ORIGINAL ARTICLE

Carotid blowout syndrome in patients treated by larynx cancer

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Abstract
Introduction: Carotid blowout syndrome is an uncommon complication for patient treated by head and neck tumors, and related to a high mortality rate.
Objective: The aim of this study was to study the risk of carotid blowout in a large cohort of patients treated only by larynx cancer.
Methods: Retrospective analysis of patients older than 18 years, treated by larynx cancer who developed a carotid blowout syndrome in a tertiary academic centre.
Results: 197 patients met the inclusion criteria, 192 (98.4%) were male and 5 (1.6%) were female. 6 (3%) patients developed a carotid blowout syndrome, 4 patients had a carotid blowout syndrome located in the internal carotid artery and 2 in the common carotid artery. According to the type of rupture, 3 patients suffer a type I, 2 patients a type III and 1 patient a type II. Five of those patients had previously undergone radiotherapy and all patients underwent total laryngectomy. We found a statistical correlation between open surgical procedures (p = 0.004) and radiotherapy (p = 0.023) and the development of a carotid blowout syndrome.
Conclusion: Carotid blowout syndrome is an uncommon complication in patients treated by larynx tumours. According to our results, patient underwent radiotherapy and patients treated with open surgical procedures with pharyngeal opening have a major risk to develop this kind of complication.

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Introduction

Carotid blowout syndrome (CBS) is an uncommon complication for patients treated by head and neck tumours (HNT). The incidence of carotid blowout in patients who underwent surgical procedures involving head and neck cancers ranged from 2.9% to 4.3%.[1-3] In those who received re-irradiation because of recurrent head and neck cancers, the incidences of carotid blowout varied from 2.6% to 10%.6,7 In this way, CBS is more frequent in patients with HNT and those cases where radiation induced necrosis, recurrent tumours, wound complications from neck dissection, or vessel erosion from pharyngocutaneous fistulas.1

The mortality rate of carotid blowout was reported to range from 3% to over 50% in the literature.[3,5,7,10] Therefore, in a recent meta-analysis, the mortality rate of carotid blowout after re-irradiation in those patients treated by head and neck tumours was as high as 76%.[8] On the other hand, the neurological sequelae reported in those patients who survived an acute episode of carotid blowout, was from 16% to 50%.[9]

In the past, the traditional approach to treat this kind of complication was the surgical revision or ligation.[4,5] However, these tendencies have changed in recent years into a less aggressive approach, and nowadays, endovascular techniques, including balloons, destructive (embolization) and constructive (stent grafting) techniques, performed by interventional neuroradiologists are gaining popularity and having promising results.[1,9,10]

Few studies have discussed the relevant risk factors of carotid blowout occurred in patients treated by head and neck cancer in general. However, the aim of this research was to study the risk of carotid blowout in a large cohort of patients treated only by larynx cancer.

Methods

A retrospective analysis was performed on previously untreated patients, diagnosed with squamous cell carcinoma (SCC) of the larynx (cT1-cT4), N−/−, M−/− according to criteria of the Union Internationale Contre le Cancer (UICC) and the American Joint Committee on Cancer (AJCC) between January of 2009 and January of 2012. Identification of cases was achieved by informatic research on the medical records of our database, using the International Classification of Diseases (ICD-9). This study was approved by the ethics committee of our centre. The demographic data (age, sex), past medical history, comorbidities, stage, type of surgery, CBS as a complication, were obtained by a review of medical history.

Prior to surgery, all cases were discussed in an interdisciplinary committee of head and neck tumours. Preoperative examination of the lesion was carried out by indirect laryngoscopy, videolaryngoscopy and CT scan or MRI of the neck to evaluate the cartilage, preepiglottic and paraglottic space and lymph node involvement. Fine needle biopsies of the neck nodes were performed usually under ultrasonographic control. Those patients with lesions suspicious of malignancy were scheduled for laryngeal microsurgery and panendoscopy with biopsies, followed by a total laryngectomy (TL), horizontal partial laryngectomy (HPL), transoral laser microsurgery (TLM), and radiotherapy alone or accompanied
Carotid blowout syndrome in patients treated by larynx cancer

