Risk factors of recurrent carotid blowout syndrome and strategy of endovascular management

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Abstract

Background: Carotid blowout syndrome (CBS) is a catastrophic complication after aggressive head and neck cancer treatment. Endovascular embolization is an effective modality to manage CBS. However, some CBS may have recurrent CBS (rCBS) after endovascular management. This study aims to report the potential rCBS risk and endovascular management strategy.

Methods: Of the 225 patients with CBS referred for embolization in 13 years, 31 men and one woman (mean age, 55 years) with 35 rCBS with pseudoaneurysms formation were identified after endovascular management. Moreover, the rCBS preembolization angioarchitecture, rCBS cause, rCBS time interval, embolic materials selection, and final embolization clinical/angiographic outcomes were retrospectively analyzed.

Results: rCBS with pseudoaneurysm due to disease progression (DP) occurred in 17 patients, while 15 patients had insufficient embolization (IE) with 18 rCBS. The mean rCBS timing interval was 76 days with 129 and 12 days due to DP or IE. The most common rCBS locations were the carotid bulb and the main trunk of the external carotid artery (n = 20, 57%), followed by internal carotid artery (n = 8, 23%), distal branch of the external carotid artery (n = 4, 11%), and common carotid artery (n = 3, 9%). Endovascular management was technically successful in all patients by reconstruction (n = 7, 20%) or destruction (n = 28, 80%) techniques. Three patients (9%) had procedure-related complications. No rCBS was observed in all affected arteries after the last embolization in a mean 11-month clinical follow-up.

Conclusion: rCBS may result from DP or IE. The common location of IE-related rCBS usually occurred in the carotid branches. It occurred within two weeks of CBS largely because of the underestimation of the extension of the affected carotid artery. In addition, DP is natural in head and neck cancer after aggressive treatment. Thus, endovascular management remained an effective method to manage rCBS.

Keywords: Carotid blowout syndrome; Embolization; Head-neck cancer; Recurrence

1. INTRODUCTION

Carotid blowout syndrome (CBS) is carotid artery rupture or segmental carotid artery exposure in patients following aggressive head and neck cancer (HNC) management. It is classified as acute, impending, or threatened based on its severity.[1,2] CBS is always associated with catastrophic bleeding. Most patients will have a fatal shock if left untreated.[3,4] Identification of bleeding points and early commencement of endovascular management are critical life-saving procedures with promising clinical outcomes.[5–10] However, some patients may have recurrent CBS (rCBS) after aggressive endovascular management of previous CBS. The cause and angioarchitecture of rCBS have not been evaluated well. Understanding the potential risk factor may be helpful to predict a patient's clinical and angiographic outcomes and avoid rCBS occurrence.

This paper aimed to assess the angioarchitecture and risk factors of rCBS and endovascular management strategy.

2. METHODS

From September 2005 to August 2018, the institute where this study took place saw 225 patients with HNC-related CBS for diagnostic angiography and endovascular embolization to aggressively manage intractable oronasal or neck hemorrhage. From the database, 35 patients with 38 rCBSs had pseudoaneurysm (PA) formation verified by carotid digital subtraction angiography (DSA) with (active rCBS) or without contrast leakage (impending rCBS). All patients had HNC and underwent radiation and chemotherapy (n = 33) or combination treatment with surgical tumor removal (n = 21). This study was approved by the institutional review board of the current study before study initiation. All informed consents were obtained from the patients or the patient's families. Table 1 summarizes information on these 35 patients with 38 rCBS, including the patient's age and gender, rCBS number/location, rCBS angioarchitectures, rCBS cause, and CBS/rCBS timing interval as well as embolization technique and treatment outcomes. Of the patients, 31 (97%) were

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Table 1

Demography and characteristics of 32 patients with 35 rCBSs

	Value
No of patients of CBS	225
No of patients of rCBS enrolled	32 (14%)
Mean age (y)	
Gender	55 (range 42-81)
Female	1 (3%)
Male	31 (97%)
Number, location of rCBS	
Total number of rCBS	
No of acute rCBS	35
No of impending rCBS	21 (60%)
Location of rCBS	14 (40%)
CCA	3 (9%)
ICA	8 (23%)
CB	10 (29%)
mECA	10 (29%)
dECA	4 (11%)
Disease progression of rCBS	
No of patients/rCBS	17/17
Mean age of DP of rCBS	56 yrs
Day interval of CBS/rCBS (mean)	38-320 (129)
Insufficient embolization of rCBS	
No of patient/rCBS	15/18
Mean age of IE of rCBS	53 yrs
Day interval of CBS/rCBS (mean)	1-27 (11)
Technique of embolization of rCBS	
Reconstruction	7 (20%)
Destruction	28 (80%)

CB = carotid bulb; CBS = carotid blowout syndrome; CCA = common carotid artery; dECA = distal branch of external carotid artery; ICA = internal carotid artery; mECA = main trunk of external carotid artery; rCBS = recurrent carotid blowout syndrome.

men, and one (3%) was a woman. Patients were 33–81 years old (mean age, 55 years old). All patients had recent r acute oronasal bleeding, managed by oronasal packing. Before DSA initiation, the CTA of the skull base and neck were performed for all patients to assist subsequent DSA for the localization of the bleeding points.

