Novel treatment (new drug/intervention; established drug/procedure in new situation)

Advanced and rapidly progressing head and neck cancer: good palliation following intralesional bleomycin

Keith Ian Quintyne,¹ Shirley Baker,¹ Fintan Wallis,² Neville Shine,³ Rajnish Gupta¹

¹Department of Medical Oncology, Mid-Western Regional Hospital, Limerick, Ireland;

²Department of Radiology, Mid-Western Regional Hospital, Limerick, Ireland;

³ENT Department, Mid-Western Regional Hospital, Limerick, Ireland

Correspondence to Dr Keith Ian Quintyne, keithi.quintyne@hse.ie

Summary

The authors herein report the case of a 61-year-old man undergoing adjuvant therapy for locally advanced laryngeal cancer, who developed parastomal recurrence in his radiation field around his tracheotomy site, while he was undergoing radiation therapy, and compromised the secure placement of his tracheotomy tube and maintenance of his upper airway. MRI restaging and biopsy confirmed recurrence and progressive disease in his mediastinum. He underwent local therapy with intralesional bleomycin with good palliation, and ability to maintain the patency of his upper airway.

BACKGROUND

Head and neck cancers are a heterogeneous group of conditions, that may arise from any of almost 30 anatomical sites; the majority of which include oral cavity, oropharynx,

larynx, sinuses and base.^{1 2} Therapeutic options available traditionally include a combination of surgical intervention, chemotherapy, biological therapy and radiotherapy; due to the natural history of these disorders, issues related

Figure 1 MRI soft tissue-face and neck – axial T2 weighted image demonstrating parastomal nodule, obstructing tracheotomy.

Figure 2 Patient on day 1 on intralesional bleomycin.

to disease recurrence and toxicity from therapy maybe encountered, with affected patients often having a complex and protracted course of illness that is plagued with quiescent phases from disease and symptoms interspersed with bouts of serious illness, debility, disfigurement and depression.^{2 3}

Management of postlaryngectomy stomal recurrence poses a clinical conundrum, because most of the initial primary intervention is aggressive and given upfront, hence leaving few therapeutic options and is hence normally associated with poor outcome;⁴ we herein report the case of a 61-year-old Caucasian man of Irish extraction who presented with clinical and radiological features of rapidly progressive head and neck cancer, with parastomal disease and outline his management and clinical path.

CASE PRESENTATION

A 61-year-old gentleman presented with a 6 week history of progressive shortness of breath, dry cough and hoarseness. These symptoms were associated with loss of appetite and weight loss of 15 kg (approximately 25% of his body weight). He denied any significant medical illnesses. He gave a 50 pack year history of smoking and admitted to minimal alcohol usage. He was reviewed by the Ears, Nose and Throat (ENT) surgical team and his diagnosis of supraglottic laryngeal carcinoma, T₄ N₂ C₀ M₀, grade III squamous cell carcinoma with nine out of 47 positive lymph nodes, with evidence of perineural and lymphovascular invasion was established following a total laryngectomy and bilateral lymph node dissection.

Clinical examination revealed that he was a pleasant and co-operative gentleman, with an Eastern Cooperative Oncology Group (ECOG) performance status of two.⁵ The remainder of his clinical assessment was otherwise normal, with note made of his functioning tracheostomy. He

embarked on his adjuvant radical radiotherapy without cisplatin (due to his borderline ECOG performance status) and was to receive 64 Grays in 32 fractions, but this was halted at 54 Grays in 27 fractions, due to development of an infield parastomal recurrence. This nodular swelling at his tracheotomy site prevented the secure placement of his tracheotomy tube. MRI of the soft tissue of his face and neck was undertaken and revealed a 2.0×1.5 cm nodule, but also noted mediastinal lymphadenopathy that was in direct contact with the proximal portion of the subclavian vein, hence making it Sisson's disease classification III.⁶ This is shown below in figure 1.

Biopsy was undertaken of the nodule and histological confirmation of recurrence was obtained. Further surgical intervention or radiotherapy, following multidisciplinary team (MDT) meeting review was thought not appropriate, given his level of pretreatment, declining ECOG performance status and extent of his disease. Systemic therapies with weekly methotrexate or cetuximab were reviewed, but the patient declined these options. The possibility of intralesional bleomycin every 2 weeks was raised to facilitate local control to all the safe and secure placement of his tracheotomy tube, and the patient was amenable to the option. Intralesional bleomycin was started at a dose of eight units diluted in 2% lignocaine to a volume of 4 ml and administered every 2 weeks without apparent complication. His clinical images through his therapy are shown below in figures 2, 3 and 4.

OUTCOME AND FOLLOW-UP

Following his local therapy, the patient was able to more easily place his tracheostomy tube, and allowed for his discharge into the community after palliative care services were formally introduced, to attend a wedding of his niece.

