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Original Article

Management of Complex Jugular Paragangliomas: Surgical Resection and Outcomes

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BACKGROUND: This study aimed to review tumor control and cranial nerve function outcomes in patients with complex jugular paragangliomas and to refine the surgical strategies for complex jugular paragangliomas.

METHODS: We describe our experience with 12 patients with complex jugular paragangliomas diagnosed in our institution from January 2013 to June 2020. The main outcomes included tumor control, complications, and function of facial nerve and lower cranial nerves, postoperatively.

RESULTS: Gross-total resection was achieved for 9 (75%) patients, and subtotal resection was achieved for 3 (25%) patients. The surgical tumor control rate was 100% after a mean follow-up of 45.5 months (range, 13-111 months). Postoperatively, 10 patients (83.3%) obtained unchanged or improved facial nerve function. However, new lower cranial nerve deficits occurred in 2 patients (16.7%) due to surgical removal of the concurrent vagal paraganglioma and scar tissue enclosing the IX and XII nerves.

CONCLUSION: Our refined surgical techniques, including tension-free anterior facial nerve rerouting, sigmoid sinus tunnel-packing, and push-packing techniques, could be a choice for the treatment of complex jugular paragangliomas to achieve tumor control and cranial nerves preservation. A 2-stage surgery should be applied to minimize the risk of bilateral cranial neuropathies and the influence on cerebral circulation in patients with bilateral paragangliomas. The preoperative endovascular intervention such as coil embolization or internal carotid artery stenting can be employed for the management of paragangliomas with internal carotid artery-associated lesions.

KEYWORDS: Jugular paraganglioma, carotid body tumor, vagal paraganglioma, carotid artery, infratemporal fossa approach

INTRODUCTION

Jugular paragangliomas (JPs) are the most common primary benign tumors of the jugular foramen region, which are aggressive lesions that can infiltrate surrounding bony structures, blood vessels, posterior fossa, cranial nerves, and even the intracranial cavity.[1] The management of JPs is challenging because the tumors are always hypervascular and intimated with the internal carotid artery (ICA), lower cranial nerves (LCNs), and inferior petrous sinus. With a better understanding of the natural history of JPs, "wait and scan," surgery, and radiotherapy have been applied as primary treatment modalities for JPs.[2-6] However, surgery also plays a crucial role to offer a chance of disease-free survival for patients with JPs. Complex jugular paragangliomas (CJPs) have been defined as fulfilling one or more of the following criteria[7,8]: (1) very large size; (2) great intradural extension; (3) extension to the cavernous sinus foramen magnum and clivus; (4) significant involvement (encasement and stenosis) of ICA; (5) single ICA on the lesion side; (6) involvement of the vertebral artery; (7) dominant or unilateral sigmoid sinus on the lesion side; (8) bilateral or multiple paragangliomas; and (9) recurrence after previous surgery. Patients with CJPs pose an extreme challenge to skull base surgeons, and there are few studies focused on the surgical management of CJPs. In this study, we aimed to review surgical strategies, tumor control, complications, postoperative facial nerve (FN) and LCNs damage, and functional recovery in our unique series of CJPs patients.

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METHODS

Design and Participants

A retrospective clinical database was queried to identify 12 patients who met the criteria for CJPs from January 2013 to June 2020. All patients underwent surgery with histopathological confirmation of the diagnosis. This study was approved by the ethics committee of Eye, Ear, Nose, and Throat Hospital, Fudan University (No.2021048). All patients were informed of the risks and benefits of all available treatment modalities, including surgery, radiotherapy, and "wait and scan." Informed consent forms were signed by all patients.

Preoperative and Intraoperative Evaluation

All patients underwent a preoperative otoscopic examination, assessment of hearing, FN, and LCNs function, trans-abdominal sonography, catecholamine secretion screening, enhanced temporal bone MRI, CT scanning, magnetic resonance angiography, and digital subtraction angiography (DSA). Temporal bone paragangliomas were graded according to Fisch's classification.[9] Facial nerve function was graded according to the House Brackmann (HB) grading system. Superselective endovascular embolization was routinely performed for all patients 2 days before surgery. Facial nerve monitoring was routinely conducted in patients with normal preoperative FN function. The tumor extension or growth patterns were defined based on preoperative radiological and intraoperative findings.

