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Preoperative Endovascular Embolization of Glomus Jugulare Tumors: A Retrospective Case Series of 22 Embolizations in 20 Patients and Literature Review

Embolização endovascular pré-operatória de tumores de glômus jugular: Uma série de casos retrospectiva de 22 embolizações em 20 pacientes e revisão da literatura

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Abstract

Objective Glomus jugulare tumors, or tympanojugular paragangliomas, are rare, highly vascularized skull base tumors originated from paraganglion cells of the neural crest. With nonabsorbable embolic agents, embolization combined with surgery has become the norm. The authors assess the profile and outcomes of patients submitted to preoperative embolization in a Brazilian tertiary care hospital.

Methods The present study is a single-center, retrospective analysis; between January 2008 and December 2019, 22 embolizations were performed in 20 patients in a preoperative character, and their medical records were analyzed for the present case series.

Results Hearing loss was the most common symptom, present in 50% of the patients, while 40% had tinnitus, 30% had dysphagia, 25% had facial paralysis, 20% had hoarseness, and 10% had diplopia. In 7 out of 22 embolization procedures (31%) more than a single embolic agent was used; Gelfoam (Pfizer, New York, NY, USA) was used in 18 procedures (81%), in 12 of which as the single agent, followed by Embosphere (Merit Medical, South Jordan, UT, USA) (31%), Onyx (Medtronic, Minneapolis, MN, USA) (9%), and polyvynil

Keywords
- endovascular procedures
- glomus jugulare
- therapeutic embolization

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alcohol (PVA) and Bead Block (Boston Scientific, Marlborough, MA, USA) in 4,5% each. The most common vessel involved was the ascending pharyngeal artery, involved in 90% of the patients, followed by the posterior auricular artery in 15%, the internal maxillary artery or the occipital artery in 10% each, and the superficial temporal or the lingual arteries, with 6% each. Only one patient had involvement of the internal carotid artery. No complications from embolization were recorded.

Conclusions Preoperative embolization of glomus tumors is safe and reduces surgical time and complications, due to the decrease in size and bleeding.

Resumo

Objetivo Tumores de glômus jugular, ou paragangliomas timpanojugulares, são tumores de base de crânio raros, altamente vascularizados, originados das células paragangliônicas da crista neural. Com agentes embólicos não-absorvíveis, embolização combinada com cirurgia se tornou a norma. Os autores avaliam os perfis e desfechos de pacientes submetidos a embolização pré-operatória em um hospital terciário brasileiro.

Métodos O presente estudo é uma análise retrospectiva realizada em centro único; entre janeiro de 2008 e dezembro de 2019, 22 embolizações foram realizadas em 20 pacientes em caráter pré-operatório. Seus registros médicos foram analisados para a presente série de casos.

Resultados Hipoacusia foi o sintoma mais comum, presente em 50% dos pacientes, enquanto 40% tinham tinnitus, 30% tinham disfagia, 25% tinham paralisia facial, 20% tinham rouquidão e 10% tinham diplopia. Em 7 das 22 embolizações (31%), mais de 1 agente embólico foi utilizado; Gelfoam (Pfizer, Nova York, NY, EUA) foi usado em 18 procedimentos (81%), em 12 dos quais como agente único, seguido de Embosphere (Merit Medical, South Jordan, UT, EUA) (31%), Onyx (Medtronic, Minneapolis, MN, USA) (9%), e polyvynil alcohol (PVA) e Bead Block (Boston Scientific, Marlborough, MA, EUA) (4,5% cada). Os vasos mais comumente acometidos foram a artéria faríngea ascendente (90% dos pacientes), seguida da artéria auricular posterior (15%), a artéria maxilar interna e a artéria occipital (10% cada) e as artérias temporal superficial e lingual (6% cada). Apenas um paciente teve acometimento da artéria carótida interna. Não houve complicação secundária a embolização.

