- and extradural TJP (patient 8). (c, d) DSA demonstrates feeding vessels of intradural tumor from the vertebral artery

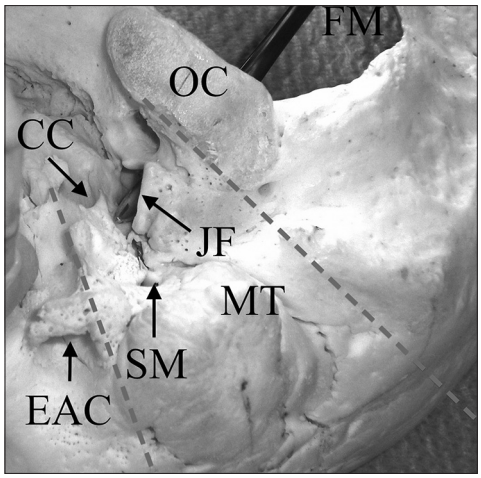

Figure 4: Inferolateral view of the skull with demonstration of our surgical trajectory. FM: Foramen magnum; OC: Occipital condyle; CC: Carotid canal; JF: Jugular foramen; MT: Mastoid tip; SM: Stylomastoid foramen; EAC: External auditory canal

RESULTS

Operative procedure and postoperative course

Radical tumor resection was achieved in 10 patients. Near-total resection was achieved in the remaining four patients. There was no operative and postoperative mortality. There were no major complications such as large vessel injury, intracranial bleeding, or ischemia. There were no cases of postoperative ataxia or temporary limb palsy. In two patients with secondary surgery and in another patient with initial facial nerve palsy HB grade IV due to tumor invasion of the Fallopian canal, the preexisting facial nerve palsy remained unchanged. Temporary facial nerve palsy HB grade V occurred postoperatively in two other patients. A complete sensineural hearing loss was postoperatively observed in two patients. Postoperative lower cranial nerve impairment was present in three patients. One patient (patient 1) developed postoperative severe aspiration pneumonia and required tracheotomy and temporary percutaneous endoscopic gastrostomy. However, she recovered during long-term follow-up.

Long-term outcome

Clinical and radiological follow-up was available for all patients. Radiological follow-up with CT or MRI was performed after 3 months and then every year. Data were collected from the outpatient aftercare and from a phone survey. Patients were followed up for a mean of 57 months (range 8–124 months). There were no mortalities. Recurrence was experienced in one patient (patient 8) in the cohort. After two previous surgeries, he presented with tumor regrowth along the carotid canal into the cavernous sinus. He was referred to radiation therapy. Hearing was preserved in patients with a normal or minimally impaired preoperative audiogram. Otherwise postoperative worsening of hearing did not improve in two patients during long-term follow-up. In three patients, the preoperative facial nerve palsy remained unchanged and in two other patients, postoperative facial nerve palsy resolved during long-term follow-up to HB grade II. Dysphagia resolved in all patients with lower cranial nerve impairment. Three patients with vocal cord palsy suffered chronic hoarseness and were treated by silicone thyroplasty. Overall recovery based on the Karnofsky performance scale after long-term follow-up was 100% in 10 patients and 90% in 4 patients.

DISCUSSION

The combined expertise of neurosurgery, ENT surgery, and interventional neuroradiology in high-volume centers is mandatory for successful surgical treatment of TJP. The present series, together with review of the literature, revealed good long-term results with low morbidity and high tumor control rates.[1,4,6,7,10,28,31,32,34,36-39,42-44]

Clinical considerations

TJP are rare slow-growing, benign, but locally destructive lesions and account for only 0.6% of all head and neck tumors.[32] They are typically found in patients in the fifth and sixth decade, although they can appear at any age. In concordance with the literature, women are affected more often than men.[16,33,38] Malignant variants with lymph node, lung, and liver metastasis are associated with mutations of the succinate dehydrogenase subunit B (*SDHB*) gene and have been reported in 2–3% of all cases.[5,32] Only 1–3% of TJPs are associated with hypertension and tachycardia caused by catecholamine secretion.[32] However, preoperative assessment for catecholamine secretion by the tumor should be performed in all patients to avoid perioperative wide fluctuations of blood pressure and tachycardia. In case of catecholamine-secreting tumors, pretreatment is warranted and an extensive workup should be performed to exclude the possibility

