

Acute haemorrhage in patients with advanced head and neck cancer: value of endovascular therapy as palliative treatment option

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Abstract

Aims: Acute or subacute haemorrhage is one of the most frightening complications in patients suffering from advanced head and neck cancer. Few articles report experience with superselective endovascular therapy for this purpose. Is endovascular therapy underestimated in the field of palliative head and neck cancer therapy? This study set out to investigate this question.

Patients and methods: A review was undertaken of the clinical courses of seven patients (six men, one woman) suffering from incurable, advanced head and neck cancer (four pharyngeal, two laryngeal, one neck) and treated with superselective endovascular strategies as an emergency procedure for acute bleeding.

Results: All patients were successfully treated without evidence of neurological complication. Patients reached a median survival of 20 weeks (range eight–168 weeks). Following endovascular treatment all patients were discharged from the hospital within several days. Three patients survived almost free of symptoms for several weeks and were able to stay at home with their families until their death.

Conclusion: We conclude that in the field of palliative care, superselective endovascular therapy deserves to be considered alongside standard treatment options for the management of acute haemorrhage from advanced head and neck cancer.

Key words: Therapeutic Embolization; Head and Neck Cancer; Carotid Artery, External; Haemorrhage

Introduction

One of the most frightening but rare complications in patients suffering from advanced head and neck cancer is acute or subacute haemorrhage. In most cases patients suffer from recurrent or residual disease following palliative treatment. Due to previous treatment regimens (i.e. major flap surgery, neck dissection or radio(chemo)therapy) or even to huge tumour masses or metastases, percutaneous access to the site of haemorrhage is often complex or difficult and sometimes impossible. Even today acute and severe tumour haemorrhages are only occasionally treated by ligation of the external carotid artery or its branches. In recent years specialized centres have gained more experience providing interventional radiological procedures for endovascular treatment in daily clinical care. Since the 1980s this treatment modality has existed for several diseases of the head and neck area

(paragangliomas, angiofibromas, vascular malformations, epistaxis, etc.).^{1,2} However, surprisingly few articles report its use and efficacy in cases of head and neck cancer compared with other tumour types.³ This suggests that the value of endovascular therapy may be underestimated in the field of palliative head and neck cancer therapy.

The aim of this study was to determine the value of superselective endovascular therapy as a palliative treatment option in seven patients with acute haemorrhage due to advanced head and neck cancer. In cases of acute tumour-related bleeding the disease has already entered its terminal phase with further surgical interventions no longer a viable alternative. Since most bleeding is oral or pharyngeal, the only treatment alternative is local packing of the pharynx, which is extremely dramatic for the patient. In most cases this situation means the beginning of a phase of deep sedation with its inevitable consequences.

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Patients and methods

From 1998 until August 2004 a total of seven patients (one woman, six men) suffering from incurable, advanced head and neck cancer (four pharyngeal, two laryngeal, one neck) were treated for tumour-related acute and subacute haemorrhage with super-selective endovascular strategies in cooperation with our centre's department of neuroradiology. The patient charts were reviewed. Patient data prior to and following neuroradiological intervention are presented in Table I. All clinical bleeding scenarios except in case three were not self-limiting and so were classified according to Chaloupka *et al.*⁴ as 'acute carotid blowout'.

Immediate resuscitation was commenced under intensive care preconditions supported from the outset by an anaesthesiology team. All radiological interventions were completed under general anaesthesia. Following the intervention all patients remained intubated and ventilated until their condition was stable.

High-resolution digital subtraction imaging of the carotid artery system was obtained bilaterally. In all cases bilateral selective arteriography of the subclavian, costocervical and thyrocervical arteries as well as superselective angiograms of the external carotid artery were performed.

Embolization agents were used as follows: microcoils in cases of erosion-bleeding of larger vessels (e.g. carotid artery) and microparticles in cases of tumour bleeding from tumour neovascularity. Balloon occlusion, a reliable treatment option for the aforementioned situation, was previously described in detail by Chaloupka *et al.*⁴ but was not utilized in this series.

