Timeline for Carotid Blow-out in Head and Neck Cancer Patients, When to Expect Major Bleeding?

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Abstract

Abstract: Objectives: Carotid blow-out syndrome (CBS) is one of the uncommon yet detrimental complications in head and neck cancer patients, by presenting itself as a catastrophic bleeding. Various factors are related with CBS. There is no timeline for the development of CBS in patients with uncontrollable tumors. In this report we intended to review our cases of CBS with special emphasis on risk factors, the timeline for carotid rupture as well as the outcomes following ligation. Design, Setting and Participants: A retrospective analysis was performed on previously treated head and neck cancer patients who experienced carotid blow-out syndrome (CBS) following tumor recurrence between 2015 and 2020. Results: All of the patients in this study were classified as type III CBS and managed by carotid artery ligation. Three patients had previous chemoradiotherapy while five had surgery and adjuvant treatment as the primary treatment. Time to recurrence following primary treatment was ranging between 6-19 months with a mean of 8.25±5.11 months. Apart from tumor infiltration seen in all of the patients, 3 had fistula, 5 had wound infection and 6 had necrosis. Conclusion: CBS is an uncommon yet detrimental complication encountered in head and neck cancer patients, which is mostly treated by endovascular approach. However, surgical ligation is still a treatment option especially in patients with type III rupture. Since, there is a limited time for those patients preventive measures should be undertaken within 4 months following soft tissue exposure, necrosis and fistula.

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Conclusion: CBS is an uncommon yet detrimental complication encountered in head and neck cancer patients, which is mostly treated by endovascular approach. However, surgical ligation is still a treatment option especially in patients with type III rupture. Since, there is a limited time for those patients preventive measures should be undertaken within 4 months following soft tissue exposure, necrosis and fistula.

Key words: carotid blow-out syndrome; carotid rupture; carotid artery ligation; head neck cancer; radiotherapy

Key Points

1. Carotid blow-out syndrome (CBS) is one of the uncommon yet detrimental complications in head and neck cancer patients, by presenting itself as a catastrophic bleeding.
2. There are various risk factors for CBS such as prior radiotherapy, prior radical neck dissection, mucocutaneous fistula, flap necrosis, wound infection, poor nutrition and tumor recurrence.
3. Prevention may be the most effective treatment by using various reconstructive procedures such as myocutaneous flaps to hinder the exposure of carotid artery and to avoid pharyngocutaneous fistula.
4. Regardless of the treatment choice; angiography is accepted as gold standard for diagnosis, by also having the advantage of evaluating the patency of contralateral carotid system with balloon occlusion test, thus leading the treatment option.
5. Since, it has a high mortality and neurologic morbidity, preventing CBS would be the most effective treatment method, because the countdown is approximately set to 4 months.

INTRODUCTION

Carotid blow-out syndrome (CBS) is one of the uncommon complications in head and neck cancer(1)(2). It may occur due to tumor invasion or fibrosis of adventitia of the artery as a complication of cancer treatment resulting in rupture of carotid artery(3). Common presenting symptoms are catastrophic bleeding from oral cavity, oropharynx or an exposed wound on the neck. Incidence of CBS in patients with major head and neck surgery ranges between 3-4.5%(4)(5), with 7.6 fold increase with previous history of irradiation(6). There are various risk factors such as prior radiotherapy, prior radical neck dissection, mucocutaneous fistula, flap necrosis, wound infection, poor nutrition and tumor recurrence(7); with previous curative radiotherapy being the main risk factor after salvage surgery, especially a total radiation dose over 70 Gy(5)(8). Incidence of CBS following re-irradiation may increase up to 17%(5). Another factor is tumor encasement of carotid artery, infiltration of carotid wall by tumor causing inflammation and weakening of carotid artery(5)(9). Although modern surgical reconstruction methods decreased the rate of CBS, morbidity and mortality still remains with rates up to 76% for mortality(10) and 16-60% for neurologic morbidity(11).

