

Single Case

Malignant Broncho-Oesophageal Fistula following Radiotherapy for Noninvasive T3 Oesophageal Squamous Cell Carcinoma

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Keywords

Chemoradiotherapy · Esophageal fistula · Esophageal squamous cell carcinoma · Radiotherapy · Stents

Abstract

Malignant tracheo-oesophageal fistula (TEF) can result from tumour progression and invasion of adjacent organs, or a complication of treatment. In the posttreatment setting, incidence of TEF in cases with preceding airway invasion (T4b) are not infrequently reported; however, for those for whom disease was confined to organ (T1–3) at staging, this is a rare complication. Management for these cases is palliative in nature, with the goal to prevent aspiration by closing the connection and facilitate safe resumption of oral intake where possible. Herein we report a case of a 71-year-old female with a T3 oesophageal squamous cell carcinoma, who presented with new onset dysphagia 2 weeks after completing a course of definitive radiotherapy and was found to have a broncho-oesophageal fistula. This patient was managed with dual stenting of both the airway and oesophagus, an emerging management option for this condition, and was thereafter able to safely resume oral intake.

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Introduction

The following case illustrates an uncommon presentation of malignant tracheo-oesophageal fistula (TEF) in a 71-year-old female, within weeks of having completed a course of definitive radiotherapy for an early (T3) oesophageal squamous cell carcinoma (SCC). Malignant TEF is an abnormal (pathological) connection between the oesophagus and airway. Its two purported mechanisms are that it is the result of tumour progression and invasion of adjacent organs, or due to tumour regression as a result of treatment. In the posttreatment setting, tumour with preceding airway invasion (T4b) regress, but imbalance with normal tissue repopulation leaves an unoccupied tract, which is the fistula [1]. Consistent with these mechanisms, the incidence of TEF in the posttreatment setting for early oesophageal cancers (T1–3) is rare [2].

Case Presentation

A 71-year-old female presented with progressive dysphagia and weight loss. She had a background of chronic obstructive pulmonary disease and was an active smoker. Endoscopy revealed a tumour of the upper oesophagus (shown in Fig. 1a). Histology confirmed oesophageal SCC. Staging positron emission tomography (PET) showed avidity in the primary and 2 right upper para-oesophageal lymph nodes (shown in Fig. 2a). MDT recommended definitive chemoradiotherapy for early (T3N1, Stage IIb) oesophageal SCC. This patient tolerated only one cycle of chemotherapy (carboplatin, paclitaxel), receiving radiotherapy alone with 54 Gy to gross disease and 48 Gy in 30 fractions to elective regional nodes, using a volume modulated arc therapy technique, over 6 weeks. Her treatment course was complicated by moderate odynophagia, mild fatigue, and nausea. By treatment completion, this patient had lost 2.5 kg weight compared to pretreatment baseline of 46.6 kg. She continued to smoke approximately 10 cigarettes a day whilst being treated.