197 patients met the inclusion criteria, 192 (98.4%) were male and 5 (1.6%) were female. The mean age was 63.8 ± 10.13 (Min: 40/Max: 88). Of these 37 (18.5%) were diabetics and 69 (34.5%) were hypertensive. The patients had a mean postoperative haemoglobin level of 12.7 ± 1.89 g/dL and a mean albumin level of 41.0 ± 2.98 g/L. Tumoural stage of patients included 39 (19.7%) as stage I, 39 (19.7%) as stage II, 53 (26.9%) as stage III and 66 (33.5%) as stage IV. 138 (70.05%) patients were classified as N0, 14 (7.1%) as N1, 13 (6.5%) as N2A, 16 (8.1%) as N2B, 13 (6.5%) as N2C and 3 (1.5%) as N3. There were 4 (2.03%) cases of distant metastases (M1). The mean follow-up was 46.1 ± 12 months (Min: 11/Max: 72).

Regarding the type of surgery, the most common was the transoral laser microsurgery for glottis tumours (58 = 29.44%) and total laryngectomy without chemo-radiation therapy (23 = 11.6%) (Table 1).

Six (3%) patients treated by laryngeal cancer developed a CBS (Table 2), 4 patients had a CBS located in the internal carotid artery (ICA) and 2 had a CBS located in the common carotid artery (CCA). According to the type of rupture, 3 patients suffer a type I, 2 patients suffer a type III and 1 patient suffers a type II. 5 of those patients had previously undergone radiotherapy and all patients underwent total laryngectomy. However, anyone underwent a radical neck dissection (Table 2).

About the cause of CBS, 3 patients suffered radiation induced necrosis proved by pathological and image study, 2 patients present vessel erosion from pharyngocutaneous fistulas and tumour recurrence was proved by pathological examination in 1 patient. Nonetheless, 2 cases were managed with embolization, 1 case was managed with surgery and one patient was treated with a stent (Fig. 1). The other 2 patients died due to severe bleeding in the emergency room. Neurological sequelae were evident in 2 patients due
to cerebral stroke, 1 patient after ligation and the other one after ICA embolization (Table 3).

**Discussion**

CBS can be considered as an iatrogenic complication of HNT treatment. The syndrome was described at first in 1962, since then, several surgical and endovascular treatment options have been attempted. At the beginning, CBS could be treated only with surgical ligation or surgical bypass of the carotid artery. However, these techniques were associated to high mortality and to high neurologic morbidity with rates about 40% and 60%, respectively. In the mid of 80s, endovascular techniques to managed acute CBS were introduced. Then, this treatment has gradually gained popularity due the ease of the approach and lower morbidity and mortality rates compared to the surgical approach.

Short and long term effects of radiation over arteries have been reported. A total radiation doses of 40 Gy over a 10 day duration could induce damage to the vasa vasmorum of large arteries and it might be related to the rupture of great arteries in dogs according to McCready et al. Free radicals produced by radiation were also found to cause thrombosis and obliteration of vasa-vasorum, adventitial fibrosis, premature atherosclerosis, and the weakening of the arterial wall in the histological examination of resected carotid arteries. We also found a significant statistical difference in the appearance of CBS, in those patients who received RT treatment before surgery (5/6 = 83.3%) (p = 0.023) (Table 4).

Furthermore, some authors suggest the underestimated role of infections in CBS (tissue necrosis or fistula), and the relation of bacterial inflammation as a cause of vasa vasmorum thrombosis, and secondary arterial wall damage. This is why summarizing the effects over vasa-vasorum of radiation and infection, it is necessary to take into consideration the importance of these factors, due to the adventitial layer, which carries about 80% of the blood supply to the remaining walls of the carotid artery. In our series of patients affected by CBS, 2 (2/6 = 33%) patients suffered a pharyngo-cutaneous fistula in the early post-operative period, and 3 (3/6 = 50%) other patients suffered radiation inducing tissue necrosis.

Neck surgery is another significant factor related to CBS, because this type of surgeries could compromise the nutrition of the carotid artery during cervical nodes resection, resulting in injury to the adventitial layer, and this deleterious effect occurs independently of radiation. Radical neck dissections render the carotid artery more vulnerable to rupture because of the lack of supporting healthy tissues. Moreover, in those patients with accompanying pharyngeal surgery, there is a higher risk to develop a CBS due to major proportion of salivary fistula formation and when a hemithyroidectomy has also been carried out, the carotid artery lies very close to the skin and the tracheal stoma increasing the risk of damage over the artery. In relation to larynx tumours, Chen et al. found an incidence of 0.9% of CBS in patients treated by larynx tumours, a lower percentage compared with our results. However, previous literature review reports the larynx as the most common primary tumour site in almost 23% of patients who suffered a CBS.