of a synchronous pheochromocytoma or a sympathetic paraganglioma.[1,3,27,40] Symptoms relate to the location of the tumor and invasion of the neural and vascular structures. Similar to other series, pulsatile tinnitus and hearing loss were the most prevalent initial symptoms in our series, caused either by impairment of vibration of the ossicles or invasion of the cochlea. Distortion or invasion of the lower cranial nerves may result in paralysis of the tongue, dysfunctional swallowing, and disturbed vocal cord function.[5,32] A less-frequent symptom may be affection of the facial nerve. Further growth in the posterior fossa may lead to cerebellar and/or brainstem compression and even to occluding hydrocephalus. Symptoms of this usually range from gait disturbance, ataxia, and hemiparesis to reduced consciousness.[10] Despite the high vascularity of TJP, intracranial hemorrhage from a paraganglioma has been only published once.[49] The time interval between the first symptom and diagnosis is estimated to be 4–6 years.[26]

Treatment

In a prospective study by Jansen *et al*., tumor growth was observed in 60% of the paragangliomas and the median tumor doubling time was 4.2 years with a range of 0.6–21.5 years.[22] Therefore, a wait and scan strategy for patients with TJP has been proposed, based on older series with poor surgical outcome.[46] With advancement of microsurgical techniques and intraoperative monitoring, this strategy cannot be further supported, and observation should only be reserved for selected patients without significant symptoms and serious morbidity.

Endovascular occlusion of TJP is performed by superselective catheterization of the supplying branches and transarterial embolization. Because of the complex angioarchitecture with multiple, small feeding branches, and anastomosis between the internal carotid artery, the external carotid artery, and the vertebral artery, embolization of large tumors is challenging. The blood supply of TJP is mainly derived from the ascending pharyngeal artery, the occipital artery, and the posterior auricular artery. In case of intracranial extension (Fisch Class D), they can be supplied by the clival meningeal branches of the carotid artery and the meningeal branches of the vertebral artery. TJPs extending intradurally in the posterior fossa are supplied by the posterior inferior cerebellar artery and the anterior inferior cerebellar artery.[29,47] Endovascular embolization of the feeding arteries results in significant reduction of tumor size, tumor consistency, and blood loss during operation.[27,38,47] These effects improve the surgical conditions similar to cerebral arteriovenous malformation (AVM) in terms of tumor exposure and the identification of anatomical structures during surgery.[20,30,43] Embolization as a single treatment represents a merely palliative option due to a high rate of revascularization.[35,47]

Surgery for large TJP is demanding because of its close anatomical relationship and involvement of the internal carotid artery, sigmoid sinus, jugular bulb and internal jugular vein, lower cranial nerves, cochlea, labyrinthine, and the Fallopian canal. Therefore, the surgical approach for complex TJP represents one of the most difficult skull base approaches. Many approaches depending on the anatomical tumor location at the JF have been described in the literature.[12,27,33,36]

Extensive lateral approaches have been frequently used in the past such as the infratemporal approach Fisch type A.[1,8,23,33,35,39,38] The key elements of this approach are anterior rerouting of the facial nerve and the permanent obliteration of the middle ear space. This approach allows wide exposure and surgical control of the internal carotid artery (ICA) with coagulation or ligation of the afferent vessels during tumor removal.[23,33,39,38] The infratemporal approach type A gives access to large extradural TJP. Disadvantages include hearing loss and temporary or permanent facial nerve palsy.[6,7,23,33,35,38,39] Therefore, the use of anterior transposition of the facial nerve is controversial.[6,7,27] Many modifications of the infratemporal type A approach have been published in the literature.[1,8,23,33,35,38,39] Liu *et al*. proposed full skeletonization of the facial nerve without anterior transposition.[6,7,27] During surgery, the facial nerve is translocated anteriorly to obtain a better exposure of the ICA. However, any degree of transposition may be associated with facial nerve palsy.[6,7,27] Furthermore, Borba *et al*. described the infralabyrinthine approach without rerouting of the facial nerve.[6,7,27] According to our experience, if the facial nerve is not infiltrated by the tumor, it is not necessary to remove it from its bony canal. We routinely performed a retro- and infralabyrinthian approach and the Fallopian bridging technique that allows two surgical routes anterior and posterior of the facial nerve. Even large TJP type C2 and C3 can be removed by this approach using standard microsurgical techniques and high magnification under the operating microscope. Moreover, the infratemporal approach type A does not permit access to the intradural part of the JF. Many authors, therefore, prefer a two-staged procedure for tumors invading the posterior fossa.[35,38,43] In concordance with other series, we combined the retro- and infralabyrinthian approach with a retrosigmoid craniotomy and generally performed a single-stage resection in the case of posterior fossa involvement.[10,27,36] More recently, Bruneau and George have described the juxtacondylar approach to TJP.[9] The juxtacondylar approach permits access to the posterior and inferior part of the JF via a transcervical route with proximal control of the vertebral artery. Advantages are control of major vessels and lower cranial nerves and limited petrous bone drilling. However, this approach allows limited access to the superior and anterior part of the JF. Also, the removal