Details of Surgical Procedure

Infratemporal fossa approach (ITFA) was applied in the present study. If the perineurium of the FN was intact, we performed the tension-free anterior FN rerouting technique. The key point is to suture the parotid gland with the inferior temporal muscle to reduce the distance between the genicular ganglion to the stylomastoid foramen of the FN, while the digastric muscle, FN, and parotid gland underwent anterior transposition.[10] If the FN was infiltrated by the tumor and had to be sacrificed, grafting with the great auricular nerve was performed to reconstruct FN.

To control bleeding, we decreased tumor vascularity with bipolar coagulation cauterizing. After the jugular foramen was exposed, we separated the tumor from the ICA and then ligated the jugular vein. The sigmoid sinus was occluded with Surgicel (Ethicon, Somerville, NJ) and bone wax. We applied sigmoid sinus tunnel-packing and push-packing techniques to control bleeding from the inferior petrous sinus.[11] Intrabulbar dissection and preservation of the medial wall of the jugular bulb were used to preserve LCNs function, as long as the tumor had not penetrated the medial wall of the jugular bulb or infiltrated the LCNs.

Follow-Up

All patients underwent regular enhanced temporal bone MRI and clinical examination postoperatively, which was usually performed 3 months postoperatively and annually thereafter. The follow-up period was defined as the period extending from surgery to the most recent clinical visit or patient contact.

RESULTS

Surgical Outcomes

All patient characteristics and tumor status is summarized in Table 1. Meanwhile, the descriptive analysis of patient demographics and clinical presentation of CJPs is summarized in Table 2. In 12 patients, hearing deficit and pulsatile tinnitus were the most common symptoms. Facial nerve involvement was seen in 8 patients (4 patients with HB grade I and 8 patients with HB grade III-VI). Two patients with previous surgery history presented with lower cranial nerve impairment preoperatively.

Gross total tumor resection was achieved for 9 patients (75%), and subtotal resection was achieved for 3 patients (25%). Multiple paragangliomas on the ipsilateral side were removed in a single stage in 3 patients. A 2-stage resection was conducted in 5 patients with bilateral lesions. The average intraoperative blood loss was 1001 mL. Case 8, who lost 2500 mL blood during operation, suffered from mild hemiparesis (muscle strength grade 4) as a result of a postoperative lacunar cerebral infarction but resolved (muscle strength grade 5) 2 months after surgery. There was no mortality, and all patients were discharged from the hospital 7-10 days postoperatively. Pulsatile tinnitus and otalgia resolved in all patients. Tumor control of 100% was achieved at a mean follow-up of 45.5 months (range, 13-111 months). The details of surgical outcomes are summarized in Table 3.

Facial Nerve and Lower Cranial Nerves Function

Postoperatively, 10 patients (83.3%) obtained unchanged or improved FN function. The preoperative FN function was H-B grade I in 4 patients and H-B grade VI in 5 patients, except for 1 patient deteriorated to H-B grade III from grade I and 1 patient improved to H-B grade III from grade VI, but the postoperative FN function remained stable for other patients at the last follow-up. The remaining 3 patients showed H-B grade III-V function before surgery, and improvement was shown in 1 patient from grade V to grade IV.

Intrabulbar dissection and preservation of the medial wall of the jugular bulb were applied to 10 patients, except for 2 patients with previous surgery history. Two patients (cases 2 and 10) experienced newly developed LCNs deficit postoperatively. Case 2 suffered vocal cord paralysis after surgical removal of the vagal paraganglioma (VP) and JP. Case 10 had to remove the IX and XII nerves due to encapsulated scar tissue from previous surgery.

MAIN POINTS

- Attempts have been made to achieve tumor control and prevent cranial nerve damage or dysfunction or other complications, postoperatively.
- The infratemporal fossa approach with our unique refined surgical techniques including tension-free anterior facial nerve rerouting, sigmoid sinus tunnel-packing, and push-packing techniques can be a considerable treatment option for complex jugular paragangliomas.
- For patients with bilateral paragangliomas, a 2-stage surgery should be applied to minimize the risk of bilateral cranial neuropathies and the impact on cerebral circulation.
- Endovascular intervention such as coil embolization or internal carotid artery (ICA) stenting can be employed for the management of paragangliomas with ICA-associated lesions.
- In case ICA has to be a permanent occlusion, the surgeon should prudentially balance blood pressure, blood loss, and tumor removal to prevent cerebrovascular accident intraoperatively.

