

An Unusual Case of Bronchogenic Carcinoma and Oral Cavity Cancer: Metastatic Oral Cavity Disease or a Second Primary Tumor

Şule Akçay, MD; Beyhan Demirhan, MD

Başkent University, Faculty of Medicine, Departments of Pulmonary Diseases, Pathology, Ankara, Turkey

Abstract

We report a case of bronchogenic carcinoma and subsequent oral cavity tumor. After the initial intervention for lung cancer, an oral lesion that was causing dysphagia was observed. Both punch biopsies of the bronchial and oral lesions led to diagnosis of squamous cell carcinoma. These histopathological results pointed to the origin of oral cavity

disease being either lung cancer metastasis or a second primary oral cavity cancer and we discussed these two possibilities.

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Introduction

Multiple primary tumors of the aerodigestive tract are not rare. The development of such tumors has been linked to etiologic factors such as smoking, alcohol consumption, heredity and nutrition, among others. Various studies have reported the incidence of primary tumors of the aerodigestive tract as 5% to 30% (1-4).

The primary tumor that is first discovered in a patient is referred to as the "index tumor". When head and neck cancer is labeled the index tumor, there is a higher probability of developing a second primary cancer in the aerodigestive tract (oral cavity, larynx, lung, or esophagus) (2). However, in cases of primary lung cancer, it is rare to see the development of second primary upper aerodigestive cancer before the lung disease causes death.

Here we present an unusual case of squamous cell bronchial carcinoma and subsequent oral cavity tumor, and discuss whether the oral cavity disease represented lung cancer metastasis or a second primary oral cavity cancer.

Case Report

A 59 year-old man was hospitalized in April 1997 with complaints of hemoptysis, weight loss (5 kg. per month)

Correspondence:

Şule Akçay, MD
Başkent University Hospital
Fezî Çakmak Bulvarı
10. Sok. No:45
06490 Bahçelievler-Ankara-TURKEY

E-mail: sulea@b.baskent.edu.tr

and night sweats. He was a heavy smoker (70 pack.years) and had a history of an elective cholecystectomy 10 years ago. In his physical examination, there were decreased breath sounds in the right lower lung field. Other systems were normal, and routine hematological and biochemical results were unremarkable. The patient's chest x-ray revealed right lower lobe atelectasis (Fig-1). Computerized tomography (CT) of the thorax showed that a mass of 4.5x4.5x5 cm in the basal segments of the right lower lung lobe, and unilateral multiple clustered lymphadenopathy at the hilum and mediastinum. Fiberoptic bronchoscopy revealed an endobronchial mass in the bronchus of the right lower lobe. Pathological examination of the bronchial punch

biopsies revealed squamous cell carcinoma (Fig.2). The patient was staged as T3 N2 M0 (Stage III-A), since there was no evidence of metastasis.

The patient received curative radiotherapy, and returned to good clinical condition. He needed no further medical attention until eight months later when he noticed an oral lesion that was causing dysphagia. Upon hospitalization in December 1997, a tumoral lesion in his mouth was observed in his physical examination (Fig-3). A punch biopsy of this lesion demonstrated squamous cell carcinoma (Fig.4). A chest x-ray showed massive pleural effusion on the right side, and diagnostic thoracentesis revealed empyema, based on gross observation of pus and on biochemical properties (glucose: 20 mg/dl, LDH: 3200 IU/L, PH < 6.8). However, pleural fluid cultures were negative for acid-fast bacilli, fungi, and aerobic and anaerobic bacteria. A drain was placed percutaneously and systemic anti-anaerobic antibiotics were

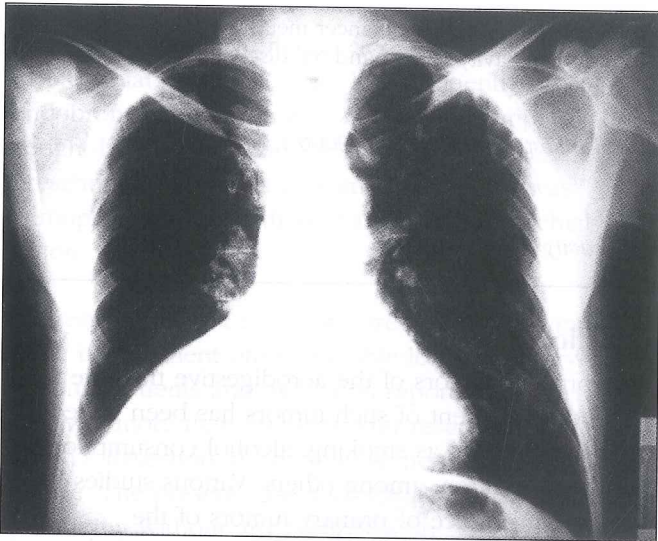


Fig. 1. Chest X-ray on admission. Right lower lobe atelectasis was present.

