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Case Report

Large apical lung cancer treated with CT-guided percutaneous cryoablation☆,☆☆

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ABSTRACT

Percutaneous lung ablation is increasingly used in the treatment of lung malignancies with good outcomes, but recurrence is commonly reported in ablation of lesions size larger than 3 cm. We report a 50-year-old female with a 9 cm nonsmall cell lung cancer involving the right upper lobe and apical chest wall causing severe neuropathic shoulder pain and significantly disturbing her daily activities. CT-guided percutaneous cryoablation was performed using a 4-phase protocol with complete eradication of the tumor. Follow-up imaging showed no evidence of recurrence 6 months after the procedure. The neuropathic pain was significantly improved after the procedure, and she was pain-free until her death due to metastatic disease elsewhere. To our knowledge, this is the first case of successful cryoablation for an exceptionally large lesion.

Introduction

Surgical resection is currently the standard of care for early-stage nonsmall cell lung cancer (NSCLC) treatment. However, an increasing number of inoperable patients has made the use of image-guided percutaneous ablation more frequent in the treatment of lung malignancies. Previous studies have shown that approximately 75% of patients with NSCLC were diagnosed at advanced stages, where surgery was not suitable. Guideline review suggests the main indication for percutaneous lung ablation is inoperable stage IA NSCLC, although inoperable NSCLC at other stages can also be considered for ablative treatment [1–3].

Percutaneous lung ablation techniques include: radiofrequency ablation, microwave ablation and cryoablation. They are usually suitable for small tumors with 3 cm diameter or less, although larger lesions may be considered [1,2]. Previous studies have shown that size is one of the most crucial factors for predicting recurrence after ablation treatment, with

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unsuccessful ablation more likely in lesions size larger than 3 cm [2,4]. To the authors' knowledge, successful ablation of an exceptionally large lesion has not been reported in the literature. We report successful treatment of a large apical lung lesion with diameter of 9 cm, using cryoablation.

Case report

A 50-year old female patient was diagnosed with NSCLC with sarcomatoid features involving the right upper lobe and apical chest wall (Fig. 1). She was previously treated with chemotherapy (cisplatin and etoposide) and concurrent radiotherapy. She had been experiencing progressively worsening right shoulder pain for 3 months with neuropathic features and dull ache in the axilla which was radiating to the back of her arm and elbow. As she was right-handed, these symptoms significantly disturbed her daily activities.

CT-guided percutaneous cryoablation was performed in supine and prone positions using Boston Scientific Cryoablation System. Eight probes (IceFORCE, Galil Medical) measuring 2.1 mm in diameter and 175 mm in shaft length were used. Four probes were used simultaneously (Fig. 2). Four-phase cryoablation protocol was utilized, which consisted of 3-minute, 7-minute, 10-minute, and 10-minute freeze. After each freeze, there was a 2-minute passive thawing and 1-minute active thawing. Following the four-phase protocol completion, the probes were repositioned to begin another four-phase protocol, and the process was repeated multiple times to cover all parts of the tumor. Total time of the procedure was seven hours. Non-contrast chest CT scan immediately after the procedure showed complete ablation of the tumor (Fig. 3).

The postprocedural period was uneventful, and she was discharged to home 2 days later with no immediate complications.

Her right hand felt weaker after procedure, but this symptom improved with steroid therapy (Dexamethasone 6 mg bd for 1 week, followed by 4 mg bd for 1 week, and then 2 mg bd for 1 week and finally 2 mg once per day for 1 week).

