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Endovascular Therapy for Management of Oral Hemorrhage in Malignant Head and Neck Tumors

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Abstract

Purpose: To evaluate the efficacy and safety of endovascular therapy in oral hemorrhage from malignant head and neck tumors.
Methods: Ten patients (mean age 56 years) with oral hemorrhage caused by malignant head and neck tumors underwent a total of 13 emergency embolization procedures using gelatin sponge particles, steel and/or platinum coils, or a combination of these embolic materials. Angiographic abnormalities, technical success rate, clinical success rate, recurrence rate, complications, hemostatic period, hospital days, survival days, and patient outcome were all analyzed.
Results: Angiographic abnormalities were identified during 85% of procedures (11/13). The technical success rate was 100% (13/13 procedures). The primary and secondary clinical success rates were 77% (10/13 procedures) and 67% (2/3 procedures), respectively. The overall clinical success rate was 92%, and the recurrence rate was 22% (2/9 procedures) in patients whom we were able to observe during the 1-month period after embolization. No major complications occurred. Several patients in whom gelatin sponge particles had been used complained of transient local pain after the procedure. The median hemostatic period was 71 days (range 0–518 days). Median hospital and survival days were 59 days (range 3–209 days) and 141 days (range 4–518 days), respectively. Three patients survived and 7 patients died during the observation period. Only 1 of these 7 patients died from hemorrhage.
Conclusions: In conclusion, our findings suggest that endovascular therapy is an effective, safe, and repeatable treatment for oral hemorrhage caused by malignant head and neck tumors.

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Key words: Arteries, therapeutic embolization—Head and neck neoplasms—Hemorrhage—Interventional procedure, utilization

Oral hemorrhage caused by malignant head and neck tumors is refractory and sometimes presents a life-threatening situation. Even if hemorrhage is controlled by conservative treatments, tumors can rebleed at unpredictable intervals; therefore, the risk of fatal hemorrhage is still high. Recently, various endovascular treatments for hemorrhage from the head and neck regions have been reported, but most have occurred in trauma and postsurgical patients [1–3]. Except for case reports [4–9], original articles about endovascular therapy, in particular, embolization for hemorrhage from malignant head and neck tumors, have been rare [2, 10–14]. We retrospectively reviewed our experience to evaluate the efficacy and safety of endovascular therapy for oral hemorrhage caused by malignant head and neck tumors.

Materials and Methods

Patients

Between November 1998 and January 2004, 10 consecutive patients (6 male, 4 female) age 20–85 years (mean 56 years), who had previously been treated with conservative therapies, presented with uncontrollable oral hemorrhage from advanced malignant head and neck tumors and underwent emergency or near-emergency endovascular therapy at our institution in Japan (Table 1). Written informed consent was obtained before treatment from patients or their family members. Diagnoses included nasopharyngeal carcinoma (n = 1), oropharyngeal carcinoma (n = 4), oropharyngeal malignant lymphoma (n = 1), hypopharyngeal carcinoma (n = 1), parapharyngeal lymph node metastasis from thyroid carcinoma (n = 1), maxillary bone metastasis from renal cell carcinoma (n = 1), and mandibular bone metastasis from hepatocellular carcinoma (n = 1). The existence of primary or recurrent viable tumors had been confirmed in all patients. Tumor locations were

Table 1. Case details

Patient no.	Age/Sex	Diagnosis	Tumor location	Previous treatment	Shock index[a]	No. of sessions of embolization
1	20/F	Nasopharyngeal Ca	Widespread	CTx+RTx	1s: Mild 2nd: Mild	2
2	51/M	Oropharyngeal Ca	Localized	CTx+Ope	Mild	1
3	46/M	Oropharyngeal Ca	Localized	CTx+RTx	Moderate	1
4	85/F	Oropharyngeal Ca	Localized	RTx	None	1
5	72/M	Oropharyngeal ML	Widespread	None	Moderate	1
6	54/M	Oropharyngeal Ca	Widespread	CTx+RTx	1st: Moderate 2nd: Moderate	2
7	54/F	Hypopharyngeal Ca	Widespread	CTx+RTx	Mild	1
8	58/F	Parapharyngeal LN Mets from thyroid Ca	Localized	Ope	None	1
9	64/M	Maxillary bone Mets from RCC	Localized	None	None	1
10	61/M	Mandibular bone Mets from HCC	Localized Localized	CTx CTx+RTx+RFA+Bone cement	1st: None 2nd: Mild	2

Ca, Carcinoma; ML, Malignant lymphoma; LN, lymph node; Mets, Metastasis; RCC, renal cell carcinoma; HCC, hepatocellular carcinoma; CTx, chemotherapy; RTx, radiation therapy; Ope, operation; RFA, radiofrequency ablation; Bone cement, injection of bone cement.
[a]Shock index (= heart rate/systolic blood pressure). None, 0.5–1.0; mild, 1.0–1.5; moderate, 1.5–2.0; severe, >2.0.

classified into two groups: localized (i.e., localized to one side of the neck) and widespread (i.e., on both sides of the neck) by clinical examination and computed axial tomography (CAT) and/or magnetic resonance imaging (MRI). Six patients had localized tumor and in 4 the tumor was widespread. Six patients had received chemotherapy and/or radiation therapy; 2 patients had postoperative recurrence; and 2 patients had not undergone any treatment. Three patients had undergone endovascular therapy twice because of rebleeding, and a total of 13 embolization procedures had been performed in 10 patients.

