

Vanishing a primary lung carcinoma following irradiation of cranial metastasis: "the abscopal effect"

Kraniyal metastaz radyoterapisi sonrasında kaybolan primer akciğer karsinomu: "Abskopal etki"

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ABSTRACT

The abscopal effect is a phenomenon which refers to disappearance of primary solid tumors following radiotherapy applied to their distant metastatic lesions. There are very few documented cases of this unusual clinical situation and are extremely rarely seen in non-small cell lung carcinomas. A 68-year-old male patient was admitted to our outpatient clinic with dyspnea. Thoracic computed tomography revealed a 12 mm ground-glass opacity lesion with a nodular component located at the superior segment of the lower lobe of the right lung. The lesion had an increased fluorodeoxyglucose uptake on positron emission tomography-computed tomography (SUV_{max}: 7.2). Transthoracic fine needle aspiration revealed non-small cell lung carcinoma. There was no mediastinal lymph node metastasis by cervical mediastinoscopy. Cranial magnetic resonance imaging showed a metastatic nodule in the pons. The patient initially received cranial radiotherapy. The surveillance positron emission tomography-computed tomography revealed the disappearance of the lesion located in the right lung parenchyma without a fluorodeoxyglucose uptake. The patient was scheduled for surgery; however, he refused to have any treatment and was put in follow-up. After six months of the initial diagnosis, repeated positron emission tomography-computed tomography revealed re-appearance of the lesion on the same area measured as 10 mm with a slightly increased fluorodeoxyglucose uptake (SUV_{max}: 2.4). The patient, then, underwent superior segmentectomy of the right lower lobe and lymph node dissection through video-assisted thoracoscopic surgery. The pathological examination result was reported as an adenocarcinoma with a predominant lepidic pattern. He remained recurrence-free during a 25-month follow-up.

Keywords: Abscopal effect; immune system; non-small cell lung carcinoma; radiotherapy.

ÖZ

Abskopal etki fenomeni, primer solid tümörlerin uzak metastatik lezyonlarına uygulanan radyoterapi sonrasında ortadan kaybolmasıdır. Bu olağan dışı klinik duruma ilişkin çok az bildirilmiş olgu vardır ve küçük hücreli dışı akciğer karsinomlarında çok nadir görülür. Altmış sekiz yaşında erkek hasta, nefes darlığı şikayeti ile polikliniğimize başvurdu. Toraks bilgisayarlı tomografisinde sağ akciğer alt lobunun üst segmentinde nodüler içeriği olan buzlu cam görünümlü 12 mm bir lezyon izlendi. Pozitron emisyon tomografi-bilgisayarlı tomografide lezyonun florodeoksiglukoz tutulumunda artış vardı (SUV_{maks}: 7.2). Transtoraksik ince iğne aspirasyonu sonucunda, küçük hücreli dışı akciğer karsinomu izlendi. Servikal mediastinoskopide lenf nodu tutulumu saptanmadı. Kranial manyetik rezonans görüntüleme de ponsda metastatik nodül izlendi. Hastaya ilk olarak kraniyal radyoterapi uygulandı. Takip pozitron emisyon tomografi-bilgisayarlı tomografide, florodeoksiglukoz tutulumu olmaksızın sağ akciğer parankimi yerleşimli lezyonun kaybolduğu izlendi. Hastaya cerrahi önerildi; ancak herhangi bir tedavi almayı reddeden hasta, izleme alındı. İlk tanıdan altı ay sonra çekilen pozitron emisyon tomografi-bilgisayarlı tomografide, artmış florodeoksiglukoz tutulumu ile aynı bölgede 10 mm ölçülen lezyonun yeniden ortaya çıktığı görüldü (SUV_{maks}: 2.4). Ardından hastaya video yardımlı torakoskopik cerrahi ile alt sağ lobun superior segmentektomisi ve lenf nodu diseksiyonu yapıldı. Patolojik inceleme sonucu, baskın lepidik paternli adenokarsinom olarak bildirildi. Hastada 25 aylık izlem süresince nüks saptanmadı.

Anahtar sözcükler: Abskopal etki; immün sistem; küçük hücreli dışı akciğer karsinomu; radyoterapi.



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The abscopal effect for lung cancer is described as regression of the lung tumor following radiotherapy to the metastatic lesions distant from the primary site.^[1,2] The pathophysiology and underlying mechanism of the abscopal effect for lung and other tumors have not been completely understood. Herein, we report a case with a vanishing lung adenocarcinoma following irradiation of the cranial metastasis.

