Synchronous lung adenocarcinoma associated with bullous lung disease

Büllöz akciğer hastalığı ile ilişkili senkronize akciğer adenokarsinomu

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The relationship between lung cancer and bullous lung diseases has been described in the literature. Herein, we presented a 45-year-old male patient who was asymptomatic when bilateral bullae and bilateral synchronous primary lung adenocarcinoma were detected. Computed tomography revealed a giant bulla in the upper right lobe with a nodular lesion in the bulla wall, and multiple bullae in the upper left lobe with a nodule in the parenchyma adjacent to the bulla. Initially, malignancy was not considered. Pulmonary function test was restrictive. Thoracotomy was performed for the giant bulla in the right upper lobe. Frozen section analysis of the nodular lesion in the bulla wall revealed poorly differentiated adenocarcinoma. Upper right lobectomy was performed. Mediastinal lymphadenopathy was not observed. Two weeks later, the patient underwent a left thoracotomy for the intraparenchymal nodule. Adenocarcinoma was reported on frozen section analysis and upper left lobectomy was performed. Following surgery, the patient received chemotherapy. No recurrences were detected within a follow-up period of 20 months. This is an interesting case showing the relationship between bullous disease and lung cancer, reminding that bilateral synchronous primary lung cancer may be encountered in bullous lung disease.

Key words: Adenocarcinoma; blister/complications; lung diseases; lung neoplasms; neoplasms, multiple primary.

Akciğer kanseri ile büllöz akciğer hastalığı arasındaki ilişki giderek daha fazla vurgulanmaktadır. Bu yazıda, iki taraflı bül ve iki taraflı senkronize primer akciğer adenokarsinomu saptandığı sırada asemptomatik olan 45 yaşında bir erkek hasta sunuldu. Bilgisayarlı tomografide sağ üst lobda dev bir bül ve bül duvarında nodüler lezyon, sol üst lobda multipl bül ve büle komşu parenkimde nodüler lezyon izlendi. Ameliyat öncesinde malignite düşünülmedi. Solunum fonksiyon testi kısıtlayıcı idi. Sağ üst lobdaki dev bül için torakotomi uygulandı. Bül duvarındaki nodülün frozen sonucu az diferansiye adenokarsinom olarak bildirildi ve hastaya sağ üst lobektomi uygulandı. Mediastinal lenf nodu tutulumu izlenmedi. İki hafta sonra hastaya soldaki intraparenkimal nodül nedeniyle yapılan torakotomide frozen inceleme sonucu adenokarsinom olarak bildirilmesi üzerine sol üst lobektomi uygulandı. Cerrahiden sonra kemoterapi gören hastada 20 aylık takip süresi içinde nüks gözlenmedi. Sunulan olgu, büllöz akciğer hastalığı ile akciğer kanseri arasındaki ilişkiyi göstermesi ve büllöz akciğer hastalığında iki taraflı senkronize akciğer kanserinin görülebileceğini hatırlatması açısından ilginç bulundu.

Anahtar sözcükler: Adenokarsinom; bulla/komplikasyon; akciğer hastalığı; akciğer neoplazileri; neoplazi, çoklu primer.

The relationship between lung cancer and bullous lung diseases has been increasingly described in the literature. In various publications, it was reported that malignancy incidence increased 32 folds in patients with bullous emphysematous disease. In many cases, it was radiographically demonstrated that lung cancer associated with bullous disease is near the bulla or adjacent to the thickened wall of the bulla.[1]

In this case report, we presented bilateral bullae and synchronous primary lung adenocarcinoma in an asymptomatic patient.