Conclusão Embolização pré-operatória de glômus jugular é segura e reduz tempo e complicações cirúrgicas, pela redução em tamanho e sangramento.

Palavras-chave
- procedimentos endovasculares
- gomo jugular
- embolização terapêutica

Introduction

Glomus jugulare tumors, more recently described as tympanojugular paragangliomas, are rare, highly vascularized though slow-growing skull base tumors that originate from paraganglion cells of the neural crest.[1] Even though their histological substrate is benign, they often present as aggressive lesions, invading the temporal bone, the upper neck, the middle ear, and the jugular foramen itself.[2] The approach for these lesions remains controversial: while radiosurgery, radiotherapy, and gamma knife radiosurgery as primary treatments showed high rates of growth afterwards, they had low morbidity[3–7]; meanwhile, neurosurgeons are often faced with challenges due to the rich vascularization of the lesions as well as to the intimate relationship with neural and vascular structures.[1,2,8,9] To minimize the risks for the patient and ensure total resection, a combined approach involving neurosurgeon, interventional radiologist, and ear, nose, and throat (ENT) surgeon is ideal.[10] After the introduction of modern, nonabsorbable embolic agents, embolization combined with surgery after at least 2 days has become the norm. Since 2008, the authors have treated 20 patients with this combined approach; in the present series, we present the results of a retrospective analysis of this group.

Patients and Methods

Between January 2008 and December 2019, 22 paraganglioma embolizations were performed in 20 patients in a preoperative character in the Neurological Institute of Curitiba (INC, in the Portuguese acronym), a tertiary reference center in Southern Brazil. There were 11 women (55%) and 9 men (45%), with a mean age of 51.25 ± 16.3 years old (range: 23 to 87 years old). A total of 50% of the lesions were on the

right side. All patients with glomus jugulare who presented to our service underwent both embolization and surgery afterwards. Every single patient is still alive and in regular follow-up with the team.

The present study is a retrospective analysis of a series of cases treated by the same team (neurosurgeons and interventional neuroradiologists); the procedures were performed in either a Siemens AXIOM system (Siemens, Munich, Germany) (before 2013) or a Philips Allura Xper FD20 system (Philips, Amsterdam, Netherlands) (since 2013). Given the retrospective nature of the present case series, institutional approval was obtained from the Committee of Ethics in Research of our institution (approval protocol 4.211.396) but the need to obtain a consent form was waived.

As previously reported by the group, embolization of glomus jugulare tumors was performed through super selective catheterization of feeder arteries between 3 to 5 days prior the surgical procedure; feeders from the external carotid artery (ECA [ascending pharyngeal, internal, maxillary, and occipital arteries, for instance]) and internal carotid artery (ICA [through carotid tympanic branches]) were embolized with gelatin foam (Gelfoam; Pfizer, New York, NY, USA), polyvinyl alcohol foam, or polyvynil alcohol (PVA) (Ivalon; Nycomed, Paris, France) particles, embolic spheres (Embosphere; Merit Medical, South Jordan, UT, USA), Bead Block (Boston Scientific, Marlborough, MA, EUA), and ethylene-vinyl alcohol copolymer, or EVOH (Onyx; Medtronic, Minneapolis, MN); the choice of the materials was subject to medical indication as well as to authorization by the health insurance provider of each patient. The aim of the treatment was radical and complete tumor removal in one surgical procedure with preservation of the cranial nerves.[10]

Results

Of the 20 patients who presented to our department for evaluation, 11 (55%) had already been submitted to previous neurosurgical procedures (►**Table 1**). Hearing loss was the most common symptom, present in 10 patients (50%), while 8 (40%) had tinnitus, 6 (30%) had dysphagia, 5 (25%) had facial paralysis (classified as House-Brackmann [HB] 2 in 2 patients, HB 3 in 1 patient, and HB 4 in 2 patients), 4 (20%) had hoarseness, and 2 (10%) had diplopia. While 11 patients (55%) reported no previous medical condition, hypertension was found in 6 patients (30%), diabetes and dyslipidemia were found in 2 patients each (10%), clinically-diagnosed generalized anxiety, tabagism, and atrial fibrillation were reported in 1 patient each (5%).

