Endoscopically detected multicentric squamous cell carcinoma of the esophagus; Case presentation and literature review

Serkан Yalaki1, Hüseyin Pülat2, Oktay Karaköse3, Serdar Şenol4
1 Department of Gastroenterology, Mersin City Training and Research Hospital Mersin
2 Department of Surgical Oncology, Mersin City Training and Research Hospital Mersin
3 Department of Surgical Oncology, Samsun Training and Research Hospital Samsun
4 Department of Gastroenterological Surgery, Samsun Training and Research Hospital Samsun, Turkey

Abstract
Esophageal cancer is the 8th most common cancer worldwide and the 6th most common cause of cancer-related deaths. In general, the majority of esophageal cancer cases are more common in underdeveloped regions and are more common in males than females. Esophageal squamous cell carcinoma (ESCC) tends to occur in the proximal and middle esophagus and is the dominant sub-type worldwide, accounting for approximately 90% of all esophageal cancers. In a single patient, the simultaneous detection of an esophageal tumor endoscopically at multiple sites is very rare. Here, we aimed to discuss the case and literature in which endoscopic examination revealed all foci to be ESCC on biopsy.

Keywords
Endoscopy; Carcinoma; Squamous cell
Introduction
Esophageal cancer is the 8th most common cancer worldwide and the 6th most common cause of cancer-related deaths. Its incidence shows differences according to countries and even regions in the same country. In general, the majority of esophageal cancer cases are more common in underdeveloped areas and are more common in males than females [1]. In our country, it is most commonly seen in Eastern Anatolian and Eastern Black Sea regions [2,3]. The incidence is reported to be 5-10 / 100.000 in the general population.

Esophageal cancer has two primary subtypes; esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma (EAC) are the most common subtypes and are seen more commonly in the 7th and 8th decades of life. ESCC tends to occur in the proximal and middle esophagus and is the dominant sub-type worldwide, accounting for approximately 90% of all esophageal cancers in regions with the highest incidence of esophageal cancer worldwide, especially from Northern Iran to the Northern-Central China and Russia [4]. Although the formation of more than one independent SCC is described in 14-31% of cases; these cases could be determined by examining surgical preparates. These secondary cancers are mostly in situ carcinomas and superficial ESCCs [5-8]. In a single patient, the simultaneous detection of an esophageal tumor endoscopically at multiple sites is very rare. Here, we aimed to discuss the case and literature in which endoscopic examination revealed all foci to be ESCC on biopsy.

Case Report
A 52-year-old female patient applied with pain complaint during swallowing. It was known from her medical history that she had been suffering from diabetes for 15 years and had been on hemodialysis program for 5 years due to chronic renal failure. As the result of the upper gastrointestinal endoscopy, between esophageal 30th-35nd centimeters a malignant looking ulcerovegetative mass which narrowed the lumen was detected (Figure 1A,B); 4-8 mm diameter nodular lesions independent of each other with swollen surfaces were observed between esophageal 28th-22nd centimeters (Figure 1C); and finally a vegetative mass narrowing the lumen between the esophageal 20th-17th centimeters was observed (Figure 1D).

Tumoral lesions with dark-colored, oval and distinct nuclei, containing widespread mitosis and showing single-cell keratinization within nests on the desmoplastic stromal floor were observed on biopsies taken from all the lesions separately. It was detected with PanCK, P40 and P53 stainings in the immunohistochemical examination. It was reported as ESCC. PET-CT showed a significant increase in the involvement of the esophagus segment approximately 50 mm in length, extending at the level of T1-T3 vertebrae, which caused wall thickening in the proximal esophagus and completely covering the passage in some areas (SUVmax: 13,2). Esophageal wall thickening and prominent involvement were observed at the level of the T5-T9 vertebrae, approximately 91 mm in length from the subcarinal area to the distal esophagus (SUVmax: 15.9).
Discussion
Esophageal cancers constitute 1.5-2% of all cancers worldwide and 5-7% of gastrointestinal cancers and 1.8% of all cancer-related deaths are related to esophageal cancer [1,2]. Squamous cell carcinoma and adenocarcinomas are the most common types of esophageal cancers. In regions where esophageal malignancies are common in the world, histologically it has been found that 90% of these malignancies are ESCC [2]. Although there is no definite incidence in our country, it is mostly observed in the regions of Eastern Anatolia and the Eastern Black Sea regions [3].

The incidence of esophageal cancer increases with age and peaks during the 7th and 8th decades of life, and it is more common in men than women [4-6]. The fact that our patient was young female is not compatible with the literature.

SCC typically occurs in the middle and lower third of the esophagus, with only 10%-15% occurring in the upper one-third segment [7]. Endoscopically, they are usually identified as single, ulcerated or ulcerovegetative lesions. Malignant lesions with similar characteristics were observed in the upper and lower esophagus [6,7].

Two theories have been described to explain the appearance of multiple carcinomas. The theory of monoclonal neoplasia predicts that a strain from a single transformed cell can spread to produce multiple tumors. In some cases, individual tumor nodules are seen in the esophagus or stomach wall. By examining the resected esophageal specimens, this situation called intramural metastasis may be detected in about 11-16% of cases. These metastases are thought to be caused by intramural lymphatic spread [8]. In our case, in accordance with this information, metastatic nodular formations, which were thought to be caused by an ulcerovegal malignancy in the lower segment of the esophagus, were detected.

In the field-effect model, it is predicted that independent tumors develop as a result of genetic effects of carcinogens. It is thought that viral infections, nutritional deficiencies and dietary habits play a role in the carcinogenicity process and that the mucosa becomes sensitive to the development of multiple tumors as a result of this. According to the field carcinogenesis theory, atypical epithelial hyperplasia, metaplasia, pre-invasive carcinoma (in situ) and fully developed carcinoma areas can be found in various regions in the upper aerodigestive canal [8]. In 20.2% of patients with esophageal carcinoma, synchronous or metachronous carcinoma was detected in another region. Patients with upper aerodigestive system tumors are at greater risk for developing of second primary cancers in the same region [7,8].

In conclusion, it should be kept in mind that multicentric malignancies as well as intramural metastatic lesions, may frequently occur in individuals with esophageal carcinoma. Therefore, careful evaluation should be done to prevent another lesion from being missed during endoscopic examinations.

Scientific Responsibility Statement
The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Conflict of interest
None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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