CASE REPORT

A 45-year-old male who worked for a telephone relay station was referred to our clinic for a radiolucent image in the right upper zone on his standard chest X-ray. The oldest of his routine annual microfilm was dated back to seven years. It was noted that the same radiolucent image had existed, but it couldn't be diagnosed since it was a microfilm. He had no symptoms. He had a history of smoking (30 packets/year). Breathing sound could not be heard at the right upper zone. Other systemic examinations were normal. The results of pulmonary function

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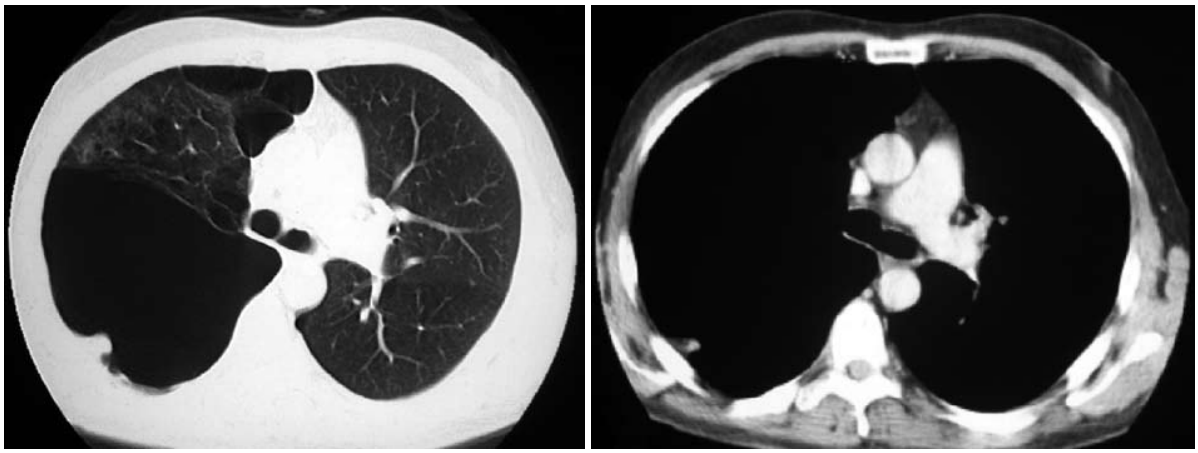

Fig. 1. Chest computed tomography showing a giant bulla and a nodular lesion in the bulla wall in the upper right lobe.

test were as follows: forced vital capacity (FVC) 64.0%, forced expiratory volume at the first second (FEV_1) 70%, FEV_1/FVC 90. Alpha1-antitrypsin level was normal.

The right upper zone was radiolucent on the chest X-ray. A computed tomography (CT) scan showed a giant bulla in the upper right lobe, and a nodular lesion on the bulla wall (Fig. 1). Paraseptal bullous and scattered centrilobular emphysematous changes were seen in the upper left lobe and a nodule was present in the parenchyma adjacent to the bulla (Fig. 2).

Preoperatively, malignancy was not considered. A right thoracotomy was performed. During exploration, a giant bulla measuring 15x15 cm and a whitish gray, semisolid lesion, 2x1.5 cm in size, were observed on the bulla wall. Frozen section analysis of the lesion revealed poorly differentiated adenocarcinoma. Mediastinal lymphadenopathy was not observed and upper right lobectomy was performed. Tumor stage was assessed as IA ($T_1N_0M_0$). Cranial and abdominal tomographies and systemic scintigraphic bone scan were found to be normal. The nodule in the left upper lobe was thought to be a second primary malignancy because no mediastinal lymphadenopathy was observed in the first thoracotomy. A left thoracotomy was performed two weeks after the right thoracotomy. On exploration, multiple bullae in the upper left lobe and a nodule, 4x4 cm in size, in the parenchyma attached to the visceral pleura were observed. There was no infiltration into the mediastinal pleura. Adenocarcinoma was reported from frozen section analysis and then upper left lobectomy was performed. Wedge resection was performed for the bullous lung parenchyma. Pathological examination showed that the hilar and interlobar lymph nodes were reactive and that surgical margins were tumor-free. Tumor stage was assessed as IB ($T_2N_0M_0$). Following surgery, the patient received chemotherapy. No recurrences were detected within a follow-up period of 20 months.