2.1. rCBS definition

rCBS is the presence of PA in the carotid artery after endovascular management of previous CBS. Those patients with self-limited tumor bleeding or bleeding point not detected by DSA were excluded. rCBS due to disease progression (DP) was considered if PA was found at the contralateral side or in another (Fig. 1) or similar arterial territory (e.g., internal/external/common carotid artery) with remote to (longer than 5 cm) previously demonstrated PA. On the contrary, rCBS due to insufficient embolization (IE) was considered when the PA occurred on-site (Figs. 2 and 3) or within 5 cm of previously managed PA (Fig. 3).

2.2. DSA protocol and endovascular management principle to rCBS

The femoral arteries of patients were catheterized with a percutaneous technique under local anesthesia. The DSA of the aortic arch, bilateral carotid, and vertebral arteries were assessed for potential PA formation, bleeding points, and intracranial hemodynamic circulation. Rotational and three-dimensional reconstruction DSA were routinely obtained in patients for whom bleeding points were difficult to identify.

The occlusion of the affected artery by liquid adhesive or coil(s) was performed in rCBS with involving ECA branch. In those CBS involving internal or common carotid artery (ICA/CCA), balloon occlusion test (BOT) was routinely used to evaluate the collateral flow. If the patient could tolerate the BOT, the patient underwent a deconstructive technique by the coil or liquid adhesives occlusion of affected ICA/CCA. The reconstructive method, by a cover stent, was selected when the patient failed to tolerate BOT or the affected carotid ICA/CCA was vital to maintaining cerebral circulation, such as when contralateral ICA was already occlusive or high-grade stenosis. For those patients with a deconstructive method to ICA occlusion, patients were hydrated by daily intravenous fluid administration of 1,500–2,000 cm^3 and kept systolic pressure at about 140–160 mmHg for 2 days to avoid watershed or delayed ischemic stroke. Regarding pharmacological therapy for the cover stent, clopidogrel (150 mg) and aspirin (200 mg) were given daily for 3 days before embolization. After stenting, patients were given clopidogrel (75 mg) and aspirin (200 mg) daily for 6 months, followed by clopidogrel (75 mg) and aspirin (100 mg) daily for the next