Results

Case 1

About 24 months after first diagnosis of a T₄ cancer of the larynx a 61-year-old male patient was readmitted to the department for acute haemorrhage from a suprastomal pharyngeal fistula. Because of significant haemorrhage, intubation packing of the pharynx and the oral cavity was performed immediately. The patient was then transferred to the angiography unit. A significant, hypervascular tumour bleeding from the right superior thyroid artery was diagnosed angiographically and successfully embolized with polyvinyl-alcohol emboli after careful removal of the tamponade. Following the intervention the patient was monitored under intensive care for 24 hours and no neurological defect was noted. Fourteen weeks after endovascular treatment the patient received palliative chemotherapy with trofosamid because of his strong demand for therapy. Because of progressive disease recurrent mild haemorrhage occurred from the exophytic tumour during palliative chemotherapy. The patient died 19 weeks after receiving endovascular treatment.

Case 2

Due to recurrence of a T₄ squamous cell carcinoma of the hypopharynx a 48-year-old patient developed

an initially small fistula in level III on the right side of the neck. A computed tomography (CT) scan revealed a large tumour involving the entire right side of the neck with thrombotic occlusion of the internal jugular vein and encasement of the external carotid and parts of the common carotid artery by the tumour. About four weeks later the patient presented with acute, massive bleeding from the above-mentioned fistula especially when turning his head to the left. Angiography revealed heavy bleeding around a tumourously transformed branch of the external carotid artery. Immediate occlusion of the source of the bleeding (pseudoaneurysm) and of the distal and proximal parts of the external carotid artery (Figure 1) was performed utilizing four long Guglielmi electrolytically detachable coils (GDCs) resulting in occlusion of the entire external carotid artery. Following the intervention the patient complained about mild ododynia with slight temporary immobility of the right arm. No further neurological symptoms were recognized. More than six months following angio-embolization the patient died at home from another sudden, massive haemorrhage out of the right malignant neck fistula and mouth. Until this time he had received analgesic medication and palliative therapy with methotrexate 50 mg/week orally.

Case 3

A 74-year-old woman suffering from residual oropharyngeal cancer presented to the out-patient department reporting mild but continuous haemorrhage from her mouth for several days. Flexible endoscope pharyngoscopy revealed haemorrhagic oozing from the base of the tongue. At that time the patient's haemoglobin was 94 g/l. Angiography was arranged for the following day. During this procedure a pseudoaneurysm of the left lingual artery emerged as the cause of the haemorrhage. Embolization was subsequently performed utilizing polyvinyl-alcohol emboli. Neurological defects were not observed. Seven weeks later a sudden, massive haemorrhage occurred from the base of the tongue, which was successfully treated by bipolar coagulation under general anaesthesia. After discharge from hospital this patient was transferred to a hospice where, 12 weeks after the intervention, she died.

Case 4

A rapidly growing, malignant fibrous histiocytoma of the neck (Figure 2) caused several self-limited episodes of acute haemorrhage in a 41-year-old patient. Nearly six years after initial diagnosis of the tumour in another country, severe, diffuse bleeding occurred from the right side of the neck, which was considered to be treatable by angio-embolization. Angiography revealed a diffuse, hypervascular bleeding area fed by the right superior thyroid artery. This was successfully embolized with polyvinyl-microparticles. In this particular case because of the huge, heavily vascularized tumour

TABLE I
PATIENT DATA

Patient	1	2	3	4	5	6	7
Age at diagnosis (years)/gender	61/m	48/m	74/f	41/m	51/m	62/m	41/m
Tumour localization	Larynx	Hypopharynx	Oropharynx	Neck	Larynx	Oro-hypopharynx	Oro-hypopharynx
Histology and TNM stage	SCC T ₄ N ₀ M ₀	SCC T ₄ N ₀ M ₀	SCC T ₄ N _{2c} M ₀	MFH –	SCC T ₄ N _{2c} M ₀	SCC T ₃ N _{2b} M ₀	SCC T ₄ N ₀ M ₀
Coincident carcinoma	Lung SCC	–	–	–	–	–	Floor of mouth SCC
Recurrence/residual	Recurrence	Recurrence	Residual	Recurrence	Residual	Recurrence	Recurrence
Previous therapy	LE, NDil, RT (GHD 60 Gy); Res, RFF, NDcl	CO ₂ laser res, NDil, tracheo; RT (GHD 66.6 Gy); Palliative chemo	Primary RT (GHD 66 Gy), tracheo	Primary chemo-RT (GHD)*; NDil, multiple chemo	Primary RT (GHD 71.4 Gy), tracheo; Palliative chemo	Primary chemo-RT (GHD 66 Gy); LE, ND	LE, NDil, RT (GHD 50 Gy); CO ₂ laser res, NDcl; ia chemo (cisplatin)
Duration of disease before haemorrhage (months)	24	13	7	68	16	7	168
Site of initial bleeding	Sup thyroid a	ECA	Lingual a	Sup thyroid a	ECA	Facial a	Facial a
Embolized vessel	Sup thyroid a	Entire ECA	Lingual a	Distal parts of ECA	Distal parts of ECA	Facial a & maxillary a	ECA
Embolization material	PVA	Platinum coils	PVA	PVA	Platinum coils	PVA	Platinum coils
Survival after embolization (weeks)	19	25	12	9	8	168	37