In 7 out of 22 embolization procedures (31%) more than a single embolic agent was used; Gelfoam was used in 18 procedures (81%), in 12 of which as the single agent, followed by Embosphere in 7 procedures (31%), Onyx in 2 procedures (9%), and PVA and Bead Block in 1 each (4,5%).

Concerning the arterial feeder, 5 patients (25%) had multiple arteries involved; the most common vessel was the ascending pharyngeal branch of the external carotid artery, involved in 18 patients (90%), followed by the posterior auricular artery in 3 cases (15%), the internal maxillary artery and the occipital artery in 2 cases each (10%), and the superficial temporal and the lingual arteries, with 1 case each (5%). Only 1 patient (5%) had involvement of the ICA; she was submitted to 3 procedures, and after the 1st the ICA supply was terminated; later, she underwent direct lesion injection of Onyx as well, our sole procedure with direct percutaneous injection of any agent.

The embolization was deemed total by the interventionist in 13 procedures (59%), partial in 4 procedures (18%), and was not reported in the remaining 5 (►**Table 2**). No complications were reported after the embolizations. Surgical resection, on the other hand, was considered total in 12 (60%) of the patients and partial in 8 (40%). Further microsurgery was indicated in 2 patients (10%), and stereotactic radiosurgery (Leksell Gamma Knife Perfexion; Stockholm, Sweden), in 4 patients (20%).

Postoperative symptoms included dysphagia in 4 patients (20%), worsening of hearing loss in 3 patients (15%), cerebrospinal fluid (CSF) leak in 2 patients (10%), and worsening of facial paralysis or surgical site granuloma in 1 patient each (5%), with tracheal laceration, necrosis of skin graft, and bone exposition in a specific patient. All patients are alive to this date; ►**Figs. 1** and **2** provide clinical examples.

Discussion

While rare, slow-growing and histologically benign, glomus jugulare tumors are considered aggressive lesions; invasion of temporal bone, of the middle ear, of the neck, and of vascular structures is common. Their most defining aspect is their hypervascularization, which directly influences both imaging and treatment.[1,2]

Concerning imaging features, preoperative digital subtraction angiogram (DSA) is still a vital component of both a correct diagnosis of glomus jugulare tumors, allowing for differential diagnosis with schwannomas, for instance, as well as of the dynamic evaluation of the lesion, identifying a hypervascular mass with rapid arterial blushing, the feeder arteries, which are often hypertrophied, as well as a possible involvement of the internal carotid artery, and venous drainage, often enlarged, possible compression or enlargement of the jugular vein, not to mention size and possible occlusion of the jugular bulb or involvement of the middle ear.[10,11] Magnetic resonance imaging (MRI) with gadolinium injection displays the characteristics, size, and extension of the lesion, as well as its relationship with neighboring structures.[12,13] Glomus jugulare tumors appear as well vascularized lesions, with heterogeneous gadolinium enhancement on T1WI in the typical "salt and pepper" pattern, representing dark vascular flow voids and intense contrast enhancement; on T2WI, the tumors are heterogeneous with dark flow voids.[11,14] Computed tomography (CT) may be useful for analysis of neighboring bone structures and possible invasion[11]; a noncontrast CT typically shows a poorly defined soft tissue mass along with a destructive bony aspect within the jugular foramen.[12,15,16]

Concerning the treatment rationale, tumor embolization is a centenary idea; Dawbarn first described in 1904 a

