The Journal of Laryngology & Otology (2012), ***126***, *111–115*.

doi:10.1017/S0022215111002416

REVIEW ARTICLE

Management of vascular complications of head and neck cancer

J RIMMER[1], C E B GIDDINGS[2], F VAZ[1], J BROOKS[3], C HOPPER[1]

Departments of [1]Head and Neck Surgery and [3]Interventional Radiology, University College Hospital, London, and [2]Department of Otolaryngology and Head & Neck Surgery, Bart's and The London Hospitals, London, UK

Abstract

Background: Major vascular complications in patients with head and neck cancer have previously been thought of as terminal events. However, it is now possible to intervene in many situations, with benefits for quality of life as well as survival. Endovascular techniques have reduced morbidity and mortality in many situations, both emergency and elective.

Method: We describe the techniques that can be employed in such situations, and present illustrative case reports. Life-threatening haemorrhage, carotid compression and radiation-induced carotid stenosis are all discussed.

Conclusion: It is possible to predict where complications may arise, and to take prophylactic steps to allow treatment to continue. Early intervention can reduce both morbidity and mortality in this high-risk patient group.

Key words: Injuries, Carotid Artery; Carcinoma, Squamous Cell; Carotid Stenosis; Stents

Introduction

Major vascular complications in patients with head and neck cancer have previously been thought of as terminal events. While this may still be true in some cases, it is now possible to intervene in many situations, with benefits for patient quality of life as well as survival. Advances in interventional radiological techniques have drastically reduced the morbidity and mortality of many such sequelae; furthermore, the risks associated with these interventions have also been reduced.

Squamous cell carcinoma (SCC) of the head and neck has a high incidence of metastasis to cervical lymph nodes. Many patients with SCC present with advanced disease involving the neck, whilst others only relapse in the neck after treatment of the primary tumour. The proximity of the deep cervical chain of lymph nodes to the carotid sheath and major vessels in the neck is a factor in the development of vascular complications due to both haemorrhage and vessel occlusion. Even without cervical involvement, the primary tumour itself can involve adjacent vasculature, with similar effects. Treatment of both primary and secondary disease can contribute to, or directly cause, vascular complications.

The major complication of bleeding arises most commonly from the extracranial carotid arteries – so-called 'carotid blow-out' – but can also occur from other major vessels of the head and neck. Carotid stenosis and occlusion, with resultant neurological sequelae, can also be a significant and underestimated problem for these patients. This is not only due to such patients' general comorbidity and risk factors, but also occurs as a late side effect of radiotherapy treatment.

In this review, we discuss new strategies in the management of these vascular complications, illustrated with case reports, as there is a paucity of good evidence on this topic.

Discussion and case reports

Carotid blow-out syndrome

Perhaps one of the most disastrous vascular complications seen in head and neck cancer patients is that of carotid blow-out. This is rupture of the extracranial carotid arterial system, and occurs in 3–5 per cent of patients with major head and neck resections.[1] It can also be seen in patients treated with radiotherapy alone.[2]

Carotid blow-out is now commonly described as a syndrome, with three distinct clinical entities.[3] The first is 'threatened' carotid blow-out, when there is a clinically exposed carotid artery or radiological evidence of carotid invasion by tumour. In 'impending' carotid blow-out, a herald bleed has settled, either spontaneously or with packing and compression. The third category is 'acute' carotid blow-out, with

Accepted for publication 12 April 2011 First published online 5 September 2011

profuse, uncontrollable bleeding that requires immediate resuscitation and treatment if appropriate.

Overall, carotid blow-out syndrome carries a 40 per cent mortality rate, despite surgical treatment with emergency ligation of the involved carotid artery.[4,5] Sadly, neurological sequelae are reported in 60 per cent of survivors following such surgical intervention.[6] A survival rate of 62 per cent at six months following emergency carotid ligation has been reported.[1]

Advances in interventional radiology techniques have been reported in recent years. Initially, this was with endovascular balloon occlusion of the bleeding vessel.[3,4] As progress was made within this field, embolisation was advocated.[6,7] More recently, techniques have evolved to allow endovascular stent repair of carotid rupture.[5,8–10] A study of 25 patients treated with endovascular stent-grafts reported a 100 per cent technical success rate for stent placement, with no major or minor neurological complications.[9] Thirteen of these patients had carotid blow-out syndrome; others were treated for pseudoaneurysms or stenosis of the carotid artery. There were two intra-procedural arterial wall dissections, managed successfully at the time, and a 15 per cent short-term complication rate (i.e. within 30 days). The overall mortality in this study was 36 per cent, although the authors did not specify the time period. Unsurprisingly, all deaths occurred in patients treated for carotid blow-out syndrome.

