Effective, same-day preoperative embolization and surgical resection of carotid body tumors

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Abstract

Backgroud: The aim of this study was to evaluate the efficacy of the procedure by analyzing the blood loss and duration of carotid body tumor (CBT) surgery following same-day preoperative embolization.

Methods: We reviewed the medical records of subjects retrospectively. Fifteen patients with 16 CBTs were enrolled in this study. Our same-day procedure comprises preoperative embolization of the feeding arteries in the morning followed by surgery within 3 hours after the embolization is completed.

Results: The mean operative time and the mean amount of blood loss were 138 min and 29.3 ml, respectively. The tumor volume after embolization was markedly reduced and the mean reduction rate was 50%. We found that 13 CBTs had more than 3 feeding arteries. Almost all the postoperative complications, mainly cranial nerve paralyses, resolved within months after surgery.

Conclusions: Our same-day procedure is a safer and superior alternative to traditional CBT surgery, having good outcomes.

1 | INTRODUCTION

Carotid body tumor (CBT) is a rare disease that develops from carotid body paraganglion cells. The characteristic features of this tumor are a rich vascular network within the lesion and a capsule supplied by many feeding arteries.[1] Molecular biological studies have revealed that this tumor has various types of gene alterations such as point mutations in the succinate dehydrogenase (SDH) gene family.[2-4] The disease concept of “hereditary paraganglioma-pheochromocytoma syndrome” has arisen to describe familial paraganglioma patients, and it applies to CBT patients with a family history of the disease and gene alterations.[5-7]

It is well known that as malignant tumors cannot always be identified by their morphological features in histopathological examinations, they are distinguished from their benign counterparts through clinical findings such as their metastatic activity. The need for surgical resection depends on the potential for such metastatic activity. Head and neck surgeons must consider surgical resection of CBT once a patient is referred to their hospital.

The aim of this study was to evaluate the efficacy of the preoperative embolization of feeding arteries of CBTs by analyzing the blood loss and operating time of the CBT surgery following same-day preoperative embolization. We previously reported the efficacy of our preoperative embolization procedure as a letter.[8] We described here the efficacy of our procedure more precisely and remarkably by increased number of the patients for the surgeons to help perform the resection of carotid body tumor safely and effectively.

2 | METHODS

2.1 | Patients

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. This study was approved by our institutional review board and written informed consent was obtained from each patient. We reviewed the medical records of patients retrospectively.

From March 2013 to August 2018, 15 consecutive patients were referred to our hospital with 16 CBTs that were resected. Four patients had a family history of paragangliomas and of these patients, two had bilateral CBTs.

2.2 | Preoperative embolization

We have provided a detailed description the method of preoperative embolization in a previous study.[8] A dose of intravenous (IV) heparin was administered intra-procedurally (500–1000 IU added every hour) to prevent thromboembolic complications related to the catheterization procedure. A 5-Fr sheath was introduced after puncturing the right femoral artery. Selective angiography of the external carotid or common carotid artery was performed via the 5-Fr headhunter-type catheter (Glidecath^{TM}, Terumo, Tokyo, Japan). Super-selective catheterization of the arteries feeding the CBT was performed using a 2.2-Fr microcatheter (Progreat-b^{TM}, Terumo, Tokyo, Japan) and a 0.014-inch guide wire (AQUA, Cardinal Health Japan, Tokyo, Japan). One millimeter of gelatin sponge (GS; Gelpart, Nihon-kayaku, Tokyo, Japan) was mixed with contrast material and slowly introduced into the feeding arteries using a 1-mL lock syringe. The free-flow condition during GS injection was monitored using X-ray fluoroscopy. Injections were repeated until a significant blood flow reduction was obtained. Additional super-selective catheterization and embolization procedures were performed whenever other feeding vessels were identified on angiography.

2.3 | Surgical resection

Surgical resection was carried out appropriately and routinely within 3 hours following the preoperative embolization procedure. The surgeries were performed under general anesthesia using endotracheal insertion of the tracheal tube. A transverse skin incision was made just above the CBT in an upper neck skin crease. The fascia of the sternocleidomastoid muscle was incised and the muscle was retracted laterally to expose the internal jugular vein (IJV) followed by the common carotid artery (CCA). The vagal nerve was found and preserved between the IJV and the CCA. Lymph nodes overlying the CBT were removed and frozen sections of these lymph nodes were examined histopathologically for evidence of metastasis. The hypoglossal nerve, like the vagal nerve, was also identified, dissected, and preserved. The carotid sheaths were incised and opened under the carotid bifurcation and the CCA was exposed, dissected around the surface, and secured by a vessel loop. Dissection of the tumor began along the CCA in a subadventitial plane to the carotid bifurcation. Owing to the potential of the surface of the capsule of the tumor to bleed easily, meticulous hemostasis with electrocautery was required to maintain adequate hemostasis and minimize blood loss. Once dissection of the CCA was completed, the carotid bifurcation was visible and further dissection was carried out. First, careful dissection of the internal carotid artery (ICA) was performed to ensure that it was kept intact. Following this, dissection of the external carotid artery (ECA) was carried out by ligating or cauterizing the feeding arterial branches of the ECA. Resection of the CBT was completed by dissecting it from the ICA and ECA and from the inner space of the neck. Through these procedures, the cranial and sympathetic nerves were carefully preserved.