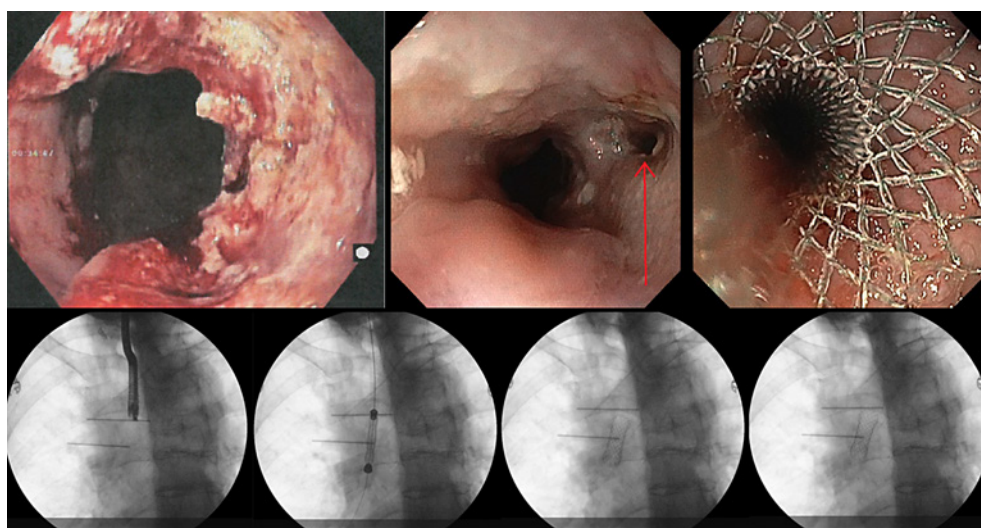


Fig. 1. Endoscopy and stenti. **a** Pretreatment. Tumour of the middle oesophagus, involving two-third of the circumference, 20 cm distal to incisors, extending 5 cm. **b** Posttreatment. Malignant-appearing, intrinsic moderate stenosis was found 22 cm from the incisors, measured 4 cm (in length) and associated fistula is seen (red arrow). **c** This was stented with an 18 mm × 12.3 cm with a partially covered metallic stent under fluoroscopic guidance. **d** Fluoroscopy demonstrating the placement of 12 mm × 3 cm metallic silicone covered stent in the right main bronchus, under bronchoscopy.

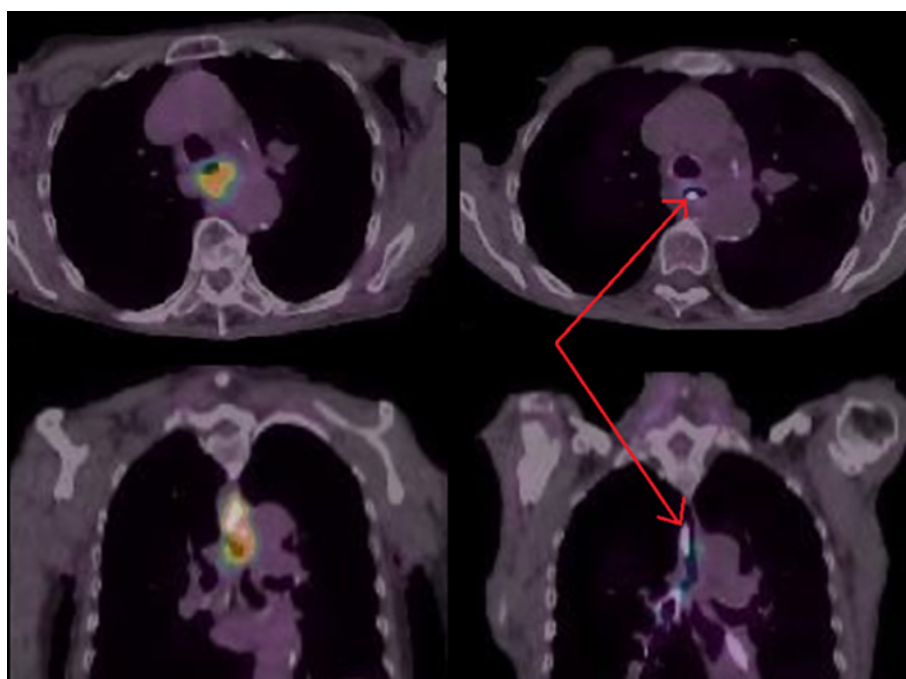


Fig. 2. Position emission tomography (PET). **a** Pretreatment PET. There is a large area of intensely increased FDG uptake into the mid portion of the oesophagus over approximately 5 cm, SUV max 9.4. There was moderate uptake into 2 right upper para-oesophageal lymph nodes, more superior to the oesophageal uptake. **b** Posttreatment PET at 11-weeks. Previously identified intense uptake related to the mid oesophagus has resolved. Mild activity persists, SUVmax 4.9 (previously 9.4). Uptake into the 2 right para-oesophageal lymph nodes has resolved. Nasogastric tube in-situ (red arrow).

