



MALIGNANT TRACHEO-ESOPHAGEAL FISTULA IN ADVANCED ESOPHAGEAL CANCER: REPORT OF TWO CASES

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ABSTRACT **Introduction:** Malignant tracheo-esophageal fistula (TEF), a relatively uncommon entity, can be seen in advanced esophageal cancer. However, development of TEF in these patients whether due to advancement of disease or due to medical intervention like radiation therapy (RT), chemotherapy is a matter of debate. Here, we reported two cases of malignant TEF in advanced esophageal carcinoma. **Case Summary:** The first patient was 46-year-old male, with progressive dysphagia diagnosed as middle thoracic esophageal cancer, squamous cell type. Patient was managed with palliative RT 39 Gy/13 fractions. Within 1-month of RT completion, patient developed TEF and succumbed to death. The other one was 54-year-old male presented with history of progressive dysphagia and diagnosed as having upper thoracic squamous cell carcinoma of esophagus. He was given palliative RT 20 Gy/4 fractions. Unfortunately, this patient also developed TEF on first follow-up and despite best efforts patient declared dead in ICU. **Conclusion:** These two cases showed that treating oncologist should be aware of potential TEF occurrence in cases of advanced esophageal cancer treated vigorously. As, management of established TEF is cumbersome, precaution should be taken to prevent it. Further case reports and series with different management approach will enlighten about standard protocol in management of such patients.

KEYWORDS : Esophageal cancer; malignant trachea-esophageal fistula; radiation therapy

INTRODUCTION

Malignant tracheo-esophageal fistula (TEF) is relatively a rare condition, the incidence of TEF from esophageal cancer ranges from 4.3–12%. [1] The causes are multiple like advanced esophageal cancer (EC), lung cancer etc. [1] The two proposed mechanism causing malignant TEF are tumor progression and invasion of adjacent organs, or owing to the imbalance between tumor shrinkage and normal tissue repair. [2] In both the scenario, it presents as grave challenge to the treating clinician because the survival of patient diagnosed with terminal stage esophageal cancer is poor; developing the complication due to intervention, prognosis is even poorer. Sometimes, TEF developed even due to the therapeutic intervention like inappropriate, high dose radiation therapy (RT). [3] Here, we present two cases of EC patients who developed TEF following radiotherapy, each receiving distinct radiation treatment schedules.

Case Summary

Case 1: A 46-year-old man presented to our Radiation Oncology Out-patient Department (OPD) with a 3-month history of dysphagia, which was both to solid & liquid, and progressive in nature. On general physical examination and systemic examination, no significant abnormality was seen. Contrast enhanced computed tomography (CECT) of the thorax showed a heterogeneously enhancing soft tissue growth for a length of 6.5 cm corresponding to T2-T5 vertebral body level with distal end of thickening being 8 cm above gastro-esophageal junction. Upper gastro-intestinal (UGI) endoscopy revealed the growth at 24 cm from incisor teeth, beyond which the scope was not negotiable. Histopathological examination from esophageal growth confirmed moderately differentiated squamous cell carcinoma (MDSCC). In view of the progressive nature of the disease, and unresectability of the tumor, the patient underwent palliative radiotherapy with 39Gy in 13 fractions over 2.5 weeks (five days a week). Patient tolerated the RT well and was kept on follow-up. However, patient came back to OPD within 1 month with complains of absolute dysphagia and cough. On evaluation with CECT thorax, heterogeneously enhancing mural thickening with maximum thickness of 0.8 cm was seen for length of 4.4 cm corresponding to T3-T4 vertebral body level esophagus with presence of fistulous communication between trachea and upper thoracic esophagus with no significant response from radiotherapy. As dysphagia worsened progressively, and patient was having difficulty in consuming food, the patient was referred for the placement of a feeding jejunostomy to address nutritional requirements. Patient general condition

deteriorated gradually and developed respiratory distress requiring oxygen support. However, despite best efforts, patient developed respiratory failure and declared dead in hospital.

Case 2: A 54-year-old man presented with history of progressive dysphagia for 4-month duration, starting with solid food and progressed to liquid also, but not associated with any pain. He also had significant weight loss (>15 kg) for the same duration with no other complains. General physical and systemic examination revealed patient was cachexic and having significant pallor. UGI endoscopy showed esophageal growth at 22 cm from incisors, beyond which the scope was not negotiable. Histopathological examination from the growth revealed MDSCC. Radiological examination with CECT of the thorax showed the growth having a length of 7.5 cm corresponding to T1-T4 vertebral level. After thorough evaluation, patient was found to be unresectable and palliative radiotherapy was advised in view of progressive nature of the tumor and poor general condition of the patient. Patient was given 20Gy radiation in 4 fractions over 4 days. He tolerated RT well, but on first month follow-up patient did not have any symptomatic relief from RT and referred to surgery for feeding jejunostomy for meeting nutritional demand. On further evaluation with CT scan, fistulous communication was found between trachea and esophagus with presence of residual disease (figure 1). Patient underwent feeding jejunostomy under general anaesthesia. However, during postoperative period patient declared dead due to respiratory failure in intensive care unit.