We classified the severity of hemorrhage by shock index (i.e., heart rate/systolic blood pressure: normal range 0.5–0.7), which was a sensitive guide to the degree of hypovolemia following hemorrhage [15] on admission to the interventional radiology unit. Shock index was classified into four groups: none (0.5–1.0), mild (1.0–1.5), moderate (1.5–2.0), and severe (> 2.0). During 13 embolization procedures in 10 patients, the shock indexes were none in 4 procedures, mild in 5 procedures, moderate in 4 procedures, and severe in 0 procedures.

Procedure

Endovascular therapy was performed using the transfemoral approach with the patient under local anesthesia except for the second procedure in patient no. 6, which was performed under general anesthesia due to the patient's critical condition. To identify the bleeding and feeding arteries of the tumors, routine angiography of the bilateral common, internal, and external carotid arteries was obtained on biplanar views using a 5 Fr Headhunter catheter (Headhunter Cerebral; Cook, Bloomington, IN, USA). In some sessions, superselective angiograms of the external carotid artery's branches were additionally performed with a microcatheter (Microferret; William Cook Europe, Bjaeverskov, Denmark). On finding neovascularity and tumor stains, pseudoaneurysms, or irregularity of vessel walls, these arteries were immediately embolized. In procedures during which no remarkable findings were noted, the suspected bleeding arteries were embolized by referring to bleeding sites and tumor locations according to the otorhinolaryngologist's observations and the CAT and/or MRI imaging.

Embolic materials used were either gelatin sponge particles (Yamanouchi, Tokyo, Japan), steel and/or platinum coils (Cook), or a combination of both. Gelatin sponge was cut into 1- to 2-mm pieces (i.e., gelatin sponge particles) and injected with contrast medium. Gelatin sponge particles were mainly used in patients with occlusion in the peripheral branches of external carotid arteries. In patients with isolation of the main trunk of internal and external arteries, steel and/or platinum coils were used. In some patients, platinum coils were also used to block the flow of gelatin sponge particles into unrelated arteries with hemorrhage, in particular the meningeal branches. This technique prevented unnecessary embolization, so that when the main trunk of the maxillary or external artery was embolized with gelatin sponge particles the proximal part of a middle meningeal artery or a superficial temporal artery was occluded with coils in advance. Embolization was stopped when the target arteries became invisible or when hemorrhage ceased.

Analysis

Angiographic abnormalities, technical success rate, clinical success rate, recurrence rate, complications, hemostatic period, hospital days, survival days, and patient outcome were analyzed. Technical success of the procedure was defined as when the target arteries had been completely embolized and hemorrhage had been decreased or had ceased immediately after the procedure. Clinical success was defined as when hemorrhage had been decreased or had ceased and further conservative treatment had been possible for at least >1 month after the procedure or up until time of death. Recurrence was defined as rebleeding that occurred >1 month after embolization.

Results

Results are listed in Tables 2 and 3. Embolizations were performed twice in 3 patients because of rebleeding. Second embolizations were performed on hospital days 1 (patient no. 6), 51 (patient no. 1), and 194 (patient no. 10), respectively, after the initial embolization. The target arteries of oral hemorrhage were identified during 85% of procedures (11/13). Frequent findings included neovascularity and tumor stains (Fig. 1) in 54% (7/13), vessel wall irregularities

