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## Synchronous triple squamous cell carcinoma of the esophagus

Andy Petroianu\*, Kelly Renata Sabino, Maurício Buzelin Nunes

Department of Surgery, School of Medicine, Federal University, Minas Gerais, Brazil

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## ABSTRACT

**BACKGROUND:** Synchronous multiple primary malignancies of the esophagus and other organs are relatively unusual, but only five articles have published two synchronous cancers, both in the esophagus. This is the first published case of a triple esophageal carcinoma.

**CASE REPORT:** A 43-year-old man was referred to our hospital with severe progressive dysphagia and epigastric pain for almost one year. Endoscopy and imaging exams revealed three tumors located in upper, middle and lower esophagus. The upper and middle esophageal cancers were irresectable, and the patient was treated with radio- and chemotherapy. He survived 11 months after the diagnosis and died due to severe undernutrition and bilateral pneumonia.

**CONCLUSION:** In presence of squamous cell carcinoma of the esophagus, propedeutics should be carefully performed in order to verify the occurrence of other synchronous tumors in the esophagus and other organs, mainly head and neck and bronchial regions.

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## 1. Introduction

Reports of multiple synchronous cancers have been increasing due to prolonged lifespan and improvements in diagnostic techniques [1] range from 5% to 20% in the literature [1,2,4–14]. The most well known is with head and neck and lung similar cancers [1,2,4,11,14,15]. The association between different SCC can be explained from exposure to common carcinogenic agents such as tobacco smoke and alcoholism [4–6,11]. Smoking-induced tumor formation through DNA methylation is a common risk factor for patients with multiple primary malignancies, being an example of epigenetic field cancerization induced by exposure to carcinogenic factors [15].

Synchronous multiple cancers in the same organ are well known in colon, stomach and thyroid, but is extremely rare in esophagus. The literature registered only five cases of synchronous and metachronous double SCC of the esophagus [2,4,5,10,12] work has been reported in line with the SCARE criteria.

## 2. Case report

A 43-year-old man was referred to our institute with severe progressive dysphagia and epigastric pain for almost one year. Previously he smoked circa 60 cigarettes/day and was alcohol addicted for more than 20 years. Diagnostic evaluation included a complete

medical history, physical examination, laboratory blood analyses, and pulmonary and cardiac function tests. All lab exams were normal except for the lower level of the albumin 2.5 mg %. The patient underwent esophagogastrosomy with biopsies, esophagography, chest-abdomen CT with contrast enhancement and bronchoscopy. Tumor stage was determined according to the TNM staging system.

Endoscopy and imaging exams revealed three tumors located in upper (20 cm from teeth arcade), middle (29 cm from teeth arcade) and lower (38 cm from teeth arcade) esophagus. The biopsies of the three tumors confirmed the endoscopic impression of squamous cell carcinomas (Fig. 1). The bronchoscopy revealed a hard compression of the right main bronchus due to the middle esophagus tumor invasion. The chest CT demonstrated a three-centimeter node in the left lung lower lobe suggesting metastasis. A screening to search for other diseases did not show any disorder.

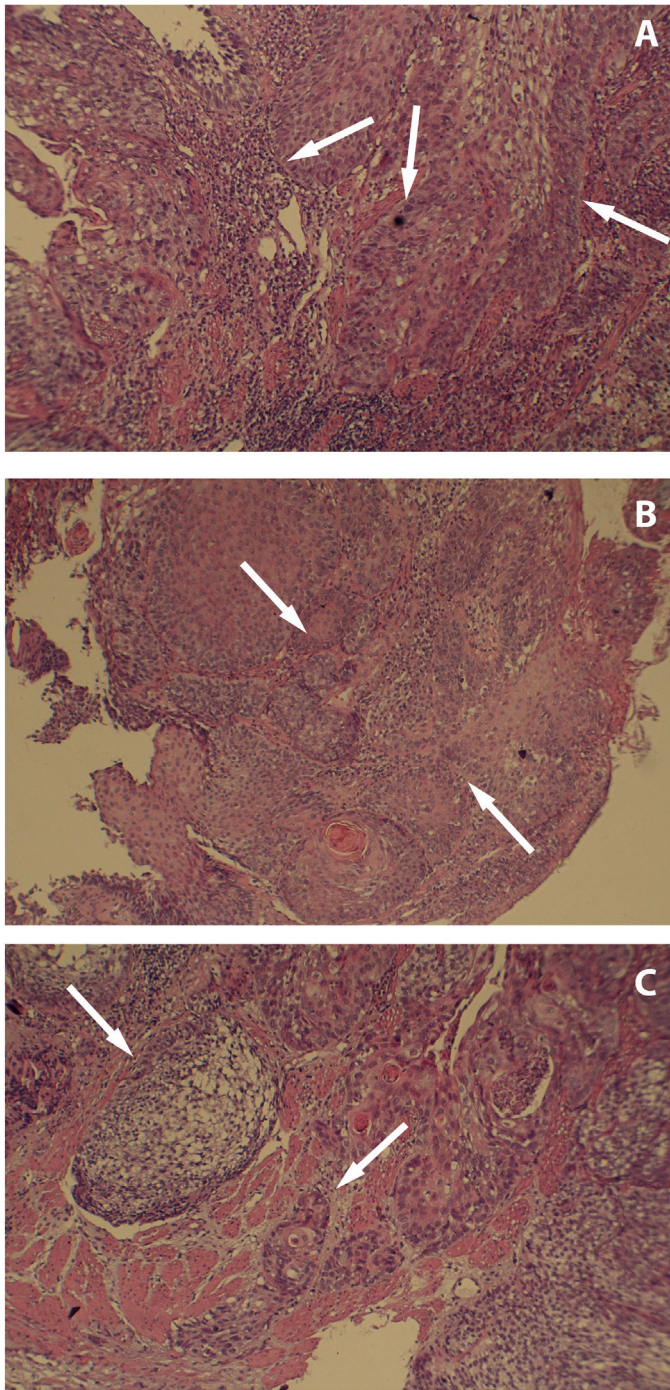
Esophageal surgical procedure was not considered due to the upper and middle esophageal cancers, which were irresectable, and to the pulmonary metastases. The patient was treated with four cycles of chemoradiotherapy (cisplatin plus fluoropyrimidine) with concurrent 25 cycles radiotherapy.