2.4 | Tumor volume

Tumor volume was estimated on computed tomography (CT) and/or magnetic resonance (MR) images preoperatively. The size of the CBT was measured in terms of major (longitudinal) diameter (A), minor (transverse) diameter (B), and thick diameter (C). Postoperative size of the tumor was estimated using surgically removed specimens as well as its major (longitudinal) (A), minor (transverse) (B), and thick (C) diameters. The volume was calculated by the following formula: $\frac{4}{3}\pi$ x $\frac{1}{2}$A x $\frac{1}{2}$B x $\frac{1}{2}$C, assuming that the tumor was an ellipsoid.

2.5 | Histopathological examination

Several serial, 10% formalin-fixed paraffin-embedded 3-μm sections were obtained from a representative block of the tumor. These sections were stained using hematoxylin and eosin (HE).

2.6 | Statistical analysis

Statistical analyses were carried out using Students' t-test.

3 | RESULTS

The patient characteristics are shown in Table 1. There were 9 females and 6 males and their mean and median ages were 46.0 and 53 years, respectively, with their ages ranging from 23 to 62 years. One patient had a tumor classified as Shamblin type I (Case 7), and 15 had type II tumors, including one patient who had bilateral CBTs (Cases 11 and 12). Three patients had the germline mutation SDHD exon4 c.317G>A (p.Gly106Asp) (Cases 2, 11 (12) and 14)., and two patients had the germline mutation SDHB exon3 c.201-2 A>C (Cases 1 and 8). One patient had the germline mutation SDHB exon5 c.424-7 A>C and exon5 c.424-6_427deletion CCACAGGATT (Case 9), and another had the mutation SDHD exon4 c.337_340delGACT(p.Asp113Metfs) (Case 15).

Figure 1. shows the typical results of our procedure for Case 8. The patient had right CBT classified as Samblin II, with a preoperative volume of 18398 mm^3. Since the patient's CBT had feeding arteries from the right ascending pharyngeal, occipital, and lingual arteries, preoperative embolization was carried out in the morning followed by resection of the CBT in the afternoon. An almost complete embolization of the feeding arteries was performed by our radiologist and significant reduction of the blood supply was achieved adequately (Figure 1D). When we resected the CBT, all the cranial nerves were safely preserved; the operating time and blood loss were 138 minutes and 14 ml, respectively. The estimated tumor volume from the excised specimen was 8206 mm^3 indicating that a 55% volume reduction was achieved by preoperative embolization (Figure 1G). Histopathological examination showed embolization materials within the tumor vessels and tumor tissues showed no edema (Figure 1H and I).

Table 2 shows the results of CBT surgery and their respective outcomes. The mean operative time and the mean amount of blood loss were 138 min and 29.3 ml, respectively. The median operative time and the mean amount of blood loss were 118 min and 8 ml, respectively. The operative time and volume of blood lost from one patient (Case 4), who underwent resection of the carotid artery followed by reconstruction with an artificial vessel, were 300 minutes and 341 ml, respectively. Exclusion of Case 4 yields a mean operating time and mean volume of blood loss of 128 min and 8.5 ml, respectively.

The feeding arteries of these patients are shown in Table 3. The most predominant feeding artery was the ascending pharyngeal artery (APA) and 14 out of 16 tumors were fed by this artery. Closely following the APA were the superior thyroid artery (STA) and the occipital artery (OA), which fed CBTs in 11 and 10 tumors, respectively. Surprisingly, 5 tumors were fed by a direct feeder from the ECA. Additionally, the accessory superior thyroid artery fed one CBT. These arteries were not found in normal individuals and thought to be exceptions. Five tumors had 4 feeding arteries, 8 tumors had 3 feeding arteries, 2 tumors had 2 feeding arteries, and one tumor had only one feeding artery.

Preoperative tumor volumes were calculated based on the measured diameters of the tumor in CT and/or MR images, and postoperative tumor volumes were calculated based on the direct measurement of the tumor size from removed specimens. The mean values of preoperative and postoperative tumor volumes of 15 cases were 13769 and 7436 mm^3, respectively (Table 2 and Figure 2). Case 1 was omitted because there was no precise measured value of the tumor size after surgery. Reduction rates of tumor volume ranged from 76% to -7% and the mean reduction rate was 46%. These results indicate that the tumor volume can be expected to be reduced by approximately 50% by preoperative embolization of feeding arteries.

Postoperative complications are shown in Table 2. The most frequent postoperative complications were first bite syndrome and X paralysis, leading to recurrent nerve palsy and hoarseness. Most of them were transient and resolved within several days to months postoperatively. One patient (Case 8) exhibited transient Horner's syndrome. Case 4 showed paralysis of nerves IX, X and XII postoperatively but these resolved within weeks.