Table 1. Patient Characteristics and Tumor Status

	Age	Sex	Fisch Type	Tumor Size (cm)	Previous Surgery	Concurrent Tumor	Removal Method	FN Procedure	Blood Loss (mL)	Follow-up Period (Months)	H-B Grade		LCN Deficit	
											Preoperation	Postoperation	Preoperation	Postoperation
1	47 years	M	C2	1.5×2.4×1.6	NO	CBT	Gross total	Transposition	350	111	I	I	—	—
2	32 years	F	C3	1.5×2.2×1.8	NO	VP; CBT	Gross total	Graft	300	73	III	III	—	X
3	58 years	M	C3De1	3.8×4.0×4.8	NO	VP	Gross total	Graft	1700	68	VI	VI	X	X
4	37 years	M	C3	4.5×3×2.7	NO	CBT	Subtotal	Transposition	300	57	I	I	—	—
5	51 years	F	C2	4.8×3.7×3.5	NO	—	Gross total	—	400	58	VI	III	—	—
6	23 years	M	C3Di2	5.0×4.0×3.5	NO	CBT	Subtotal	—	2000	44	VI	VI	—	—
7	36 years	F	C3	1.6×3.1×2.9	YES	—	Gross total	—	500	38	VI	VI	XII	XII
8	52 years	M	C3Di1	3.7×4.8×4.2	NO	CBT	Subtotal	Graft	2500	21	I	III	—	—
9	39 years	F	C3Di1	2.7×2.7×3.3	YES	ICA ANEURYSM	Gross total	Transposition	300	16	III	III	—	—
10	54 years	M	C3	3.0×2.0×1.8	YES	—	Gross total	—	250	14	VI	VI	X	X; IX; XII
11	76 years	F	C3De2	4.0×2.5×2.8	NO	—	Gross total	—	300	13	V	IV	—	—
12	34 years	M	C3	2.2×3.2×2.4	NO	CBT	Gross total	Transposition	200	44	I	I	—	—

F, female; M, male; LCN, lower cranial nerve; FN, facial nerve; JP, jugular paraganglioma; ICA, internal carotid artery; CBT, carotid body tumor; VP, vagal paraganglioma

Table 2. Descriptive Analysis of Patient Demographics and Clinical Presentation of CJPs

Variable	No. of Patients (n = 12, %)
Male	7(58.3)
Female	5 (41.7)
Age, years (mean)	44.9 (23–76)
Left	5(41.7)
Right	7 (58.3)
Most common symptoms	
Deafness	8(66.7)
Mixed hearing loss	3(25)
Pulsatile tinnitus	11(91.7)
Ear pain	6(50)
Facial paralysis	8 (66.7)
X CN deficit	1(8.3)
XII CN deficit	1(8.3)
FN palsy	8(66.7)
Prior surgery	3(25)
Fisch type	
C2	2 (16.7)
C3	5(41.7)
C3De1	1(8.3)
C3De2	1(8.3)
C3Di1	2 (16.7)
C3Di2	1(8.3)
Complex factors	
Giant tumor	6(50)
JP with CBT	6(50)
Ipsilateral CBT	1(8.3)
Contralateral CBT	5(41.7)
JP with VP (ipsilateral)	2(16.7)
JP with ICA aneurysm	1(8.3)

CN, cranial nerve; FN, facial nerve; JP, jugular paraganglioma; ICA, internal carotid artery; CBT, carotid body tumor; VP, vagal paraganglioma; CJPs, complex jugular paragangliomas.