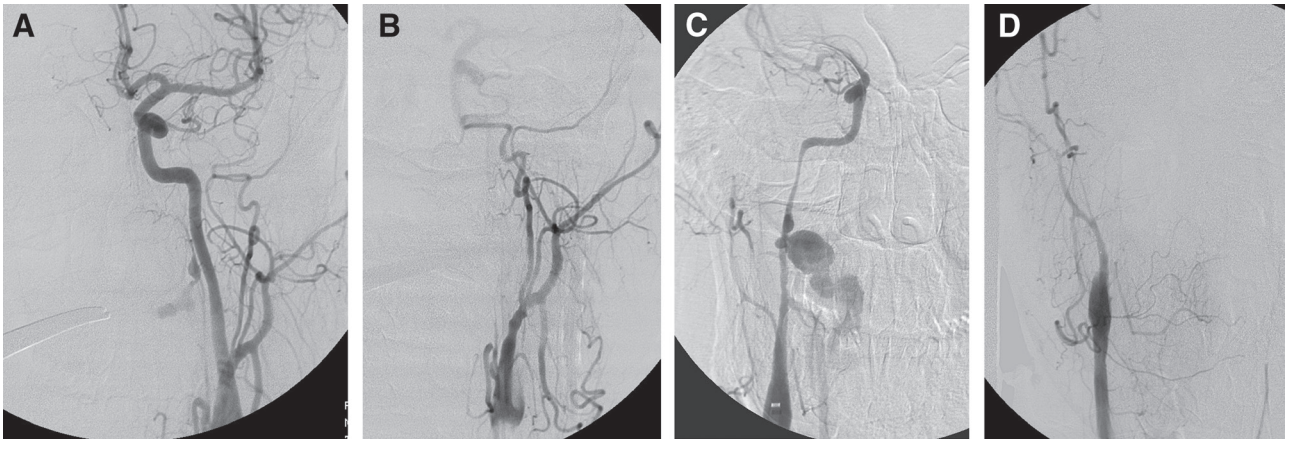

Fig. 1 A 33-year-old man with nasopharyngeal carcinoma following combined chemotherapy and radiotherapy presented with rCBS due to disease progression. **A**, **B**, Preembolization left frontal common carotid artery angiogram revealed acute CBS in the distal branch of the ascending pharyngeal artery. The patient underwent transarterial liquid embolic material embolization leading to obliterate CBS. **C**, The patient developed acute rCBS at the right cervical internal carotid artery with a 90-day interval of previous CBS. **D**, After the balloon occlusion test, the right ICA and acute rCBS were obliterated by detachable balloon and liquid embolic materials. CBS = carotid blowout syndrome; ICA= internal carotid artery; rCBS = recurrent carotid blowout syndrome.

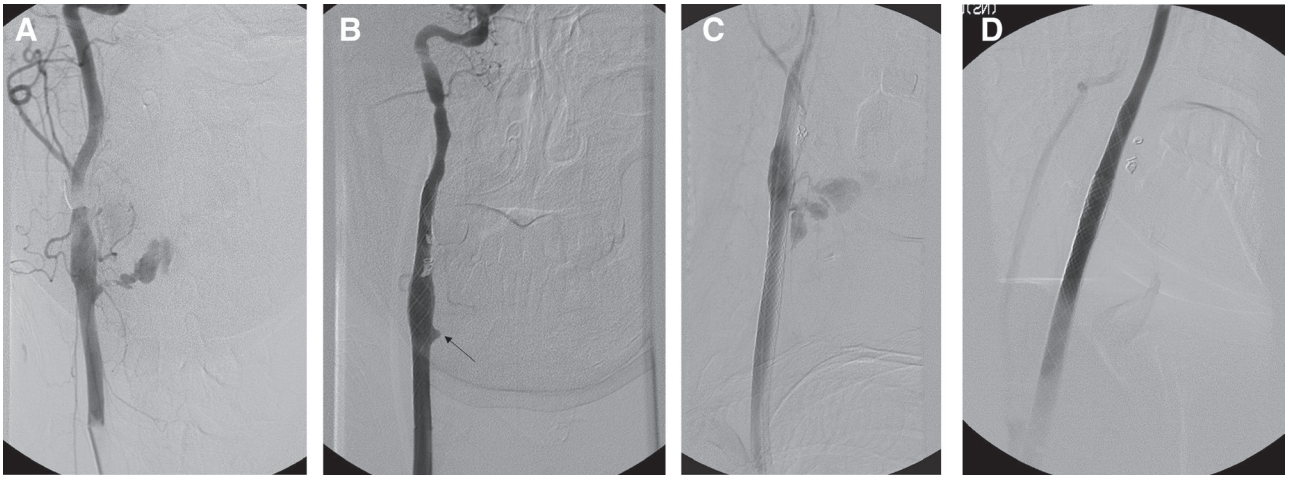

Fig. 2 A 58-year-old man with hypopharyngeal carcinoma following tumor resection and CCRT. The patient had IE-related acute rCBS. **A**, Preembolization of the right carotid angiogram revealed an active CBS in the carotid bulb; the patient failed to tolerate BOT. **B**, The patient underwent endovascular cover stent management. However, a small residual pseudoaneurysm (*arrow*) was found because of endoleak. **C**, The patient developed active rCBS 2 days after the previous stenting due to IE. **D**, A second cover stent was deployed into the affected carotid artery leading to total PA occlusion with ICA flow preservation. BOT = balloon occlusion test; CBS = carotid blowout syndrome; ICA= internal carotid artery; IE = insufficient embolization; PA = pseudoaneurysm; rCBS = recurrent carotid blowout syndrome.

