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Abstract

We report the clinical experience of radiofrequency ablation followed by radiation therapy for large primary lung tumors. Two patients with large primary lung tumors were treated with combined radiofrequency ablation and radiation therapy, and good local control was observed. Combined radiofrequency ablation and radiation therapy that involves minimally invasive techniques appears to be promising for the treatment of large lung tumors.

KEYWORDS: radiofrequency ablation, lung cancer, radiation therapy

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Case Report

Radiofrequency Ablation Followed by Radiation Therapy for Large Primary Lung Tumors

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We report the clinical experience of radiofrequency ablation followed by radiation therapy for large primary lung tumors. Two patients with large primary lung tumors were treated with combined radiofrequency ablation and radiation therapy, and good local control was observed. Combined radiofrequency ablation and radiation therapy that involves minimally invasive techniques appears to be promising for the treatment of large lung tumors.

Key words: radiofrequency ablation, lung cancer, radiation therapy

There are limited treatment options for patients with non-small cell lung cancer (NSCLC) who are not surgical candidates. Radiofrequency (RF) ablation presents a potentially less invasive option for these patients. RF ablation is a relatively new modality that has been successfully used for the treatment of hepatic tumors [1]. During the past few years, an increasing number of reports have described the use of RF ablation for treating malignant lung nodules [2-4]. The success of this method, however, is limited by tumor size [4]. We treated 2 patients with large lung tumors with combined RF ablation and radiation therapy.

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Case Report

Two patients with large lung tumors were treated with combined RF ablation and radiation therapy. Written informed consent was obtained from both patients. Approval of our institutional review board was obtained for RF ablation of the lung tumors; however, the board's approval was not required for performing the combined therapy.

Case 1. The first patient was an 82-year-old man who had been previously diagnosed with T2N0M0 squamous cell carcinoma of the lung. Chest computed tomography (CT) demonstrated a 6-cm tumor in the right lower lobe of the lung (Fig. 1A, B). The patient was not considered a good candidate for surgery or chemotherapy because of his advanced age and poor pulmonary function. The tumor appeared too large to be treated completely by RF ablation alone or radiation therapy alone. Therefore, we decided to treat the tumor by combining RF ablation and external beam radiation therapy.

First, RF ablation was performed under CT guidance (Fig. 1C). The treatment was performed under local anesthesia and conscious sedation that was achieved by means of intravenous fentanyl chloride infusion. A cluster internally cooled electrode (Cool-Tip, Radionics/ValleyLab, Boulder, CO, USA) was placed inside the tumor under CT fluoroscopic guidance. Once proper electrode positioning was confirmed, we attached the electrode to a 500-kHz monopolar radiofrequency generator (Cosman Coagulator-1, Radionics/ValleyLab). Overlapping ablations were performed by repositioning the needle in an attempt to ablate the entire tumor. Pneumothorax developed after RF ablation, necessitating chest drainage and pleurodesis.

External beam radiation therapy was performed 2 months after RF ablation (Fig. 1D). Radiation therapy was performed by using a linear accelerator (10 MV) with an anterior-posterior parallel opposed pair of portals. The patient received 50 Gy in 25 fractions. The total dose was administered to the radiation field that consisted of the primary tumor