Table 1 Baseline characteristics of the patients

Patient	Age (years old)	Sex	Previous diseases	Clinical features	Lesion laterality	Arterial supply	Previous surgery
1	87	Female	Arterial hypertension, dyslipidemia	Hearing loss, vertigo, facial paralysis (House-Brackmann 3), hoarseness, cough, dysphagia	Right	Ascending pharyngeal artery, posterior auricular artery	Yes
2	49	Male	Arterial hypertension, tabagism	Hearing loss, dysphagia	Right	Posterior auricular artery	Yes
3	63	Female	Not reported	Not reported	Left	Ascending pharyngeal artery, occipital artery	Not reported
4	37	Male	Not reported	Not reported	Right	Superficial temporal artery	Not reported
5	65	Female	Arterial hypertension	Tinnitus	Right	Ascending pharyngeal artery	No
6	51	Female	None	Hoarseness	Left	Ascending pharyngeal artery	No
7	70	Female	None	Hearing loss, tinnitus, facial paralysis (House-Brackmann 2)	Right	Ascending pharyngeal artery	Yes
8	41	Male	None	Asymptomatic (incidental finding)	Right	Ascending pharyngeal artery	Yes
9	60	Female	None	Dysphagia, diplopia	Right	Ascending pharyngeal artery	Yes
10	32	Female	None	Hearing loss, hoarseness	Left	Ascending pharyngeal artery	No
11	36	Male	None	Hearing loss, facial paralysis (House-Brackmann 2), diplopia	Left	Ascending pharyngeal artery	Yes
12	40	Male	Arterial hypertension	Tinnitus	Right	Ascending pharyngeal artery	Yes
13	81	Female	Arterial hypertension, type 2 diabetes	Facial paralysis (House-Brackmann 4), hearing loss	Left	Ascending pharyngeal artery, maxillary artery	Yes
14	55	Male	Generalized anxiety	Dysphagia, hoarseness	Left	Ascending pharyngeal artery	Yes
15	55	Female	None	Tinnitus, dysphagia, facial paralysis (House-Brackmann 4), hearing loss, lesion extrusion through external acoustic meatus	Right	Ascending pharyngeal artery, maxillary artery, internal carotid artery	Yes
16	23	Male	None	Hearing loss, tinnitus	Right	Ascending pharyngeal artery	No
17	44	Male	None	Hearing loss	Left	Ascending pharyngeal artery, lingual artery	Yes
18	60	Female	Arterial hypertension, atrial fibrillation, type 2 diabetes, dyslipidemia, interatrial communication	Tinnitus, auricular discomfort	Left	Ascending pharyngeal artery, posterior auricular artery	No
19	43	Female	None	Tinnitus, hearing loss, facial paresthesia	Left	Ascending pharyngeal artery, occipital artery	No
20	33	Male	None	Tinnitus, dysphagia	Left	Ascending pharyngeal artery	No

Table 2 Embolization and microsurgical characteristics of the patients

Patient	Embolic agent	Complete embolization?	Complications from embolization	Complications from surgical resection	Outcome	Necessity of new surgical approach
1	Gelfoam	Yes	None	None	Complete resection	None
2	PVA	Yes	None	Complete hearing loss	Complete resection	None
3	Embosphere and Gelfoam	Yes	None	None	Complete resection	None
4	Gelfoam	Yes	None	None	Complete resection	None
5	Embosphere and Gelfoam	Yes	None	Local granuloma	Incomplete resection	Open surgery
6	Embosphere	Yes	None	None	Incomplete resection	Gamma Knife radiosurgery
7	Embosphere and Gelfoam	Not described	None	Not reported	Complete resection	None
8	Embosphere and Gelfoam	Not described	None	None	Incomplete resection	Open surgery
9	Embosphere and Gelfoam	Not described	None	Cerebrospinal fluid leak	Incomplete resection	Gamma Knife radiosurgery
10	Gelfoam	Not described	None	None	Complete resection	None
11	Embosphere and Gelfoam	Partial	None	None	Complete resection	None
12	Gelfoam	Yes	None	None	Complete resection	None
13	Gelfoam	Yes	None	Worsening of facial paralysis (House-Brackmann 5)	Incomplete resection	Gamma Knife radiosurgery
14	Gelfoam	Not described	None	Worsening of dysphagia	Complete resection	None
15	Gelfoam - first embolization	Partial	None	Tracheal laceration, necrosis of skin graft, bone exposition	Incomplete resection	None
	Gelfoam - second embolization	Partial	None			
	Onyx - third embolization (intralesional)	Partial	None			
16	Gelfoam	Yes	None	Cerebrospinal fluid leak, worsening of hearing loss, dysphagia, and tinnitus	Incomplete resection	Gamma Knife radiosurgery
17	Gelfoam, Onyx, Bead Block	Yes	None	None	Incomplete resection	None
18	Gelfoam	Yes	None	None	Complete resection	None
19	Gelfoam	Yes	None	Dysphagia	Complete resection	None
20	Gelfoam	Yes	None	Worsening of dysphagia	Complete resection	None