4 | DISCUSSION

The issue of significant blood loss and prolonged operating time of the surgery associated with resection of CBTs has been a topic of much debate. This is because the hyper-vascular network of the tumor capsules makes the dissecting procedure from carotid arteries quite difficult.[9-11] There have been several attempts to reduce the blood loss associated with CBT surgeries by preoperative embolization.[12-17] We investigated patients with CBTs in Japan by analyzing the case report files from head and neck surgeons all over the country in the study group called the Japan Carotid Body Tumor Research Group (JCBTRG).[18] Our study revealed that the most predominant feeding artery of these CBTs was the APA followed by the STA and OA. Preoperative embolization of these arteries was essential in reducing blood loss but operative time in Shamblin types I and II tumors. However, there has been a clear consensus on the efficacy of preoperative embolization in reducing blood loss and/or operative time, as well as a postoperative complications such as cranial nerve paralysis. Although two reports on meta-analyses of preoperative embolization in CBT surgery have been published, these reports present different and controversial results.[19,20] One report stated that preoperative embolization before surgical resection of CBTs appears to decrease blood loss and operative time compared with that without preoperative embolization,[19] while another reported that preoperative embolization does not confer any operative and postoperative advantage to patients with CBT.[20] However, our results indicate that if surgeons apply preoperative embolization and resection of CBT according to our method, at least blood loss would be reduced dramatically and some postoperative complications such as cranial nerve paralysis would be avoided to some degree.

Regarding feeding arteries, most tumors had multiple feeding arteries with aberrant ones originating from the ECA directly. These conditions were thought to be the cause of easy bleeding and much blood loss during the CBT resection surgery. In fact, 5 out of 16 tumors in our series of patients had direct feeding arteries from the ECA and one tumor had an aberrant accessory STA.

Although there have been several reports describing preoperative embolization and resection surgery, interval time between preoperative embolization and successive surgery were various ranging from hours to several days. Table 4 shows a review of the literature on blood loss and operative time associated with CBT resection. Although in these studies, preoperative embolization reduced the blood loss of the patients who underwent the procedure compared with that of patients without preoperative embolization, the mean blood loss reported was 314 ml. Our results showed that our same-day procedure led to a more significant reduction in blood loss compared to these previous reports, with the mean blood loss being 29.3 ml. However, the operative time of the patients who underwent preoperative embolization was not significantly reduced compared to that of the patients who did not undergo that procedure. Indeed, the operative time of the patients who underwent our same-day procedure was 138 min (2.3 hours) and, although this was short, it was not remarkable. We have reported in previous studies that a reduction in blood loss was obvious in patients who underwent preoperative embolization, but the reduction of the surgery duration was not.[18] These results are consistent with the results presented in those reports.

Regarding the timing of the preoperative embolization, it is unclear as to why our same-day procedure is effective in the reduction of blood loss. CBTs naturally have rich vascular networks both within the lesion and in their capsules, which are supplied by many feeding arteries. Once preoperative embolization has been completely carried out, recanalization of the blood vessels from collateral feeding arteries should be considered. For this reason, the resection surgery must be performed as soon as possible after preoperative embolization is completed. In fact, during our procedure of preoperative embolization, in some patients, occasionally, new collateral feeding arteries were visible after main feeding artery was obstructed by the gelatin sponge. In general, an intentional delay of 1 or 2 days between preoperative embolization and surgery is considered to allow time for edema to resolve, but that is enough time to allow reconstitution or recruitment of feeding arteries or for the inflammation that may occur with waiting.[20] Since no edema was observed in the surgically resected specimen (Figure 1H and I), our results indicated that this intentional delay was not necessary for CBT surgery.

Although measurement methods were different between preoperative and postoperative tumors and values of the calculated volumes were somewhat predicted in this point of view, one remarkable advantage of our procedure was marked shrinkage of the tumor after preoperative embolization leading to an easy resection and blood loss reduction. Difficulties of dissection of the tumor from the carotid arteries and easy bleeding of the tumor and its capsules in some patients were difficult problems the surgeons faced. Additionally, the patients who underwent CBT surgery had some complications after surgery such as cranial nerve paralysis and so on. Our procedure can be the landmark of CBT surgery and provide the patients with a better quality of life after surgery. Although our same-day procedure may be difficult to carry out in some facilities because of the unavailability of angiography and/or surgery room, ability of the IVR radiologist, and so on, it is worthy to consider resecting CBTs.

5 | CONCLUSION

Our results show little blood loss and possibly less operative time, indicating that our same-day procedure is superior to other methods of preoperative embolization of feeding arteries and resection of CBTs. This procedure is a safer alternative to traditional CBT surgery, is easier to perform, and has good outcomes, which provide patients with a better quality of life after surgery.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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FIGURE LEGENDS

FIGURE 1. Typical result of preoperative embolization followed by surgery using our one-day procedure (Case 8).

