

# Enigma of Esophageal - Respiratory Fistula in Advanced Esophageal Cancer

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## ABSTRACT

**Background:** The incidence of malignant esophageal-respiratory fistulas in esophageal cancer patients is not so frequent. The fistula development in esophageal cancer may be due to advanced disease or a radiotherapy-related complication. Rarely, a pulmonary abscess may develop, which is the most dreadful complication resulting in dismal outcomes. Here, we reported 2-cases of esophageal-respiratory fistula; one with esophageal bronchial fistula and the other with esophageal pleural fistula.

**Case reports:** A 46-year-aged man presented with complaints of difficulty in swallowing for 4 months. CECT chest showed an esophageal growth of 8.5 cm in the lower esophagus. The patient received palliative radiotherapy followed by palliative chemotherapy and showed some improvement in dysphagia.

Nine months after the start of treatment, the patient's dysphagia began to worsen, and he was put on oral metronomic chemotherapy. After 1-year of metronomic chemotherapy, the patient developed cough and chest pain and was diagnosed with an esophageal-pleural fistula with chest wall collection and pleural effusion. The patient was managed conservatively and later lost to follow-up. Another 65-year-old patient presented with dysphagia for 3-months. CECT chest showed an esophageal growth of 5.5 cm in the middle esophagus. The patient received palliative radiotherapy, after which the dysphagia improved. In 3rd month of follow up patient's dysphagia worsened; barium swallow showed esophageal-bronchial fistula. The patient was managed symptomatically and later lost to follow-up.

**Conclusions:** Fistula formation and subsequent abscess results in a poor prognosis. With advancing disease and compromised general condition of the patient, palliation of symptoms is a significant challenge. Treatment becomes difficult due to the rare occurrence of fistulas and the non-standardization of the treatment protocol. Invasive treatment includes esophageal-pulmonary resection, endoscopic placement of self-expandable covered stents, drainage of empyema and obliteration of empyema cavity, esophageal diversion, and non-invasive treatment includes best supportive care. However, even with appropriate treatment, the outcome is dismal.

**Keywords:** Esophageal-pleural/bronchial fistula, Esophageal cancer.

**INTRODUCTION:**

The incidence of malignant esophageal-respiratory fistulas in esophageal cancer patients ranges from 5% to 13% [1,2]. Most lesions are localized between the esophagus and the tracheobronchial tree, but a subgroup (3–11%) presents with direct fistulas into the pulmonary parenchyma and empyema [1,3,4]. Fistula formation and subsequent empyema results in a poor prognosis. Advanced esophageal cancer can result in esophageal-respiratory fistula formation. As the tumor grows, it invades the adjacent structures leading to fistula formation [5,6]. Anatomically, the esophagus is in direct contact with the lung pleura for a considerable distance on the right side. In contrast, on the left side, the aorta lies between the esophagus and the pleura, except for a short distance above the diaphragm. Therefore, right-side pleural involvement is more common than left [7].