Prevention may be the most effective treatment by using various reconstructive procedures such as myocutaneous flaps to hinder the exposure of carotid artery and to avoid pharyngocutaneous fistula(7). Ligation of common carotid artery (CCA) or internal carotid artery (ICA) is the traditional management of CBS with higher rates of neurologic sequela(4). Yet another and more frequent option is embolization or stenting of carotid artery by endovascular approach with less complication rates. However, not every patient is suitable for endovascular approach; patients with open wound and active bleeding are still being managed by ligation.

There is no timeline for development of CBS in patients with uncontrollable tumors. In few reports regarding salvage surgery, carotid rupture was seen within 10-40 days following surgery(5), yet there is no knowledge in literature about the time to carotid rupture due to unresectable tumors or patients with open wounds. In this report we intended to review our cases with CBS with special emphasis on risk factors, timeline for carotid rupture as well as the outcomes following ligation.

MATERIALS AND METHODS

Design, Setting and Participants

A retrospective analysis was performed on previously treated head and neck cancer patients who experienced CBS following tumor recurrence between 2015 and 2020. From medical records of 348 patients, 8 patients

with CBS who had open approach surgical ligation of carotid artery were detected. Patients treated with endovascular intervention, untreated cancer patients and patients lost to follow-up were excluded. All of the patients had head and neck cancer with primary surgery and adjuvant treatment or salvage surgery and referred to our center with active bleeding due to CBS who were treated by open surgery with carotid ligation. CBS was classified as type I (threatened) CBS occurring when carotid artery was exposed through soft tissue breakdown, type II (impending) with limited, sentinel bleeding and type III (rupture) with active bleeding as suggested by Chaloupka et al(1) and Powitzky et al(12). Demographic data (age, sex), primary site of tumor, neck stage during primary treatment, type of surgery, radiotherapy history, predisposing factors (fistula, wound infection, necrosis), site of rupture, time to recurrence of tumor and time to CBS from exposure of neck soft tissues were obtained by a review of medical history. Variables were expressed as percentage, mean ± standard deviation. The reporting guideline of choice was STROBE (Strengthening the Reporting of Observational studies in Epidemiology) for this article. (13)

Ethical Consideration

Ethics committee approved the study design and informed consents were obtained from patients or their caregivers.

RESULTS

Demographics, previous N stage, type of surgery, time to recurrence and time to carotid rupture of 8 patients were presented in Table 1. All of the patients in this study were type III CBS and managed by carotid artery ligation. Age of the patients was between 54 and 69 with a mean of 62.75±5.6 years.

All of the patients had untreatable locoregional recurrence. Primary site was oral cavity in 3(37.5%), oropharynx-hypopharynx in 3(37.5%) and larynx in 2(25%) patients with primary N stages as N1 in 1(12.5%), N2 in 3(37.5%) and N3 in 4(50%) patients. Three patients(37.5%) had previous radiotherapy or chemoradiotherapy for curative intent. Five patients (62.5%) had surgery and postoperative adjuvant treatment, radical neck dissection was performed in 3 (60%) and functional neck dissection was performed in 2(40%)(Table 1). Time to recurrence following primary treatment was between 6-19 months with a mean of 8.25±5.11 months. Apart from tumor infiltration seen in all of the patients, three had fistula, 5 had wound infection and 6 had necrosis at bleeding site(Table 1). Bleeding was from CCA near bifurcation in 5(62.5%), ICA in 2(25%) and from main trunk of external carotid artery just above bifurcation in one(12.5%) patient(Table 1). Time from detection of recurrence-soft tissue exposure to CBS was ranging from 2 to 12 months with a mean of 5.37±3.11 months and in patients having fistula and necrosis blow-out was earlier(6 patients; 2-4 with a mean of 4±1.2 months). Postoperatively 2 patients had major neurologic morbidity (hemiplegia; 25%). In postoperative follow-up period 7 patients were detected to be deceased(87.5%) and mean time to death was 7.71±6.15 months(1-17 months).