After five months, a gastrostomy was performed due to dysphagia. The patient survived 11 months after the diagnosis and died due to severe progressive undernutrition and bilateral pneumonia.

The ethical approval for the publication of this case was exempted by our institution due to the absence of risk to the patient and his family by this article and no research related to this case.

\* Corresponding author at: Avenida Afonso Pena, 1626 – apto. 1901, Belo Horizonte, MG 30130-005, Brazil.

E-mail address: [petroian@gmail.com](mailto:petroian@gmail.com) (A. Petroianu).



**Fig. 1.** Photomicrographs of synchronous triple esophageal squamous cell carcinoma (SCC).

A – Invasive SCC associated with chronic inflammatory infiltration. Carcinoma invasion into the upper third of esophageal wall, observe nuclear atypia (arrows). (HE, 100 $\times$ ).

B – Panoramic view of the invasive SCC into the middle thoracic esophagus. The infiltrating tumor into the esophageal corion is indicated by arrows. (HE, 40 $\times$ ).

C – Invasive SCC into the lower third of the esophageal muscle layer. Observe tumor atypical cells inside fibromuscular tissue (arrows). (HE, 100 $\times$ ).

### 3. Discussion

Patients with SCC of the esophagus have an increased risk of synchronous cancers, mainly in the aerodigestive tract organs, such as the oral cavity, pharynx, larynx and lung [4,6,8,10,15]. However multiple SCC in the esophagus is a extremely rare event. The litera-

ture has shown only five double SCC and none with higher number of tumors [2,4,5,10,12]. This is the first published triple SCC only in the esophagus.

Given the well-known harmful effects of smoking and alcohol consuming, including increased risk of cancers such as esophageal, aerodigestive tract and lung cancers, physicians should pay attention to the risk of synchronous SCC in these organs [4,6,8,10]. Recent technical progress in diagnostic methods may affect the clinical features of SCC of esophagus [13]. Endoscopy and PET-CT are the standard modality for SCC of the esophagus diagnosis and staging, demonstrating 100% sensitivity and 89% positive predictive values for endoscopy, and 91% sensitivity and 69% positive predictive values for PET-CT. Conventional CT on its own can miss early malignant lesions due to the mobility of body structures and normal variation [4,13].

In this case with three advanced esophageal cancers, the endoscopy easily diagnosed the three cancers of esophagus and was useful to biopsies of the three tumors. Probably due to the fact all cancers were advanced, the diagnosis and staging these tumors were easily done by the conventional CT without the necessity to perform a PET-CT. For smokers and long-term alcohol consumption, such as the patient of this case, the risk of esophageal SCC is increased, and this tumor should be always considered during the initial medical assessment.

Multidisciplinary approach was used for treating this patient [3]. Treatment plans for the three SCC was not optimal due to the unfeasibility of surgical treatment specifically for the upper and middle esophageal carcinomas. The treatment plans for esophagectomy and gastric transposition were altered to non-surgical treatment including definitive chemotherapy radiotherapy and palliative therapy [3]. Under-nutrition was an important negative prognostic factor for this patient.

### 4. Conclusion

Physicians should be aware of the co-existence of two or more squamous cells carcinoma of the esophagus during the initial study. In presence of esophageal cancer, propedeutics should be carefully performed in order to verify the occurrence of other synchronous tumors in the esophagus and other organs, mainly head and neck and bronchial regions.

### Conflicts of interest

All authors declare NO conflict of interest related to this article.

### Funding

All authors declare NO funding sponsored this work and article.

### Ethical approval

The ethical approval for the publication of this case was exempted by the Department of Surgery of the School of Medicine of the Federal University of Minas Gerais and by the Santa Casa Hospital of Belo Horizonte due to the absence of risk to the patient and his family by this article and no research related to this case.

### Consent

The patient signe the consent form for the publication of this article.

### Author contributions

Andy Petroianu is the head of the Surgical Service of Santa Casa Hospital and was responsible for the management of this patient. He wrote the manuscript.

Kelly Renata Sabino is Assistant surgeon of the Surgical Service of Santa Casa Hospital and was responsible for the management of this patient. She also wrote the manuscript.

Maurício Buzelin Nunes was the Pathologist of this patient. He made the pictures and manuscript.

### Registration of research studies

This is not a study, but a case report.

### Guarantor

The authors Andy Petroianu, Kelly Renata Sabino and Maurício Buzelin Nunes.

### Human rights statement

The authors declare all procedures followed have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

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