Endovascular stent complications have been reported, and some authors have advocated stents only as an interim measure whilst more definitive management is planned.[5] Concerns relate to the stent as foreign material, with infection an inevitable late complication. More ruinous is extrusion or occlusion of the stent, with subsequent cerebrovascular accident, obviating the primary treatment aim.[11] Another group has reported rupture of the carotid artery following stent placement.[12]

Despite these concerns, use of such endovascular techniques has been advocated in non-surgical candidates, as there is minimal morbidity related to the procedure itself.[13] Obviously, there are also complications pertaining to the angiography required for stent insertion. One study prospectively reviewed the risk of neurological sequelae following cerebral angiography, in almost 3000 patients.[14] A complication rate of 1.3 per cent was reported, with only 0.5 per cent of patients suffering permanent neurological deficits. This series was published in 2003, and the authors noted previously recorded complication rates of up to 12.2 per cent for transient events, and rates as high as 5.4 per cent for permanent neurological deficits. This risk appears to have reduced over time, perhaps as interventional radiology has emerged as a subspecialty and endovascular procedures have become more common. Another study, published in 2007 and involving a series of 2924 cerebral angiograms, reported an incidence of transient neurological events of only 0.34 per cent, with no permanent neurological sequelae.[15] Other complications included puncture site haematomas (0.41 per cent) and asymptomatic vessel dissections (0.44 per cent). Of note, however, was a slightly increased overall risk of complications when the procedure was undertaken in an emergency setting.

The complication rate is low, and patients with impending carotid blow-out syndrome may be effectively palliated with stents and discharged home or to a hospice, without the dramatic and distressing event of carotid haemorrhage. Late complications are less of a concern in such cases, and preventing carotid blow-out can successfully prolong life, with good quality, to allow a more dignified and controlled ultimate death.

Case report one. A 53-year-old woman had been treated for a primary tumour stage (T) 1, node stage (N) 0, metastasis stage (M) 0 right lateral tongue SCC with surgical resection, right selective neck dissection and post-operative radiotherapy to the neck. She represented nine years later with a new primary in the tongue, and was treated with surgical resection, neck dissection and post-operative radiotherapy (66 Gy in 33 fractions). Eleven months following completion of radiotherapy, further recurrence and airway compromise necessitated an emergency tracheostomy, which was performed under local anaesthetic, with subsequent haemorrhage noted from the tracheostomy site. Acute deterioration and cardiac arrest prompted resuscitation and neck exploration. Ulceration and active bleeding were observed from the anterior aspect of the right common carotid artery bifurcation. The defect was repaired with a 4/0 non-absorbable monofilament suture, and haemostasis was achieved. Computed tomography (CT) angiography performed three days post-operatively showed an 80 per cent stenosis of the distal right common carotid artery, suspected to have occurred as a result of the surgical repair. The patient underwent percutaneous endoluminal stent insertion using a self-expanding covered stent in the right common carotid artery, with good improvement of the lumen. She survived with no focal neurological deficit, and went on to have palliative chemotherapy.

Other major head and neck vessel haemorrhage

Much less is written about haemorrhage from other major vessels in the head and neck. However, this can pose just as great a problem, particularly if associated with other complicating factors. Previous radiotherapy, recurrent carcinoma, and surgical complications such as infection and fistula formation may all contribute to the onset of such bleeding, and may make controlling it more difficult. Exploring the post-radiotherapy neck conveys additional morbidity and even mortality. Previous reports of lingual artery haemorrhage controlled with angiography and selective embolisation have shown this technique to be a safe and effective alternative to surgical ligation of the

https://doi.org/10.1017/S0022215111002416 Published online by Cambridge University Press

vessel.[16] In our experience, this has also been shown to be the case; however, there may be ever-increasing difficulty in locating these vessels within previously chemo-irradiated tissues.

