RECURRENCE AND METACHRONOUS LUNG CANCER DEVELOPING AFTER CHEMOTHERAPY IN A PATIENT WITH SMALL CELL LUNG CARCINOMA

KÜÇÜK HÜCRELİ AKCİĞER KANSERLİ BİR OLGUDA TEDAVİ SONRASI REKÜRRENS VE METAKRON TÜMÖR GELİŞMESİ

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SUMMARY

Small cell lung cancer (SCLC) is a kind of disease with a good response to chemotherapy, however it usually recurs in a short time and the most important reason of mortality is relapses. A sixty-two-year old male patient was diagnosed as SCLC, with an inoperable lesion in left lung. After 6 cycles of carboplatin and etoposide chemotherapy and radiotherapy, there was a total regression of the lesion. In following months, there was a new right pulmonary mass seen in thorax computed tomography (CT) which had the diagnosis of adenocarcinoma by transthoracic needle biopsy. It was accepted as a metachronous lung carcinoma and a new chemotherapy regimen including carboplatin and gemsitabine was administered, which created a total regression of the tumour for the second time. Nine months later, a mass invasing mediastinum was recognized in the same location with firstly diagnosed tumour, SCLC.

ÖZET

Akciğer Tüberküloz'u (TB) ülkemizde önemli derecede morbitide ve mortaliteye neden olmaktadır. Mycobacterium tüberculosis complex'in infeksiyonu oldukça heterojendir. Farklı radyolojik görünümle karşımıza çıkan ve metastatik akciğer kanserini taklit eden akciğer TB olgusunun sunulması uygun görüldü.

Elli dokuz yaşında erkek hasta nefes darlığı, göğüs ağrısı şikayeti ile başvurduğu merkezimizde çekilen PA akciğer grafisinde; bilateral multipl sayıda nodüler lezyonlar, üst zonlarda hiperlüsensi saptandı. Bilgisayarlı toraks tomografisinde; bilateral multipl sayıda, multisentrik özellikte lezyonlar ve büllöz amfizem görünümü mevcuttu. Biyokimyasal ve hematolojik laboratuar bulguları normal sınırlar içerisinde idi. Yapılan bronkoskopide bronşiyal sistem doğal olarak izlendi. Balgam ve bronş lavaj sıvısında ARB negatif olarak bulundu. Tüm vücut malignite taramalarında patoloji saptanmadı. Hastaya sağ mini torakotomi ile nodul eksizyonu

This situation was named as recurrence of SCLC and the prior chemotherapy was administered again. We want to present this interesting case with the unexpected behaviour of tumour that contains both metachronous cancer and recurrence in a short time, and with the perfect response to the platin-based chemotherapy at every attack of the tumour.

INTRODUCTION

Small cell lung cancer (SCLC) is the most agressive and one of the most frequent tumours in all types of cancers. However it is highly responsive to chemotherapy and radiotherapy, it is characterized with a short survival time or rate. Overall response to chemotherapy can be seen as 80-100% in limited stage disease when it is 60-80% in extensive stage disease SCLC (1,2). We generally see a relapse in a short time in SCLC patients (1,2).

Multiple primary lung cancers can develop in 2-3% per year in successfully treated lung cancers, and they are characterized as either synchronous or metachronous tumours (3,4). Synchronous lung tumour is described as two different pulmonary tumours existing in different lobes or different sides of the lungs at the same time (5). Metachronous lung cancer is defined as a type of tumour that appears as a second or third primary lesion after the curative treatment of lung cancer (6). That type of cancer is generally seen in 2-4 years after the diagnosis and treatment of primary lung cancer.

In this case, a metachronous lung cancer (adenocarcinoma) existed after a complete response to chemotherapy given for SCLC - limited stage. We would like to present this interesting case who had a metachronous tumour and relapse in a short time, also with an unexpected high chemosensitive pattern of different types of lung cancers.

yapıldı. Patoloji sonucu amfizem, interstisyel pnömoni bulguları ve kazeifiye granulomatöz hastalık olarak raporlandı.

Radyografide yaygın nodüler lezyonları olan olguların ayırıcı tanısında granülomatöz hastalıklar mutlaka düşünülmeli, ülkemiz şartlarında akciğer TB'unun hala ilk sıralarda değerlendirilmesi gerektiği unutulmamalıdır.