Abbreviation: PVA: polyvynil alcohol.

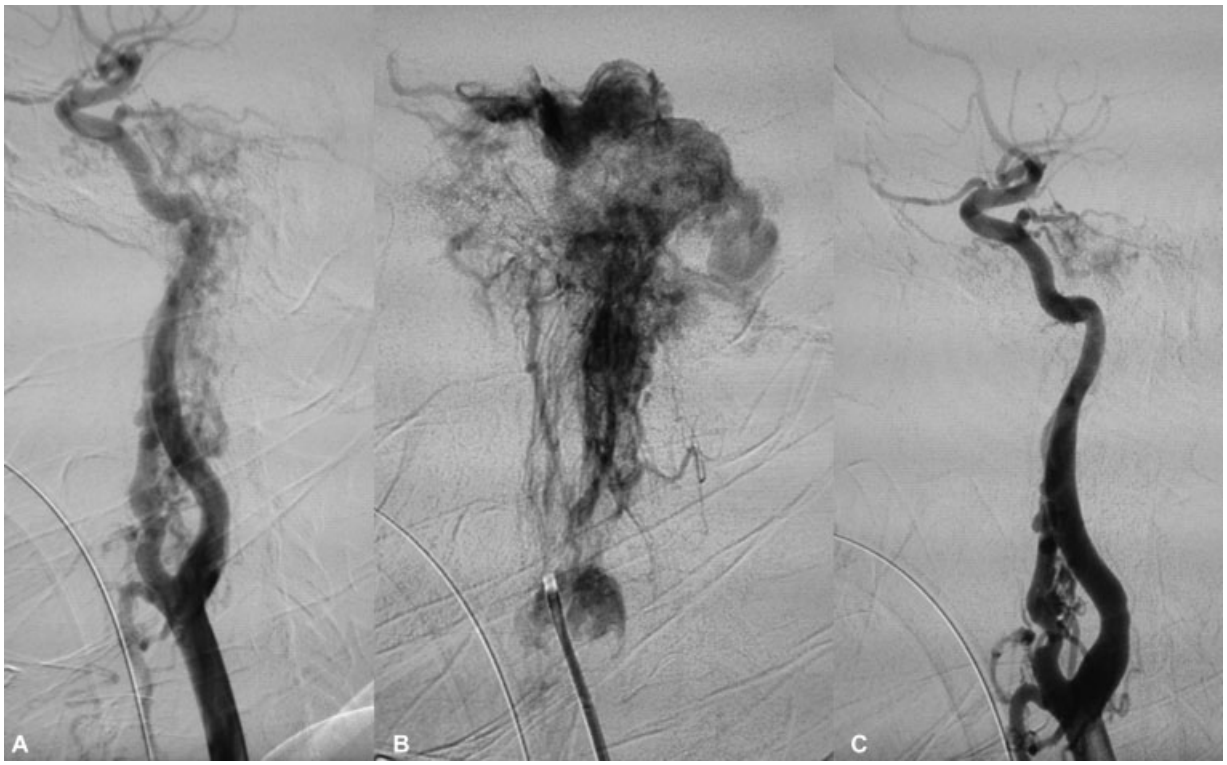

Fig. 1 A 36-year-old male who first presented with hypoacusia, with later development of HB 2 facial paralysis, had been previously operated without embolization. He had no known comorbidities. He was evaluated at our institution and was submitted to embolization of glomus jugulare tumor with Gelfoam and Embosphere by selective catheterization of the left ascending pharyngeal artery, which was shown by angiography to be the main feeder. The patient had no complications from the procedure and underwent surgery without complications as well, achieving complete resection and needing no further treatment. All images are lateral DSA acquisitions during embolization. A: early arterial phase of vast left side hypervascularized, invasive tumor fed by the ascending pharyngeal artery. B: late arterial phase after selective catheterization of the ascending pharyngeal artery. C: control early arterial acquisition showing significant decrease of the lesional blood supply.

"starvation plan" for facial sarcomas and carcinomas[17]; after surgical access, the ECA would be cannulized and liquid paraffin would be injected. In 1930, Brooks reported the use of autologous muscle to close a post-traumatic carotid-cavernous fistula.[18] Cerebral angiography, as we know it, also had a long history, since the days of Egas Moniz and his studies on surgically exposed cervical carotid arteries,[19,20] passing through the technical advances of Seldinger in 1953, creator of the modern percutaneous arterial access,[21] and Djindjian, who first described superselective catheterization of branches of the ECA.[22]

The first reported case of glomus jugulare tumor embolization was in 1973, by Hekster,[23] with autologous muscle; the first uses of Gelfoam, Silastic (American Heyer Schulte, Goleta, CA, USA) spheres, and adhesives through ECA branches was published by Hilal in 1975.