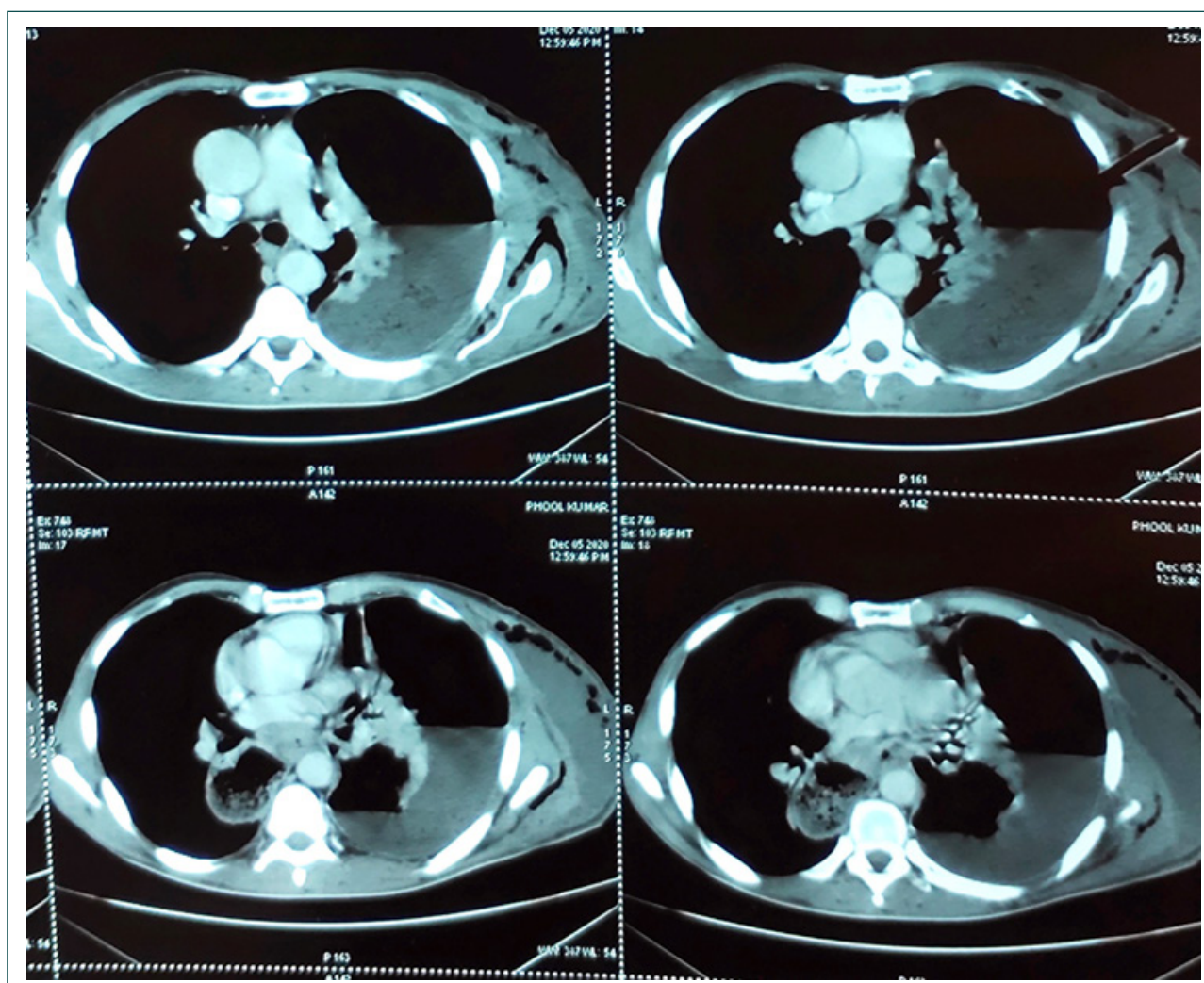
With advancing disease and compromised general condition of the patient, palliation of symptoms and dysphagia is an important challenge. The fistula development in esophageal cancer may be due to advancing disease or a therapeutic complication. Either of these situations results in grave difficulties in managing such patients. The uncommon presentation of this condition and lack of standard protocol for treating such patients makes the situation more complicated. Here, we reported 2-cases of esophageal-respiratory fistula; one with esophageal bronchial fistula and the other with esophageal pleural fistula with abscess formation.

**Case Reports**

**Case 1:** A 46-year-aged man presented with dysphagia for 4-months. The patient was able to take semisolids but with some difficulty. On examination, the patient's Karnofsky Performance Status (KPS) was 50. All hematological and biochemical parameters were within normal limits. The systemic examination of the patient was normal. Upper gastrointestinal endoscopy (UGIE) showed a fungating growth at 30 cm from incisors, and the scope could not negotiate further. Biopsy from the growth revealed moderately differentiated squamous

cell carcinoma. Barium swallow showed irregular luminal narrowing of the lower 1/3rd of the esophagus with shouldering and proximal hold up of contrast. Contrast-enhanced computed tomography (CECT) chest showed 8.5 cm long esophageal growth in the lower esophagus opposite to the D7-D11 vertebra along with pre-tracheal, para-tracheal, sub-aortic, and sub-carinal lymph nodes. The patient was diagnosed with a case of locally advanced carcinoma esophagus. The patient received palliative radiotherapy to the whole esophagus (20Gy/5fractions/1-week) followed by intravenous palliative chemotherapy with injection carboplatin (area under the curve [AUC]= 5) and 5-fluorouracil (750 mg/m<sup>2</sup>) after which there was an improvement in dysphagia. A Follow-up CECT scan after intravenous combination chemotherapy revealed residual disease, and the patient was put on oral metronomic chemotherapy with tablet cyclophosphamide 50 mg twice daily, following which the patient had stable disease. After 16 months of continuous oral chemotherapy, the patient developed a fever, cough, and chest pain. CECT chest showed a linear defect in the left esophageal wall communicating with the left lower lobe of the lung with chest wall abscess and pleural effusion, indicating esophageal pleural fistula formation (Figure-1); an esophageal thickening from D6-D12 vertebral level was also noted. The patient was managed with intravenous antibiotics and drainage of abscess, but unfortunately, the patient later lost to follow-up.