Illustrative Cases

Ipsilateral Vagal Paraganglioma + Jugular Paraganglioma and Contralateral Carotid Body Tumor

A 32-year-old woman (case 2) presented with symptoms of otalgia and severe mixed hearing loss. Physical exam showed a reddish tumor behind the eardrum. Enhanced temporal bone MRI revealed the presence of multiple paragangliomas: a JP and VP on the right side and a carotid body tumor (CBT) on the left side (Figure 1). We initially resected the left CBT in an attempt to preserve the LCNs, jugular vein, and CA in the first stage. The FN function on the right side progressed from HB I to III within 3 months before her second-stage surgery. After removing the VP and JP, a new X deficit developed, but the FN function was maintained at H-B III following grafting with the great auricular nerve. In addition, removal of the VP definitely results in vocal cord paralysis postoperatively. All efforts were made to preserve the LCN function on at least one side and the cerebral

Table 3. Details of Surgical Outcomes

Parameter	No. of Patients (n, %)
Surgery	
Gross total resection	9 (75)
Subtotal resection	3 (25)
Management of LCNs (2 patients)	
Resection of IX	1 (8.3)
Resection of X	2 (16.7)
Resection of XII	1 (8.3)
FN procedure	
ITFA with FN transposition	4 (33.3)
ITFA with FN interposition graft	3 (25)
ITFA with FN not grafted (HB,VI)	5 (41.7)
Tumor control	12 (100)
FN function	
Unchanged	8(66.7)
Improved	2 (16.7)
Deteriorated	2 (16.7)
LCNs function deterioration	2 (16.7)

LCNs, lower cranial nerves; ITFA, infratemporal fossa approach type A; FN, facial nerve.

circulation. This case demonstrated that a 2-stage surgical strategy is applicable for patients with bilateral multiple paragangliomas.

Jugular Paraganglioma with Abundant Feeding Arteries

A 52-year-old man (case 8) complained of right pulsatile tinnitus, deafness, vertigo, and headache. Physical exam showed a red tumor behind the eardrum. The FN and LCN functions were normal preoperatively. A giant JP was detected on enhanced temporal bone MRI (Figure 2). The patient underwent surgery to remove an ipsilateral CBT 18 years ago, and his right external CA was ligated intraoperatively. Preoperative DSA showed that the right ICA, vertebral artery, thyroid cervical trunk, and contralateral external CA fed the JP. Given that the ICA was the main feeding artery, the branches could not be embolized; furthermore, the ICA was encased by the tumor, and the balloon occlusion test was negative, the right ICA was completely occluded preoperatively. The blood supply of the patient's right cerebral hemisphere was well compensated despite the ICA occlusion. However, the surgical process presented a great challenge to the surgeon, who had to balance intraoperative blood pressure, bleeding, tumor removal, and maintenance of the brain blood supply. Due to massive intraoperative blood loss (approximately 2500 mL), a subtotal resection was performed. The patient suffered from mild hemiparesis as a result of a postoperative lacunar cerebral infarction, which we considered associated with right ICA occlusion and extensive blood loss. Fortunately, this patient resolved 2 months after surgery. The LCNs were preserved and no cerebrospinal fluid leakage developed. This case showed that complex vascular conditions developed after a previous intervention with an adverse outcome of a ligated external CA.

Jugular Paraganglioma Concurrent with Internal Carotid Artery Aneurysm

A 37-year-old female (case 9) presented with a history of surgical resection of a right JP and deafness 11 years ago and FN paralysis (H-B III) 2 years ago. The temporal bone MRI and CT demonstrated a recurrent JP. Preoperative magnetic resonance angiography revealed mild dilatation at the junction of the horizontal and vertical segments of the intratemporal ICA, and an aneurysm was confirmed by DSA (Figure 3). The aneurysm was embolized with coils, and an endovascular stent was placed in the ICA preoperatively. The JP was removed by planned surgery after oral anticoagulant for approximately half a year. The FN was resected and grafted with the great auricular nerve to reconstruct the FN. The FN function remained HB III 1 year after surgery. The LCNs function was intact. This case demonstrates that a meticulous preoperative review of temporal bone images can reveal hidden lesions and prevent disastrous complications.