CASE REPORT

A 62-year-old man was referred to our hospital with back pain localizated at his left shoulder in July 2004. He had a smoking history for forty-five years without the existence of any other known diseases. In his chest X-ray, there was a suprahilar mass with 3x5 cm; also in the thorax CT scan it was seen as a lesion invasing mediastinum (Figure 1 a,b). In the fiberoptic bronchoscopy, there was no endobronchial lesion. The patient had the diagnosis by anterior mediastinotomy, as the biopsy material revealed small cell lung cancer (Figure 1c). After the staging investigations, it was classified as limited disease small cell lung cancer (SCLC).

Combination chemotherapy was planned with the drugs including cisplatin and etoposide. After one cycle of chemotherapy, acute renal failure had started, so cisplatin agent was exchanged with a less nephrotoxic agent; carboplatin. After four cycles of chemotherapy and also radiotherapy (RT) for primary tumor, the patient was evaluated with a new thorax computed tomography (CT), and it was seen that the tumor had totally regressed in December 2004 (Figure 2). Afterwards, the patient had a prophylactic cranial RT and following process without treatment had started.

In the first year of the following, a new lesion in the superior lobe of the right lung invasing chest wall was detected in the new

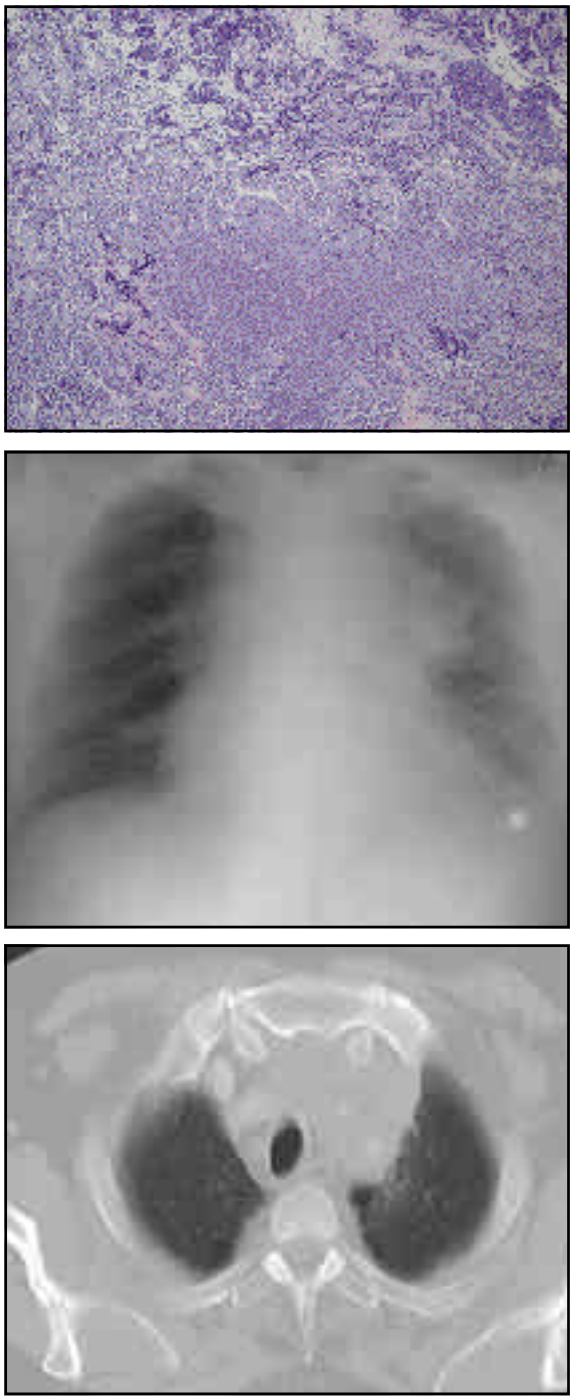

Figure 1 a-b. A lesion invasing mediastinum in the superior lobe of the left lung in chest X-ray and thorax CT having the diagnosis of SCLC (July 2004), **c.** Mediastinotomy biopsy material revealed as small cell lung cancer, HE X 10