**Case 2:** Another 65-year-old male presented with dysphagia for the 3-months duration. The patient was able to take semisolids but with some difficulty. On examination, the patient's KPS was 60. All hematological and biochemical investigations were within normal limits. The systemic examination of the patient was normal. CECT chest showed an esophageal growth of 5.5 cm in length in the middle esophagus. Due to poor general condition, the patient received palliative radiotherapy (30 Gy/10 fractions/2-weeks), after which the dysphagia improved. In 3rd month of follow-up, the patient's dysphagia worsened; barium swallow showed esophageal-bronchial fistula (Figure-2). The patient's general condition was poor,



**Figure.1.** CECT chest (axial view) showing communication between the left esophageal wall and left lower lobe of the lung, indicating esophageal pleural fistula formation; left-sided pleural abscess is also noted.

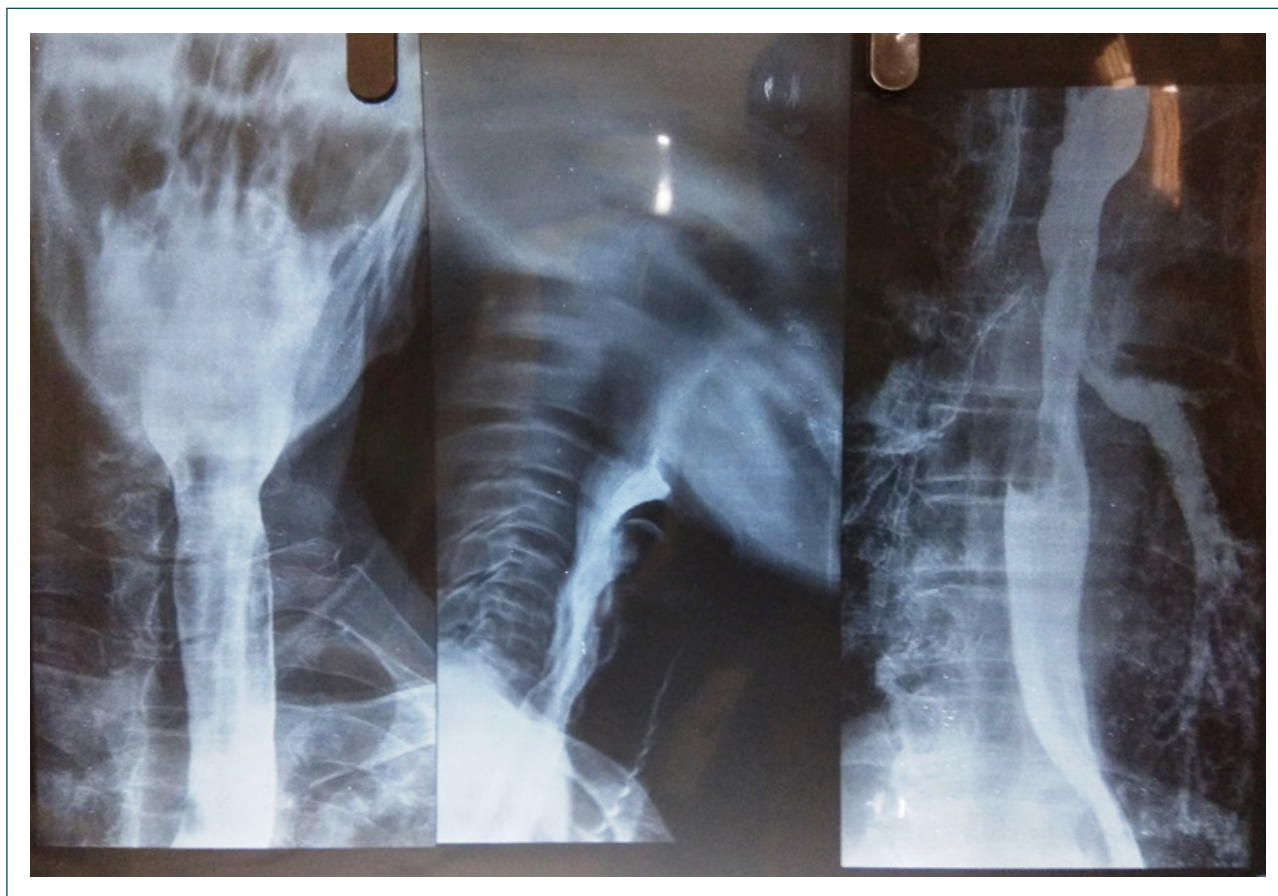
and he was managed conservatively. Later, the patient lost to follow up.