DISCUSSION

The incidence of lung cancer associated with bullous lung disease was reported as 2% to 6%.[2] Lung cancers associated with bullae are usually non-small cell lung cancers. Although there are reports on occult cancers at

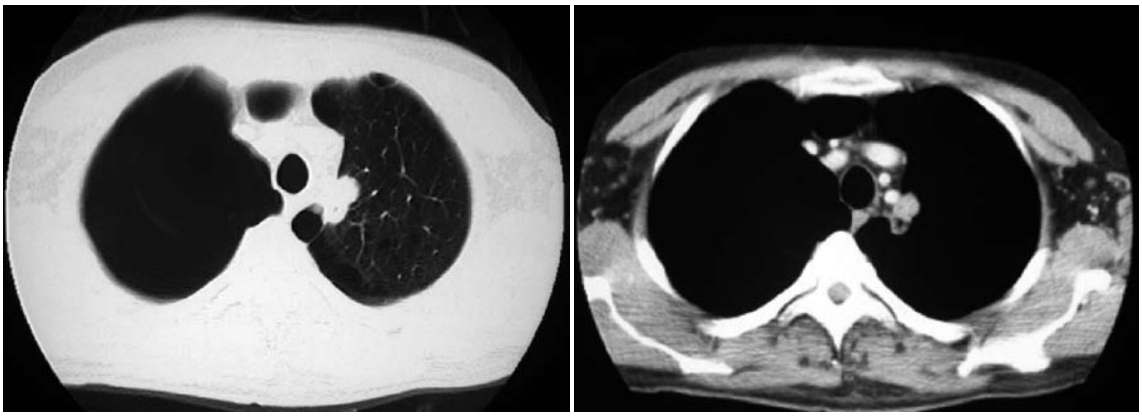

Fig. 2. Chest computed tomography scans showing paraseptal bullous, scattered centrilobular emphysematous changes and a nodule in the parenchyma adjacent to the bulla in the upper left lobe.

the wall of the bullae or nodular lesions adjacent to the bullae, we could not find any reports on synchronous bilateral bullae and bilateral malignancy of the same histological type. In the present case, poorly differentiated adenocarcinoma in the bulla wall in the upper right lobe and adenocarcinoma infiltration in the parenchyma adjacent to the bulla in the upper left lobe were observed. Mediastinal lymph node involvement and distant metastasis were not found. We considered the case to be synchronous primary lung adenocarcinoma.

Particular attention should be paid to the radiological evaluation to be able to diagnose lung cancer accompanying bullous lung disease at an early stage. Tsutsui et al.[1] reported 26 cases that had radiological findings of this type of lung cancer. There were nodular opacities adjacent to the bullae and focal or diffuse thickening of the wall of the bullae. In our case, the lesion in the upper right lobe was in the wall of the bulla, whereas there was intact parenchyma between the bulla and the nodular lesion in the upper left lobe.

Several mechanisms have been proposed for the relationship between bullous disease and bronchial cancer. It is thought that inhibition of anti-elastase enzyme by carcinogens leads to interalveolar septal destruction, which results in the formation of bulla. It has been suggested that the inner surface of the bulla may be more susceptible to metaplastic transformation, and impaired ventilation in bullous lung may facilitate the deposition of carcinogens on the inner surface of the bulla. The identification of epithelial metaplasia in the wall of congenital cysts supports this theory.[3]

It has been reported that smoking, the presence of scar, and entrapment of air in the bulla may contribute to the development of cancer.[4] In general, patients with both pulmonary bullous disease and primary lung cancer have very poor prognosis, because the tumor is at an advanced stage when detected.[5]

Subsequent thoracotomy can be performed in 2 to 6 weeks.[6,7] In patients with high risk for malignancy, subsequent thoracotomy should be planned as soon as possible depending on general physical condition of the patient. In our case, the second thoracotomy was performed two weeks later, during which general physical condition and breathing function of the patient improved to a sufficient level.

In conclusion, in patients with bullous lung disease, the standard chest X-ray and CT scan may reveal a malignant pathology accompanying the bulla. It must be kept in mind that bilateral bullous lung disease is associated with high risk for cancer development, and patients with bilateral nodular lesions should be investigated for synchronous lung cancer. Furthermore, even in bullectomy cases without evidence for parenchymal lesions, surgical resection of the bulla should be as complete as possible and an accurate pathological examination of all resected material should be made. Patients with bilateral bullous lung disease should be closely followed-up for the possibility of an occult lung cancer.

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