Case report two. A 74-year-old man underwent total laryngectomy and bilateral level II–IV neck dissection for a T_4 laryngeal SCC. On the eighth post-operative day, he developed bleeding from the oral cavity; this settled spontaneously, with no obvious source identified. Six hours later, there was a further episode of haemorrhage, controlled with oropharyngeal packing. Carotid angiography the next day revealed no obvious bleeding point. The packs were removed under general anaesthetic after three days; again, no obvious source of bleeding was identified. However, further, profuse bleeding occurred later the same day, requiring repacking. Carotid angiography was repeated, which showed a right lingual artery aneurysm. Embolisation was undertaken with four coils. The packs were successfully removed, with no further haemorrhage, and the patient made an uneventful recovery. Planned post-operative radiotherapy commenced. Twelve months later, the patient remained well and disease-free, with no further bleeding or neurological sequelae.

Carotid artery stenosis or compression

Patients with head and neck cancer often have significant comorbidity, with many risk factors for cerebrovascular disease. Cervical metastases can cause direct compression of the carotid vasculature, and metastatic deposits within the neck can invade the vessels directly. However, the treatment itself can also cause complications.

Radiotherapy has well recognised acute side effects, which are managed symptomatically at the time of treatment. The late complication of large vessel injury secondary to radiotherapy is also well recognised, causing subsequent occlusive vascular disease. Despite growing reports in the literature, routine screening for post-radiotherapy carotid stenosis is not standard practice.[17]

Three mechanisms of radiation damage have been identified: damage to the vasa vasorum causing ischaemic necrosis with subsequent fibrosis; adventitial fibrosis with narrowing; and acceleration of the atherosclerotic process.[18] Therapeutic irradiation has been shown to increase the carotid artery intima media thickness (i.e. the thickness of the vessel wall) over the first year after treatment.[19] This process appears accelerated compared with control subjects, and is known to be a reliable predictor of future cerebrovascular disease.[20]

External beam radiotherapy has long been associated with carotid stenosis, particularly when given for nasopharyngeal or laryngeal carcinoma.[21] Time elapsed after treatment does seem to play an important role, and studies have shown that after five years the risk is significantly higher.[22] Screening with carotid ultrasound has been suggested after this time, but is not routinely undertaken at present. Radiotherapy has been postulated to cause acceleration of carotid atherosclerosis, and has been shown to be an independent risk factor for this.[23] Several studies support these findings, and active screening for carotid stenosis in such patients has been advocated.[24] Whilst many studies have looked specifically at patients treated with radiotherapy for SCC of the head and neck, other groups have also been studied. Long-term survivors of lymphoma and seminoma, also treated with radiotherapy but lacking many of the usual SCC comorbidities and risk factors, have also been investigated. These patients have also been shown to develop accelerated, non-coronary atherosclerotic disease after a median interval of 15 years.[25] Radiation-induced vessel injury occurs elsewhere in the body as well, for example within the abdomen causing intestinal angina. Findings in these patient groups support the use of routine vessel surveillance after radiotherapy; Patel *et al.* advocate careful auscultation at the very least.[25] In their series, carotid bruits were heard in five patients, who went on to have successful treatment of their stenosis with no neurological incidents. Interestingly, radiotherapy appears to cause more widespread and atypical patterns of carotid stenosis than is seen in the normal, non-irradiated population, something that needs to be taken into account when planning treatment.[26]

It has been suggested that all post-radiation patients under regular follow up in the head and neck clinic be considered for baseline carotid duplex ultrasound five years after completion of radiotherapy, or sooner should patients have significant risk factors for arterial disease. This non-invasive investigation could help to identify those patients with a significant degree of carotid stenosis, before symptoms develop. This would enable appropriate treatment, be it endovascular or surgical, prior to the occurrence of a significant neurological event.

Photodynamic therapy involves administration of a photosensitising agent which is then focally activated in the presence of oxygen, using light of a specific wavelength. The photosensitiser is preferentially absorbed by neoplastic tissue and the light is directed to the appropriate site, allowing site-specific tumour treatment.[27] Studies have demonstrated that photodynamic therapy does not damage normal, healthy vessels.[28] Following photodynamic therapy, the risk of thrombosis or rupture of normal arteries is low, as collagen and elastin are preserved.[29] However, there is good evidence that photodynamic therapy should not be used if there is any concern that the tumour has invaded adjacent vasculature, such as the carotid artery in the neck.[27] In such cases, the risk of carotid blow-out is significant. Care should also be taken if carotid vessels are being compressed by tumour bulk, as transient post-treatment oedema is almost inevitable. In cases of such compression, endovascular stenting of

https://doi.org/10.1017/S0022215111002416 Published online by Cambridge University Press

the artery in question offers a low-morbidity method of maintaining vessel patency during this time, and thus minimises the risk of adverse neurological sequelae in what are often palliative cases. This technique is now being employed regularly in our practice, prior to delivering palliative photodynamic therapy, where there is significant impingement of disease on the carotid system. The following case serves as an example.