*Procedure was performed in the USSR. m = male; f = female; chemo = chemotherapy; cl = contralateral; ECA = external carotid artery; a = artery; RFF = radial forearm flap; ia = intra-arterial; il = ipsilateral; LE = laryngectomy; MFH = malignant fibrous histiocytoma; ND = neck dissection; PVA = polyvinyl-alcohol particles; res = resection; RT = radiotherapy; SCC = squamous cell carcinoma; tracheo = tracheotomy; tRTD = total radiotherapy dose



FIG. 1

Patient 2. (a) Contrast medium (CM) extravasation (arrow) from the right external carotid artery showing the tumorous destruction of the vessel. (b) Catheter lying in the common carotid artery with visible CM extravasation (arrow). (c) External carotid artery after placement of four coils without proof of CM extravasation. (d) Final radiograph for control of coils position.

angiography of the contra-lateral side was performed in the same session. At the same time the decision was made to also treat other vessels without evidence of bleeding, including the cervical trunk. Two further sessions of angio-embolization followed two and nine days later. Further bleeding episodes did not occur and no neurological defects were observed. The patient died nine weeks later from carcinomatosis during a course of palliative chemotherapy.

Case 5

Seven months after previous therapy (Table I) a 51-year-old patient was admitted to the hospital for acute bleeding from a biopsy-proven residual tumour of the larynx. After packing of the pharynx and the oral cavity with gauze tamponade the patient was immediately taken to the angiography

unit. Both common carotid arteries were explored. Severe bleeding from the right external carotid artery (pseudoaneurysm) was evident. Exploration of the right external carotid artery and successful embolization of the bleeding vessel with two platinum coils was performed. Following embolization no neurological defect was noted. During this event the patient lost about 1500 ml of blood from his mouth. He died eight weeks later at home because of a further massive bleed from an unknown site.

Case 6

A 62-year-old patient suffering from a T₃ N_{2b} M₀ staged oro-hypopharyngeal carcinoma received primary radiochemotherapy. During radiochemotherapy he developed progressive odynophagia.



FIG. 2

Patient 4. Huge exophytic cervical tumour masses in this case of malignant fibrous histiocytoma.

Subsequent panendoscopy eight weeks later revealed necrosis in the region of the right piriform sinus with sequestration of parts of the thyroid cartilage. In view of this and the persistence of large cervical lymph node metastases, the patient underwent laryngectomy and bilateral neck dissection. Four weeks post-operatively he developed massive haemorrhage from his mouth. Under general anaesthesia an immediate pharyngoscopy was performed. The examination revealed severe bleeding from the hypopharynx. The pharynx including the oral cavity was packed with gauze tamponade. Two hours later angiography determined that the right facial artery was the source of bleeding. After embolization with microparticles the bleeding reduced but did not stop. Thus a new tamponade was placed and the patient was transferred to the intensive care unit, still intubated and ventilated. The following day a second angiography was performed. Persistent haemorrhage from the maxillary artery became visible, which was embolized with microparticles as well. Afterwards no further bleeding was observed and the gauze tamponade was carefully removed. Eight days later another fulminant haemorrhage occurred from the mouth and nose. Within a few minutes the patient went into shock. The patient was again tamponaded in the operating room and transferred to

the angiography unit. After localization of the bleeding the external and internal carotid as well as the common carotid artery were embolized utilizing several fibred platinum coils of different sizes. The course of the disease was neurologically uneventful. Following the intervention a right-sided, extracranial swelling became visible presumably because of progressive secondary lymphoedema following radical neck dissection on this side. Several days later during wound care and inspection of persistent right pharyngeal fistula platinum coils became visible outside the embolized external carotid artery. These were carefully removed. After receiving four cycles of palliative chemotherapy with cisplatin and 5-fluorouracil the patient died at home 14 months after angi-embolization. According to his general practitioner the cause of death was fulminant erosion bleeding of unknown origin from the mouth.