A: The axial image of enhanced CT and B: the anterior coronal view of the MR image at the CBT tumor. The tumor was located at the right carotid bifurcation and its estimated size was 47×34×22 mm on the image. C: The lateral view of the DSA image before the embolization of the feeding arteries. D: The same view as C after the embolization. The feeding arteries from the ascending pharyngeal artery, occipital artery, and lingual artery were selectively injected by gelatin sponge (see Materials and Methods). Almost all blood supply was obstructed by the embolization procedure. E: The operative view of CBT surgery. The ICA and ECA were covered by tumor (arrow head) and not visible. The CCA (open arrow), vagal nerve (arrow), and IJV were preserved and secured by a vessel loop. F: The operative view after resection of the CBT. The ICA (arrow) and ECA (open arrow) were preserved and secured by vessel loops. The hypoglossal nerve was preserved. The operative time and blood loss were 138 minutes and 14 ml, respectively. G, The lateral view of the removed specimen. H, The cut surface of the specimen. Most areas showed ischemic color, but a few areas showed injection. The tumor size was 35×28×16 mm by direct measurement. I and J, Hematoxylin and eosin staining of the specimen showed embolization materials in tumor vessels. The longitudinal view (I) and transverse view (J) are shown. Magnification, 40×.

FIGURE 2. Reduction of tumor volume after preoperative embolization. The tumor volume of each CBT except for Case 1 was estimated in CT and /or MR images preoperatively (PRE). Postoperative size was directly measured using surgically removed specimens and the tumor volume was estimated (POST). The volume was calculated assuming that the tumor was an ellipsoid as described in the Methods. Although only one tumor (case 2) showed almost equal volume in PRE and POST, most tumors showed reduction of the tumor volume to some extent. Tumor volume is indicated by mm^3. The mean reduction rate was 46% (Table 2).

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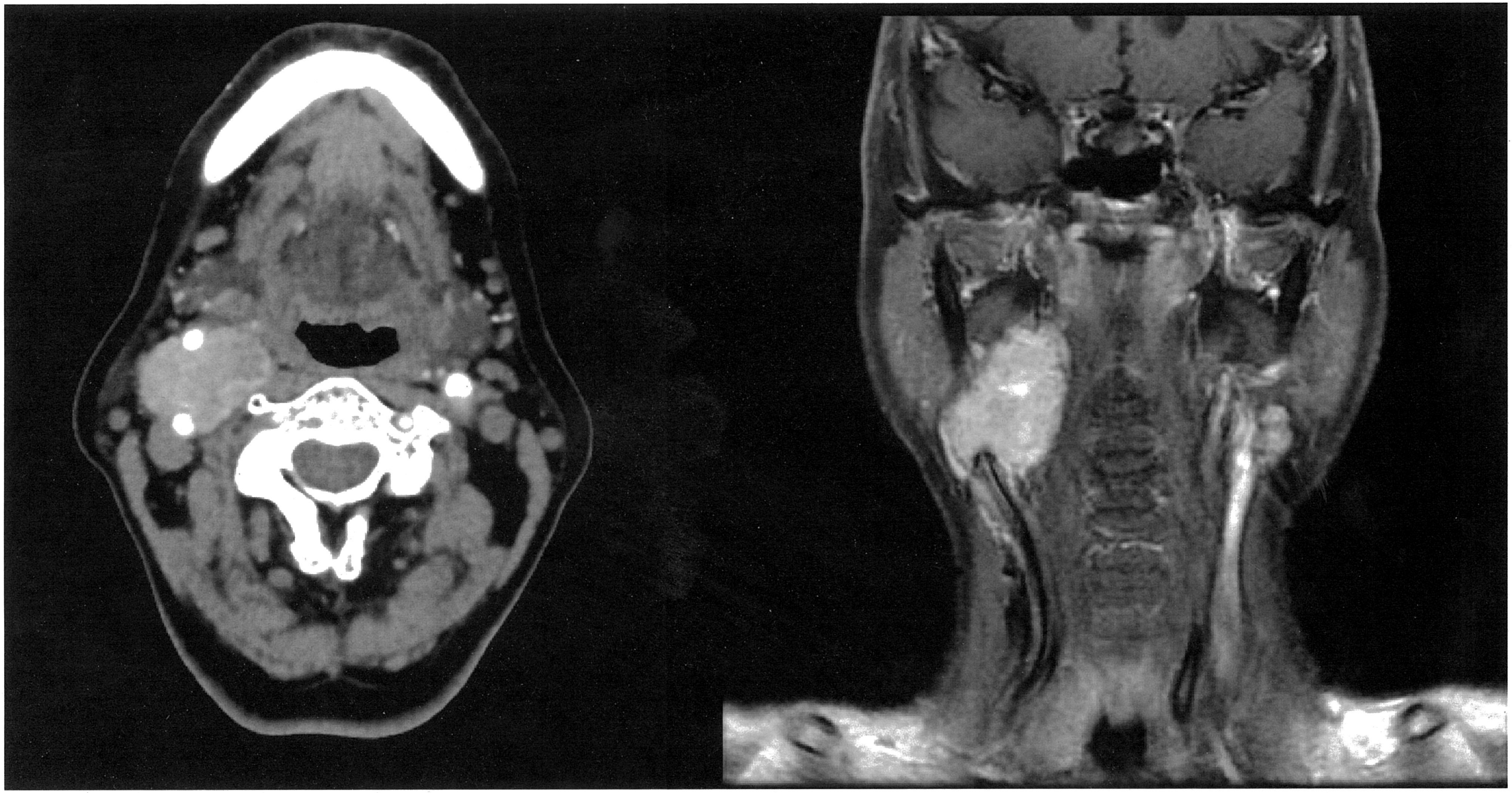

