Radiological and Pathological Correlation of Lung Malignant Tumors Treated with Percutaneous Radiofrequency Ablation

Osamu Hataji, Koichiro Yamakado, Atsuhiro Nakatsu, Shuichi Murashima, Hajime Fujimoto, Yoichi Nishii, Hiroki Nakahara, Hiroyasu Kobayashi, Esteban C Gabazza and Osamu Taguchi

Abstract

Radiological and histological correlation was evaluated in patients with malignant tumors of the lung that underwent radiofrequency ablation (RFA). One of the patients had a primary lung tumor and another patient had three metastatic lung tumors. RFA was performed under computed tomography (CT) fluoroscopic guidance. CT showed ground glass shadows around the tumoral lesions immediately after RFA, but one week later homogenous opacification without tumoral enhancement was noted. Two months after RFA, most lesions showed cystic changes without activity on FDG-PET. Histological evaluation showed massive coagulation necrosis throughout the tumor and some viable cells at the peripheral areas in all lesions. Although RFA is a promising therapeutic approach for malignant lung tumors, some viable cells may persist in peripheral areas of the tumor.

Key words: radiofrequency ablation, lung tumor, radiological features, pathological findings

Introduction

Lung cancer is one of the leading causes of death for malignancy. The death rate for cancer still remains high (about 30 per 100,000) in the United States (1). In Japan, lung cancer became the leading cause of death for malignancy in men (2). There has not been much progress in the therapeutic strategies for lung cancer. The use of cytotoxic drugs and radiation therapy has not substantially improved the clinical outcome of lung cancer patients (3, 4). The ideal therapy is the surgical approach but most primary and secondary malignant tumors of the lung are in advanced stages of disease at the time of diagnosis, and thus they are not suitable for surgical resection. For these reasons, novel therapies are currently being evaluated to improve the prognosis of patients with malignant tumors of the lung.

One of the new therapeutic modalities that is currently being assessed is minimally invasive techniques such as laser ablation, cryoablation and radiofrequency ablation (RFA) (5–7). Among these, RFA has recently become the focus of much attention as a promising approach for the treatment of inoperable hepatic, renal and bone neoplasms (8, 9). RFA is a minimally invasive electrosurgical technique that uses high frequency alternating current to heat tissues leading to thermal coagulation. The use of this therapeutic approach for lung tumors has also been recently reported (9, 10). Although encouraging results have been reported in short-term follow-up period, correlation of the histopathological features and radiological findings has not been as yet reported. Correlation of pathological and radiological findings is important for a complete evaluation of the therapeutic efficacy of RFA in malignant lung tumors. Herein, we report the correlation of pathological and radiological findings in 2 patients with malignant lung tumors treated with RFA.

Materials and Methods

Patients

Eleven patients with malignant tumors in the lung were enrolled in the present study (Table 1). In this study, we re-
port the correlation of pathological and radiological findings in 2 patients in whom histopathological samples of lung tumors were obtained after RFA therapy. Of these, one patient had 3 metastatic lung tumors, while the other patient had a primary lung cancer. Written informed consent was obtained from all subjects. The Mie University Hospital Institutional Review Board approved the study protocol, and it was carried out following the principles of the Helsinki Declaration.

RFA technique

RFA was performed using a 17-gauge internally cooled straight electrode (Radionics, Burlington, MA). The RF electrode was inserted into the tumor under CT fluoroscopic guidance. The electrode was inserted in the center of the tumor in metastatic tumors measuring less than 3 cm. The electrode was inserted into 2 different positions of primary lung tumors larger than 3 cm. RF was applied for 12 minutes after insertion of the electrode into the tumor.

Results

The age of the patients ranged from 66 to 87 years old. There were 8 males and 3 females. Eight patients underwent RFA for recurrence of lung tumor after surgical treatment. Two patients were in stage IV and were unresponsive to chemotherapy. The follow-up period ranged from 3 to 19 months. All patients except one remained alive after RFA therapy. Lung tissue after RFA was available for histopathological study in 2 patients. To date, no study has described the histopathological findings of the lung in relation to radiological findings in patients treated with RFA. Here, in one patient tissue samples were obtained at autopsy, while in another patient tissue samples were obtained from surgical specimens. The size of the tumors ranges from 35–45 mm to 21×23 mm. The details of these 2 cases are described below.

Case 1

A 66-year-old man underwent RFA for treatment of 3 metastatic lung tumors from colon cancer on February 2002. Later, he also underwent RFA for metastatic liver tumors. There was 1 metastatic tumor in the right lower lung and 2 in the right upper lung. First, RFA of the lower tumor was performed and 1 week later RFA of the 2 tumors of the right lung was performed. Pneumothorax requiring 5 days of chest drainage occurred during RFA of tumors of the right lung. CT images showed ground glass shadows surrounding the tumors, probably due to hemorrhage during electrode placement; these CT findings expanded immediately after finishing the therapeutic procedure. CT scanning carried out 1 and 2 weeks after lung tumor ablation showed soft tissues around the tumor and pleural thickening. Contrast-enhanced magnetic resonance imaging showed enhancement not inside but around the tumor. 18F-deoxyglucose positron emission tomography (FDG-PET) showed no biological activity in any of the 3 lung tumors. FDG-PET was not available before RFA procedure. Four months after the first RFA procedure and despite negative findings for recurrence of the lung tumors, the patient requested complete surgical resection of his pulmonary lesions subjected previously to RFA. Microscopic evaluation of the lung tumors disclosed a fibrous capsule surrounding the tumors and coagulation necrosis throughout the tumors. Viable cancer cells were observed at the periphery of the 3 tumors particularly surrounding broncho-vascular areas (Fig. 1).