of the occipital condyle may result in chronic neck pain and even craniocervical instability.[9] Recent technical advances in endovascular devices and microsurgical instruments have resulted in the development of less-invasive approaches and less morbidity. However, due to the highly variable extension of especially large TJP, the surgical approach should be tailored individually based on the tumor location and the preference of the surgical team.

Cranial nerve injury is a main source of postoperative morbidity. Sen *et al*. performed a histological study of the normal anatomic features and compared the results with the pathological anatomic features affected by paragangliomas.[41] They demonstrated histologically that TJP may invade the neural tissue of the lower cranial nerves, as well as the adventitia of the internal carotid artery. These findings confirm our observations that complete resection of TJP is not feasible without cranial nerve deficits if the tumor invades the nerve. If the patients present preoperatively with lower cranial nerve deficits, they are able to compensate very well for postoperative nerve injuries. In their series, Sen *et al*. found that tumor infiltration of the cranial nerves may occur despite normal preoperative nerve function. In these cases, postoperative deficits take much longer to compensate for and represent serious morbidity.[41] Postoperative care and rehabilitation includes special attention to swallowing difficulties with prolonged nasogastric tube feeding or temporary gastrostomy. In case of paralysis of the lower cranial nerves, early laryngoplasty should be performed.

TJPs are relatively radiosensitive oncotypes and fractionated radiotherapy consisting of routine treatment schedules with 45–55 Gy were frequently used as a primary or a salvage treatment modality.[13,45] The most significant effect of radiotherapy is related to a radiation-induced fibrosis with obliteration of the vascular supply and not to direct destruction of tumor cells.[13,18,48] Thus, it is important to re-emphasize that radiotherapy only achieves tumor control and not a cure. Complications include radiation-induced osteonecrosis of the temporal bone, mucositis, alopecia, and radionecrosis of neural tissue.[13] Radiation-induced carcinogenesis has also been reported in the literature.[25] Recent studies have explored radiosurgery for TJP as a primary treatment.[2,4,11,14-18,24,26,45] The beneficial effects of radiosurgery are comparable to their application on cerebral arteriovenous malformations. The precise stereotactic localization and the combined steep dose gradient outside the target volume allow the application of a large single doses to a precisely defined lesion.[2,14] While radiosurgery alone is appropriate for smaller tumors, in larger tumors, especially, the potential risks of wide field radiation are still major concerns. Stereotactic radiosurgery revealed high rates of tumor growth control and relatively low morbidity in recent series.[2,4,11,14-18,24,26,45] Their results are supported by two meta-analyses that maintain the advantage of radiotherapy including radiosurgery of TJP compared to microsurgery.[21,45] The evidence is mainly based on retrospective studies. The diverse range of data presentation in the literature including tumor size and poor surgical outcome in some studies are still major limitations of such results. Also, longer follow-up periods are required to exclude later resumption of growth or transformation into a more aggressive tumor.

CONCLUSIONS

TJPs are surgically challenging lesions. Preoperative embolization and interdisciplinary microsurgical resection in specialized centers are the preferred treatment for selected healthy patients. There may be also a definite role for radiotherapy in patients with preserved cranial nerve function, recurrent tumors, and patients with serious preexisting medical conditions. However, the definite decision must be based on a precise preoperative assessment and the results of a detailed preoperative discussion with the patient.

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