DISCUSSION

Currently, the treatment modalities for patients with CJPs are still controversial. A number of studies including surgery and/or radiotherapy have demonstrated clinical experience in the management of CJPs.[7,12-14] Although complete surgical excision of JPs is technically possible, it has often been associated with a high risk of LCN injuries. In this retrospective study, we assess the clinical symptoms and

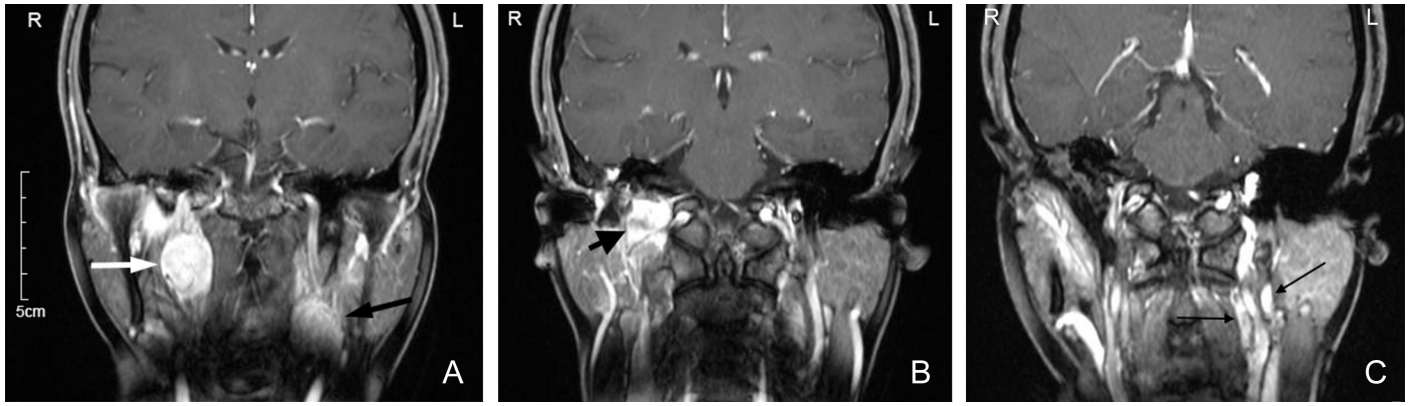

Figure 1. a-c. Enhanced coronal temporal bone MR images of a 32-year-old woman (case 2) with multiple paragangliomas. (a) Preoperatively, a right vagal paraganglioma (white arrow) and a left carotid body tumor (black arrow) are demonstrated. (b) The short black arrow shows the right jugular paraganglioma (JP). (c) Postoperatively, after a 58-month follow-up, the left internal carotid artery and internal jugular vein (thin black arrows) were completely preserved. There was no tumor residue or recurrence.