Table 2. Procedural data of embolization

Patient no.	Angiographic abnormalities	Embolized arteries	Embolic Materials
1	1st: Slight neovascularity of bil. ascending pharyngeal a. Pseudoaneurysm of Rt. ascending pharyngeal a. and slight tumor stains	Bil, ascending pharyngeal a., Rt. maxillary a.	Gelatin sponge particles
	2nd: Slight neovascularity of Lt. ascending pharyngeal a., LI, pacial a., bil. maxillary a, and slight tumor stains	LL ascending pharyngeal a., Lt. facial a., bil. maxillary a.	Gelatin sponge particles
		(Lt. middle meningial a. and superficial temporal a.)	(Platinum coils)
2	Slight neovascularity of Rt. lingual and facial a., pseudoaneurysm of Rt. lingual a, and slight tumor stains	Rt. Lingual and facial a.	Gelatin sponge particles
3	Irregularity of Rt. main trunk of external carotid a.	Rt. main trunk of external carotid a.	Steel coils
4	None	Bil, inferior dental a., Lt. lingual a.	Gelatin sponge particles
5	None	bil. ascending pharyngeal a., bil. maxillary a.	Gelatin sponge particles
6	1st: Irregularity, stenosis and dilatation of Lt. main trunk of internal and external carotid a.	bil. lingual a.,	Gelatin sponge particles
		Lt. main trunk of external carotid a.	Steel coils
	2nd: Pseudoaneurysm of Lt. main trunk of internal a.	Lt. main trunk of internal carotid a.	Platinum coils
7	Irregularity of bil. Main trunk of extern carotid a. and slight tumor stains	Rt, main trunk of external carotid a.	Steel and platinum coils
		Lt. thyrocervical a.	Platinum coil
8	Marked neovascularity of branches of Bil. external carotid a. and marked tumor stains	Bil. main trunk of external carotid a. (bil. middle meningial a. and superficial temporal a.)	Gelatin sponge particles. (Platinum coils)
9	Marked neovascularity of Lt. maxillary a. and transverse facial a. and marked tumor stains	Lt. maxillary a. and transverse facial a.	Gelatin sponge particles
10	1st: Marked neovascularity of branches of Rt. external carotid a. and marked tumor stains	Rt. main trunk of external carotid a (bil. middle meningeal a. and superficial temporal a.)	Gelatin sponge particles (Platinum coils)
	2nd: Moderate neovascularity of Rt. facial and maxillary a.	Rt. facial and maxillary a.	Gelatin sponge particles

Rt, right; Lt, left ,Bil, bilateral; a. artery.
Words in parentheses: Embolic arteries and material for blocking the flow of gelatin sponge particles.

Table 3. Results of procedural and clinical data

Patient no.	Technical success	Clinical success	Complications	Subsequent treatment	Hospital days (days)	Survival days (days)	Follow-up or outcomes
1	1st: Yes	Yes	None	None	(51)	(51)	
	2nd: Yes	No	None	None	(4)	(4)	
					55	55	Died of primary disease
2	Yes	Yes	None	None	209	209	Died of primary disease
3	Yes	Yes	None	None	339	339	Died of primary disease
4	Yes	Yes	None	None	29	71	Alive
5	Yes	No	None	None	4	4	Died of hemorrhage
6	1st: Yes	No	None	None	(1)	(1)	
	2nd: Yes	Yes	None	CTx	(76)	(76)	
					77	77	Died of primary disease
7	Yes	Yes	None	None	58	58	Died of primary disease
8	Yes	Yes	None	None	3	397	Alive
9	Yes	Yes	None	RTx	114	518	Alive
10	1st: Yes	Yes	None	RTx+RFA+bone cement	(49)	(194)	
	2nd: Yes	Yes	None	None	(11)	(11)	
					60	205	Died of primary disease