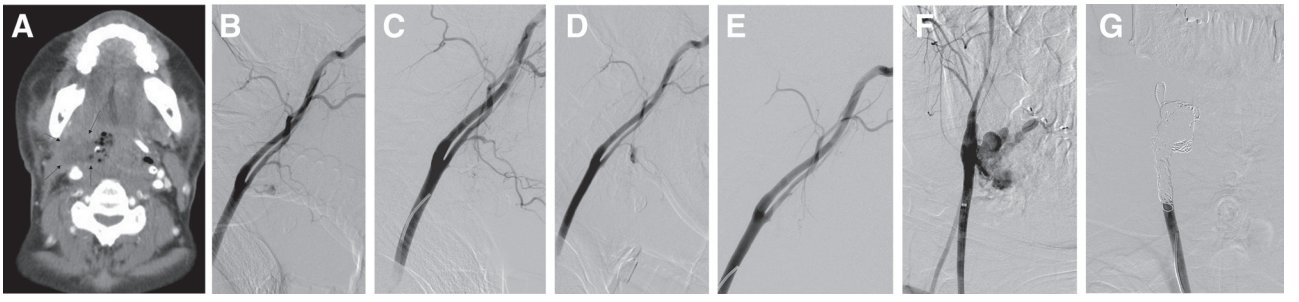

Fig. 3 A 45-year-old man had hypopharyngeal carcinoma after tumor resection and CCRT. The patient had two rCBSs due to IE. **A**, Computed tomography of the neck 2 days before embolization showed a necrotic tumor (*arrows*) near the mECA and carotid bulb. **B**, **C**, Preembolization of the right carotid angiogram showed acute CBS at the proximal superior thyroid artery near the mECA. The patient underwent transarterial liquid adhesive embolization with total CBS obliteration. **D**, **E**, The patient suffered acute rCBS at the proximal lingual artery near the mECA 13 days from the previous CBS. Again, the patient underwent transarterial liquid adhesive embolization with total rCBS obliteration. **F**, **G**, Patient had second acute rCBS of the right CB 21 days from rCBS. Right ICA, ECA, and CCA were eventually occluded by fiber coils after BOT. BOT = balloon occlusion test; CCA= common carotid artery; ECA, external carotid artery; ICA= internal carotid artery; IE = insufficient embolization; mECA, main trunk of the right external carotid artery; rCBSs, recurrent CBS.

6 months, and aspirin (100 mg) for a lifetime. Postembolization DSA was routinely obtained to assess the embolization effect.

Two experienced interventional neuroradiologists with 28 and 23 years (CBL and FCC) of experience evaluated these DSA findings and treatment outcomes independently. They used the same workstation to evaluate the angioarchitectures and treatment outcomes rCBS location, rCBS cause, embolic material selection, and embolization technique. Any discrepancy in the DSA findings of these two interventional neuroradiologists was resolved through reassessment and discussion to reach an agreement.

2.3. Statistical analysis

The SPSS statistical software package (version 20) was used for all statistical analyses. Correlations between the rCBS with age, gender, DSA findings, rCBS location, rCBS time frame, and embolic material selection in both groups of DP- and IE-related rCBS were analyzed using the chi-square test for categorical variables. Continuous variables (e.g., time interval and PA formation location) were analyzed using a one-way analysis of variance with post hoc Bonferroni correction. A p value <0.05 was considered to indicate a statistically significant difference.

3. RESULTS

Table 1 lists demography, angioarchitecture, and treatment outcomes. rCBS due to PD was found in 17 patients, while IE was depicted in 15 patients with 18 rCBS. The average rCBS timing was 79 days with 129 and 12 days in DP and IE, respectively, and statistical significance (p < 0.01) was noted. rCBS occurred in the contralateral CBS side exclusively found in seven DP-related rCBS. Acute rCBS was depicted in 21 (60%) patients. The most common rCBS location was the carotid bulb (CB) and the main trunk of the external carotid artery (mECA; n = 20, 58%), particularly those IE-related rCBS (n = 15, 83%) and showed statistical significance compared with DP-related rCBS (p < 0.01), followed by the ICA (n = 8, 23%), distal ECA branch (dECA; n = 4, 11%), or common carotid artery (n = 3, 9%). Seven (20%) and 28 (80%) reconstructive or destructive techniques to manage rCBS were noted, respectively. Procedure-related

complications occurred in three patients (9%) with permanent (n = 1) or transient neurologic deficit (n = 2). After embolization, 35 patients achieved complete bleeding cessation. Nineteen patients (59%) expired during the follow-up period due to advanced tumor progression. The clinical follow-up period for these patients was 0.5–31 months, with a mean of 11 months.

4. DISCUSSION

The skull base, face, and neck have rich vascular networks fed by CCA, ICA, and numerous ECA branches. Healthy arteries usually should have abundant blood flow to supply their walls by vasa vasorum. The normal surrounding soft tissue to support and protect the carotid artery is also crucial to maintain arterial function.[11] After composite treatment by surgical resection, radiation, or chemotherapy to control and eradicate the HNC, tumor necrosis usually occurred with cavity formation. Moreover, the damage of normal adventitia and vaso vasorum through various processes leads to the loss and weakness of the carotid artery wall thickness. Eventually, it causes CBS/rCBS associated with severe hemorrhage. Recurrent bleeding is not uncommon after aggressive endovascular CBS management. The cause of recurrent bleeding commonly results from tumor bleeding, angiographic hyperemic change, exposed affected artery, or more severe CBS form with PA formation. Chaloupka et al. reported that the recurrent bleeding occurred in 26% of 46 consecutive patients after endovascular CBS management, and most bleedings resulted from tumor bleeding.[12] No published data of rCBS with PA formation after aggressive endovascular management of previous CBS currently exist. The rCBS incidence in the current series was 14% of 225 patients.