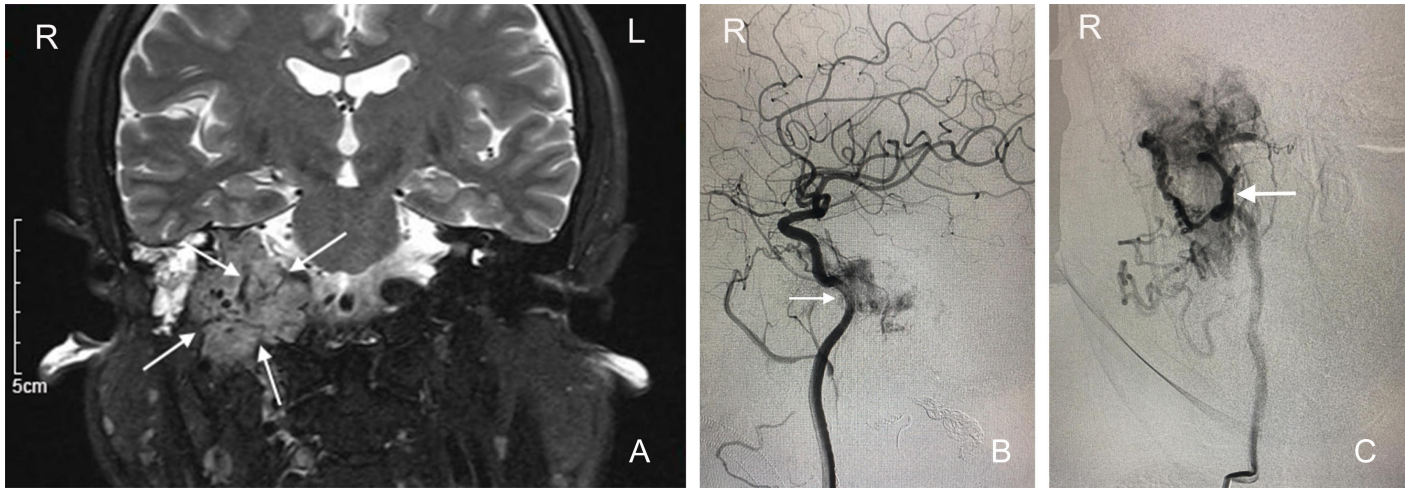

Figure 2. a-c. A 52-year-old man (case 8) with a surgical history of right carotid body tumor removal and right external carotid artery (CA) ligation 18 years ago. T2-weighted coronal MR image reveals a giant jugular paraganglioma with flow voids, suggesting a hypervascular tumor (a) and development of new feeding vessels from the internal CA (b) and vertebrobasilar artery (c).

discuss individualized surgery strategies to achieve tumor control and cranial nerves preservation in 12 patients with CJPs.

Clinical Characteristics

The typical clinical manifestations of JPs are pulsatile tinnitus, hearing loss, and a reddish mass behind the eardrum or in the external auditory canal.[5,15] Our patients did not present with any significant variation with respect to typical clinical presentations, but a higher proportion of hearing loss (91.6%) and facial paralysis (66.7%) were shown. Giant tumors are rare and usually considered inoperable or have a high risk of morbidity and mortality.[7] However, there is no clear standard for defining a "giant tumor." In our series, a giant tumor was defined as having a maximum diameter greater than 4 cm, which means that at least the horizontal segment of the ICA was involved. Because the common location of VPs arises from the superior vagal ganglion, the differential diagnosis of VPs from JPs is difficult. Imaging features may help to distinguish between these 2 types. We noticed that the internal jugular vein was always pushed outward or inward by VPs (Figure 4 b1 and b2), but JPs always spread inferiorly within the internal jugular vein lumen on temporal bone MRI images (Figure 4 a1 and a2).

Surgical Approaches

Various surgical approaches are applied in clinical practice: the retrosigmoid approach, the far lateral approach or its variations, and ITFA.[16-18] The first 2 approaches have limitations in controlling anterior lesions around the ICA, and their advantages are able to expose tumors with intradural extensions. We prefer the ITFA which provides optimal control of the upper parapharyngeal space, the ICA, and the LCNs following FN anterior rerouting. However, some surgeons criticize the FN dysfunction postoperatively. With the application of the tension-free FN anterior rerouting technique, we were able to achieve good FN function.[10]

Multiple Paragangliomas

In our series, approximately 66.7% (8/12) of patients presented with multiple paragangliomas and 41.7% with bilateral paragangliomas. The management of multiple paragangliomas is controversial, particularly when bilateral LCNs or ICA are involved. Van der Mey et al[15] supported that a wait-and-scan policy should be considered for such patients. Al-Mefty et al[7] indicated that ipsilateral tumors could be excised simultaneously, and the opposite side should be treated surgically only if the first resection did not cause essential cranial nerve