Two weeks after treatment, she developed dysphagia to liquids and proceeded to a video fluoroscopic swallow study, concerning fistula formation (shown in Fig. 3a), and CT confirmed a broncho-oesophageal fistula between the mid-oesophagus and the right main bronchus (Fig. 3b). Endoscopy revealed severe stricture and fistula; biopsy of this returned persistent oesophageal SCC (shown in Fig. 1b). She underwent urgent stenting of the right main bronchus to prevent aspiration (shown in Fig. 1d), and a plan was made to provide further upper GI stenting, therefore completion of dual stenting, as an outpatient. The second stent was offered to facilitate safe and comfortable resumption of oral intake. Several factors were considered in this delay to the second stent; time for the initial stent to settle, but also given the patient's wishes to be back at home with her family for a period prior to re-hospitalisation. She was discharged home, remaining on nasogastric tube feeding, to await her second procedure. Endoscopy and oesophageal stent placement took place 7 weeks later (shown in Fig. 1c). Between stenting, repeat PET 11 weeks posttreatment showed mild persistent avidity at the site of primary alone (shown in Fig. 2b). Following this procedure, oral intake was safely resumed with a minced and moist diet.

Discussion/Conclusion

Malignant fistula following completion of radiotherapy treatment for oesophageal cancer with preceding airway invasion (T4b) has an incidence rate of up to 33% in some case series [1]. It is thought that this results from an imbalance between tumour destruction and normal

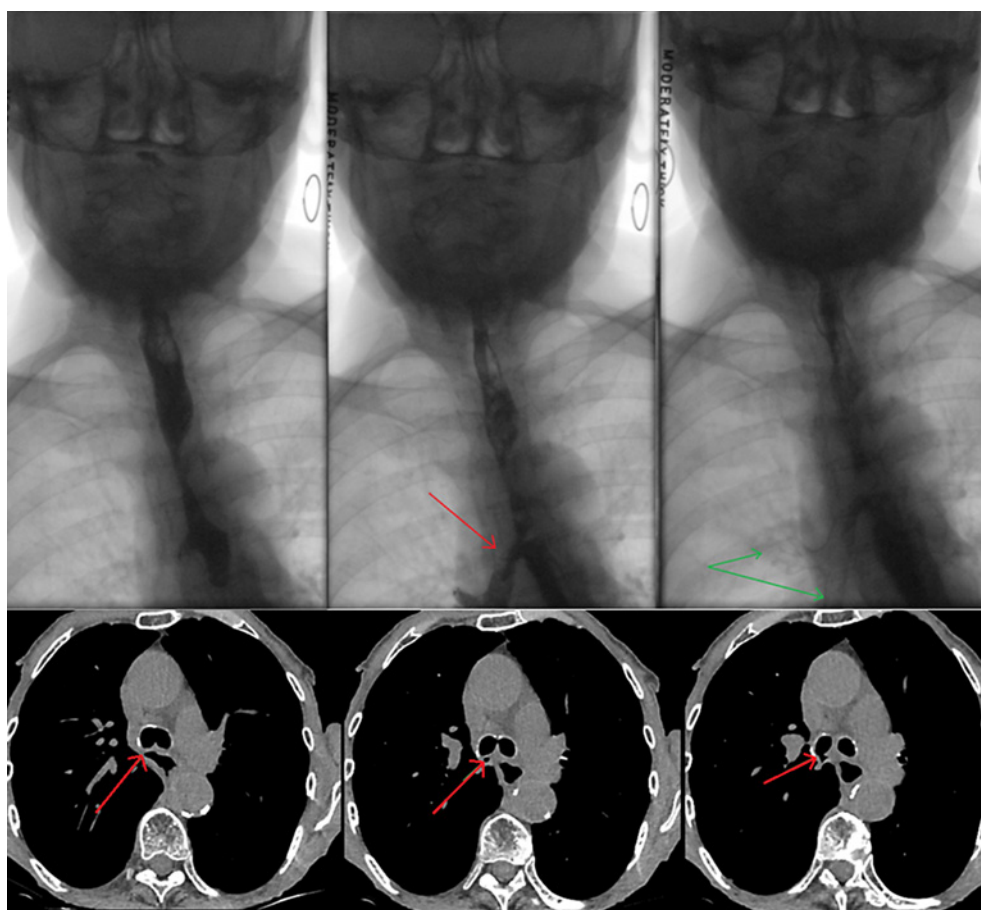


Fig. 3. a Video Fluoroscopic Swallow Study (VFSS). There is evidence of a tracheo-oesophageal fistula at the level of the carina with contrast seen extending from the oesophagus into the right main bronchus (red arrow) and the peripheral bronchi (green arrows), especially of the right lower lobe. The examination was aborted immediately, and no further oral contrast was given. **b** CT neck and chest. The CT confirms the presence of a broncho-oesophageal fistula with connection of the mid oesophagus with the right main bronchus inferior to the carina (red arrow).

cell repopulation. However, cases of TEF complicating T1–3 disease are very infrequent, with one case series going as far as to describe the risk of fistula formation in non-organ invading tumours as “clinically irrelevant” [2].