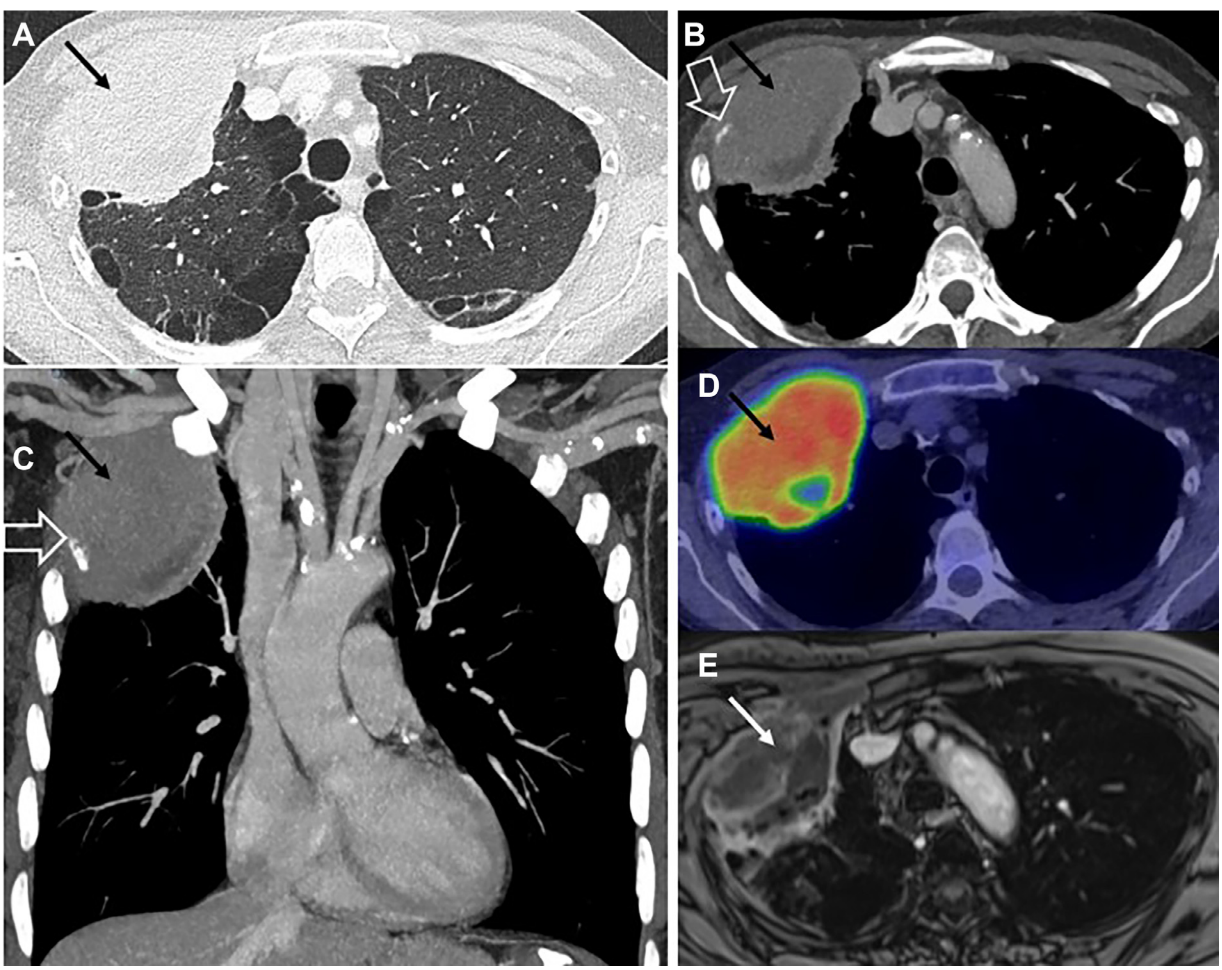

Fig. 1 – Pre-procedure imaging. Contrast-enhanced chest CT scan (A) axial slice lung window, (B) axial slice mediastinal window, (C) coronal slice mediastinal window, showing heterogeneously enhancing solid mass (*solid arrow*) involving the right anterior apical chest wall and right upper lobe, eroding the upper ribs (*open arrow*), measuring approximately 8.5 x 4.8 x 9 cm (D)PET-CT scan showing avid FDG uptake by the mass (*arrow*), and (E) contrast-enhanced MR showing heterogenous enhancement in the mass (*arrow*).