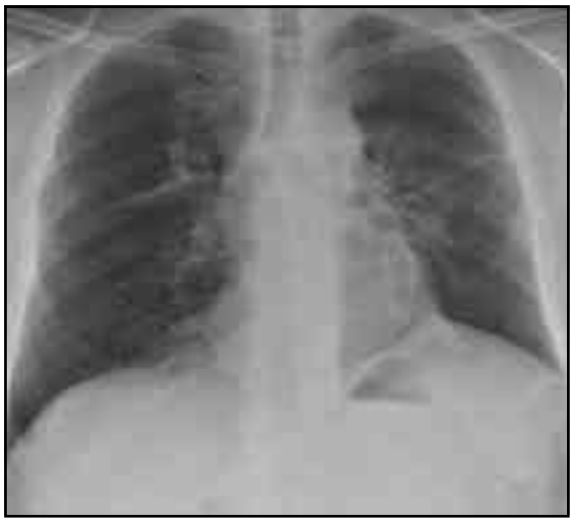

Figure 2. The total regression of the primary tumour after four cycles of chemotherapy (December 2004).

thorax CT of the patient in October 2005. That was an independent lesion and had a different location compared with the first known mass (Figure 3a). In fiberoptic bronchoscopy (FOB), no endobronchial lesion was seen; so CT-guided transthoracic needle biopsy was executed for diagnosis. The hystopathological diagnosis of the biopsy was well-differentiated adenocarcinoma which was accepted as a metachronous lung cancer (Figure 3b). Pathology preparats (first preparat: representing SCLC, second: adenocarcinoma) were revised by pathologs to confirm these two different results at diagnosis. The final evaluation was told that there was no doubt about the hystopathological reports of the specimens; the existence of the metachronous tumour with a different hystopathological type from the primary tumour was confirmed.

The treatment regimen of carboplatin-gemcitabine chemotherapy was administered for the non-small cell lung cancer (NSCLC) metachronous tumour and after 2 cycles of this treatment regimen, with the new thorax CT it was seen that the lesion forming

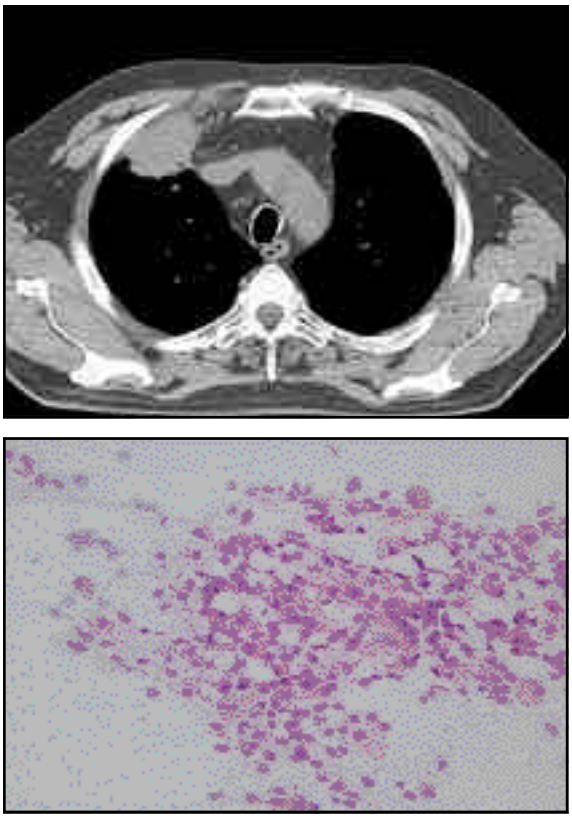

Figure 3 a. A new lesion in the superior lobe of the right lung invasing chest wall in the thorax CT in the first year of following (October 2005), **b.** Diagnosis as adenocarcinoma by transthoracic needle aspiration biopsy, HE X 10