The rCBS cause could be attributed as DP or IE related. DP-related rCBS was presumed as a natural course of treated HNC after endovascular CBS management. DP-related rCBS could be considered as an isolated CBS and nonrelated to previously managed CBS. In this series, 17 rCBS was assumed to be DP because it occurred in the contralateral carotid artery or different carotid territory or remote to the previous CBS location. DP-related rCBS was commonly found in the larger tumor, affecting the different carotid territories. In addition, patients underwent a second aggressive treatment of recurrent/residual tumors. In this series of the DP group, the timing interval of CBS and rCBS is 129 days. In terms of the location of DP-related rCBS, it occurred in more evenly distributed in different carotid territories compared with those of IE-related rCBS. On the contrary, IE-related rCBS usually occurred onsite or nearby carotid branch(es). The mean interval time is 11 days and showed a much shorter time frame than DP with statistical significance ($p < 0.01$). IE more frequently occurred in the CB (29%) or main ECA trunks (29%) in which carotid is bifurcate or has several ECA branches. DSA is a gold standard to evaluate the cerebrovascular lesion and hemodynamic and guide to manage cerebrovascular lesion because DSA can preciously detect the small PA that CTA or other imaging modalities may overlook. However, DSA may underestimate the extension of the ongoing CBS,[5] and the endovascular CBS with PA management in a single branch of the carotid artery may be insufficient, particularly in those patients with larger necrotic tumor or cavity potentially affecting other carotid branches. CT/CTA can be a supplement imaging modality to DSA to search the CBS extension. Therefore, the scope of embolization should rely on both DSA and CTA findings to avoid rCBS.[11]

Endovascular management of natural intracranial arterial aneurysms obliterates the aneurysm sac by coiling and parent artery preservation. However, the PA of the CBS is a different entity than the natural aneurysm because the PA lacks an arterial wall.[13] Complete angiographic obliteration by coiling PA may be temporally achieved on DSA. However, the packing density is usually <30% with insufficient blockage of blood flow into the PA, and the recurrent PA was inevitable and usually found in a few days. Therefore, PA occlusion alone is not enough to cease future bleeding. To avoid rCBS, complete and permanent PA and nearby carotid artery obliteration are mandatory. Endovascular occlusion of ECA branches is usually easier and safer[10,11] because numerous arterial networks and collateral flow in the face and neck are noted. In contrast, if CBS involves the ICA, carotid bulb, or CCA, endovascular management would be more complex and riskier because these vital carotid arteries supply the brain's blood flow. Although cover stents have been used to manage CBS involving the ICA, CCA, and carotid bulb by preserving the flow of the affected carotid artery,[14–17] the best method to manage the CBS of the CCA/ICA is via endovascular coil occlusion. Moreover, the preservation of the involved and weakened unhealthy carotid artery is typically impossible and extremely complicated.[13] The major risk involved in the endovascular occlusion of the ICA/CCA is ischemic stroke. The BOT of the ICA/CCA helps understand the risk of both acute and delayed hemodynamic ischemia related to the ICA/CCA occlusion. The advantage of the cover stent to manage CBS is to preserve the flow of the affected artery with less ischemic complication than the destruction method of the ICA or CCA occlusion, which is particularly useful when contralateral ICA was previously sacrificed due to previous CBS or high-grade stenosis due to radiation or natural arteriosclerotic change. The disadvantage of the cover stent is poor apposition of of stent leading to endoleaking with rCBS.[14] Dual antiplatelet treatment is necessary for the reconstructive method by deploying the cover stent to the affected carotid artery to prevent postprocedural thromboembolic complications, which may worsen tumor bleeding if it occurs. The major limitation of the cover stent is the difficulty to deploy the stent in the tortuous carotid artery with lacking satisfy apposition of the stent.

In conclusion, rCBS may occasionally occur due to DP or IE. IE-related rCBS usually occurred within 2 weeks after the first embolization and is commonly found in the CB and mECA of the carotid branches. PD is another risk factor of rCBS due to the natural course of the aggressive HNC management, and it occurred with a longer time interval after previous CBS management. Thus, endovascular embolization remained an effective method to manage rCBS.

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