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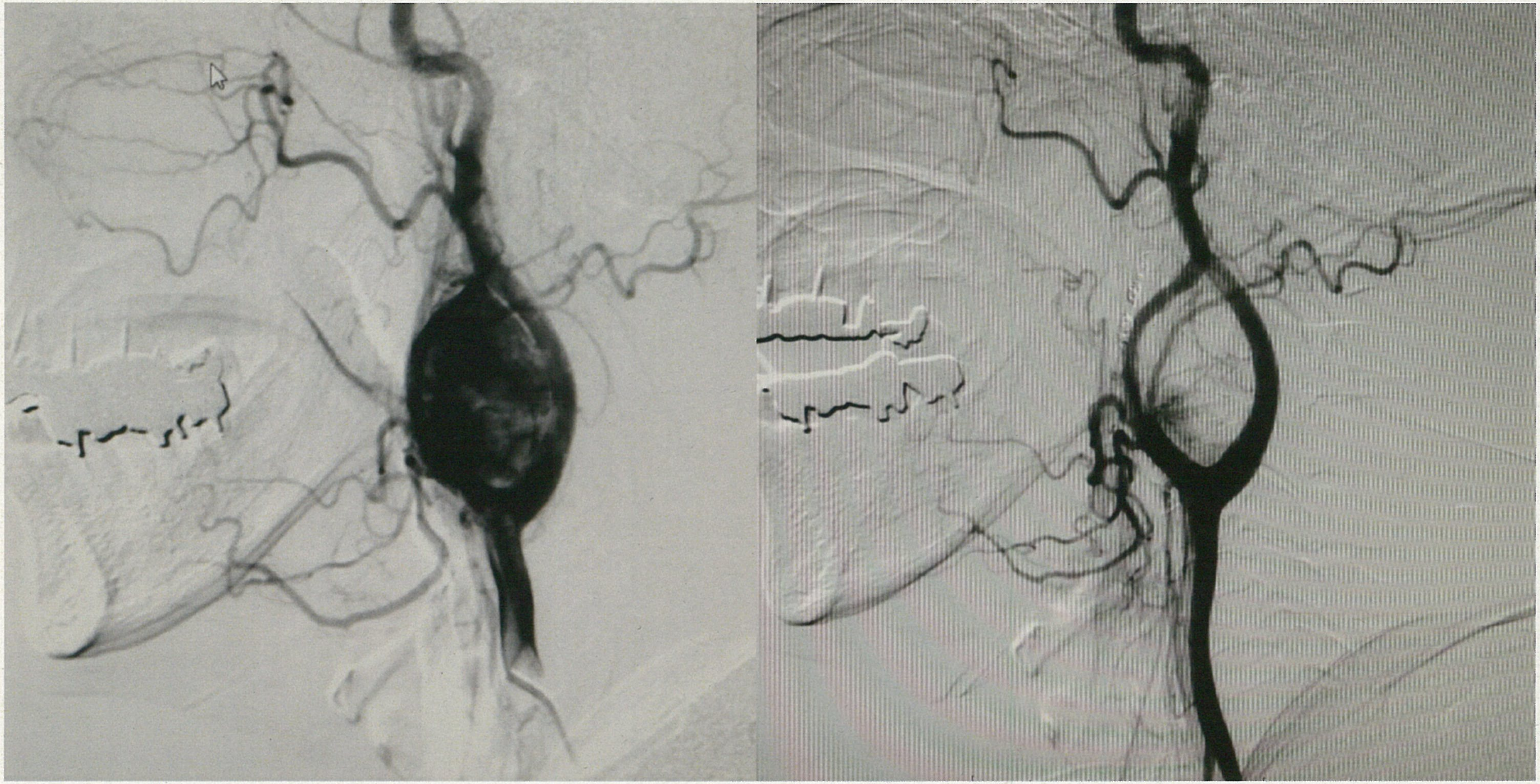

