

Metastasis to the Esophagus from Primary Adenocarcinoma of the Lung. Case Report and Literature Review

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Abstract

Background

Esophageal metastases from distant primary tumour are rare. The diffusion could derive from direct infiltration in most cases, but it can rarely derive from lymphatic or hematogenous spread.

Methods

We present a case of a patient who was referred to our institution for esophageal metastasis from a primary lung cancer. PubMed, EMBASE, and Web of Science were consulted until January 2019 to review the current evidence about this rare event.

Results

A 59-year-old man with previous history of lung cancer (thyroid transcription factor TTF-1 +) in complete remission after 37 cycles of Gefitinib therapy was referred to our department because of the detection at the follow-up Positron Emission Tomography (PET) of hypercaptation in the lower third of the esophagus. An upper gastrointestinal endoscopy showed a 12-mm nodular lesion of the cardias. Esophageal biopsies were suggestive for TTF1+

adenocarcinoma metastasis from lung cancer. A resection of the esophago-gastric junction was successfully performed. Overall, 102 cases were retrieved from current literature. The most common primary tumor location were breast (46%), followed by lung (21.6%), and skin melanoma (10.7%). Dysphagia (89%), weight loss (84%), and regurgitation (64%) were the most commonly reported symptoms. The time range from primary tumor diagnosis to esophageal metastasis evidence ranged from 0 to 10 years. Endoscopic palliation and systemic chemotherapy represent the most common approach while surgical resection was adopted in few patients.

Conclusions

The mucosal growth of an esophageal metastasis from a primary lung tumor is a rare event. Immunohistochemistry is useful to confirm the diagnosis of primary tumor. Despite its rarity, metastasis to the esophagus from primary lung cancer should be considered as a possible event and in case of complete remission, surgical resection may be considered in selected patients with good performance status.

Keywords: Distant metastasis; Esophageal carcinoma; Esophageal Resection; Lung adenocarcinoma

Introduction

The esophagus is a rare site of metastasis from other organs' tumor. The esophageal secondary cancer often develops upward from the submucosa with UGE usually demonstrating esophageal narrowing, with smooth mucosal surface. That characteristic makes the histopathological diagnosis difficult, and the use of immunohistochemical markers has proven useful in identifying the primary site of tumour. The most common mechanism of diffusion to the esophagus is direct invasions and infiltrations from adjacent organs or nodes. However, hematogenous or lymphatic diffusion has been reported. Dysphagia, regurgitation, and weight loss are common symptoms in such patients [1].

Lung carcinomas metastasize by lymphatic as well as blood vessels. The most reported sites of diffusion from lung neoplasm are liver, bone, adrenal glands, brain, kidney, etc, while sporadic reports are presents about esophageal metastasis. The presence of Thyroid transcription factor1 (TTF-1) is useful in detecting the pulmonary primitiveness in case of distant metastatic disease. TTF-1 is usually expressed in thyroid cancer and in a significant proportion of lung tumor. Due to the high specificity for pulmonary and thyroid malignancies, this marker is a useful diagnostic tool to recognize pulmonary primitiveness [2].

Case Presentation

In 2015 a 56-year-old man complained dysphonia and, after a normal chest X-ray, underwent neck US that revealed multiple pathologic nodes. His past clinical history consisted in

hypertension, dyslipidaemia, obesity, mechanical aortic valve replacement, and atrial fibrillation. A total body CT scan, brain Magnetic Resonance Imaging, and PET scan showed a 35mm node of the apical segment in the left lung with multiple mediastinal adenopathies (**Figure 1 A-B**). An Endobronchial Ultrasound (EBUS) with histological examination of a subcarinal lymphnode revealed a metastasis from lung adenocarcinoma (TTF-1 positive, CK7 positive, p63 negative, and CK5,6 negative). In consideration of the clinical stage and immunohistochemistry the patient was referred to immunochemotherapy with Gefitinib. After 37 cycles of neoadjuvant therapy the PET showed complete remission of the primary lung tumor and mediastinal lymphadenopathies (**Figure 1 C-D**).

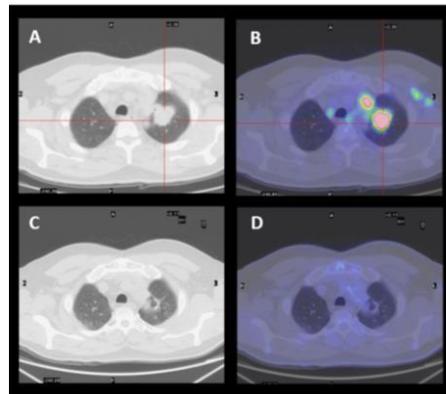


Figure 1: A-B) Computerized tomography and Positron emission tomography showing a 3.5 cm lesion in the left apical segment of the lung. C-D) Computerized tomography and Positron emission tomography images of the lesion after 37 cycles of immunochemotherapy.