Case report three. A 68-year-old man had been treated with chemoradiotherapy seven months earlier for a T_1 N_3 SCC of the left tongue base. He was diagnosed with recurrent disease and was referred for photodynamic therapy. Before treatment was commenced, he developed worsening syncopal episodes over a four-week period. Carotid artery duplex examination showed no significant stenosis in either carotid system; however, a CT angiogram revealed significant external compression of the left common carotid artery secondary to metastatic cervical disease. As photodynamic therapy can cause temporary post-treatment oedema, there was concern that the compression might worsen with treatment. The patient went on to have endovascular stent-grafting to the left common carotid artery, with no complications or neurological sequelae. His syncopal episodes fully resolved after this intervention, and he was able to proceed with the planned photodynamic therapy without complication.

Conclusion

Vascular complications occur in head and neck cancer patients, both as a result of the disease and its progression, and of our treatments for it. Advances in interventional radiology over the last decade have significantly altered outcomes in such cases. Life-threatening haemorrhage can often be safely controlled with minimal morbidity to the patient, allowing definitive treatment of the disease or continuing palliation of symptoms. Open surgery in a previously irradiated field is clearly a difficult option as regards vascular control, and carries its own morbidity. If treatment is being planned, potential vascular problems may be identified early and preventative measures taken, such as stenting a compressed artery prior to photodynamic therapy. Less acute problems occur as a result of radiotherapy, with strong evidence to support the theory of accelerated atherosclerosis and carotid stenosis in these patients, several years after completion of their treatment.