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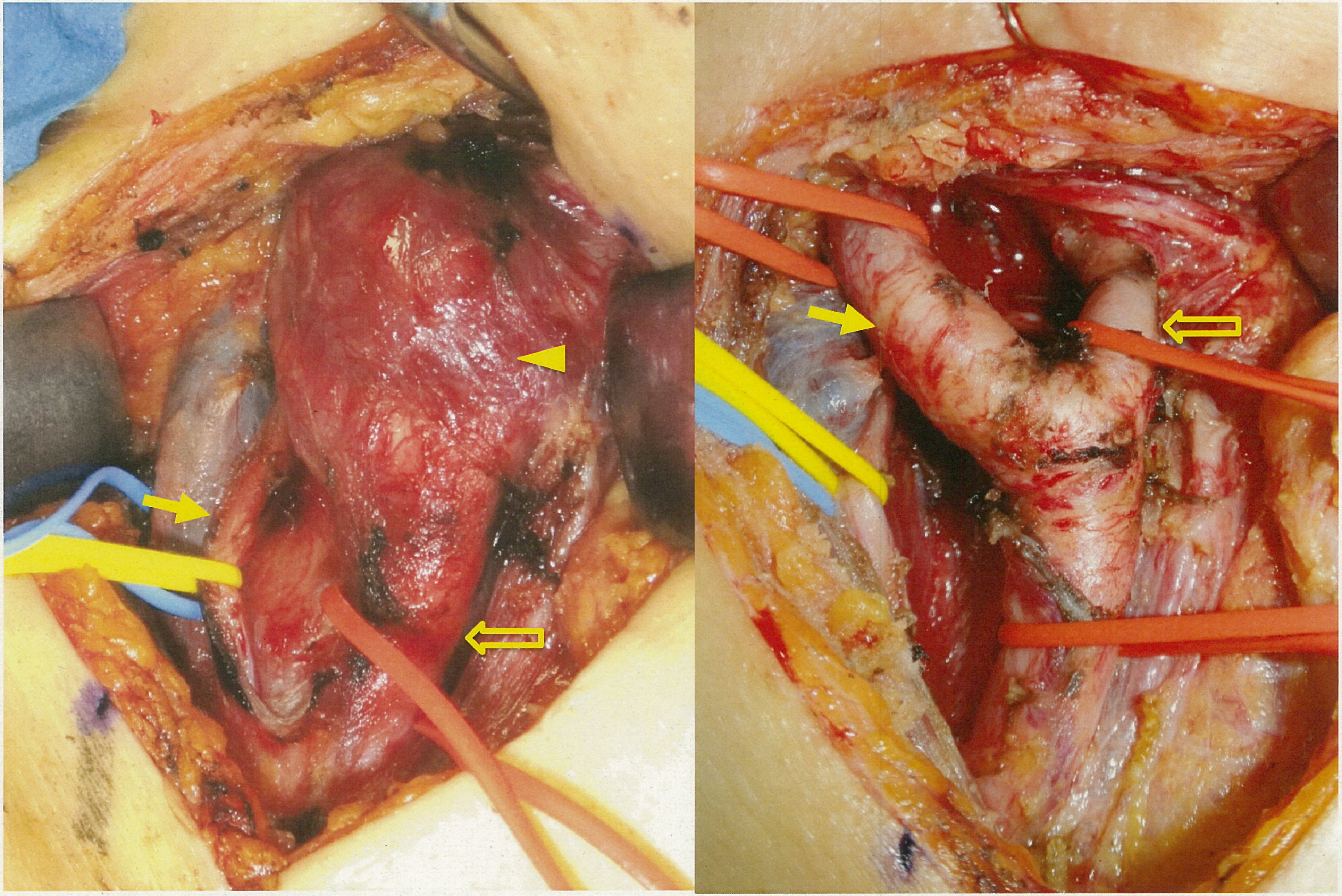