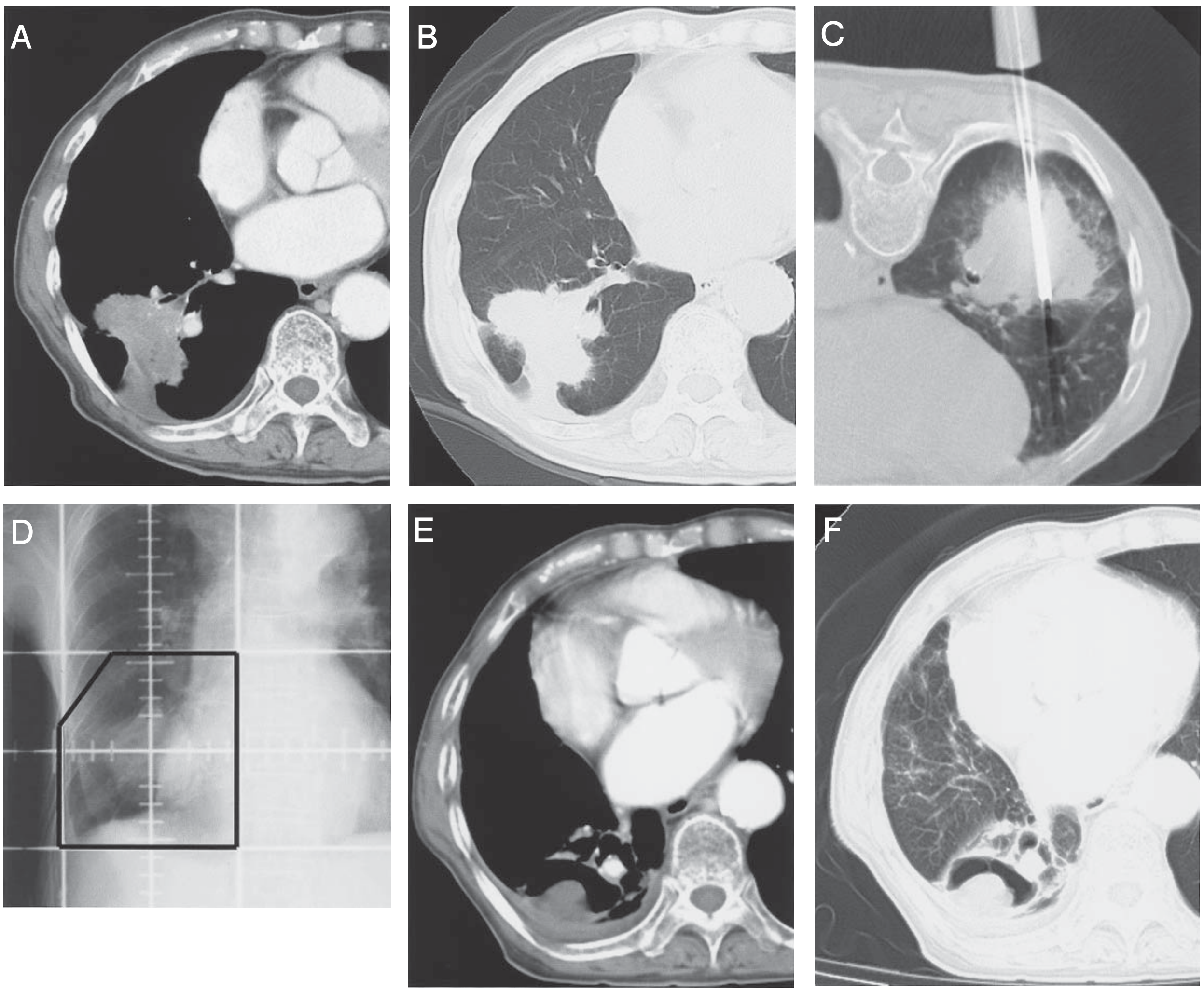

Fig. 1 Case 1. An 82-year-old man who had been previously diagnosed with T2N0M0 squamous cell carcinoma of the lung.
A, B, Contrast-enhanced chest CT demonstrated an enhanced 6-cm tumor in the right lower lobe of the lung; C, CT fluoroscopy image shows the radiofrequency electrode in the tumor; D, Radiation therapy was performed 2 months after RF ablation. The patient received 50 Gy in 25 fractions; E, F, CT images obtained 9 months after the completion of the combined therapy do not show any evidence of tumor enhancement. The tumor shrinkage and cavity formation are visible.

including the movement area by respiration. The ipsilateral hilum was not included in the radiation field because lymph node metastasis was not detected. Although administration of a total dose of 60 Gy was initially planned, radiation therapy was discontinued when a total dose of 50 Gy had been administered due to granulocytopenia.

The CT images obtained 5 months after the completion of the combined therapy showed tumor shrinkage (4.5 cm in diameter) without contrast enhancement (Fig. 1E, F). The CT images obtained 14 months after the completion of the combined therapy showed no evidence of tumor recurrence, although radiation fibrosis was observed. The patient died of acute heart failure 17 months after the completion of the combined therapy.

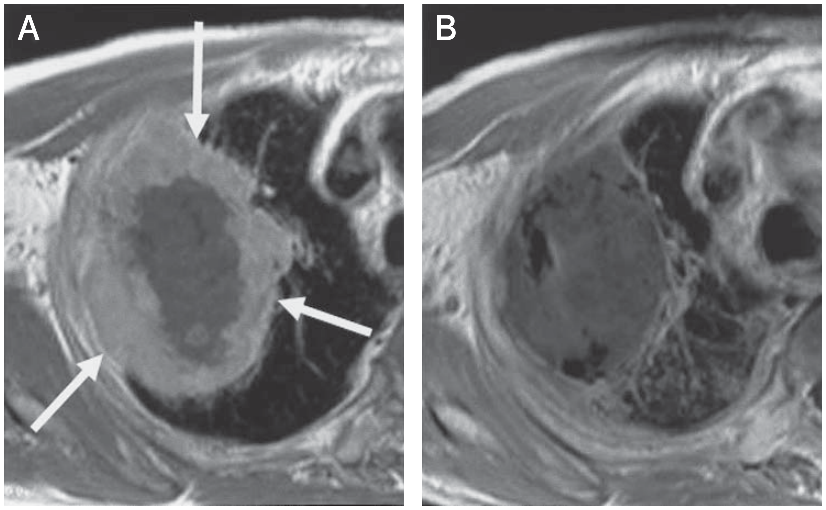

Fig. 2 Case 2. A 61-year-old man with T2N0M0 adenocarcinoma of the lung. **A**, Contrast-enhanced T1-weighted MR images obtained 3 months after the second RF ablation shows an enhanced residual tumor at the periphery (arrow); **B**, Contrast-enhanced T1-weighted MR images obtained 4 months after the completion of the combined therapy do not show any evidence of tumor enhancement.