Recently published meta-analysis of 17 studies, which explored the risk factors for oesophageal perforation for oesophageal cancer treated with radiotherapy, found age <60 years, SCC, T4 stage, ulcerative type lesion, failure to achieve complete remission, 5-FU based regimen, and stenosis to be associated with increased oesophageal fistula formation [1]. A history of smoking, and persistent smoking following a diagnosis of oesophageal cancer, is associated with a poorer prognosis [3]. Yet, to the best of our knowledge, no study has yet been undertaken to investigate the impact of smoking during a radiotherapy treatment course and direct toxicity to the oesophagus, including fistula formation, in the setting of oesophageal radiotherapy. Nicotine induces vasoconstriction, which can reduce oxygen to the mucosa [4]. Subsequent hypoxia would result in reduced radiation sensitivity and reduced healing capacity of the tissue. Anecdotally, these patients who continue to smoke during treatment do suffer from a greater degree of odynophagia. The authors question whether persisting smoking during treatment could have contributed to this outcome.

Prognosis is poor, with most patients deceased within 3 months [1, 5]. One of the largest case series of malignant TEF ($n = 207$) found sepsis related to pneumonia to be the most common cause of death (82%), followed by bleeding (12%) [5]. Management is therefore palliative. These cohorts who develop posttreatment malignant TEFs are invariably nonsurgical candidates with most undergoing definitive chemoradiotherapy. They generally have poor performance status, are malnourished, and may already have respiratory compromise – as was the case for this patient.

Stenting is the mainstay of treatment. By blocking the fistula, the aim was to prevent infection, improve nutrition by facilitating resumption of oral intake, and by doing so, improve quality of life [6]. In patients who are suitable for stenting, the question is then which side of the fistula to stent. A recent review on the matter proposed a management algorithm, in which single oesophageal stents are initial management of choice, with the exception of cases where stenting was deemed high risk of critical airway obstruction or for fistulas located at the proximal/mid oesophagus [6]. Oesophageal stent carries known risks of migration, extrinsic airway compression, bleeding, and perforation [7]. Whilst use of single airway stents may have fewer catastrophic complications, the rate of closure of fistula is reported at 71%, and the durability of single metal airway stents has been called into question with a 12% incidence of metal fatigue resulting in stent fracture [8, 9]. However, it should be noted that the median time to such an event in a large retrospective case series was 686 days, which is significantly beyond life expectancy in this context and cohort [8].

This patient was managed with dual stenting, which is controversial as its use is based on anecdotal success and small case series, which report better outcomes, without head-to-head prospective trial data [10, 11]. Stenting of the airway, followed by the oesophagus, is thought to mitigate the risk of extrinsic airway compression from an oesophageal stent and stent migration or erosion into the airway. Theoretically, it also provides “back-up” in the event of single stent failure due to migration or rupture but carries the risk of enlarging the fistula by applying opposing radial forces [6, 12].

In summary, malignant TEF is an uncommon complication of radiotherapy for T1–3 oesophageal cancer. Awareness by both the clinician and patient is necessary for prompt recognition, investigation, and intervention. Dual stenting is an emerging management option for these patients, which carries theoretical advantages but lacks prospective head-to-head data. Lastly, there seems to be a gap in the literature with regard to investigated association between active smoking and oesophageal toxicity on treatment. Given the catastrophic consequences of treatment toxicities such as fistula formation and the nutritional and functional impact of odynophagia, investigation is certainly warranted.

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Statement of Ethics

This manuscript complies with the Declaration of Helsinki (revised 2013) and has been reviewed under the Wide Bay Hospital and Health Service’s research governance processes. The Health Service determined that formal Human Research Ethics Committee review and approval was not required for this case report. The patient provided written informed consent for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors have no financial or nonfinancial competing interests to declare.

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Author Contributions

Dwayne Reading and Bryan Burmeister wrote the manuscript. Both the authors contributed equally to the preparation of the manuscript. Both the authors gave final approval of the manuscript.

Data Availability Statement

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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