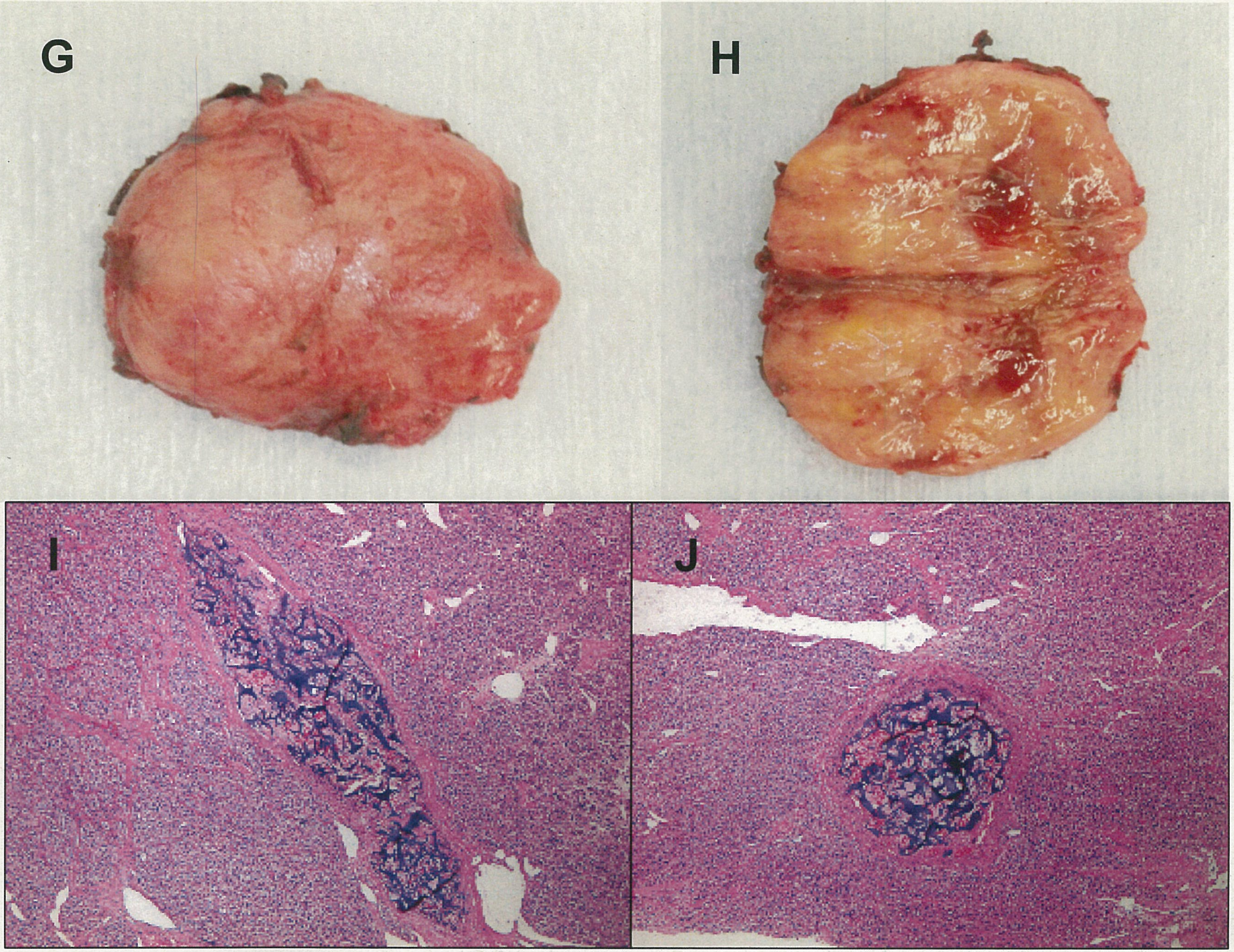
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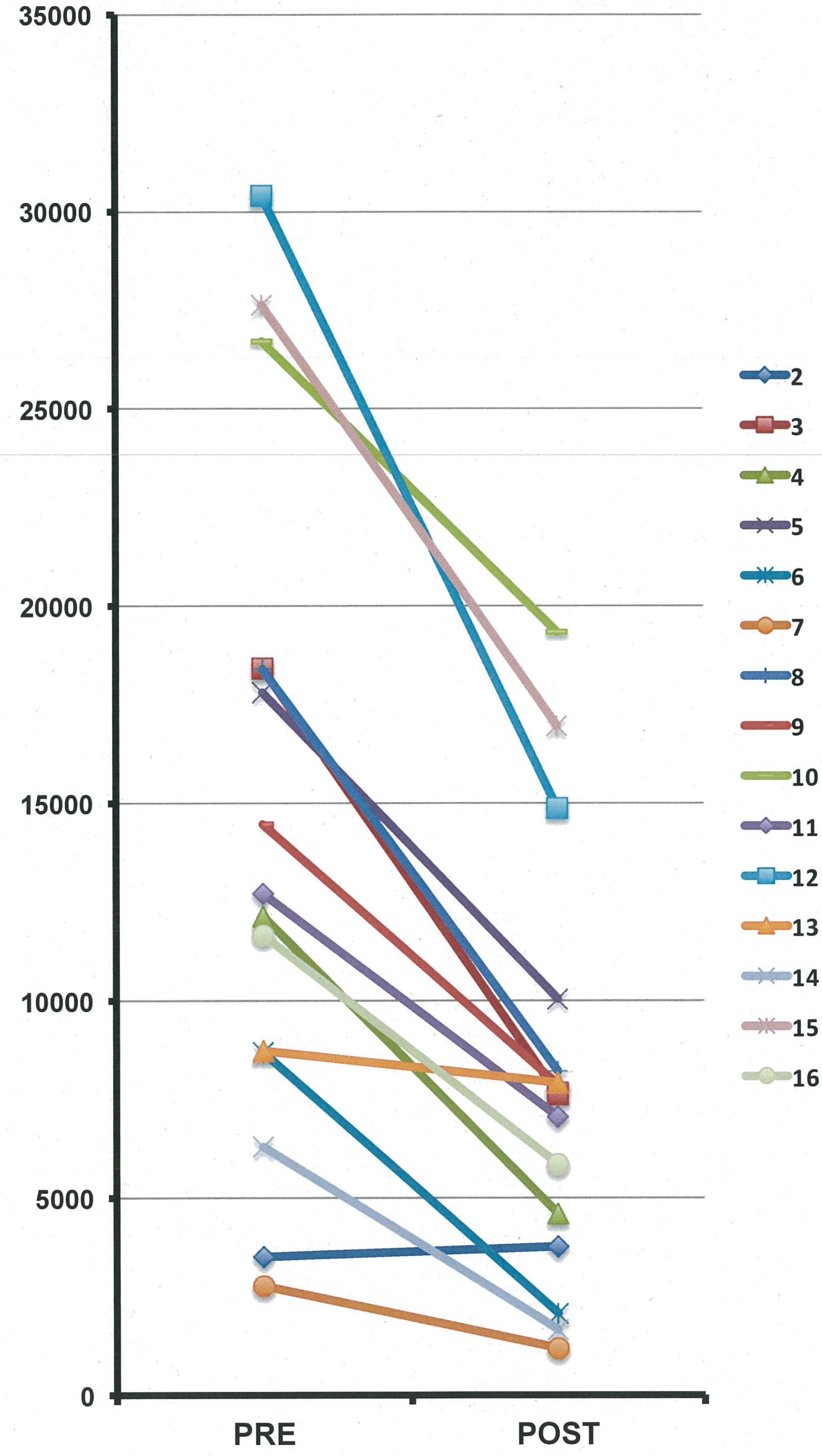