Case 7

After two cycles of intra-arterial chemotherapy with cisplatin a 41-year-old patient was admitted for a third cycle because of recurrent oro-hypopharyngeal carcinoma. At this time severe bleeding occurred from his mouth and pharyngeal fistula resulting in significant blood loss. Angiography revealed bleeding from the right facial artery. The external carotid artery was occluded utilizing three platinum coils. The neurological status was unchanged following the intervention. Further episodes of tumour-related bleeding did not occur during the following four months. However, during this time the pharyngeal fistula was progressive and the patient received palliative treatment with methotrexate 50 mg/week and pain therapy. Five months after the intervention the patient developed recurrent mild daily bleeding from the fistula. The patient finally died at home after acute rupture of the left external carotid artery. The bleeding was managed by his wife who did not want to call a doctor for this purpose.

Discussion

Acute haemorrhage is a rare cause of death in head and neck cancer patients and occurs in less than five per cent of all cases.⁵ However sudden, acute haemorrhage is the most frightening and dreaded complication^{2,6} in the field of head and neck oncology. It mostly occurs in cases of advanced, inoperable disease in its terminal phase. Previous radiation therapy, radical surgery, flap necrosis, wound infection, pharyngo-cutaneous fistula and recurrent or persistent carcinoma have all been implicated as potential risk factors.⁷ Spontaneous bleeding can result from erosion of vessels by the tumour or from tumour ulceration. Furthermore, primary or post-operative radiotherapy can predispose to acute haemorrhage because fibrosis of the adventitia and fragmentation of elastic filaments of the tunica media, due to obliteration of the vasa vasorum, may occur. As a result the wall of the

vessel weakens and bleeding can occur more easily. In all cases in this series bleeding issued from the external carotid artery and its branches. In this context it should be clarified that bleeding from the external carotid artery and its branches represents a subset of such patients; common carotid artery and internal carotid artery pseudoaneurysm and haemorrhage are more common.

In cases of acute, severe bleeding the time window for active treatment is very short. Bleeding most often originates from the carotid arterial system and if it cannot be controlled locally external compression must be applied. Sedation, intubation and, if possible, packing of the pharynx and the oral cavity in cases of heavy bleeding from the upper aerodigestive tract is essential and represents the most effective emergency procedure. In cases of mild haemorrhage with little blood loss a rigid endoscopy of the upper aerodigestive tract should always be performed so that local treatment such as cautery may be attempted. The next step is to decide which approach should be used to definitively stop the bleeding. Reports in the literature focus mainly on emergency ligation of the carotid artery in cases of acute haemorrhage.^{8–10} The external approach to the artery is certainly the fastest. However, transcatheter access is often difficult due to heavy scar formation and fibrosis following previous interventions (e.g. neck dissection, extended flap surgery or

even high-dose radiotherapy) and subsequently accompanied by extended wound-healing problems. Moreover pharyngo-cutaneous fistulas or tumour masses growing from the inside of the neck or on the skin surface can make external access to the carotid artery or its branches almost impossible. Because of a relatively high mortality rate the surgical approach is not an issue in many cases. This treatment option may also result in prolonged hospital stay as the patient recovers from the surgery.¹¹ In this setting it is often helpful to introduce other strategies to manage heavy bleeding.

A valid alternative is the option of endovascular therapy as a radiological intervention, a method which has been described by several authors in the field of head and neck oncology (Table II). This treatment option requires the availability of an experienced interventional radiologist to perform the procedure. The access is rapidly performed via a femoral approach. At present the technique of angio-embolization is an established and standard procedure offered by interventional radiologists. The role of endovascular therapy has rapidly expanded during the last few years not only as a pre-operative measure to minimize intra-operative blood loss and as a primary therapy in vascular malformations and other diseases but also as a palliative treatment option in oncology (e.g. in metastatic

TABLE II
ANGIO-EMBOLIZATION OF HEAD AND NECK CANCER PATIENTS REPORTED IN THE LITERATURE (1984–2005)