Figure 3 Patient on day 15 on intralesional bleomycin.

The effect derived from the intralesional bleomycin was short-lived, as 8 weeks following completion of his therapy, he had further development of subcutaneous nodules outside his previous intralesional therapy treatment area, and he declined any further intervention at this time. He passed away peacefully 6 weeks following his final appointment in the out patients' clinic, where his progressive disease was noted.

DISCUSSION

Within the European Union, head and neck cancers account for approximately 139 000 new cases diagnosed per annum, with 90% of these being squamous cell carcinomas.^{3–7} Laryngeal squamous cell carcinoma (LSCC) is a common subtype of head and neck cancer, with early stage (i.e. stage I and II) having a favourable outcome following surgical intervention or radical radiotherapy, but this not the same for advanced (i.e. stage III and IV), and consequently the sequencing of therapeutic modalities employed remains controversial,⁸ consequently, MDT management remains the safest option to co-ordinate the most appropriate therapeutic path to reduce unnecessary toxicity from treatment and maximise quality of life.

Incidence of relapse with parastomal disease for patients with LSCC has been described in the literature as occurring less than 10% of cases for patients undergoing laryngectomy.^{4–9} The main factors that have been associated with stomal recurrence, include advanced T-stage (T4 stage especially), subglottic involvement of the primary tumour, advanced N-stage (pre or para- tracheal lymph node involvement), preoperative tracheostomy and failed postoperative radiotherapy.^{4–10} Many of these were seen in

this case, as the patient had T4_A N2_C LSCC and had early failed postoperative radiotherapy.

In 1976, Sisson *et al.* described patterns of recurrence by anatomical involvement using a numeric system where: I—localised and discrete nodule in superior half of stoma without oesophageal involvement; II—tumour involved the superior half of the stoma with oesophageal involvement; III—tumour involving inferior half of stoma and direct extension into mediastinum; and IV—extension laterally and often under either clavicle.⁵ These criteria were used to help stratify patients and potentially allow using a standard treatment algorithm. It also allowed for prognosticating patients based on the patterns of recurrence.

Therapeutic options for recurrent or progressive stomal LSCC is limited, and therefore needs to be designed for each individual patient, and is best undertaken in the MDT setting.³ Surgical intervention remains the best option for localised recurrence,^{3–10} however, in this case, given the extent of his disease and his declining ECOG performance status, he was not a suitable or fit candidate for surgery. Palliative radiotherapy may also be considered as an option, but given this patient's stomal disease while undergoing therapy, it was not thought to be suitable in this case. Systemic therapy with palliative chemotherapy remains the standard option, with patients of adequate ECOG performance and without significant co-morbidities receiving combinations of cetuximab with cisplatin or carboplatin plus 5-fluorouracil.³ However, palliative chemotherapy given after failure of initial therapy is hampered by the fact that the response rates are generally poor and of short duration.^{11–12} In this case, the patient declined any systemic therapy, but even if he had agreed, options would have been limited to tolerate polychemotherapy given his

Figure 4 Patient on day 75 on intralesional bleomycin.

poor ECOG performance status, but could have included weekly infusions of methotrexate or cetuximab.³

Other novel alternatives for therapy, include the intral-lesional delivery of bleomycin in an effort to afford local tumour control, and has been listed in several case reports within the literature;^{13–15} this practise is limited by the lack of availability of prospective data that have been statistically validated. Further extrapolation using the bleomycin model, which is proven to have biological effectiveness for squamous cell carcinoma cell lines,¹⁶ the employment of electroporation, that is, the application of short and intense electrical pulses to a localised area in conjunction with the administration of a sensitising agent such as bleomycin, has been proven to have a statistically better outcome than administration of bleomycin on its own.¹⁶ This was not entertained for this patient, as it was not an available therapy available to our unit, and given the impending concerns regarding his tracheotomy and progressive disease while undergoing radiotherapy, embarking on only local therapy with bleomycin was best viable option.

With any management strategy employed for patients with advanced disease, appropriate palliation and dedication to maintain best quality of life is paramount, this is most ideally achieved with having an honest but compassionate communication and supportive environment facilitated with the involvement of palliative care services, both in the home and hospital settings.¹² This was achieved with this patient, as his greatest concern, following the progression of his disease was to be alive and well enough to walk with his only niece down the aisle on her wedding day, which was met and surpassed by allowing him a more pleasant end-of-life experience.

Learning points

- ▶ Patient had clinical, histological and radiological features of rapidly progressing head and neck cancer with stomal disease.
- ▶ Given his poor ECOG performance status, and his declining systemic therapy, good palliation without significant toxicity was achieved with intralesional bleomycin.
- ▶ This offers insight into therapeutic options for local control.
- ▶ Insured and improved patient's end-of-life experience, without significant toxicity from intervention.

Competing interests None.

Patient consent Obtained.

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