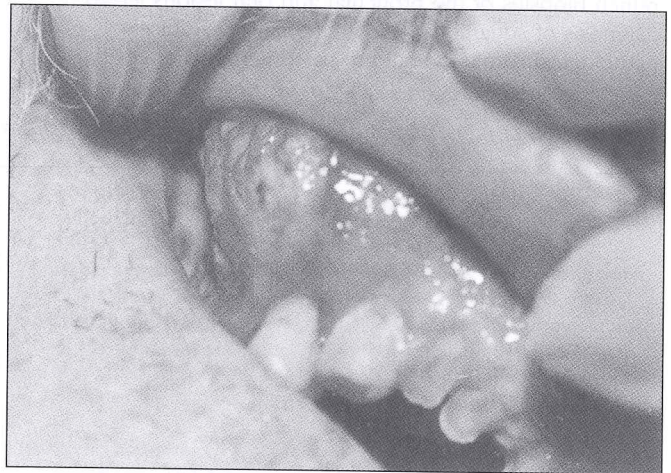


Fig. 3. An oral lesion showing close to right maxillary bone

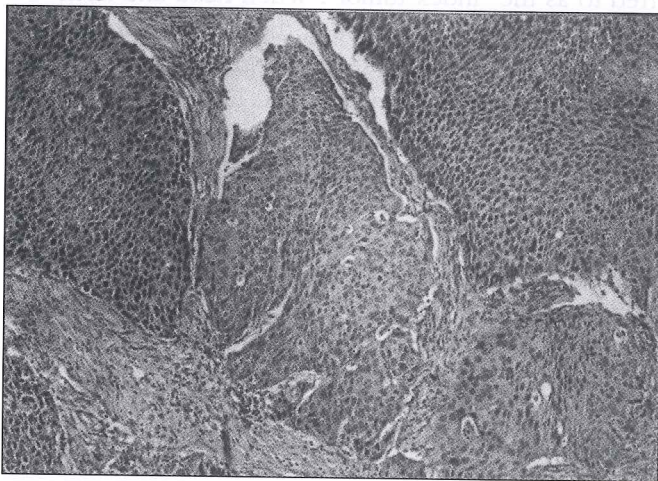


Fig. 2. Microscopic findings of a bronchial punch biopsy revealing squamous cell carcinoma

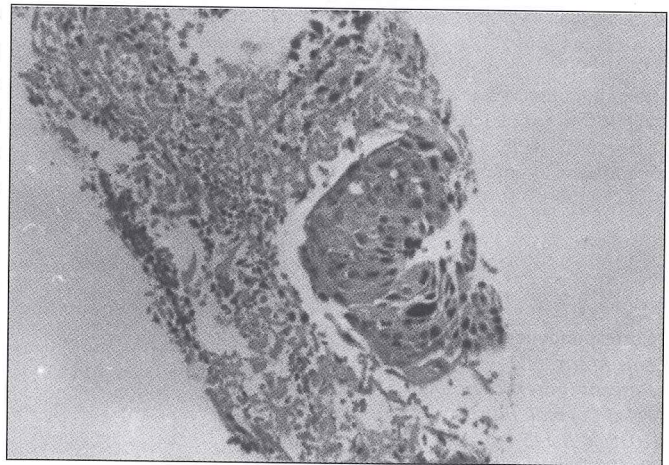


Fig. 4. Histopathological examination of oral cavity tumor showing squamous cell carcinoma

administered. Although pleural fluid was drained successfully, the patient's clinical condition did not improve as well as expected. A repeat x-ray showed a large mass in the right lower hemithorax. At that point we were able to undertake only the palliative approach to the patient's lung and oral cavity cancer due to his poor condition. The patient was discharged on systemic antibiotic therapy for empyema and nutritional support. He died one week after discharge.

Discussion

Multiple malignancies of the aerodigestive tract are relatively common. Multiple primary tumors may occur simultaneously (synchronous tumors) or consecutively (metachronous tumors). Synchronous primary aerodigestive cancers are less common than metachronous cancers.