Author	Year	Patients (n)	Embolization material	Neurologic deficit	Survival post-embolization
Osguthorpe & Hungerford ¹²	1984	1	8-mm steel Dacron coil	Right-sided hemiplegia for 24 h	Not indicated
Bhansali <i>et al.</i> ⁶	1986	3	Ivalon TM tantalum	1 × hemiparesis for 48 h 2 × no neurologic deficit	2 × 8 weeks 1 × unknown
Wilner <i>et al.</i> ¹³	1987	8	3 × PVA 5 × IBCA & iophendylate	None	1 week to >39 weeks Median: >8 weeks
Feifel <i>et al.</i> ¹⁷	1991	1	PVA	None	54 weeks
Chaloupka <i>et al.</i> ⁴	1996	18	14 × permanent balloon occlusion 6 × platinum coils or Histoacryl	2 × transient ischemic attack	Not indicated
Morrissey <i>et al.</i> ¹¹	1997	4	1 × microparticles & platinum coils 3 × platinum coils	None	>1 week to >54 weeks Median: >34 weeks
Kramann <i>et al.</i> ¹⁴	1997	12	4 × PVA & platinum coils 3 × PVA 4 × platinum coils	None	1–64 months
Remonda <i>et al.</i> ²	2000	3	1 × Histoacryl & Lipiodol glue 2 × Guglielmi detachable coils	Not indicated	Not indicated
Sittel <i>et al.</i> ⁹	2001	1	Ethibloc TM & Lipiodol	None	>36 weeks
Low & Goh ¹⁵	2003	14	Not indicated	1 × transient drowsiness 2 × permanent neurologic deficit	3–690 days
Luo <i>et al.</i> ¹⁶	2003	17	13 × permanent balloon occlusion 2 × platinum coils 2 × Histoacryl (alone)	3 × transient ischemic attack 2 × hemiparesis	2–48 months
Sesterhenn <i>et al.</i> (present article)	2006	7	3 × platinum coils 4 × PVA	1 × temporary immobility of right arm	8–56 weeks Median: 20 weeks

PVA = polyvinyl-alcohol; IBCA = isobutyl-2-cyanoacrylate

liver disease).^{3,9} Superselective chemo-embolization can also be performed utilizing this technique. The risks of this technique include strokes, blindness, seizure, haemorrhage and thrombosis.⁶

A review of the literature (Table II) reveals only a few articles on endovascular treatment for palliation of patients with advanced head and neck cancer who develop acute bleeding. These authors favour this technique compared with the open surgical approach because of its effectiveness and safety.^{2,6,9,11,17} As an alternative to angio-embolization, similar articles report their authors' experience with angiographic occlusion of the bleeding vessel utilizing detachable balloons inflated with liquid.^{4,7,16,18} In the seven cases presented here (but also in agreement with the literature) there is evidence for low complication rates and satisfactory survival rates after angio-embolization with coils and microparticles (Table I). Notably, severe neurological complications such as stroke or hemiplegia were not observed. Following the intervention some of the patients in our series could even maintain a relatively good quality of life for a certain period of time. Following successful angio-embolization three patients were discharged from hospital and were enabled to stay at home with their families without pain for at least several weeks until their death. Patient three was discharged from the hospital and transferred to a hospice where she died in the presence of her family. After successful endovascular treatment the tumour was progressive so that six patients suffered further haemorrhage and four of them died from this. In the literature detailed follow-up information, especially on cause of death, is often missing so that outcomes are hard to compare. Chaloupka *et al.* reported 15 surviving patients in their series of 18 individuals suffering from carotid blowout syndrome.⁴

Endovascular therapy is an effective and mostly safe procedure which allows, if possible, a quick remobilization of the patient. This treatment option should be considered in carefully selected individual cases and should, if possible, be discussed in detail with the patient and their relatives. The precondition to successful endovascular treatment of patients is close cooperation with a radiology department with an interventional focus. The possibility of superselective endovascular therapy in the palliative management of acute haemorrhage in advanced head and neck cancer deserves consideration alongside standard treatment options in centres with an oncologic focus providing the above-mentioned preconditions have been taken into account.

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- **This paper describes the treatment of severe haemorrhage in patients with advanced head and neck cancer, with selective endovascular embolization**
- **This therapy was used successfully in seven patients with terminal disease. In all cases bleeding occurred from the external carotid artery and its branches**
- **Radiological endovascular embolization is a viable alternative to arterial ligation in this challenging group of patients**

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