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<th>Table 3</th>
<th>Patient treated by carotid blowout syndrome at our institution.</th>
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<tr>
<td>Sex</td>
<td>Treatment</td>
</tr>
<tr>
<td>Male</td>
<td>TL + CND + QT + RT</td>
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<td>Male</td>
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<td>Male</td>
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<th>Table 4</th>
<th>Statistical analysis of factors commonly associated with carotid blowout.</th>
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<tr>
<td>Variable</td>
<td>p = 0.05</td>
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<tr>
<td>RT</td>
<td>0.023</td>
</tr>
<tr>
<td>Neck dissection</td>
<td>0.151</td>
</tr>
<tr>
<td>Open surgery</td>
<td>0.004</td>
</tr>
<tr>
<td>Fistula</td>
<td>0.842</td>
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</table>
In our series, we only included all those patients who came to the emergency room due to a CBS, treated previously by a larynx tumour. In this way, it is important to emphasize that all of them underwent a total laryngectomy with bilateral cervical neck dissection (6/6 = 100%). This is why, according to the type of larynx procedure, we found a statistical correlation between open surgical procedures and the development of a CBS (p = 0.004). However, we did not find statistical correlation between neck dissection and CBS (p = 0.151) when we include all of our patients (open and endoscopic laryngeal procedures). Furthermore, it is important to underline that any patient in our series, underwent a radical neck dissection developing a CBS, in this way, we can suggest that selective neck dissection can be related with the appearance of CBS too, maybe not as a main factor, but it could be associated with other treatment strategies or complications (Table 4).

Another factor related to CBS in previous studies is the presence of mobile foreign bodies in the head and neck like tracheostomy tube, nasogastric tubes, or the presence of wet guazes. In this case wound healing can be interrupted because of chronic irrigation and inflammatory response. According to Chen et al. this could explain why those patients with open wounds in the neck require wound care with wet dressing having a 4-fold increased risk of developing carotid blowout. Nutritional factors have also been related to the risk of CBS, and this can be explained by the less soft tissue coverage, causing the carotid arterial wall to weaken in the cervical region. Moreover, in their study Chen et al. found a 2-fold increased risk of developing carotid blowout in patients with a BMI of <22.5 kg/m².

The incidence of cerebral complications in patients affected by CBS, up to 87% when hypotension is present at the time of ligation compared to 28% in normotensive patients. Furthermore, in those patients who survived an acute episode of carotid blowout, the neurological sequela reported was from 16% to 50%. Moreover, in a recent study, authors found out that patients with carotid blowout underwent surgical intervention had a higher neurologic complication rate and mortality rate when compared with those of patients received endovascular procedures. In our series 2 (33.3%) patients showed up neurological sequela after bleeding, one of them died in the first 10 days after the initial episode due to a re-bleeding, and the other patient suffered and hemiparesis as a long term sequela.

About the best option to treat this complication on these days, there exists a trend in favour of endovascular techniques. However, recent studies show that there is no statistical significant difference in technical and hemostatic outcomes between reconstructive and deconstructive endovascular techniques. Moreover, other authors suggest that permanent vessel occlusion results in higher immediately cerebral ischaemia, but stent grafting induces potentially delayed complications, such as infections, rebleeding or stent thrombosis.

Finally, our study has a number of limitations. Primarily, its retrospective nature and the small sample size can limit the validity of our results. Moreover, we only included patients treated by larynx tumours, and this kind of complications can affect all those patients treated by head and neck tumours. In this way, a prospective study comparing the results of different types of treatments could be necessary.

Conclusion
Carotid blowout syndrome (CBS) is an uncommon complication in patients treated by larynx tumours. According to our results, patients underwent radiotherapy and patients treated with open surgical procedures with pharyngeal opening, have a major risk to develop a CBS. In this way is necessary to trying to predict the risk in all of our patients and take the appropriate actions to prevent this kind of complications.

Conflicts of interest
The authors declare no conflicts of interest.

References