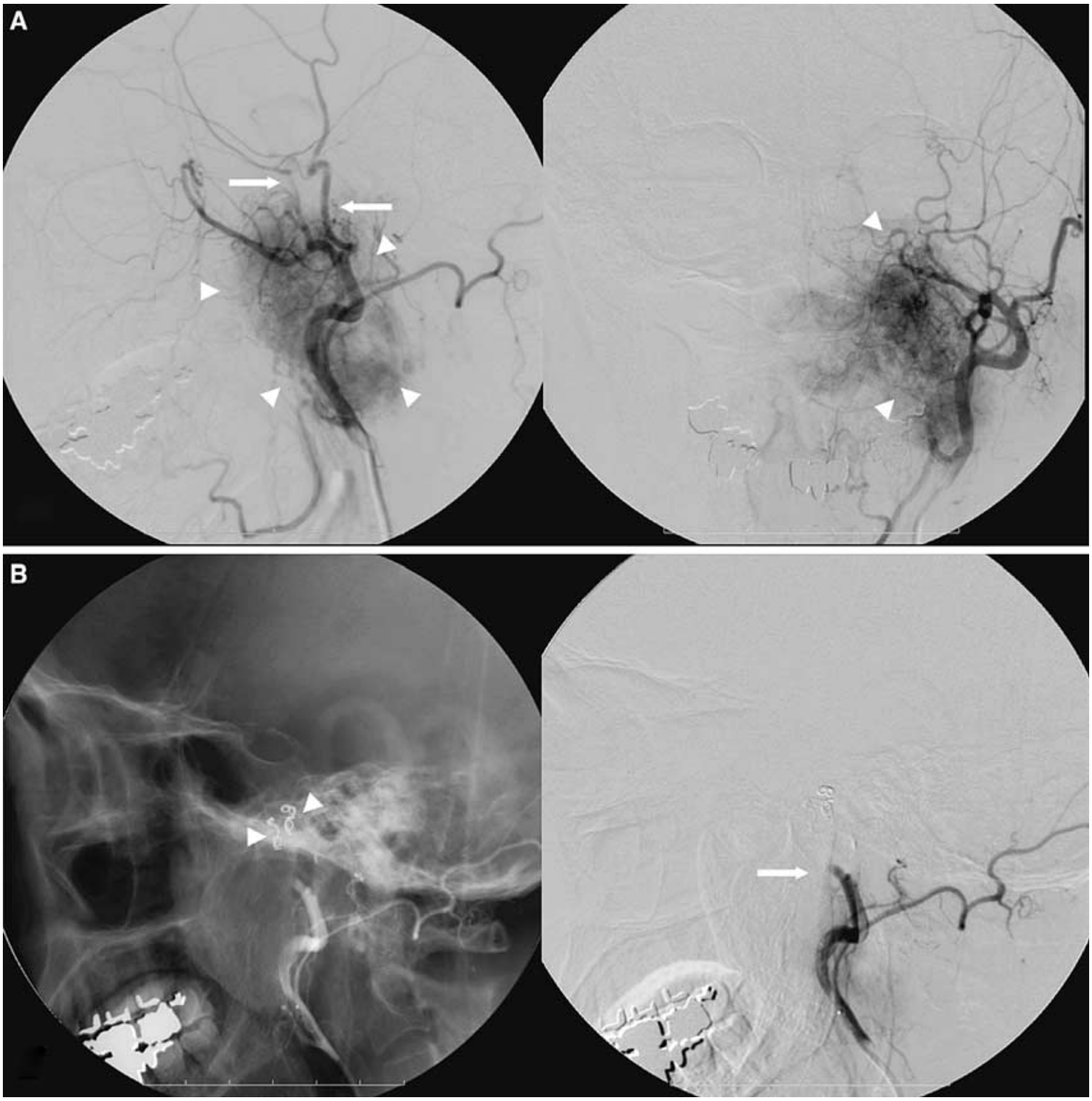

Fig. 1A, B. Patient no. 8: parapharyngeal lymph node metastasis from thyroid carcinoma. **(A)** Arteriogram of the left external carotid artery (left: lateral view; right: posteroanterior view) showed marked neovascularity and tumor stains (arrowheads). Middle meningeal and superficial arteries were not feeding vessels (arrows). **(B)** Embolization was performed from the main trunk of the external carotid artery (arrow) with gelatin sponge particles after embolization of the middle meningeal and superficial arteries with platinum coils (arrowheads). Tumor stains completely disappeared.

(Fig. 2) in 23% (3 of 13), pseudoaneurysms (Fig. 3) in 23% (3 of 13), and unremarkable findings (Fig. 4) in 15% (2/13; patients nos. 4 and 5) of procedures. In most of the patients with primary head and neck cancers, angiography showed slight neovascularity and tumor stains and sometimes pseudoaneurysms and vessel wall irregularities (Figs. 2. 3). All 3 patients with metastasis to the lymph nodes from thyroid carcinoma and to the bones from renal cell carcinoma and from hepatocellular carcinoma showed hypervascularity and tumor stains (Fig. 1).

Technical success rate was 100% (13/13 procedures), and target arteries were completely embolized in all sessions. However, hemorrhaging continued after 3 of the 13 procedures (the second procedure for patients nos. 1 and 5 and the first procedure for patient no. 6), yielding a primary clinical success rate of 77% (10/13 sessions). Patient no. 1 died from primary disease 4 days after the second embolization procedure; patient no. 5 patient died from hemorrhage 4 days after embolization; and repeat embolization was performed in patient no. 6 the day after the first embolization, and hemorrhage ceased completely. The secondary clinical success rate was thus 67% (2/3 procedures), and the overall clinical success rate was 92% (primary = 77% and secondary = 67%, respectively).