DISCUSSION

First described in 1962 by Borsany(14), CBS still is an important complication in head and neck cancer, with a mortality of 40% and neurologic morbidity of 60%(1)(15). Prior radiotherapy, prior radical neck dissection, mucocutaneous fistula, flap necrosis, wound infection, poor nutrition and tumor recurrence can be counted as risk factors for CBS(5)(7)(8). Tumor encasement and infiltration of carotid artery causing inflammation and weakening of carotid artery wall, also plays an important role(5)(9). Overall incidence of CBS in head and neck cancer ranges from 2.5% to 4.5%(2)(5)(10). After examination of medical records of 348 patients treated for head and neck cancer in our clinic, 8 patients with CBS treated by open approach carotid artery ligation, were determined, having a slightly lower rate compared to the literature(2.3%).

CBS was classified as type I(threatened) CBS occurring when carotid artery was exposed through soft tissue breakdown, type II(impending) with limited, sentinel bleeding and type III(rupture) with active bleeding(1)(12). Type III is the most common type of CBS(over 60%) followed by type II and I, respectively(12)(16). Chaloupka et al., reported their findings on endovascular treatment of CBS. Among 4 patients with type I, 10 patients with type II and 5 patients with type III CBS; most common pathologic finding

was pseudoaneurysms, followed by tumor encasement(1). However, in another study, extravasation was the most common pathologic finding(in 8 out of 10 patients), while pseudoaneurysm was seen in only 2 patients, which could be explained as all these 8 patients were type III CBS(17). All of our patients presented with acute rupture(type III CBS), thus most common finding was extravasation, followed by pseudoaneurysm.

CCA emerged as the most common site of origin of rupture in our study, which was consistent with the literature reporting a rate of over 60% (5)(12)(17)(18). Bleeding was found to be from CCA near bifurcation in 5(62.5%), ICA in 2(25%) and from main trunk of external carotid artery just above bifurcation in one(12.5%) patient. However, in a study consisting of 6 patients with CBS, ICA was found to be the most common site(in 4 out of 6 patients), followed by CCA(2). In addition, in a larger scale study, again ICA was reported to be the most common site with a rate of greater than 50%, while CCA was being the least common(1).

Previous radiotherapy is considered to be the most important risk factor, by increasing the risk up to seven fold(6)(19), even to 14-fold in case of a radiation dose of >70 Gy(8). After exclusion of patients who were previously irradiated, CBS rate was found to be only 0%–2.4%; however, when patients received radiotherapy analyzed separately, CBS rate increases to 4.5%–21.1% (5). Free radical production triggered by radiotherapy is considered to be causative agent by inducing thrombosis of vaso vasorum, fibrosis of adventitia, and premature atherosclerosis; eventually resulting in weakening of arterial wall(19). In Estomba et al.'s study, except for one out of six patients with CBS had a previous history of radiotherapy and cause of CBS was proved to be radiation induced necrosis in 3 patients, pharyngocutaneous fistula in 2 patients, and tumor recurrence in 1 patient(2). Durmaz et al., stated that history of radiotherapy was the common future in all of their 10 patients with CBS, 7 with recurred cancer and 5 with pharyngocutaneous fistula(17). In a large review by Powitzky, among 140 patients and 161 CBS cases, previous history of radiotherapy was found to be the most common shared feature(89%), followed by nodal metastasis(69%), neck dissection(63%), necrosis(55%), mucocutaneous fistula (40%)(12). Being another risk factor, neck dissection - especially radical neck dissection, with stripping of the carotid – was reported to increase the risk of CBS to eight fold(8). Among 8 patients included in this study, all had a previous history of radiotherapy, with 3 as primary curative treatment and 5 as adjuvant treatment. 3 of the latter also had a history of radical neck dissection. Pharyngocutaneos fistula in 3, wound infection in 5 and necrosis at bleeding site in 6 of the patients were seen, apart from tumor infiltration which was present in all.

