



Oxidized Regenerated Cellulose can be a Cause of False Tumor Recurrence on PET/CT in Patients with Lung Cancer Treated Surgically

Cerrahi Olarak Tedavi Edilen Akciğer Kanserlerinde Okside Rejenere Selüloz, PET/BT'de Yalancı Tümör Nüksünün Bir Sebebi Olabilir

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Abstract

Objectives: Regular follow-up of patients with lung cancer treated surgically is crucial to detect local recurrence or distant metastasis of the tumor. Postoperative follow-ups are performed with thorax computed tomography (CT) and, if necessary, positron emission tomography (PET)/CT. Sometimes, inflammatory tissue reactions due to the materials used during the surgery for hemostasis may cause the appearance of tumor recurrence in imaging modalities. In this study, we presented that oxidized regenerated cellulose (ORC) used intraoperatively may cause false tumor recurrence on PET/CT.

Methods: The records of patients who had local tumor recurrence after lung cancer surgery was reviewed retrospectively. Inclusion criteria were the presence of local recurrence of cancer on PET/CT, specification of using ORC in the surgical notes, and histopathological diagnosis of the recurrence site of tumor was reported as a foreign body reaction. Data of patients were collected according to age, gender, surgery performed, adjuvant therapy status, resolution status and time ORC, and standard uptake value of ¹⁸F-fluorodeoxyglucose on PET/CT.

Results: Eleven patients (1 female, 10 males) who met the criteria were included in the study. The median age was 64. Histopathological results of all patients were reported as foreign body reactions. The median detection time of PET/CT positivity after surgery was 139 days (range: 52-208 days). False tumor recurrence was resolved in 8 patients (72.7%) in their control radiological examinations and median resolution time was 334 days (range: 222-762 days). The median maximum standard uptake value of the lesions was 6.2 (1.7-11) on the PET/CT.

Conclusion: ORC used intraoperatively in patients undergoing surgery for lung cancer may cause false tumor recurrence in imaging modalities in postsurgical follow-ups. When tumor recurrence is suspected in the follow-up of these patients, histopathological confirmation is necessary to prevent unnecessary operations and treatments.

Keywords: Lung cancer, positron emission tomography/computed tomography, false recurrence, and oxidized regenerated cellulose

Öz

Amaç: Cerrahi olarak tedavi edilen akciğer kanserli hastaların düzenli takibi, lokal nüks ve uzak metastaz saptanmasında oldukça önemlidir. Postoperatif takipler toraks bilgisayarlı tomografi (BT) ve gerekirse pozitron emisyon tomografisi (PET)/BT ile yapılır. Bazen hemostaz sağlamak

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için ameliyat sırasında kullanılan materyallere bağlı enflamatuvar doku reaksiyonları görüntüleme modalitelerinde tümör nüksü görünümüne neden olabilir. Bu çalışmada intraoperatif kullanılan oksitlenmiş rejener selülozun (ORS), PET/BT'de yalancı tümör nüksüne neden olabileceğini göstermeyi amaçladık.

Yöntem: Akciğer kanseri cerrahisi sonrası lokal tümör nüksü gelişen hastaların kayıtları geriye dönük olarak incelendi. Dahil edilme kriterleri, PET/BT'de lokal kanser nüksü varlığı, cerrahi notlarda ORS kullanımının belirtilmesi ve tümörün nüks bölgesinin histopatolojik tanısının yabancı cisim reaksiyonu olarak bildirilmesiydi. Hastalara ait yaş, cinsiyet, yapılan cerrahi, adjuvan tedavi durumu, rezolüsyon durumu ve ORC süresi ve PET/BT'deki ¹⁸F-florodeoksiglukoz standart uptake değeri verileri toplandı.

Bulgular: Kriterleri karşılayan 11 hasta (1 kadın, 10 erkek) çalışmaya dahil edildi. Ortanca yaş 64 idi. Tüm hastaların histopatolojik raporları yabancı cisim reaksiyonu olarak rapor edildi. Ameliyattan sonra PET/BT pozitifliğinin ortanca tespit süresi 139 gündü (dağılım: 52-208 gün). Kontrol radyolojik incelemelerinde 8 hastada (%72,7) tümör görünümü düzeldi ve ortanca iyileşme süresi 334 gündü (dağılım: 222-762 gün). PET/BT'de lezyonların ortanca maksimum standart tutulum değeri 6,2 idi (dağılım: 1,7-11).

Sonuç: Cerrahi olarak tedavi edilen akciğer kanserli hastaların takibinde tümör nüksünden şüphelenildiğinde, gereksiz operasyon ve tedavileri önlemek için histopatolojik doğrulama gereklidir.