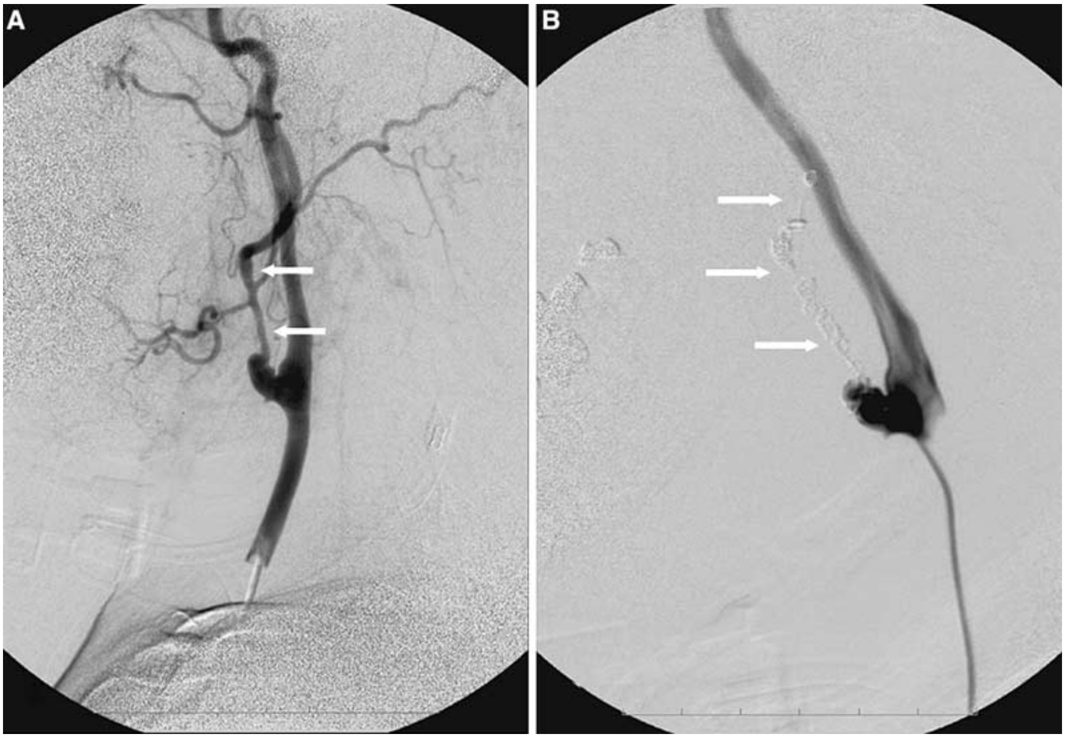

Fig. 2A, B. Patient no. 7: hypopharyngeal carcinoma. **(A)** Arteriogram of the left external carotid artery (lateral view) showed irregularity and stenosis of the main trunk of the external carotid artery (arrow). **(B)** The main trunk was embolized with two steel coils and seven platinum coils (arrowheads).

After 9 of 13 procedures it was possible to observe patients for 1 month after the first or second embolization procedure. Patients experienced rebleeding after 2 of these 9 procedures (the first procedures in patients nos. 1 and 10), thus the recurrence rate was 22%.

No major complications—including hemiparesis, blindness, or aphasia—occurred. A few patients whose procedure had been performed using gelatin sponge particles complained of transient local pain; in particular, facial pain was intense after embolization of facial arteries, but this was controlled well by analgesics. The patients were able to undergo anticancer treatment after 3 of 13 procedures. The median hemostatic period was 71 days (range 0–518 days), and hospital and survival days ranged from 3 to 209 days (median 59 days) and from 4 to 518 days (median 141 days), respectively. Three patients survived and 7 patients died during the observation period. Only 1 of these 7 patients bled to death.

Discussion

Traditional management for hemorrhage from head and neck tumors has consisted of open surgical exploration with ligation of the involved vessels. However, surgical treatment is often difficult because of fistulas, infections, radiation-induced necrosis, or previous surgical exploration. Moreover, such treatment is associated with relatively high mortality rates and high risk of neurologic complications [16]. Surgical ligation can leave a patient at risk of rebleeding from the collateral circulation [5] and, moreover, endovascular treatment becomes more difficult because of changed vascular anatomy after ligation. Our main treatment procedure is embolization and, in particular, the use of a microcatheter system, which enables superselective embolization of the affected arteries. The hemostatic effect is believed to last longer in selective embolization than in ligation because embolic materials reach all the way to the periphery [5, 7]. Even if rebleeding occurs, repeat embolization is relatively easy. In the literature, the recurrence rate of hemorrhage after embolization in patients with malignant head and neck tumors is 0 to 33% [10–14].

The recurrence rate in our study (22%) is equal to results reported in the literature. Tumor progression was believed to have been the cause of recurrence 1 month after initial embolization in patients nos. 1 and 10. After the second embolization, these patients died from their disease in shorter periods of time than did the other patients who died. The cause of recurrence the day after the procedure in patient no. 6 was deemed an insufficient first embolization, after which the irregular wall of the internal carotid artery (as seen on the first arteriogram) developed a pseudoaneurysm. However, these 3 patients did not die from hemorrhage; therefore, endovascular therapy may also be a promising treatment for tumor rebleed.