[24] Since then, the use of the technique spread and allowed for experiences with different materials. The first use of PVA was in a carotid body tumor in 1980, by Schick.[25] Since then, the use of the technique spread and allowed for experiences with different materials. In 1994, George et al. documented the first direct, intralesional injection of n-butyl-cyanoacrylate (NBCA) in paragangliomas,[26] followed by the description by Jacobs of combined arterial and venous preoperative embolization[27]; in our series, we had only one case of direct intralesional injection, and no case of combined arterial and venous approach.

Paragangliomas are often fed by branches of the ECA, especially the ascending pharyngeal artery, the occipital artery, and the posterior auricular artery; intracranial invading tissue may be supplied by the clival meningeal branches of the ICA and the meningeal branches of the vertebral artery. In case of intradural extension to the posterior fossa, both the posterior and the anterior inferior cerebellar arteries may be involved.[1,28,29]

It has been long known that embolization of glomus jugulare tumors are most successful when combined with other therapeutic modalities, due to high rates of revascularization,[1,29–32] as well as the multitude of feeding arteries and pedicles originating from eloquent branches[30,33]; preoperative embolization is vital in decreasing blood loss during surgical resection, allowing for safer surgeries.[29] It also may reduce surgical exposure time, spare a patient from thermocoagulation trauma, and prevent sinus-packing procedures.[30]

While generally safe,[29] preoperative embolization is not risk-free. Low cranial nerve palsy, presumably due to embolic ischemia of the *vasa nervorum* or tumor embolic infarction with swelling and nerve compression, stroke, due to reflux or withdraw-induced embolism, or dramatic hypotension, after embolization of a large catecholamine-secreting tumor, have all been described, even if their incidence is extremely low.[26,34–36] In our series, we had no complications arising from the embolization per se.