CASE REPORT

A 68-year-old man was admitted to our outpatient clinic with progressive dyspnea for the past few weeks. His physical examination revealed prolonged breath sounds bilaterally. He did not have any comorbidities; however, he was an active smoker with a 50-pack-year smoking history. Thoracic computed tomography (CT) showed a 12 mm lesion with a ground-glass opacity with density located at the superior segment of the right lower lobe (Figure 1a). The lesion seemed to be malignant with an increased fluorodeoxyglucose (FDG) uptake (SUV_{max} : 7.2) (Figure 1b). Positron emission tomography/CT (PET/CT) showed normal findings. For the histopathological diagnosis, transthoracic fine needle aspiration biopsy was performed which revealed

non-small cell lung cancer (NSCLC). Cranial magnetic resonance imaging (MRI) showed a 7x8 mm solid lesion located in the in the pons, which was compatible with a metastatic disease. We, therefore, performed cervical mediastinoscopy for the mediastinal staging. We sampled the right and left upper and lower paratracheal regions and subcarinal nodal station. All five stations which were excised showed no mediastinal lymph node involvement (N_0). The final clinical staging was constructed to be $cT_{1a}N_0M_{1b}$ (Stage IV). The multidisciplinary Lung Cancer Committee decided to initiate treatment from the metastatic brain lesion with follow-up. Due to the localization of the cranial lesion, the patient received cranial radiation of 3,000 cGy divided in 10 fractions. During follow-up, cranial MRI resulted in an excellent response to radiotherapy without any residual tumor in the pontine area, and no new cranial lesion was observed. Repeated thoracic CT at two months of radiotherapy revealed no lesion in the pre-existing tumor area (Figure 1c, d). Although there was no lesion, surgical resection was offered to the patient. However, the patient refused surgery and chemotherapy; therefore, he was scheduled for follow-up visits.

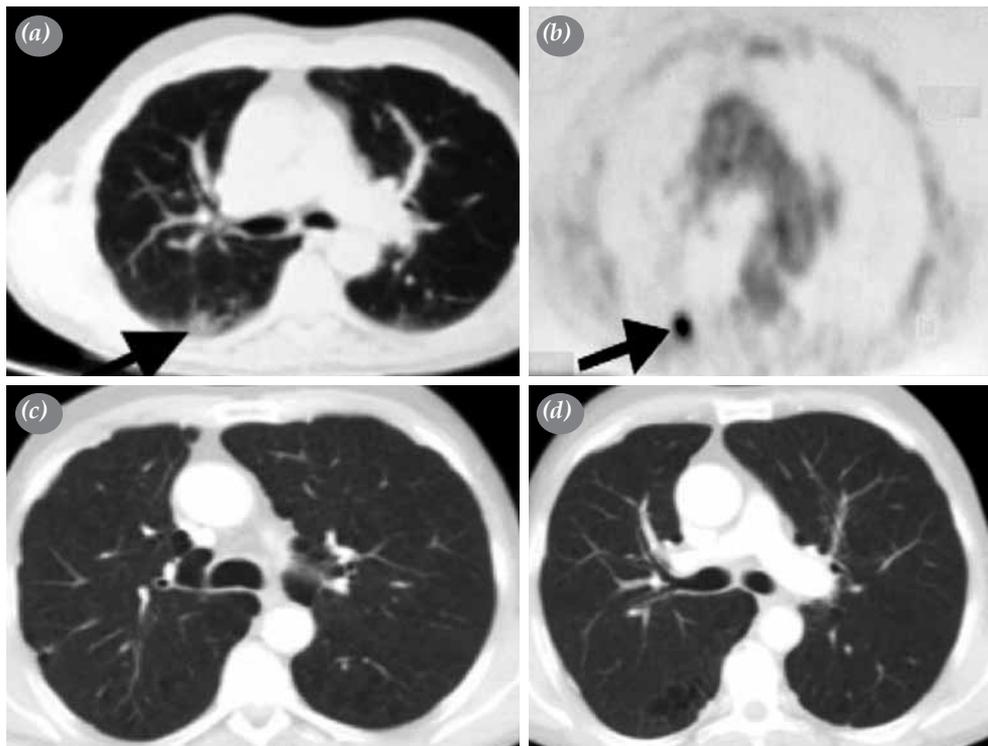


Figure 1. (a) Computed tomography scan showing a 12 mm lesion located at the superior segment of the lower lobe of the right lung (arrow) (b) Fluorodeoxyglucose-Positron emission tomography/computed tomography scan of the lesion with a SUV_{max} of 7.2 (arrow). (c, d) Computed tomography scan following radiotherapy without any sign of previously existing tumor.