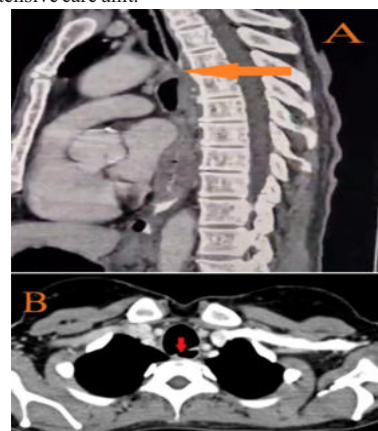


Figure 1: Contrast enhanced Computed tomography of thorax showing trachea-esophageal fistula (coloured arrow) in advanced esophageal cancer. A. sagittal view, B. axial view

DISCUSSION

Esophagus is tubular elongated organ in digestive system which connects pharynx to stomach and anatomical configuration around esophagus includes bronchi, trachea, blood vessels and mediastinum. [4] Presence of tumor in esophagus is not limited to only esophageal wall, but also has high probability to invade these surrounding critical and adjacent organs, which is related to the poor prognosis of these patients and high incidence of respiratory esophageal fistula. [5-7] In advanced EC, development of TEF is a rare, but dreaded complication; can occur due to either progression of disease or iatrogenic. [3,8] Treatment of advanced EC with patient having complete dysphagia is itself a challenging task. [9] In current scenario, there are plenty of modalities available like surgery, immunotherapy, chemotherapy, radiotherapy including external beam radiation therapy (EBRT) & brachytherapy for treatment of EC. [9,10] Despite the progressive advancement made in EC treatment to improve the outcome of the patient, still palliating the symptoms and best supportive care are the two most common intent in common practice as most of the patient are diagnosed at terminal stage. [5]

Hu et al in his study reported that T4 and N3 stage, re-irradiation, ulcerative growth, esophageal stenosis, and the maximum thickness of the tumor were the major risk factors involved in development of fistula; tumors with advanced stage like T4 has involved the whole layer of oesophagus and the probability of fistula formation is higher compared to other stage. [11] Other risk factors like body mass index (BMI), age, gender, albumin levels in blood, tumor location and length did not contribute majorly to formation of TEF. [12] Esophageal perforation caused after initiation of RT is predominantly due to the imbalance between the regression speed of tumor tissue and the repair speed of normal tissue. The rapid regression of tumor is related to the intrinsic sensitivity of tumor to the radiation, dose and speed of radiation. [12-14]

Early identification of symptoms like fever, paroxysmal coughing and refractory dysphagia should raise alarm to Radiation Oncologist during RT or after completion of RT to look for any serious adverse effect like fistula formation. [14] Moreover, these alarming symptoms can lead to severe malnutrition, recurrent infections and sepsis and this would deteriorate the existing condition of patient and presents a challenge to closure of fistula. [14] Even with good advances being made in treatment for TEF, it becomes difficult to choose the right patient for right intervention because of progressive nature of the disease. [15]

Very recently, Pao et al reported that the median interval from patient receiving radiation to the occurrence of esophageal-respiratory fistula was 4.4 months with prominent sites like esophago-pleural, esophago-tracheal, broncho-esophageal, & aorto-esophageal fistula. [16] Additionally, other prominent authors also reported similar findings in their study about formation and progression of esophageal-respiratory fistula and their unfavourable outcome. [17-19]

In the first case, our patient developed fistula after 1-month of receiving radiation for malignancy. He initially had some relief in his symptoms but later presented with worsening of symptoms. Upon evaluation, fistulous communication between esophagus and trachea was found; but, due to progressive nature of disease, patient condition deteriorated suddenly and patient expired without providing any time for intervention. In the second case, patient received less dose of radiation in comparison to first case, yet developed fistula which may be due to more advanced nature of tumor at the time of diagnosis. In this case, feeding jejunostomy was performed and patient was put on ventilator for respiratory support, but again patient succumbed either due postoperative complication or respiratory failure. These two cases showed it is difficult to predict which EC patient is prone to develop severe complication of RT. Intrinsic activity of tumor to radiation may also vary from one individual to another. [20] Our studies suggest that one cannot predict which patients can develop RT induced esophageal fistula despite taking utmost care in selecting the patient for interventions.

CONCLUSION

Esophageal fistula as an adverse effect from radiation is a grave

complication and requires prompt attention from treating clinician, timely identification of signs and symptoms and initiating the appropriate therapy at earliest like omitting RT, securing airway, administering intravenous antibiotics and surgical referral for definitive intervention. The rarity of fistula occurrences and the absence of standardized treatment protocols further complicate therapeutic approaches. Invasive interventions encompass a range of procedures such as esophageal-pulmonary resection, endoscopic deployment of self-expandable covered stents, along with esophageal diversion. Conversely, non-invasive management primarily revolves around providing best supportive care. However, even with appropriate treatment, the outcome is dismal.

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