We mainly used gelatin sponge particles as embolic material because they are easily well controlled [11, 17] and

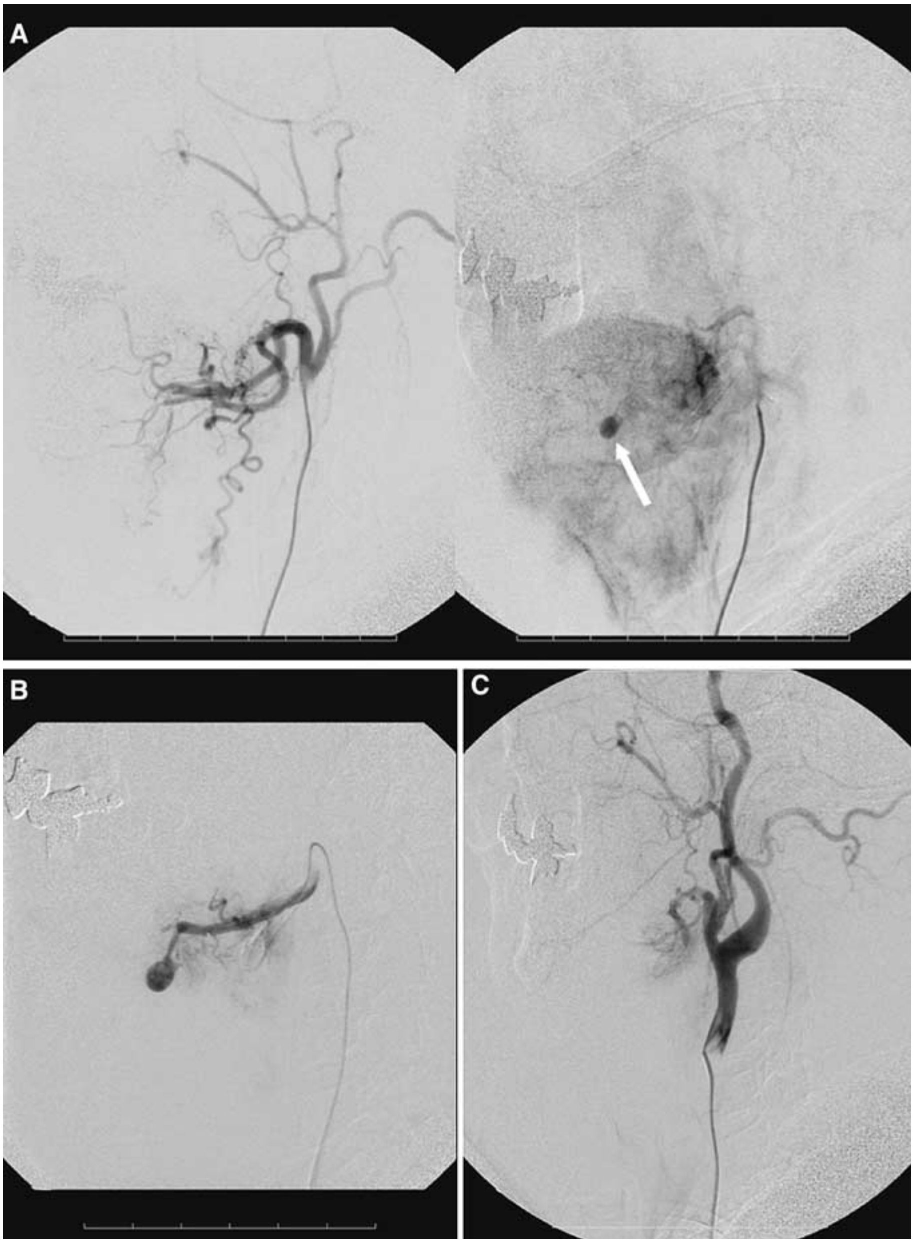

Fig. 3A–C. Patient no. 2: local recurrence of oropharyngeal carcinoma. **(A)** Arteriogram of the right external carotid artery (left: arterial phase view; right: parenchymal phase lateral view) showed a small pseudoaneurysm (arrow). **(B)** Selective arteriogram of the right lingual artery with a coaxial catheterization system showed that the vessel feeding the pseudoaneurysm was the lingual artery. **(C)** Arteriogram of the right common carotid artery after embolization with gelatin sponge particles of the right lingual and facial arteries showed complete occlusion of these arteries as well as a pseudoaneurysm.

absorbable [18, 19]. Absorbability is an advantage for postembolic re-establishment of circulation to normal tissue [19]. We believe that good absorbability induces reduced focal necrosis or a decrease in pain; indeed, pain after procedures was transient in our study. Absorbability also leads to the possibility of repeat endovascular therapy. We also used small (1- to 2-mm) particles. Berenstein et al. [20] stated that very small particles are probably contraindicated in the external carotid artery branches because they may escape into the internal carotid and vertebral arteries through normal channels. They advocated that 40- to 60-μm particles be used in the middle meningeal artery if the meningolacrimal artery is not visualized before embolization; if it is visualized beforehand, particles with a diameter larger than the anastomosis should be used to prevent emboli from entering the cerebral circulation. Even if there are invisible anastomoses, 1- to 2-mm particles will not flow into the cerebral artery. No major complications occurred in our study.