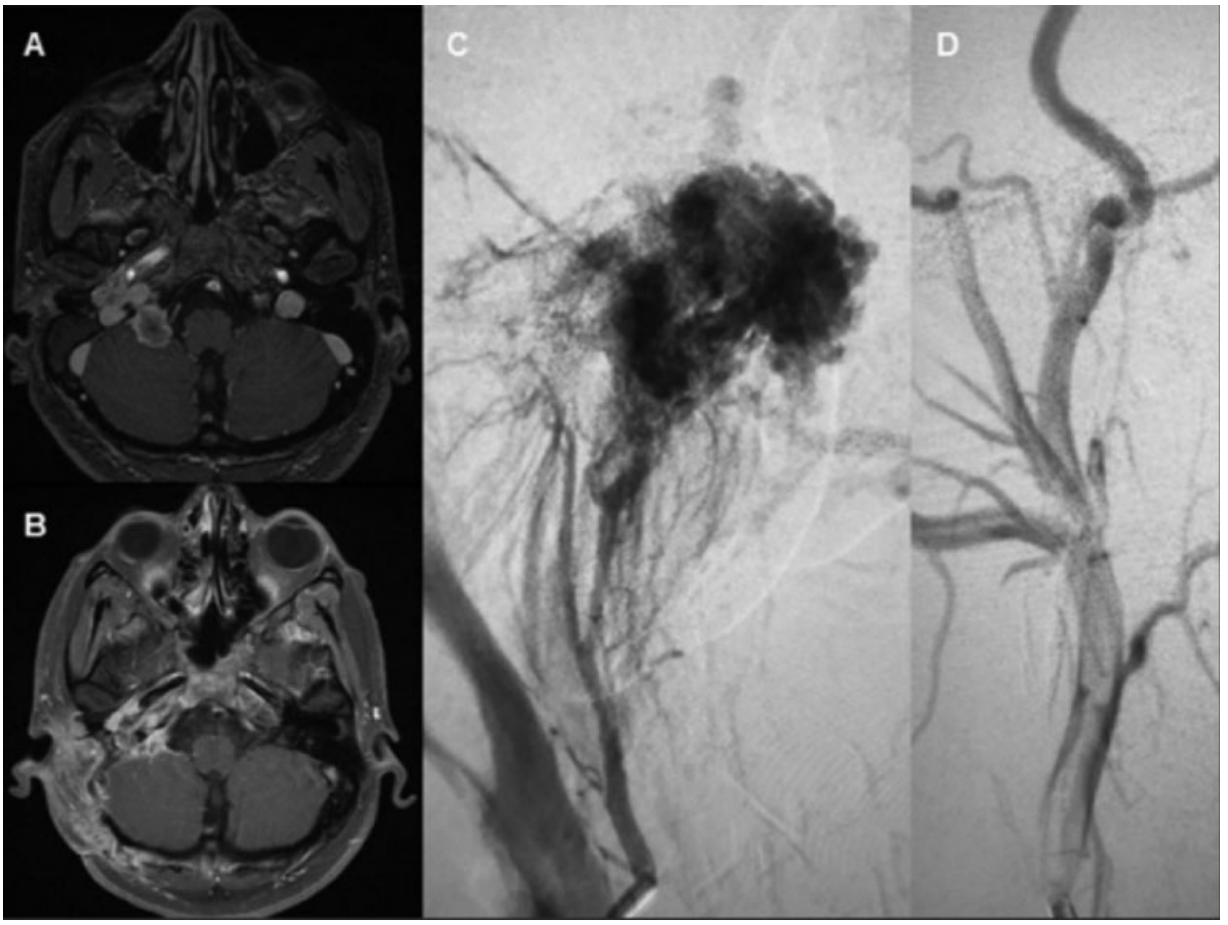

Fig. 2 A 21-year-old male complained of right side pulsatile tinnitus and hypoacusia for 10 months, as well as intermittent ipsilateral cervical pain, before admission to our hospital. ENT examinations elsewhere were without imaging, and he only performed CT and MRI examinations after our evaluation. Both revealed a large, invasive tumor in the jugulare foramen; DSA revealed the tumor was completely supplied by the ascending pharyngeal artery. The patient underwent a total embolization with Gelfoam and the tumor was resected in the same week, using a right craniocervical access. Afterwards, the patient developed CSF leak, later corrected. Due to extensive involvement of glossopharyngeal and accessory nerves, the patient underwent Gamma Knife radiosurgery (25 Gy, 50% isodose) as adjuvant treatment. A and B: axial, postgadolinium injection T1W1 images showing right side hypervascularized lesion in the foramen jugulare, before and after surgery. C: lateral DSA acquisition after selective catheterization of the ascending pharyngeal artery showing the hypervascularized glomus jugulare. D: control lateral DSA acquisition with catheterization of the external carotid artery after embolization with Gelfoam.

Many techniques have been described thus far, ranging from transarterial embolization with PVA particles to direct, percutaneous embolization with NBCA or Onyx.[30,36,37] It must be noted that not only does embolization provide better surgical outcomes but it also has positive impact in clinical manifestations such as tinnitus and vertigo.[38] Even though use of embolization as sole treatment is not advised, it may provide radiological stabilization as well.[39,40]

The following surgery should ideally be performed on the 3rd and on the 14th day after embolization, giving time for decrease of the edema generated by the embolization but before possible vessel reopening and recruiting of other arterial feeders. It is worth noting that paragangliomas may be highly compartmentalized, with independent segments fed by different branches. In our series, total embolization was achieved in 47% of the cases.

Embolization is typically done through one or more of three techniques: transarterially, injecting the embolic agent through superselective catheterization; direct percutaneous intratumoral puncture, which may close arterial supply, capillary bed, and venous drainage, but is harder to adequately gauge; and a transvenous injection, including occlusion of the inferior petrous sinus.[26,27,30]