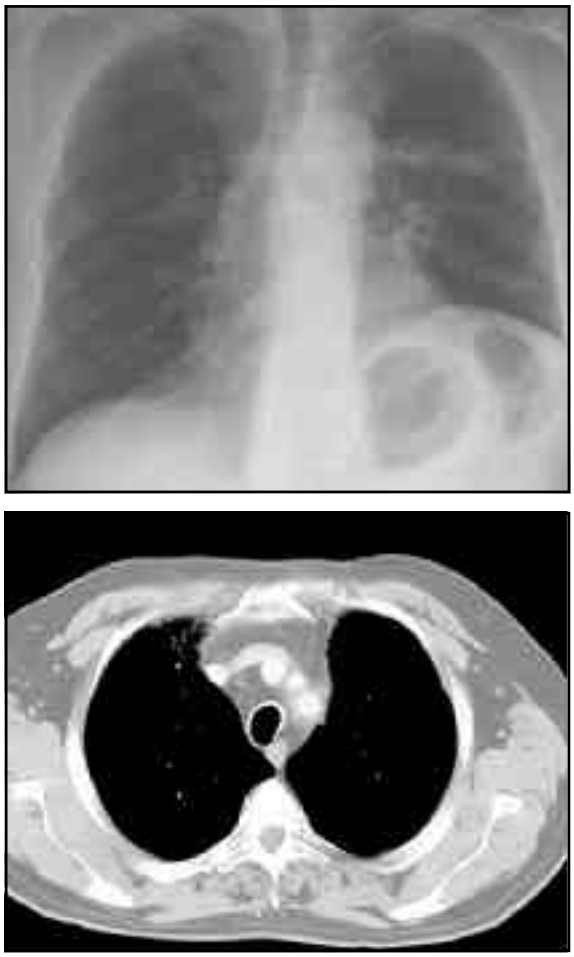

Figure 4 a-b. The total regression of the metachronous tumour after chemotherapy in chest X-ray and thorax CT (February 2006)

metachronous tumor was totally regressed (Figure 4 a,b). The final decision was to complete chemotheapy to four cycles and then follow the patient.

Nine months later, in September 2006, there was determined a recurrence this time; a mass invasing mediastinum was recognized, which was in the same location with the firstly diagnosed tumour, SCLC. (Figure 5 a,b). This situation was named to be as recurrence of the primary tumour. As SCLC patients relapsing after at least 3 months by the conclusion of first-line therapy have a great respond to the same induction regimen, it may be us eful to use not cross-resistance drugs or new drugs; so it was decided to give the patient the initial chemotherapy agents: carboplatin and etoposide.

During the treatment, the primary tumour had progression and bone metastasis had occured. The general condition of the patient got worse, which prevented going on new chemotherapy cycles after one cycle of carboplatin-etoposide administered for relapse of SCLC. The patient died because of cardiopulmonary arrest in February 2007; 9

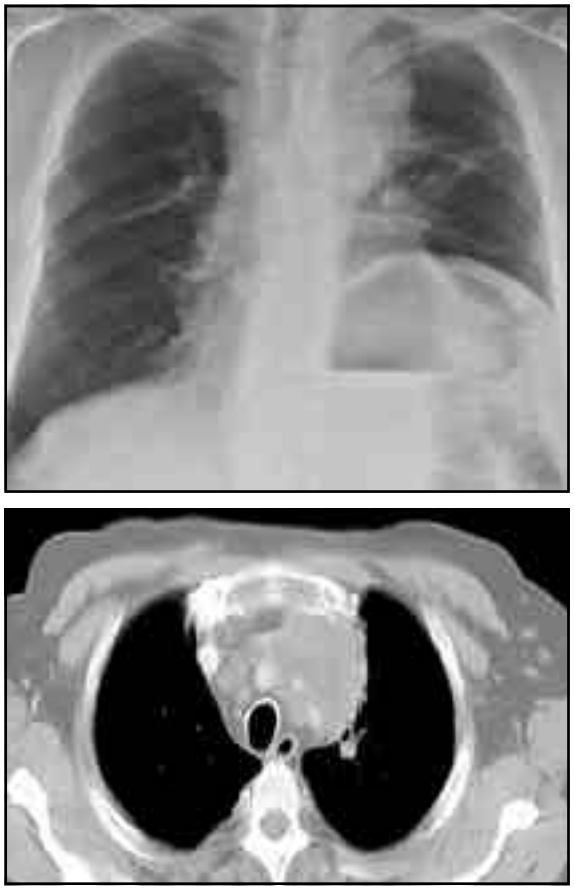

Figure 5 a-b. A mass invasing mediastinum in left lung in chest X-ray and thorax CT relapse of SCLC (September 2006)

months after relapse and 30 months after diagnosis of lung cancer.