Many investigators have reported successful embolization for hemorrhage in patients with head and neck tumors using permanent embolic materials [2, 5, 6, 8, 10, 11, 13] such as polyvinyl alcohol particles or/and isobutyl-2-cyanoacrylate. Polyvinyl alcohol particles are less commonly available in our country [8]. Isobutyl-2-cyanoacrylate is even more difficult to use and tends to penetrate the capillary vessels, often inducing focal necrosis [10]. Wilner et al. [13] treated 8 patients with cataclysmic hemorrhage from squamous cell tumors of the head and neck. They used polyvinyl alcohol particles or isobutyl-2-cyanoacrylate in-

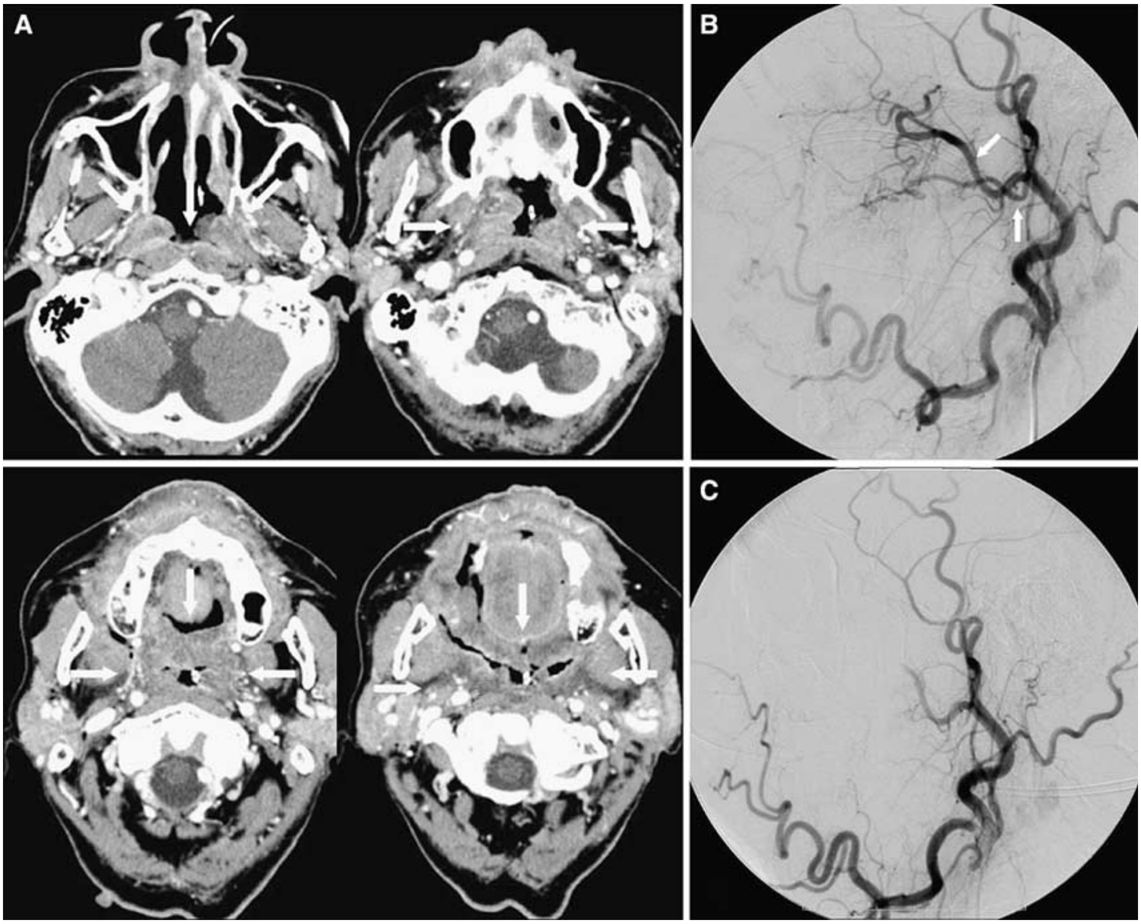

Fig. 4A–C. Patient no. 5: oropharyngeal malignant lymphoma. **(A)** CAT scan showed the oropharyngeal tumor had spread widely to both sides of the neck and to the nasopharyngeal space (arrows). **(B)** Arteriogram of the right external carotid artery (lateral view) showed no abnormality. The ascending pharyngeal and maxillary arteries (arrows) were embolized. **(C)** Arteriogram of the left external carotid artery after embolization showed the ascending pharyngeal and maxillary arteries as completely occluded; however bleeding did not cease after embolization. CAT, computed axial tomography.