Anahtar kelimeler: Akciğer kanseri, pozitron emisyon tomografi bilgisayarlı tomografi, yalancı nüks

Introduction

Surgery is the optimal treatment option for patients with clinically early-stage non-small-cell lung cancer (NSCLC). However, adjuvant treatment such as chemotherapy and/or radiotherapy, may be required depending on the patient's pathological tumor stage, complete resection status, and tumor histopathology. Despite all efforts, the 5-year survival in all stages of NSCLC is less than 50%, and the median expected survival after tumor recurrence has been reported as 11.5 months (1,2,3). Follow-up of patients after surgery for detecting local tumor recurrence or distant metastasis is usually performed with computed tomography (CT) and/or positron emission tomography (PET)/CT. PET/CT is the preferred method for follow-up due to its high sensitivity and specificity for tumor recurrence. Furthermore, it is also a suitable procedure for evaluating the response to adjuvant therapy (4,5). Oxidized regenerated cellulose (ORC) is an absorbable hemostatic material that has long been used for bleeding control in neurosurgery, hepatic surgery, renal surgery, and cardiothoracic surgery. Although some studies in the literature have reported that ORC can cause false tumor recurrence, its PET/CT findings of false tumor recurrence after lung cancer surgery are unclear (6,7,8,9). In this study, we presented ORC used intraoperatively may cause false tumor recurrence on PET/CT.

Materials and Methods

Patient Selection

Following the approval of the Gazi University Ethics Committee (no: 91610558-604.01.02, research code no: 2020-366), the medical records of patients who underwent surgery for NSCLC between January 2018 and August 2020 were examined retrospectively. An informed consent form was obtained from the patients

or their relatives included in the study. During the study period, data of patients with cancer recurrence detected on imaging modality, were collected. Inclusion criteria were, detection of local recurrence of lung cancer at the surgical side on PET/CT, specification of using ORC in the surgical notes, and reporting of histopathological diagnosis of biopsy taken from the recurrence site was the foreign body reaction. Patients whose histopathological result were reported as only "non-malignant" were not included in the study. In addition, patients whose follow-up records could not be obtained, and those whose surgical notes did not indicate the use of ORC, were excluded from the study. Data of patients were collected according to age, gender, localization of recurrence, adjuvant therapy status, smoking status, resolution status, total resolution time (day) of agent, maximum standard uptake value (SUV_{max}) on the PET/CT, stage of the tumor, comorbidity status, postoperative complication, and the detection time of false tumor recurrence.

Statistical Analysis

All analyses were performed using the IBM SPSS version 20.0 software (IBM Corp., Armonk, NY, USA). Due to the small sample size, we only performed descriptive analysis. Descriptive data were expressed in mean \pm standard deviation (SD), median (minimum-maximum) or number and frequency. The distribution of numeric variables was evaluated by histogram and Kolmogorov-Smirnov test. The mean \pm SD was used for normal distributions and median value with range (minimum-maximum) was used for skewed distributions.

Results

During the study period, we detected 293 patients undergoing surgery for NSCLC in our clinic, and 160 of them (54.7%) required adjuvant treatment. Eleven of the

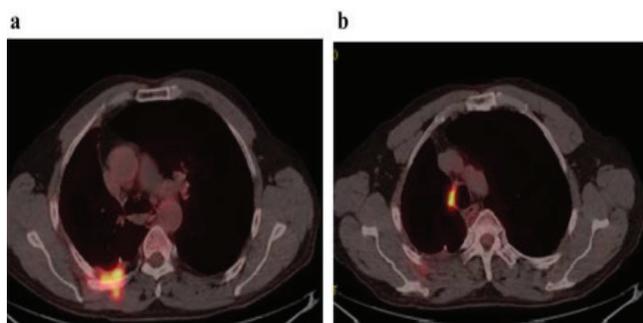


Figure 1. (a) PET/CT image of case 1. A pathological increased uptake at right posterior chest wall with SUV_{max} 9.3. Result of histopathologic examination of biopsy taken by trans-thoracic tru-cut biopsy was foreign body reaction. (b) A pathological increased uptake (SUV_{max} : 11) was detected at the right paratracheal area on PET/CT of case 2
PET/CT: Positron emission tomography/computed tomography, SUV_{max} : Maximum standard uptake value

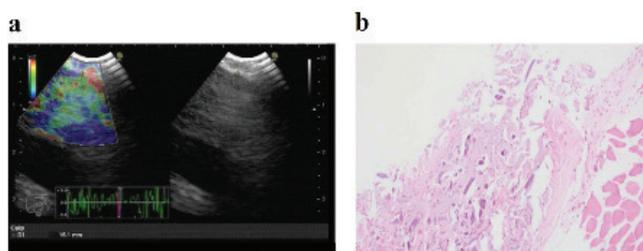


Figure 2. (a) EBUS-image of case 3 shows; indistinct margin, oval shape and heterogeneous echogenicity, partially blue partially non-blue (green, yellow and red) elastographic type in the right paratracheal area. (b) Histopathologically; granulation tissue characterized by numerous multinucleated giant cells is seen in the area adjacent to the normal muscle tissue (hematoxylin-eosin stain x100)
EBUS: Endobronchial ultrasound