Agents available for arterial use include autologous muscle, NBCA glue, Ethylene Vynil Alcohol Copolymer (EVOH) (Medtronic, Minneapolis, MN, USA), ethanol, hydrogel, microcoils, microspheres, Gelfoam gelatin sponge, PVA, and microfibrilar collagen, which may be used independently or in association with one another. Both permanent ICA ballooning and carotid stenting may be warranted in selected cases, including cases in which the tumor is extensively supplied by the ICA.[29,41,42] Factors that may influence the choice of embolic agent include, but are not limited to, the experience of the neurointerventionalist with each substance, the time lapse until the surgery, and the possibility of total occlusion. For instance, while the use of microspheres may allow for deeper penetration within the lesion and later open surgery, less experienced

neurointerventionalists may underestimate the diffusion of the substance, especially those with smaller diameters, and inadvertently generate distal venous embolization. In our case, we preferred the larger Gelfoam due to standard procedure of scheduling surgeries in the following days after the embolization and better prevention of venous emboli. This reasoning finds exception when concerning direct injection, either with Onyx, Precipitating Hydrophobic Injectable Liquid (PHIL) (Microvention, Tustin, CA, USA) or NCBA,[26,43] in which preoccupations such as incomplete embolization are also due to care to not inject into the arterial circulation.

We note that our series is one of the largest to date, with few having more patients when specifically concerning glomus jugulare lesions and not all skull base tumors. However, our case series is not without limitations, which include the single-center, retrospective nature of the analysis, the lack of a control group with nonembolized tumors, and the aforementioned bias toward the use of Gelfoam in detriment of other embolic agents.

Conclusion

Glomus jugulare tumors are complex lesions that demand a multidisciplinary approach to ensure satisfactory resection with preservation of lower cranial nerves, especially in case of intracranial extension. Preoperative embolization is essential to ensure one-stage operation of such hypervascularized lesions; there is a wide variety of techniques and material available for the interventional neuroradiologist. Complications from embolization, though rare, cannot be overlooked.

Authors Contributions
Pedro MKF: manuscript research and composition
Leal AG: manuscript research and composition
Ramina R: manuscript revision
Meneses MS: manuscript revision

Conflict of Interests
The authors have no conflict of interests to declare.

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