### Discussion

The development of esophageal respiratory fistulas in esophageal cancer is multifactorial. A fistula may develop due to disease progression; as the growing tumor invades the adjacent structures. Unfortunately, the fistula may develop due to therapeutic interventions such as chemoradiotherapy or brachytherapy.

Zhu et al. conducted a meta-analysis, the purpose of which was to identify risk factors for esophageal fistula

in esophageal cancer patients treated with radiotherapy [8]. Total of 17 articles reporting over 35 risk factors were included, and a meta-analysis was carried out for 17 risk factors. 7 of the 17 examined factors were associated with an increased risk of esophageal fistula formation: 1) Age < 60–65 years, 2) Ulcerative type, 3) Squamous cell cancer, 4) T4 stage, 5) Non-complete response, 6) Fluorouracil-based regimen, 7) and Stenosis. The 10 remaining factors (gender, hemoglobin, KPS/PS, albumin, body mass index (BMI), tumor location, tumor length, tumor size, re-radiotherapy, and concurrent chemoradiotherapy) had no significant correlation with esophageal



**Figure.2.** Barium swallow showing communication between distal esophagus and right bronchial tree, indicating esophageal bronchial fistula.

fistula formation.

The prognosis of esophageal perforation is poor, and the death rate is high; most patients will die of it within 3 months [9]. Table -1 represents the various studies on therapeutic interventions and outcomes in patients with esophageal respiratory fistulas.

The superadded infection after fistula formation poses a great therapeutic challenge. Fistula formation and subsequent empyema results in a poor prognosis of the disease. The therapeutic approach for managing esophageal respiratory fistulas may be invasive and non-invasive. Invasive treatment includes esophageal- pulmonary resection, endoscopic placement of self-expandable covered stents, and esophageal diversion. Non-invasive measures include the best supportive care to the patient [15, 16]. Most patients have a poor general conditions at the time of presentation, and in these cases, palliation is a prima-

ry goal of treatment; hence, surgery has a limited role because of surgery-related morbidity.

In cases where the fistula is complicated by empyema formation, definitive management involves complete drainage of empyema and obliteration of the empyema cavity. Systemic antibiotics should be administered for at least 4–6 weeks to sterilize the empyema cavity. However, even with appropriate intervention, the prognosis is miserable.

In our first case, the fistula occurred 16 months after palliative radiotherapy to the whole esophagus. Furthermore, after receiving palliative radiotherapy patient was on oral metronomic chemotherapy and had stable disease. In such a scenario, where the patient did not have any visible progressive disease (increase in dysphagia or pain), the likeliness of fistula formation as a direct result of advanced disease progression is less. But, the radio-

**Table 1.** Various studies (case reports/series) regarding the outcome in patients with esophageal respiratory fistulas

S.no	Study	Site of fistula formation	Treatment received	Outcome
1.	Kim et al [10]. (n=14)	Esophageal pulmonary fistula.	Metallic stents for palliative treatment.	Thirteen patients died of aspiration pneumonia, and the remaining died of cancer bleeding. Median survival 65.5 days.
2.	Rehders et al [11]. (n=2)	Esophageal pulmonary fistula with abscess formation.	Surgical.	Death of both patients at 8 and 9 months after initial surgical intervention.
3.	Guan et al [12]. (n=221)	Esophageal-respiratory and Esophageal- mediastinal fistula.	Esophageal stenting and symptomatic.	Median post-fistula survival is 3.63 months.
4.	Devydov et al [13]. (n=35)	Esophageal fistula with mediastinum, pleural cavity, lungs, bronchi, and trachea.	Surgical.	Median survival was 13 months (range 3-31) for the resection group and 3 months (range 1-6) for bypass and gastrostomy patients.
5.	Zhang et al [14]. (n=22)	Esophageal- respiratory and esophageal-mediastinum fistula		The mean survival time was 3.2 months from the development of the fistula.

therapy dose given to that patient was also less likely to cause a radiotherapy-induced acquired fistula. However, intrinsic sensitivity to radiation differs from person to person, and a comparatively small dose of radiation may cause severe toxicity in a particular individual. In the second case, fistula formation was seen after just 3-months of palliative radiotherapy. The dose used in this patient was slightly higher than the previous one but within the tolerance limit of the esophagus dose-volume threshold [17]. Moreover, fistula formation is implausible as a direct result of acute radiation toxicity within less time. Hence, fistula formation can be granted due to disease progression.