The 3-years follow-up PET scan showed an hypercaptation of the distal esophagus (**Figure 2B**). The patient was asymptomatic with no weight loss or GI bleeding reported. An upper gastrointestinal endoscopy confirmed the presence of a 12-mm pedunculated lesion located 1 cm above the esophago-gastric junction (**Figure 2A**). Biopsies showed TTF-1 + adenocarcinoma suggestive for lung cancer metastasis (**Figure 2D**). An Endoscopic Ultrasonography (EUS) showed invasion of the submucosal layer while a total body CT-scan did not show any other metastasis (**Figure 2C**). Hybrid Ivor-Lewis esophagectomy was performed with lower mediastinal and celiac lymphadenectomy. The histological examination was adenocarcinoma pT2N0G2, TTF-1 and CK7 positive, suggestive for lung metastasis. The postoperative course was uneventful, and the patient was discharged on 9th postoperative day.

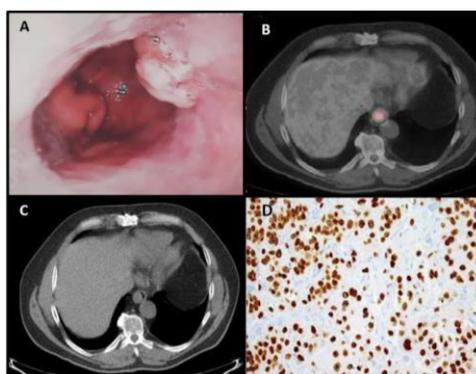


Figure 2: The esophageal metastasis at the endoscopic view (A), positron emission tomography (B), and computerized tomography (C). D) Biopsy of the esophageal lesion showing TTF-1 + adenocarcinoma.

Discussion

Esophageal metastasis usually occurs as a late event in the disease history, and the presentation is usually characterized by progressive and disabling dysphagia, weight loss, and worsening of general condition with a poor survival. Metastases to the esophagus are usually submucosal and may require biopsy under endoscopic ultrasonography guidance to make the correct diagnosis and identification. The submucosal location is probably because the well represented lymphatic plexus of the esophageal submucosal layer. By contrast, the mucosal infiltration and location of a metastatic tumor to the esophagus is even more rare, but the diagnosis can be easily obtained by biopsy and immunohistochemistry.

Secondary esophageal cancer is relatively rare. Mizobuchi et al found 112 esophageal metastases after 1835 autopsies on patients who died from cancer, with an incidence rate of 6.1% [4]. The first reported esophageal metastasis deriving from a prostate adenocarcinoma was published in 1942 and since then over 100 cases have been reported (**Table 1**). The most common primary tumor that metastasize to the esophagus are of breast origin (46%), followed by lung cancer (21.6%), and skin melanoma (10.7%). In addition, metastases from thyroid, prostate, kidney, endometrial and ovarian metastasis have been described. The time from diagnosis of primary tumor to esophageal metastasis ranged from 0 to 10 years. Dysphagia (89%), weight loss (84%), and regurgitation (64%) were the most commonly reported symptoms. The survival ranged from 6.8 to 19 months.

Primary cancer	N (%)
Breast [1, 4-17]	47 (46)
Lung [17-20]	22 (21.6)

Melanoma ^[21]	11 (10.7)
Thyroid ^[1]	6 (5.9)
Prostate ^[22-24]	3 (2.9)
Kidney ^[25, 26]	2 (1.9)
Uterus ^[1, 17]	2 (1.9)
Ovaries ^[4, 27]	2 (1.9)
Pancreas ^[1, 28]	2 (1.9)
Hodgkin Lymphoma ^[1]	1 (0.9)
Rectum ^[1]	1(0.9)
Larynx ^[1]	1 (0.9)
Osteosarcoma ^[29]	1 (0.9)
Unknown Adenocarcinoma ^[1]	1 (0.9)

Table 1. Literature review and primary tumor location.

Despite its rarity, the possible secondary location of a distant primary malignant tumor to the esophagus should be always considered especially in patients with a previous history of distant primary tumor. In most of the cases reported in the literature, the adoption of palliative techniques was considered because the delayed diagnosis and advanced stage of the disease with thoracic and abdominal lymphnodes involvement. In addition, the presence of subclinical metastasis and possible pleural or mediastinal carcinomatosis is matter of concern. Endoscopic palliation and systemic chemotherapy generally represent the first-choice approach in these patients. Esophagectomy has been described only in a few circumstances to treat solitary metastases to the esophagus from primary ovarian, breast, and lung cancer tumours [4,8,18,27]. Oka and associates reported on resection of a metastasis from a lung cancer primary after a latency period of 5 years [18]. Similarly, to Oka we decided to perform surgical resection of the gastroesophageal junction because the good performance status of the patient. The peculiarities of this case report are the mucosal growth of the secondary lesion; this allowed an easy diagnosis through endoscopic biopsies and immunohistochemistry (TTF-1+). Moreover, the apparent complete remission of the primary lung cancer and the good performance status of the patient were decisive for the choice of a surgical resection.

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