DISCUSSION

Small cell lung cancer (SCLC), which usually occurs in smokers, represents 15 to 25 percent of all lung cancers. Its rapid doubling time and the early development of widespread metastases are the basic properties of this kind of lung cancer (7).

Small cell lung cancer is one of the most agressive and the most lethal malignancies (8); the median time of survival for the disease changes from 8 to 20 months, as it is extensive or limited disease. For limited stage SCLC, five-year survival rate is 10-13% when the survival is 1-2% in extensive stage SCLC (9).

Since SCLC is a systemic disease, treatment strategies have focused on systemic therapy (10). There is a high degree of responsiveness to chemotherapy in SCLC. Also, it is proved that chemotherapy prolongs survival when compared to best supportive care (11) and without chemotherapy, the average survival is measured in weeks in SCLC. Agra et al (12) had a retrospective study based on data systems and found a result that chemotherapeutic treatment prolongs survival when compared with placebo in patients with advanced SCLC.

A second lung tumour may represent as a synchronous or metachronous tumour; as a recurrence of a primary lung tumour after noncurative therapy, or metastatic disease with the origin of a non-pulmonary tumour. Multiple lung tumours can be synchronous or metachronous, according to the time of their foundations in lung. Synchronous lung tumours are defined as more than one primary lung carcinoma presenting at the same time (13). Metachronous lung tumours, which develop after treatment of the initial lung carcinoma, are seen between two and four years after the existence of primary lung tumour (6). Metachronous cancers are the most common type of multiple primary lung cancers, representing 50 to 70% of the whole (14). The incidence of the presentation of a metachronous tumour (in group of patients with an initial total response to the treatment) is 2-14% in SCLC and 1-2% in NSCLC per year (15). In older studies, squamous cell carcinoma was said to be the most common type of multiple primary lung cancers; however the last studies report that there is an important increase in the incidence of adenocarcinoma as a second primary tumour (16).

Metachronous tumours have got a better prognosis than both synchronous tumours and relapsed lung cancers (16). As many studies have reported that resection of the second primary tumour is the most succesful way of the management (17), only near one-half of these patients with NSCLC had been operated. In patients with the history of SCLC as the initial cancer, this rate is seen as 13%. The lower rate can be explained by the short survival of SCLC patients, without a long life to develop a second lung primary tumour.

In SCLC, when recurrence exists after the third month of the completion of first-line chemotherapy, it is often named as "relapse" of SCLC. Most patients with SCLC have a relapse within 1 or 2 years (18), particularly seen in extensive stage disease. Previous studies analysing long-term survivors of SCLC reported that relapses are usually seen in 1.5 years after the beginning of combination chemotherapy; but there are some cases in the literature that late relapses may happen, even can be seen up to ten years after diagnosis of SCLC (19).

When previous reports about multiple primary lung cancers are investigated, it can be seen that metachronous tumours generally develop in 2-4 years after the diagnosis and treatment of primary lung cancer. In our case, the second primary tumour had occured nearly one year after diagnosis of the first lesion, which is an early development for a metachronous tumour.

Our patient took platin-based chemotherapy combined with different agents according to the type of the lung cancer; gemcitabine in NSCLC or etoposide in SCLC. We know that SCLC is a chemosensitive type of tumour, but to meet complete response at every cycles of chemotherapy is unpredictible. In all steps of chemotherapy; the known lesions had a complete response to chemotherapy; which is so unexpected for a patient with a multiple primary lung cancer.

In SCLC, most of tha patients are known to be in the extensive stage of the disease at the time of prognosis. As SCLC has a short doubling time, it is generally a short period for the tumour spreading to other organs and having metastasis. In our case, the first metastasis was detected after 28 month of the diagnosis, which shows that the high response of chemotherapy delayed the existence of metastasis and increased the time of survival.

We have observed three different conditions about the tumour in our patient in a short period: primary lung cancer (SCLC) and total regression after chemotherapy, metachronous lung carcinoma and total regression after chemotherapy again, and the relapse of SCLC. It is an unusual condition as we can not find any similar cases in the literature with tumour behaviours as complicated and unexpected as our case.

We wish to present this interesting case with the existence of metachronous lung carcinoma and relapse of the primary tumour at the same patient in a short period and with a high chemosensitive pattern of the tumours.

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