### Conclusion

Symptoms indicating esophageal respiratory fistula in the advanced stage of esophageal cancer should be taken seriously. Fistula formation and subsequent abscess results in a grave prognosis. With advancing disease and compromised general condition of the patient, palliation of symptoms is an important challenge. Treatment becomes difficult due to the rare occurrence of fistulas and the non-standardization of the treatment protocol. Invasive treatment includes esophageal- pulmonary resection, endoscopic placement of self-expandable covered stents, drainage of empyema and obliteration of empyema cavity, esophageal diversion, and non-inva-

sive treatment, including best supportive care. However, even with appropriate treatment, the outcome is dismal.

### Funding

The article or anything related to it was not funded by any external.

### Consent

All authors declared that written informed consent was obtained from both the patient and their attendant for the publication of these articles and accompanying images. However, the identification of the patients is not disclosed anywhere in the article.

### Conflict of interest

The authors have declared that no conflict of interest exists.

### REFERENCES

1. Duranceau A, Jamieson GG. Malignant tracheoesophageal fistula. *Ann Thorac Surg.* 1984;37:346-54.
2. Fitzgerald RH Jr, Bartels DM, Parker EF. Tracheoesophageal fistulas secondary to carcinoma of the esophagus. *J Thorac Cardiovasc Surg* 1981;82:194-7.
3. Martini N, Goodner JT, D'Angio GJ et al. Tracheoesophageal fistula due to cancer. *J Thorac Cardiovasc Surg.* 1970;59:319-24.

4. Angorn IB. Intubation in the treatment of carcinoma of the esophagus. *World J Surg.* 1981;5:535-41.
5. Cong Z, Diao, Q, Yi J et al. Esophagectomy combined with aortic segment replacement for esophageal cancer invading the aorta. *Ann Thorac Surg.* 2014;97(2):460-6.
6. Kosugi S, Ichikawa H, Kanda T et al. Clinico-pathological characteristics and prognosis of patients with esophageal carcinoma invading adjacent structures found during esophagectomy. *J Surg Oncol.* 2012;105:767-72.
7. Chuah BY, Khoo KL, Khor CJ. Clinical challenges and images in GI. Esophago?pleural fistula. *Gastroenterology.* 2008;134:919,1275.
8. Chao Zhu, Songping Wang, Yunhong you et al. Risk Factors for Esophageal Fistula in Esophageal Cancer Patients Treated with Radiotherapy: A Systematic Review and Meta-Analysis. *Oncol Res Treat.* 2020;43:34-40.
9. Burt M, Diehl W, Martini N et al. Malignant Esophagorespiratory fistula: management options and survival. *Ann Thorac Surg.* 1991;52(6):1222-8.
10. Tae-Hyung Kim, Ji Hoon Shin, Kyung Rae Kim et al. Treatment of Esophagopleural Fistulas Using Covered Retrievable Expandable Metallic Stents. *J Vasc Interv Radiol.* 2014;25:623-9.
11. Alexander Rehders, Billur Baseras, Leila Telan. Esophageal cancer complicated by esophagopulmonary fistula and lung abscess formation: A surgical approach. *Thoracic Cancer* 2014;(5):468-71.
12. Xin Guan, Chao Liu, Tianshuo Zhou et al. Survival and prognostic factors of patients with esophageal fistula in advanced esophageal squamous cell carcinoma. *Bioscience Reports.* (2020) 40 BSR20193379.
13. M. Davydov, I. Stilidi, V. Bokhyan et al. Surgical treatment of esophageal carcinoma complicated by fistulas. *European Journal of Cardio-thoracic Surgery.* 2001;20:405-8.
14. Yang Zhang, Zongjuan Li, Wei Zhang et al. Risk factors for esophageal fistula in patients with locally advanced esophageal carcinoma receiving chemoradiotherapy. *OncoTargets and Therapy.* 2018;11:2311-7.
15. Schweigert M, Dubecz A, beronm et al. Surgical therapy for necrotizing pneumonia and lung Gangrene. *Thorac Cardiovasc Surg.* 2013;61:636-41.
16. Tsai YF, Ku YH. Necrotizing pneumonia: a rare complication Of pneumonia requiring special consideration. *Curr Opin Pulmmed.* 2012; 18:246-52.
17. Werner-Wasik M, Yorke E, Deasy J, Nam J, Marks LB. Radiation dose-volume effects in the esophagus. *Int J Radiat Oncol Biol Phys.* 2010 Mar 1;76(3 Suppl):S86-93