Case 2

A 78-year-old man with primary squamous cell carcinoma of the lung associated with lung fibrosis underwent RFA for recurrence of the tumor after combined therapy with radiation and cytotoxic drugs. CT images showed ground glass shadows around the tumor immediately after RFA. This was complicated with pneumothorax and subcutaneous emphysema that resolved thereafter without any therapy. Contrast-enhanced CT study showed no enhancement inside the tumor but there was a linear enhancement at the periphery of the tumor (Fig. 2). FDG-PET performed 1 week after RFA showed no biological activity. FDG-PET was not available before RFA procedure. Thereafter, the clinical course of the patient was good. However, 2.5 months after RFA, the patient had methicillin-resistant Staphylococcus aureus-associated pneumonia. Chest CT scanning disclosed shadows compatible with interstitial pneumonia in the right lobe, and cystic formation in the outer half of the tumoral region. The patient died of pneumonia 3 months after RFA. The death of our patient was not related to the previous RFA procedure. Microscopic observation of lung samples taken at autopsy disclosed fibrous bands and marked coagulation necrosis in the original region of the lung tumor; a fibrous capsule was found to cover the tumor. Viable cancer cells were observed at the periphery of the tumor particularly surrounding broncho-vascular areas (Fig. 2).

Discussion

This report showed the use of RFA as adjuvant therapy for the treatment of patients with malignant tumors of the lung. The clinical course of the patients was relatively good in most of our patients. Most of the tumors was almost completely necrotic after 3–4 months of RFA therapy. However, remnant cancer cells were observed at the peripheral areas of the tumors; remnant malignant cells were particularly observed in broncho-vascular areas of the lung parenchyma surrounding the tumor. Some factor may limit the degree of ablation of the tumor; for example, previous studies carried out in hepatic neoplasms have shown that blood flow may cause heat loss and thereby limit the size of tumor ablation (11). The degree of tissue ablation may also depend on ventilatory conditions of the affected lung; ventilation of the air spaces of the lung may be the cause of incomplete RFA of lung tumors by acting as an air-cooled radiator (12). Technical factors may also limit the efficacy of RFA. The use of different types of electrode or a longer exposure time...
might have resulted in less residual tumor after RFA in our patients. Another factor that may limit the efficacy of RFA is the tumor size; it is commonly difficult to achieve a complete ablation of cancerous lesions in tumors with diameter larger than 3 cm (13).

Poor sensitivity of CT and FDG-PET to detect remnant cancerous tissues after RFA was observed in the present study. A previous investigation has shown that contrast-enhanced CT and FDG-PET have a high sensitivity and good specificity for detecting residual tumors after RFA when both procedures are performed in combination and after 1 and 3 months after RFA therapy (12). In the present study, FDG-PET failed to demonstrate biological activity of residual tumors 2 weeks after RFA, and both contrast-enhanced CT scanning and magnetic resonance imaging showed only enhancement of the peripheral area of the tumor. We have performed these radiological procedures 1 or 2 weeks after RFA therapy. Thus, the poor diagnostic yield achieved with both CT and FDG-PET in our cases might have been due to the premature execution of these radiological procedures after RFA therapy.

Determination of the safety margin for RFA by radiological procedures is difficult. In the present study, contrast-enhanced CT and magnetic resonance imaging showed...

Figure 1. Axial CT images of the lung tumor four months after RFA and immediately before surgical excision of the tumor (A). The surgical specimen shows the tumor in the right lower lobe (B). Loupe view of the S9 tumor shows coagulation necrosis in most part of the tumor, a central cavitation, some remaining tumor cells (T) in the periphery and a fibrous capsule surrounding the mass (C). Loupe view of the S1 tumors that became one mass (D); as described for S9 tumor, coagulation necrosis, residual cancer cells at the peripheral area and a thick fibrous tissue surrounding the tumor are found.
enhanced shadows in the peripheral areas of the tumor. Miao et al have previously demonstrated that enhanced radiological images may be due to the inflammatory response induced by the RFA technical procedure itself at the periphery of the tumor (14). Following RFA an inflammatory response occurs in the area surrounding the tumors due to the local release of high energy. In a radiologic-histopathologic correlation study in rabbits, Miao et al found that increased inflammatory response occurs at the periphery of the lung parenchyma surrounding the tumor 3 days after RFA therapy (14). However, in contrast to what we found, they have not described the presence of residual tumor cells in the lung after RFA.

In the current study, we demonstrated that some tumor cells remain viable in the pulmonary region subjected to RFA therapy, suggesting that this therapeutic procedure may not be sufficient to kill all lung tumor cells. Ground glass opacity found immediately after RFA represents coagulation necrosis that is subsequently replaced by fibrotic tissues. This fibrotic region may be useful for determining the safety margin for RFA therapy. However, the results of the present clinical observation suggest the need for more studies to determine with accuracy the tumor-free margin for RFA therapy. Methods enabling more accurate determination of the safety area may substantially improve the potential therapeutic benefits of RFA in lung malignant tumors.

Figure 2. Axial CT images show the tumor 2 weeks after RFA. There is an increased density (arrow) in half of the peripheral region of the tumor 2 (A) and 12 (B) weeks after RFA. Cavitation and a fibrous capsule can also be observed. Loupe (C) and magnified view (D) of the lung nodule at autopsy. Coagulation necrosis (N) and residual tumor cells (T) can be observed.
References