stead of gelatin sponge particles to produce more permanent hemostasis. They achieved survival times ranging from 5 to 274 days (median 60 days) and no deaths as a direct result of hemorrhage. Two of 8 patients required repeat embolization because of rebleeding. These patients experienced middle cerebral artery occlusion as a serious complication from reflux of isobutyl-2-cyanoacrylate. Remonda et al. [10] stated that the most reliable embolic material was polyvinyl alcohol particles. They treated 15 patients with acute and subacute hemorrhage from head and neck tumors using polyvinyl alcohol particles or isobutyl-2-cyanoacrylate and successfully controlled bleeding in all patients; however, 5 of the 15 patients had to undergo embolization more than once before the bleeding could be controlled. Gelatin sponge particles may not be ideal because recanalization is possible [14], which could lead to rebleeding [13]. A few reports of successful control of hemorrhage by embolization with gelatin sponge particles [7, 9, 14] have been published. Zimmerman et al. [14] reported embolization of the lingual arteries with 1×6-mm gelatin sponge particles in 4 patients with hemorrhage from tongue carcinoma and achieved immediate hemostasis in all patients. In their study, there was only 1 patient in whom there was speculation as to whether bleeding recurred as a result of recanalization or whether it was caused by more proximal extension of the carcinoma along the vessel. We consider the results of embolization with gelatin sponge particles to be almost equal to those using permanent embolic materials as published by several investigators [2, 10, 11, 13]. Our results show that gelatin sponge particles may allow the possibility of achieving clinical effectiveness in embolization of the external carotid artery's branches. To verify this finding, randomization of study participants by embolization with gelatin sponge particles and permanent embolic materials in the setting of a prospective trial is needed and expected. If our findings are verified, this may prove to be a new clinical finding for embolization in patients with bleeding from malignant head and neck tumors.

Platinum and steel coils have mainly been used in embolization with two objectives. One objective is to isolate the affected arteries and obliterate pseudoaneurysms in larger arteries such as the main trunks and branches of the carotid arteries. Coils are useful for such embolizations [2, 4, 7, 10, 12]. Another objective is to spare normal branches such as the meningeal branches before embolization with gelatin sponge particles. We believe blocking blood flow into normal branches by sparing with coils contributes to a further decrease in complications such as local pain and neurologic deficits. This technique has not been previously reported in the literature to the best of our knowledge. We embolized bleeding tumors successfully and safely in patients nos. 8 and 10 using this method despite the fact that numerous fine tumor vessels were developing in these patients. Severe neurologic complications have been reported in 0 to 10% of cases [2, 10–13]. During embolization of the external carotid artery, erratic parasitism of embolic materials should be carefully avoided, and to prevent major complications the presence of anastomosis with external and internal carotid and vertebral arteries and arteriovenous shunt should not escape notice.

Hospital and survival days varied widely in our study depending on the stage of disease, performance status, and subsequent treatments (median 59 days). After 6 of 10 clinically successful procedures, patients could not be discharged because mild oozing persisted after embolization. After these procedures, the patients were in mild to moderate shock; recovery of oral intake after massive hemorrhage from malignant head and neck tumors is difficult, if possible at all. Another factor that increased hospital stay was the subsequent treatment of the patient's disease, i.e., chemotherapy and/or radiation therapy. No patients survived >2 years after embolization. Nevertheless, death from hemorrhage occurred in only 1 patient, who represented 1 in 13 procedures. We therefore believe that embolization contributes to the prevention death by hemorrhage.

Endovascular therapy has some limitations. First, among the 4 patients with widespread tumor, clinical success was not achieved in 3 of 6 procedures (50%). Although we embolized relatively large vessels of the external carotid arteries in these patients, embolization was unsuccessful in controlling hemorrhage. Insufficient embolization was the cause of embolization failure in patient no. 5 (Fig. 4). In light of this, we should have tried to embolize sufficient regions against tumor invasion. Second, embolization in 2 of 4 patients in the moderate shock index group was unsuccessful. One patient (no. 5) with widespread tumors and moderate shock index died of hemorrhage only 4 days after the procedure. Moreover, the reason for this failure seemed to be poor vascularity, wide invasion, and diffuse capillary vessels in this patient with oropharyngeal malignant lymphoma (Fig. 4). Endovascular therapy is limited in such a case.

In conclusion, endovascular therapy is an effective, safe, and repeatable treatment for the control of oral hemorrhage caused by malignant head and neck tumors and should be offered to patients. In particular, endovascular therapy is more effective in patients with well-localized tumors and a lower shock index. Gelatin sponge particles may provide a sufficient clinical effect in most embolizations of the external carotid artery branches.

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