A number of reports in the literature note the presence of two or more synchronous or metachronous malignant primary tumors in the same patient, the majority of these tumors being squamous cell carcinomas. Gluckman et al proposed a "field squamous cancerization" theory to explain the development of multiple primary neoplasms after chronic epithelial exposure of the aerodigestive tract to carcinogens (5).

Multiple primary neoplasia was once considered a rare phenomenon, but it is now a well-recognized entity. In the original review by Warren and Gates, the incidence was 3.7% (6). Recent reviews have reported higher incidences, ranging from 5% and 30% (1-4). This increase may reflect improved survival of patients with primary tumors, as well as an increased recognition of multiple primary neoplasms by clinicians.

In particular, the association between laryngeal and lung cancer is well-described (7,8). In Rinaldo's study involving the largest series to date of patients with separate primary cancers of the larynx and lung, laryngeal tumors were usually detected clinically before primary lung carcinomas were found (7). It was suggested that this was not happening by chance and that the reason for this could be the rapid, destructive course of lung cancer. In Yellin's study, which spanned the 40 years from 1943 to 1983 and included 1.900 patients treated for lung cancer, the incidence of second primary upper airway cancer was only 0.05% (1). This suggests that patients with

lung cancer may not be at high risk for the development of upper airway cancers, including oral cavity.

Distinguishing a second primary cancer from a metastatic lesion is not always easy, if P53 immunostaining analysis is not available. In Ribeiro's study, 41 multiple primary tumors of the upper aerodigestive tract were evaluated using P53 immunohistochemical analysis to discriminate metastasis from second primary cancer (9). The P53 genotype was found to be completely discordant between separate primary tumors, however metastases had identical genotypes to the primary tumor in all cases. In another report, four multiple primary malignant neoplasms of the aerodigestive tract (tongue, tonsillary, esophageal, pulmonary respectively) were documented in the same patient (10). Tissues obtained from all cancers were analysed for the P53 gene mutation and the patient presented a different immunostaining pattern for P53 in each of four multiple primary cancers. P53 immunohistochemical staining could not be performed in our case due to technical insufficiency. Thus, we had no P53 findings to support a diagnosis of oral cavity metastasis or second primary oral cavity cancer. Still, in our opinion, the possibility of second primary oral cavity cancer seems greater than metastasis, since the patient continued to smoke cigarettes after the initial therapeutic intervention for lung cancer. In addition to smoking, dietary factors are known to contribute to the development of second primary oral and pharyngeal cancers. In our case, there was a malnourished condition too. Day et al. proved the existence of a relationship between dietary factors and the development of multiple primary cancers (11). Their results suggested a protective effect through higher intake of vegetables containing vitamin C and carotenoids. Epidemiological researches have also documented the role of retinoids as chemopreventive agents in patients with epithelial cancers.

Establishing appropriate criteria to distinguish multiple primary cancers from metastasis is essential, since treatment for the former differs entirely from that for metastasis. Complete resection of each tumor in multiple tumor cases increases the chances of patient survival, and thus should be done wherever possible (12, 13, 14). Due to the advanced stage of our patient's lung cancer as of December 1997, we were unable to apply curative therapy for the lung and oral cavity cancer, only a supportive approach was given.

With the more recent focus on curative treatment for multiple primary cancers, panendoscopy has been advocated by many investigators as a part of the tumor staging procedure (15). This enables the physician to search for further primary malignant neoplasms in patients with primary aerodigestive cancer. However, in cases where primary lung cancer is the index tumor, there is still controversy over whether panendoscopy should be performed or not. It is logical that, without an exhaustive search in these cases, multiple primary airway cancers will be underdiagnosed.

Most reports concerning multiple primary aerodigestive cancers indicate that the index tumor was generally in the upper aerodigestive tract (1, 2, 7). However, in light of our case we propose that, in the presence of initial primary lung cancer, second primary cancer can develop in virtually any other aerodigestive system. Based on only one patient, this hypothesis is speculative.

The behavioural patterns of multiple primary aerodigestive cancers must be evaluated with more cases in further studies.

In conclusion, we know that tumors of the aerodigestive tract often represent second primary cancer, and the case presented here highlights the need to focus on the possibility of multiple primary cancer development. Clinical studies of multiple primary cancers are of great importance, since they may lead to better detection of high risk patients and an exact diagnosis of this type of disease. Such

progress would, in turn, lead to higher survival rates and lower mortality in this patient group.

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