Table 2. Survival time, date of surgery, and date of false positivity on PET/CT of patients

Case	Date of surgery	Date of detection	Survivability	Survival time* (month)
1	27/03/2019	02/08/2019	Alive	36
2	13/12/2018	14/04/2019	Exitus	31
3	28/06/2019	19/08/2019	Alive	32
4	11/04/2019	05/11/2019	Alive	35
5	03/07/2019	19/11/2019	Alive	32
6	02/02/2019	06/07/2019	Alive	37
7	08/05/2019	14/10/2019	Alive	34
8	06/04/2019	02/09/2019	Alive	35
9	31/01/2019	16/05/2019	Alive	37
10	31/08/2020	13/01/2021	Alive	18
11	25/08/2020	04/01/2021	Alive	18

*Survival time was calculated according to the current date for living patients. PET/CT: Positron emission tomography/computed tomography

for patients after lung cancer surgery. The common tendency is that patients are followed up with thoraco-abdominal CT or PET/CT at intervals of 3-6 months in the first 2 years, postoperatively. In our department, postsurgical follow-up is performed out in accordance with the National Comprehensive Cancer Network guidelines (radiological follow-up is performed once every 3 months in the first 2 years and PET/CT is performed in the presence of suspected tumor recurrence). The time of local recurrence and distant metastasis after surgery are similar. Boyd et al. (7) reported that the mean durations of distant metastasis and local tumor recurrence were 12.5% and 13.6 months, respectively. However, in our study, the median time of false PET/CT positivity after surgery was 139 days. The possible reason for this difference may be that early radiological tumor recurrence tends to be false positives.

In lung cancer surgery, cellulose hemostatic agents, such as ORC, are placed to provide hemostasis, particularly in the subcarinal and paratracheal areas after lymph node dissection. It may also be necessary to place it in the posterior intercostal space in patients undergoing thoracotomy. ORC is a self-absorbable product and it completely dissolves within 2-4 weeks without causing an inflammatory reaction. However, the reabsorption time of ORC may be prolonged by some reasons, and it may cause inflammation in the localizations where it is placed, thus it may give the appearance of a false tumor recurrence in PET/CT (6,10). The presence of pneumonia or pleural infection in patients during the postoperative period may cause increased inflammation around the materials. Adjuvant treatments (chemotherapy and/or radiotherapy) may also have a similar effect. In our study, most of the patients (81.8%) had a history of adjuvant therapy, and postoperative infection was only considered as the cause of false PET/CT positivity in 2 cases. Some studies in the literature have reported that these agents have the appearance of an abscess on radiological imaging, and their unnecessary use may result in the mediastinal infection (6,10,11). In our series, there were no radiological findings of an abscess, and the histopathological results were incompatible with the infection. In addition, there was no case of mediastinitis related to the use of ORC during the study period.

Study Limitations

This study had some limitations. It is a retrospective, single-center study, and it included few patients. Thus, we could not determine whether there were any correlations between false tumor recurrence and some variables, such as smoking habit, adjuvant/neoadjuvant treatment regimens, and tumor histopathology. However, this study may be

deemed a preliminary report that may inspire researchers to conduct multicenter studies with many patients.

Conclusion

Surgeons should specify whether using ORC and its localization in the surgical notes of patients undergoing pulmonary resections for lung cancer. False tumor recurrence should be considered when radiologic early tumor recurrence is detected in the postsurgical follow-up, particularly in patients receiving adjuvant therapy and those with a history of postoperative infection. Thus, unnecessary treatment and re-surgical interventions can be prevented.

Ethics

Ethics Committee Approval: Gazi University Ethics Committee (no: 91610558-604.01.02, research code no: 2020-366).

Informed Consent: An informed consent form was obtained from the patients or their relatives included in the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.S., A.Ç., N.Y.D., G.A., İ.C.K., Concept: M.S., A.Ç., M.Ş.T., D.Ö., İ.A., O.Y., N.Y.D., G.A., İ.C.K., A.İ.T., U.A., Design: M.S., A.Ç., M.Ş.T., D.Ö., İ.A., O.Y., N.Y.D., G.A., İ.C.K., A.İ.T., U.A., Data Collection or Processing: M.S., A.Ç., M.Ş.T., D.Ö., İ.A., O.Y., N.Y.D., G.A., İ.C.K., A.İ.T., U.A., Analysis or Interpretation: M.S., A.Ç., M.Ş.T., D.Ö., İ.A., O.Y., N.Y.D., G.A., İ.C.K., A.İ.T., U.A., Literature Search: M.S., A.Ç., İ.A., O.Y., Writing: M.S., A.Ç., O.Y.

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