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TABLE 1. Clinical feature of the patients.

	Age & Gender	Side	Remarks	Germline mutation
1	31F	R		SDHB exon3 c.201-2 A>C
2	30M	R	familiar	SDHD exon4 c.317G>A(p.Gly106Asp)
3	60F	R		
4	23F	R	resection of ICA	
5	57F	L		
6	45F	L		
7	42F	R		
8	62F	R		SDHB exon3 c.201-2 A>C
9	40F	R	familiar	SDHB ①exon5 c.424-7 A>C ②exon5 c.424-6_427deleion CCACAGGATT
10	56M	L		
11	53M	L	familiar, Aortic body tumor	SDHD exon4 c.317G>A(p.Gly106Asp)
12	53M	R	familiar, Aortic body tumor	
13	57M	L		
14	47M	R	familiar, pheochromocytoma, postope.	SDHD exon4 c.317G>A(p.Gly106Asp)
15	61M	R		SDHD exon4 c.337_340delGACT(p.Asp113Metfs)
16	57F	L		

Abbreviations:F, female; M, male; SDHB, succinate dehydrogenase subunit B; SDHD, succinate dehydrogenase subunit D. Case 11 and 12 were the same patient.

TABLE 2. Results of CBT surgery

	Preoperative tumor size (mm)	preoperative tumor volume (mm^3)	removed specimen (mm)	postoperative tumor volume (mm^3)	reduction rate (%)	Operation time (min.)	Blood loss(ml)	Postoperative complication
1	31x29x19	8939	φ27			113	16	first bite syndrome
2	22x19x16	3500	27x19x14	3759	107	99	3	(-)
3	44x32x25	18421	28 x 26 x 20	7620	41	129	8	first bite syndrome, transient
4	34x31x22	12135	33x19x14	4594	38	300	341	IX,X,XII paralysis, transient
5	36x35x27	17803	32x30x20	10048	56	110	16	(-)
6	38x23x19	8690	22x18x10	2072	24	115	12	X paralysis, transient
7	22x16x15	2763	18x14x9	1187	43	113	5	(-)
8	47x34x22	18398	35x28x16	8206	45	138	14	Horner syndrome, transient
9	38x28x26	14477	34x26x17	7865	54	165	7	first bite syndrome, transient
10	44x40x29	26710	40x33x28	19342	72	118	13	(-)
11	45x30x18	12717	37x26x14	7048	55	125	11	(-)
12	44x30x44	30395	38x34x22	14875	49	161	5	X paralysis, transient
13	29x25x23	8727	30x28x18	7913	91	121	9	X paralysis, transient
14	26 x 22 x 21	6286	18x16x11	1658	26	110	2	X, XII paralysis, transient
15	40x33x40	27632	40x30x27	16956	61	179	5	XII paralysis, transient
16	33x27x25	11657	31x24x15	5840	50	105	2	(-)
Mean value		13769		7436	50	139	29.3	

TABLE 3. Feeding arteries of the CBTs.

Artery	numbers
Ascending pharyngeal artery	14
Superior thyroid artery	11
Occipital artery	10
External carotid artery (direct)	5
Lingual artery	3
Ascending palatine artery	2
Facial artery	1
Posterior auricular artery	1
Accesory superior thyroid artery	1

TABLE 4. Literature review about preoperative embolization, blood loss and operation time.

Author	Country	Number of CBTs	Interval time from embolization to surgery	Number of embolization (+) Number of embolization (-)	Blood loss (cc)	Operation time (H)	Number of carotid injury
Li et al. (2010)[12]	China	66	1-6D	36 30	354.8 656.4	2.8 3.7	3 4
Lim et al. (2010)[13]	Korea	15	within 48H	7 6	400 550	6 6	n.d.
Zeitler et al. (2010)[14]	USA	25	48-72H	10 15	305 265.5	n.d.	1 1
Power et al. (2012)[15]	USA	144	24-72H	33 71	263 599	4.1 4.4	3 14
Zhang et al. (2012)[16]	China	32	24-48H	21 8	280 450	3 3.6	n.d.
Bercin et al. (2014)[17]	Turkey	14	24-48H	7 6	375 283	2.8 2.6	4 1
Present study	Japan	16	within 3H	16 0	29.3	2.3	1

Abbreviations: CBT, carotid body tumor; n.d., not described.