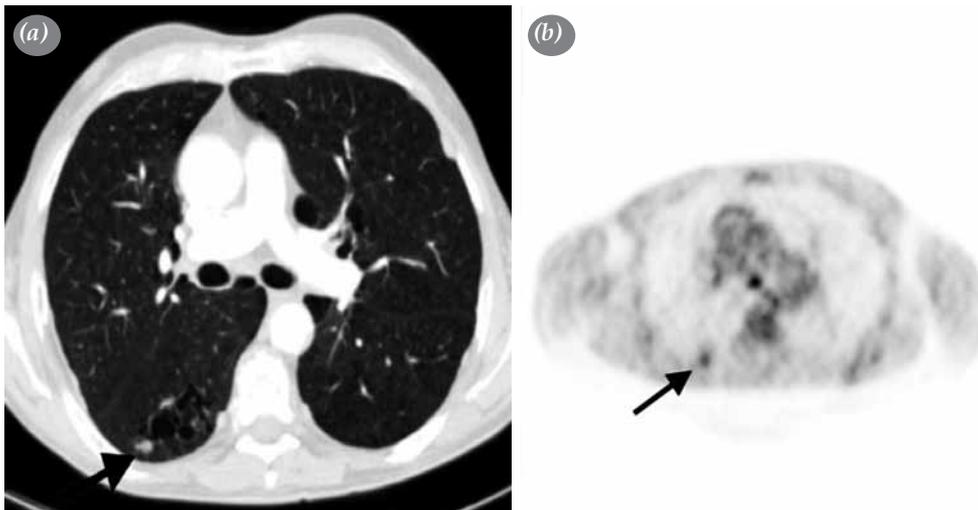


Figure 2. (a) Computed tomography scan showing re-appearance of a 10 mm tumor in the right lower lobe after six months of the initial diagnosis (arrow). (b) Fluorodeoxyglucose-positron emission tomography/computed tomography scan of the lesion with a SUVmax of 2.4 (arrow).

Unfortunately, at six months, the patient had a new lesion, as assessed by thoracic CT showing the previous right lower lobe lesion re-appearing with a less nodularity and measuring 10 mm (Figure 2a). Repeated PET/CT showed a slightly pathological FDG uptake (SUV_{max} : 2.4) (Figure 2b) without any other evident activity in the body.

The patient, then, underwent superior segmentectomy of the right lower lobe and lymph node dissection through video-assisted thoracoscopic surgery. The postoperative course of the patient was uneventful and he was discharged from hospital on Day 6. The pathological examination result was reported as an adenocarcinoma with a predominant lepidic pattern. He received six cycles of platinum-based chemotherapy following surgery. He is still recurrence-free during a 25-month follow-up.

DISCUSSION

Radiotherapy is highly effective treatment for solid tumors and related metastatic lesions. The abscopal effect as a rare clinical situation is known for more than six decades.^[1] However, the underlying mechanism of spontaneous regression of primary tumors following radiotherapy to distant metastatic lesions still remains a matter of dogma and very little is known about this phenomenon.^[1-5] The immune system has been proposed as the key component of the abscopal effect following radiotherapy (anti-tumor immunity).^[2,3] Local radiotherapy is hypothesized to induce an immunostimulatory form

of cell death defined as immunogenic cell death, leading to an immune response in the host, followed by systemic secretion of specific cytokines and chemokines, a systemic immune response against local tumor antigens released or local inflammation which can lead to a distant effect.^[2] It has also proposed that the abscopal effect is mediated by the immune system.^[4] Local irradiation of a lesion could induce the release of circulating tumor antigen or of inflammatory factors that could then mediate an augmented immune response against other, unirradiated, tumors expressing similar tumor antigens. It has been shown that local radiotherapy increases the activity of natural killer cells.^[6]

Our case had an extremely rare clinical situation for metastatic NSCLC. Although we were unable to document the immunological changes during this period, it is plausible to speculate that irradiation could have converted tumor cells into an in situ vaccine and generate the abscopal response. There are very few reported cases of NSCLC in the literature which show the abscopal effect following local radiotherapy.^[2,3] Those were cases where the abscopal effect could be responsible in combination with the other therapies; however, we observed the disappearance of the lesion following radiotherapy alone.

Regarding the different histology (adenocarcinoma) found after resection, compared to preoperative diagnosis of a squamous-cell carcinoma, it may be attributable to the tumor heterogeneity, histopathological

error or histological transformation of the tumor cells, which was previously published.^[5]

In conclusion, the mechanisms of radiotherapy-induced abscopal effect seem to be very complex due to limited knowledge and lack of prospective studies. Therefore, we suggest that further studies of this rare phenomenon should be carried out.

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