Most common tumor primary sites were larynx(23%), hypopharynx(22%) and nasopharynx (21%)(12). In a study consisting of 10 patients with CBS, in a six-year period, 3 had had primary tumor in larynx, 2 each in oral cavity, hypopharynx, nasopharynx, and 1 in salivary gland(17). In our study, primary site was oral cavity in 3(37.5%), oropharynx-hypopharynx in 3(37.5%) and larynx in 2(25%) of the patients.

Surgical ligation has been traditionally the treatment of choice for CBS(18)(20). However, after the introduction of the detachable balloons specifically for treatment of impending CBS in 1984 by Osguthorpe and Hungerford(21), there has been an increasing tendency towards endovascular approach. Over 90% of patients reported in the past fifteen years were treated by endovascular approach, either by stenting or embolization; while surgical ligation was the preferred method in less than 10%(12). Drawbacks of surgical ligation; such as hemodynamic instability complicating perioperative management, hypotension deepened with general anesthesia resulting in cerebral ischemia, consumption coagulopathy due to blood loss resulting in uncontrollable re-hemorrhage, challenging surgical dissection caused by previous operations and radiotherapy; played role in this change of treatment preferences(1). In a paper reporting 6 cases with CBS, among 3 patients managed by endovascular approach, 1 had neurologic sequel; while 1 patient managed by surgical ligation also suffered neurologic complication(2).

Regardless of the treatment choice; angiography is accepted as gold standard for diagnosis(22), by also having the advantage of evaluating the patency of contralateral carotid system with balloon occlusion test, thus leading the treatment option(23)(24). Hence, every treatment should be preceded by angiographic evaluation; yet it may not be possible in every case due to need of emergent intervention.

Average time to CBS from initial time of diagnosis was 2.7 years, mostly originating from proximal part

of the carotid bifurcation(12). Among patients who had a second regime of radiotherapy, median time for CBS to occur, from beginning of re-irradiation, was 7.5 months, ranging up to four to five years, in certain cases(10). In our patient population, time to recurrence following primary treatment was between 6-19 months with a mean of 8.25±5.11 months. Time from detection of recurrence or soft tissue exposure to CBS, was from 2 to 12 months with a mean of 5.37±3.11 months, with being earlier in patients having fistula and necrosis (6 patients; 2-4 months with a mean of 4±1.2 months). In this regard, following massive neck or local recurrence with soft tissue exposure, necrosis and fistula, carotid blow-out is to be expected within 4 months and preventive measures must be undertaken during this period.

CONCLUSIONS

CBS is an uncommon yet detrimental complication encountered in head and neck cancer patients, especially with a history of radiotherapy and radical neck dissection. It is an emergency which necessitates the use of angiography for diagnosis, and in most cases for treatment. However, surgical ligation could still be a treatment option. Since, it has a high mortality and neurologic morbidity, preventing CBS would be the most effective treatment method, especially in patients with soft tissue exposure, necrosis and fistula because the countdown is approximately set to 4 months.

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Patients	Patients	8
Age (min-max; mean±std dev)	Age (min-max; mean±std dev)	54-69; 62.75±5.6
Gender (Male/Female)	Gender (Male/Female)	7/1
Primary Tumor Site	Oral Cavity	3
	Oropharynx/Hypopharynx	3
	Larynx	2
N Stage	N1	1
	N2	3

Patients	Patients	8
	N3	4
Previous Radiotherapy	Previous Radiotherapy	3/8
Neck Dissection	Functional	2
	Radical	3
Adjuvant Treatment	RT	4
	CRT	4
Time to Recurrence Following Primary Treatment; months (min-max; mean±std dev)	Time to Recurrence Following Primary Treatment; months (min-max; mean±std dev)	6-18; 11.37±3.8
Predisposing Factors	Tumor infiltration	8/8
	Fistula	3/8
	Wound Infection	5/8
	Necrosis	6/8
Site of Rupture	Common Carotid	5
	Internal Carotid	2
	External Carotid	1
Type of Carotid Blow-out	Type III	8/8
Time to Carotid Blow-out; months (min-max; mean±std dev)	Time to Carotid Blow-out; months (min-max; mean±std dev)	2-8; 4.5±1.8

Table 1: Patient demographics and data

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