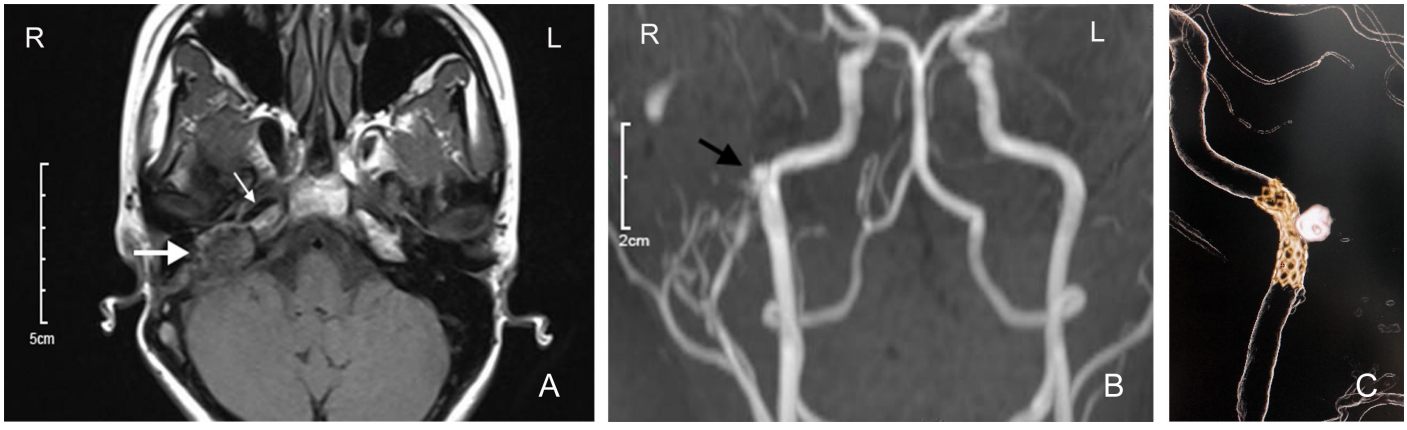

Figure 3. a-c. Imaging of a 37-year-old female (case 9) with a history of surgical resection of a right jugular paraganglioma (JP) 11 years ago. (a) T1-weighted axial MR image shows a recurrent JP (large white arrow). The small white arrow indicates the internal carotid artery (ICA). (b) MRI angiography reveals a preoperative aneurysm of the ICA (black arrow). (c) The reconstructed radiograph shows the ICA after insertion of an endovascular stent and embolization of the aneurysm with a coil.

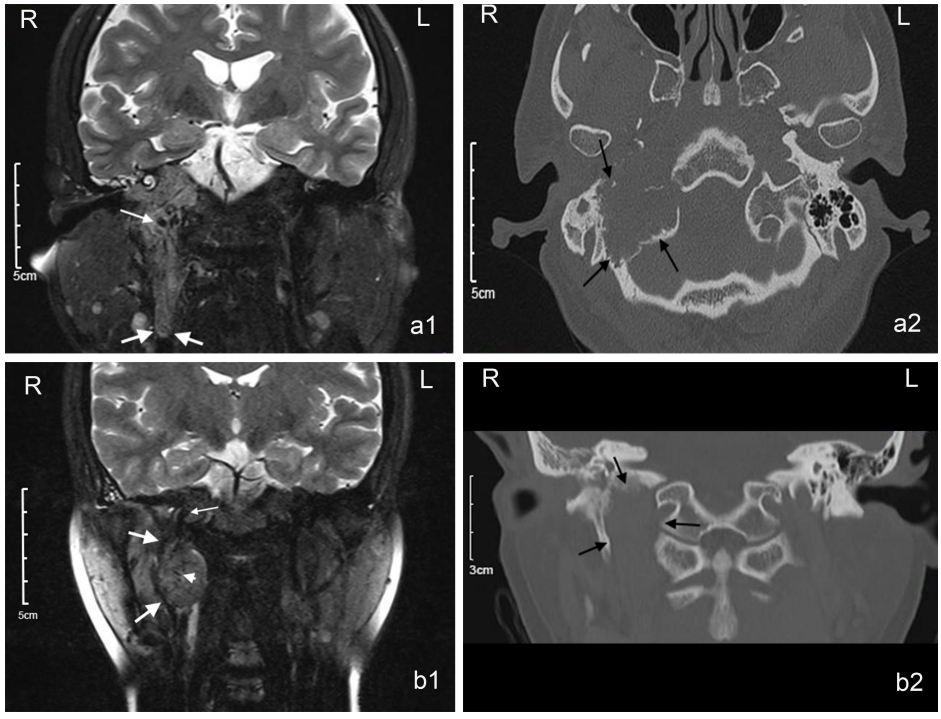

Figure 4. Temporal bone MR and CT scan images of the jugular paraganglioma (JP) and vagal paraganglioma (VP). (A1) T2-weighted coronal temporal bone MRI of the JP. The tumor is spread inferiorly along the lumen of the internal jugular vein, and the slim white arrow indicates its salt and pepper appearance. (A2) The axial temporal bone CT from the same patient indicates erosion of the jugular foramen, petrous bone, and carotid canal. (B1) T2-weighted coronal image of the VP. The internal jugular vein is pushed outward. The internal jugular vein is designated by a large white arrow. The slim white arrow indicates the ICA, and the shortest white arrow shows the internal vascular flow void of the tumor. (B2) Coronal CT of the VP indicates enlargement of the jugular foramen and bone erosion.