Case 2. The second patient was a 61-year-old man with T2N0M0 adenocarcinoma of the lung. The patient was not considered a good candidate for surgery because of poor cardiac function, and thus systemic chemotherapy was undertaken. Although the patient showed a dramatic response to chemotherapy for about 5 years, local progression of the tumor was subsequently detected. The CT examination revealed a 55-mm tumor in the right upper lobe of the lung.

At the patient's insistence, the tumor was treated twice by RF ablation alone. However, the CT and magnetic resonance (MR) images obtained 3 months after RF ablation showed local tumor progression (Fig. 2A). The tumor appeared too large to be treated completely by RF ablation alone. Subsequently, informed consent was obtained from the patient for the combined therapy. During the third treatment session, combined RF ablation and radiation therapy was performed. The CT images obtained prior to the treatment showed a 98-mm tumor in the right upper lobe of the lung; however, no obvious lymph nodes were observed in the mediastinum or hilum. First, RF ablation was performed under CT guidance by using a single internally cooled electrode (Cool-Tip, Radionics/ValleyLab). Overlapping ablations were performed by repositioning the needle in an attempt to ablate the entire tumor. External beam radiation therapy was performed 10 days after RF ablation. The patient received 60 Gy in 30 fractions. After the completion of the combined therapy, the patient suffered from ileus and was diagnosed with advanced colon cancer.

The MR images obtained 4 months after the completion of the combined therapy showed no evidence of tumor recurrence (Fig. 2B). Six months after the combined therapy, the patient died of colon cancer and pneumonia that had developed during chemotherapy.

Discussion

During the past few years, an increasing number of reports have described the use of RF ablation for malignant lung nodules. The success of this method, however, is limited by tumor size. Akeboshi *et al.* reported 54 lung neoplasms in 31 patients who were treated by RF ablation [4]. There was a significant difference in the rate of complete tumor necrosis between the tumors that were 3 cm or less in size and tumors that were larger than 3 cm (69% vs. 39%; $p < 0.05$).

External beam radiation has been traditionally used for patients who are unable to tolerate pulmonary resection. Morita *et al.* compiled the results of a study conducted in 10 institutions involving 149 patients with stage I NSCLC who were considered to be medically inoperable [5]. The mean dose of radiation administered to these patients was 64.7 Gy. The actuarial 3- and 5-year survival rates were 34.2% and 22.2%, respectively. The tumor size was of prognostic importance. When the diameter of the primary tumor was 3 cm or less, the complete response rate was 54%, but it was only 28% in patients with tumors that were more than 3 cm in diameter. To treat large tumors that are more than 3 cm in diameter, radiation therapy alone might not be sufficient.

Tissue heating by RF ablation induces coagulation necrosis and cell death, including destruction of the centrally located hypoxic tumor that is typically less responsive to chemotherapy and radiation therapy [6]. On the other hand, there are concerns regarding the presence of viable tumor cells persisting at the periphery because the aerated lung diminishes the conduction of RF current and heat. To counteract this principle, Jain *et al.* combined RF ablation with radiotherapy in the form of brachytherapy [6]. Three patients were treated with combined RF ablation and brachytherapy, and good local control was observed. We combined external beam radiation therapy with RF ablation to provide a more definitive local therapy. In our cases, the lung tumors appeared too large to be treated by brachytherapy.

In a previous study, Harkan *et al.* had reported that in a rat breast tumor model, an increased rate of animal survival was observed when combined RF ablation and radiation therapy was used than when RF ablation alone or radiation alone was used [7]. They suggested that one potential cause of this synergy might be the increased oxygenation in blood flow to the tumor, caused by local hyperthermia induced in tissues peripheral to the ablated region. Increased oxygenation has been implicated in the sensitization of the tumor to the subsequent radiation therapy. The cytoreduction induced by RF ablation could decrease the number of tumor viable cells that could be subsequently controlled by radiation. In our first patient, external beam radiation therapy was performed 2 months after RF ablation because the patient was being treated for pneumothorax. This interval between RF ablation and radiation therapy might not allow the synergy induced by increased oxygenation in the tissues at the periphery of the ablated region. The cytoreduction induced by RF ablation appears to be the main advantage of the combined therapy. Although there are concerns regarding damage to the normal lung tissue present in a radiation field, the degree of radiation fibrosis observed in our cases was acceptable.

Combined RF ablation and radiation therapy that involves minimally invasive techniques appears to be promising for the treatment of large lung tumors. However, further basic science and clinical research is required to elucidate the relationship between RF ablation and radiation therapy and their potential for combined therapy for treating lung tumors.

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