References

1 Upile T, Triaridis S, Kirkland P, Archer D, Searle A, Irving C *et al*. The management of carotid artery rupture. *Eur Arch Otorhinolaryngol* 2005;**262**:555–60
2 Katras T, Baltazar U, Colvett K, Rush D, Dunn J, Stanton P Jr. Radiation-induced arterial disease. *Am Surg* 1999;**65**:1176–9
3 Citardi MJ, Chaloupka JC, Son YH, Ariyan S, Sasaki CT. Management of carotid artery rupture by monitored endovascular therapeutic occlusion (1988–1994). *Laryngoscope* 1995;**105**:1086–92
4 MacDonald S, Gan J, McKay AJ, Edwards RD. Endovascular treatment of acute carotid blow-out syndrome. *J Vasc Interv Radiol* 2000;**11**:1184–8
5 Warren FM, Cohen JI, Nesbit GM, Barnwell SL, Wax MK, Andersen PE. Management of carotid "blowout" with endovascular stent grafts. *Laryngoscope* 2002;**112**:428–33
6 Broomfield SJ, Bruce IA, Luff DA, Birzgalis AR, Ashleigh RJ. Endovascular management of the carotid blowout syndrome. *J Laryngol Otol* 2006;**120**:694–7
7 Levy EI, Horowitz MB, Koebbe C, Jungreis CC. Target-specific multimodality endovascular management of carotid artery blowout syndrome. *Ear Nose Throat J* 2002;**81**:115–18
8 Cohen J, Rad I. Contemporary management of carotid blowout. *Curr Opin Otolaryngol Head Neck Surg* 2004;**12**:110–15
9 Hoppe H, Barnwell SL, Nesbit GM, Petersen BD. Stent-grafts in the treatment of emergent or urgent carotid artery disease: review of 25 cases. *J Vasc Interv Radiol* 2008;**19**:31–41
10 Chang F-C, Lirng J-F, Luo C-B, Wang S-J, Wu H-M, Guo W-Y *et al*. Patients with head and neck cancers and associated postirradiated carotid blowout syndrome: endovascular therapeutic methods and outcomes. *J Vasc Surg* 2008;**47**:936–45
11 Simental A, Johnson JT, Horowitz M. Delayed complications of endovascular stenting for carotid blowout. *Am J Otolaryngol* 2003;**24**:417–19
12 Kwok PC, Cheung JY, Tang KW, Wong WK. Re: Endovascular treatment of acute carotid blow-out syndrome. *J Vasc Interv Radiol* 2001;**12**:895–6
13 Koutsimpelas D, Pitton M, Külkens C, Lippert BM, Mann WJ. Endovascular carotid reconstruction in palliative head and neck cancer patients with threatened carotid blowout presents a beneficial supportive care measure. *J Pall Med* 2008;**11**:784–9
14 Willinsky RA, Taylor SM, Terbrugge K, Farb RI, Tomlinson G, Montanera W. Neurologic complications of cerebral angiography: prospective analysis of 2,899 procedures and review of the literature. *Radiology* 2003;**227**:522–8
15 Dawkins AA, Evans AL, Wattam J, Romanowski CA, Connolly DJ, Hodgson TJ *et al*. Complications of cerebral angiography: a prospective analysis of 2,924 consecutive procedures. *Neuroradiology* 2007;**49**:753–9
16 Morrissey DD, Andersen PE, Nesbit GM, Barnwell SL, Everts EC, Cohen JI. Endovascular management of hemorrhage in patients with head and neck cancer. *Arch Otolaryngol Head Neck Surg* 1997;**123**:15–19
17 Smith GL, Smith BD, Buchholz TA, Giordano SH, Garden AS, Woodward WA *et al*. Cerebrovascular disease risk in older head and neck cancer patients after radiotherapy. *J Clin Onc* 2008;**26**:5119–25
18 Lam WW, Leung S, So NM, Wong K, Liu K, Ku PK *et al*. Incidence of carotid stenosis in nasopharyngeal carcinoma patients after radiotherapy. *Cancer* 2001;**92**:2357–63
19 Muzaffar K, Collins SL, Labropoulos N, Baker WH. A prospective study of the effects of irradiation on the carotid artery. *Laryngoscope* 2000;**110**:1811–14
20 Shariat M, Alias NAA, Biswal BM. Radiation effects on the intima-media thickness of the common carotid artery in post-radiotherapy patients with head and neck malignancy. *Postgrad Med J* 2008;**84**:609–12
21 Cheng SWK, Wu LLH, Ting ACW, Lau H, Lam LK, Wei WI. Irradiation-induced extracranial carotid stenosis in patients with head and neck malignancies. *Am J Surg* 1999;**178**:323–8
22 Cheng SWK, Ting ACW, Lam LK, Wei WI. Carotid stenosis after radiotherapy for nasopharyngeal carcinoma. *Arch Otolaryngol Head Neck Surg* 2000;**126**:517–21
23 Cheng SWK, Ting ACW, Ho P, Wu LLH. Accelerated progression of carotid stenosis in patients with previous external neck irradiation. *J Vasc Surg* 2004;**39**:409–15
24 Carmody BJ, Arora S, Avena R, Curry KM, Simpkins J, Cosby K *et al*. Accelerated carotid artery disease after high-dose radiotherapy: is there a role for routine carotid duplex surveillance? *J Vasc Surg* 1999;**30**:1045–51
25 Patel DA, Kochanski J, Suen AW, Fajardo LF, Hancock SL, Knox SJ. Clinical manifestations of noncoronary atherosclerotic vascular disease after moderate dose irradiation. *Cancer* 2006;**106**:718–25
26 Halak M, Fajer S, Ben-Meir H, Loberman Z, Weller B, Karmeli R. Neck irradiation: a risk factor for occlusive carotid artery disease. *Eur J Vasc Endovasc Surg* 2002;**23**:299–302

27 Lou P-J, Jäger HR, Jones L, Theodossy T, Bown SG, Hopper C. Interstitial photodynamic therapy as salvage treatment for recurrent head and neck cancer. *Br J Cancer* 2004;**91**: 441–6
28 Kübler AC, Stenzel W, Ruhling M, Muel B, Fischer JH. Experimental evaluation of possible side effects of intra-operative photodynamic therapy on rabbit blood vessels and nerves. *Lasers Surg Med* 2003;**33**:247–55
29 Grant WE, Speight PM, MacRobert AJ, Hopper C, Bown SG. Photodynamic therapy of normal rat arteries after photosensitisations using disulphonated aluminium phthalocyanine and 5-aminolaevulinic acid. *Br J Cancer* 1994;**70**:72–8

Address for correspondence:
Miss Joanne Rimmer,
39 Handforth Road,
London SW9 0LL, UK

Fax: +44 (0)20 78339480
E-mail: jrimmer@doctors.org.uk

Miss J Rimmer takes responsibility for the integrity of the content of the paper
Competing interests: None declared