palsy in bilateral tumors. Michael G. Moore et al[19] recommended a staged fashion to minimize the risk of bilateral cranial neuropathies and/or impact on cerebral circulation when surgery is considered. Other factors such as prior treatment modalities, the patient's neurologic function, and life expectancy, as well as swallowing and pulmonary function also should be taken into account.[19] We removed ipsilateral JP and VP or CBT during the same operation. For bilateral tumors, we preferred prior surgery for the contralateral CBT, and secondary stage surgery for ipsilateral JPs or VP as a surgical strategy. If there was no LCNs injury and the internal jugular vein was preserved intact contralaterally, we were more confident in resecting the JP in the second stage. Otherwise, conservative treatments were chosen.

Vascular Considerations

Our previous study showed hemorrhage from the sigmoid sinus and inferior petrosal sinus can be effectively controlled by tunnel-packing and push-packing techniques.[11] The ICA in its upper neck and intratemporal portions is often involved in patients with paragangliomas. Angiography is a useful tool to identify the feeding arteries, evaluate the collateral cerebral circulation, detect occult vascular lesions, and determine the management strategy of the ipsilateral ICA during surgery. Al-Mefty et al[7] stated that a plane of dissection can be identified between the tumor and the ICA with the aid of a microscope. We noticed that the presence of scar tissue in the jugular foramen due to previous surgery makes it extremely difficult to navigate the ICA in the upper neck or find a normal anatomic landmark. We preferred to use the cochlea and the tympanic ostium of Eustachian tube as landmarks to identify the vertical ICA. In most cases, the tumor could be separated from the ICA. Given a benign tumor, even if a tiny piece of tumor is left, we would not sacrifice the ICA. Three patients in our study with subtotal tumor removal resulted in extensive blood loss, which put patients at risk of cerebral infarction following balloon occlusion of ICA or tumor adhered to the vascular adventitia of the ICA. In these cases, we had to make a balance between gross tumor removal and postoperative morbidity. The 3 patients who followed subtotal resection of CJPs showed no tumor growth occurred over an average of 40.7 months of follow-up. Various procedures have been described in the management of ICA preoperative, including saphenous vein bypass grafting, permanent occlusion, and endovascular stenting.[8,20,21] In our study, we used embolization coiling or endovascular stenting in the management ICA-associated lesions, which prevented disastrous incidents intraoperative.

Our study demonstrates the feasibility of surgical resection and the possibility of preserving cranial nerve function in patients with CJPs. The weakness of the present study is obvious: retrospective review study, small sample size, and lack of statistical power. Given the lower incidence of CJPs and the indolent course of these tumors, future studies will enroll more patients with multicenter cooperation to validate our treatment and increase the duration of follow-up.

CONCLUSION

There remains no consensus regarding the best treatment modalities for CJPs, particularly for younger patients and for patients who initially present with functional LCNs. With refined surgical techniques, including tension-free anterior FN rerouting, sigmoid sinus tunnel-packing, and push-packing techniques, our data suggest that surgery can reach a low incidence of residual tumor, achieve tumor

control, and cranial nerves preservation. For bilateral paragangliomas, a 2-stage surgery should be applied to minimize the risk of bilateral cranial neuropathies and the impact on cerebral circulation. The proper preoperative endovascular intervention such as coil embolization or internal carotid artery stenting should be employed in the management of paragangliomas with ICA-associated lesions.

Ethics Committee Approval: This study was approved by the ethics committee of Eye, Ear, Nose, and Throat Hospital, Fudan University (No.2021048).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – C.D.; Design – C.D., G.C.; Supervision – C.D.; Materials – G.C., Q.W.; Data Collection and/or Processing – C.D., G.C., Q.W.; Analysis and/or Interpretation – C.D., G.C., Q.W.; Literature Review – G.C., Q.W.; Writing Manuscript – G.C., Q.W.; Critical Review – C.D.

Declaration of Interests: The authors declare that they have no conflict of interest.

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