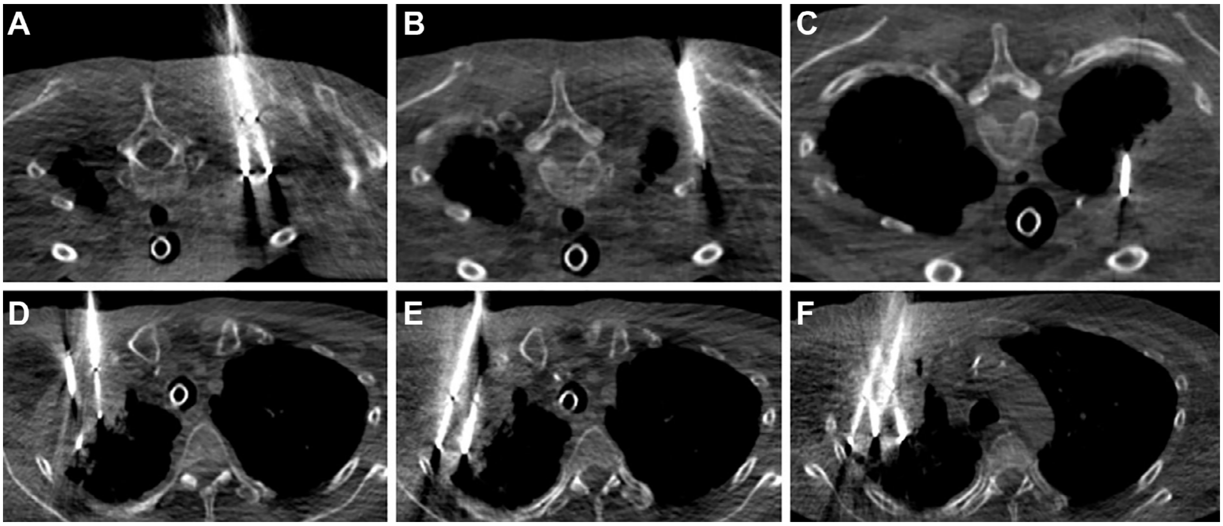

Fig. 2 – CT images showed cryoablation needles inside the mass during ablation procedure in (A,B,C) prone and (D,E,F) supine positions.

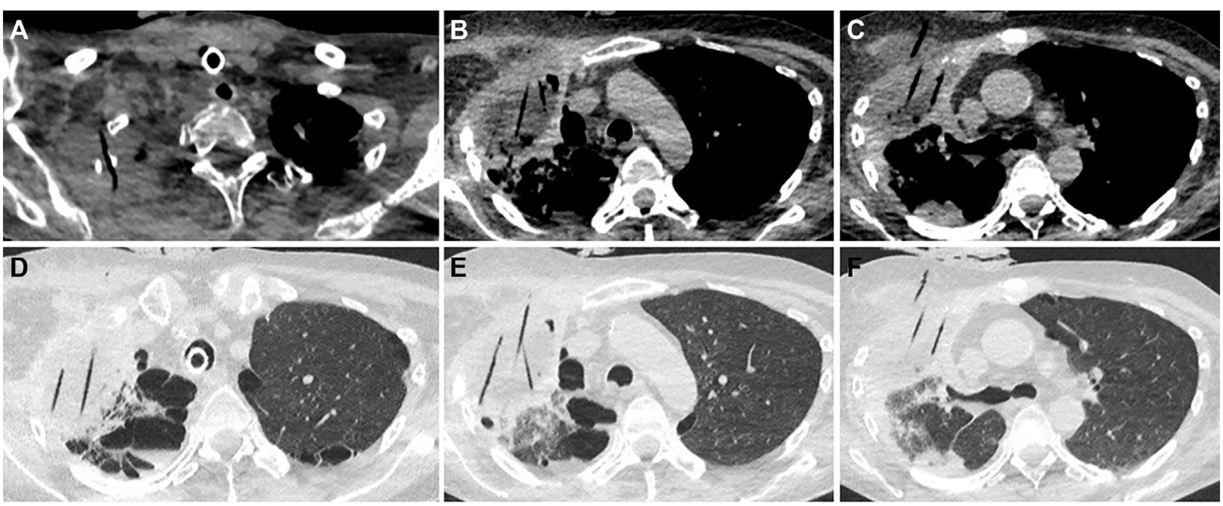

Fig. 3 – CT images in (A,B,C) mediastinal and (D,E,F) lung windows immediately after procedure, showing complete ablation of the tumor. No pneumothorax is seen.

The neuropathic pain in her right shoulder and arm significantly improved immediately after cryoablation and she was pain-free until her death (due to metastatic disease elsewhere).

Follow-up imaging at 6 months after procedure showed no recurrence in the ablated tumor (Fig. 4).

Discussion

Lung cancer is one of the leading causes of cancer-related mortality worldwide. Current British Thoracic Society guidelines for NSCLC recommend offering radical treatment for patients with T3 N0 or T3 N1 disease and no metastasis. For more advanced disease (T4N0, T4N1), radical multimodality treatment may be considered. However, in early-stage disease where patients have significant comorbidities or poor lung function, nonconventional radical treatment (other than surgery, radical radiotherapy) may be considered and discussed with patients as a valid alternative. Image-guided percutaneous lung ablation is a minimally invasive technique for both radical and palliative treatment. It has shown reasonable local disease control while preserving lung function. Patients should be selected by the MDT (multidisciplinary team) [1,2].

Our patient in this case report had a large tumor involving the right upper lobe and the chest wall (T4 disease), which should be considered for multimodality treatment based on current guidelines. She was previously treated with chemoradiotherapy, and MDT discussion recommended for image-guided percutaneous lung ablation for local disease control and symptoms management. In this patient, the neuropathic

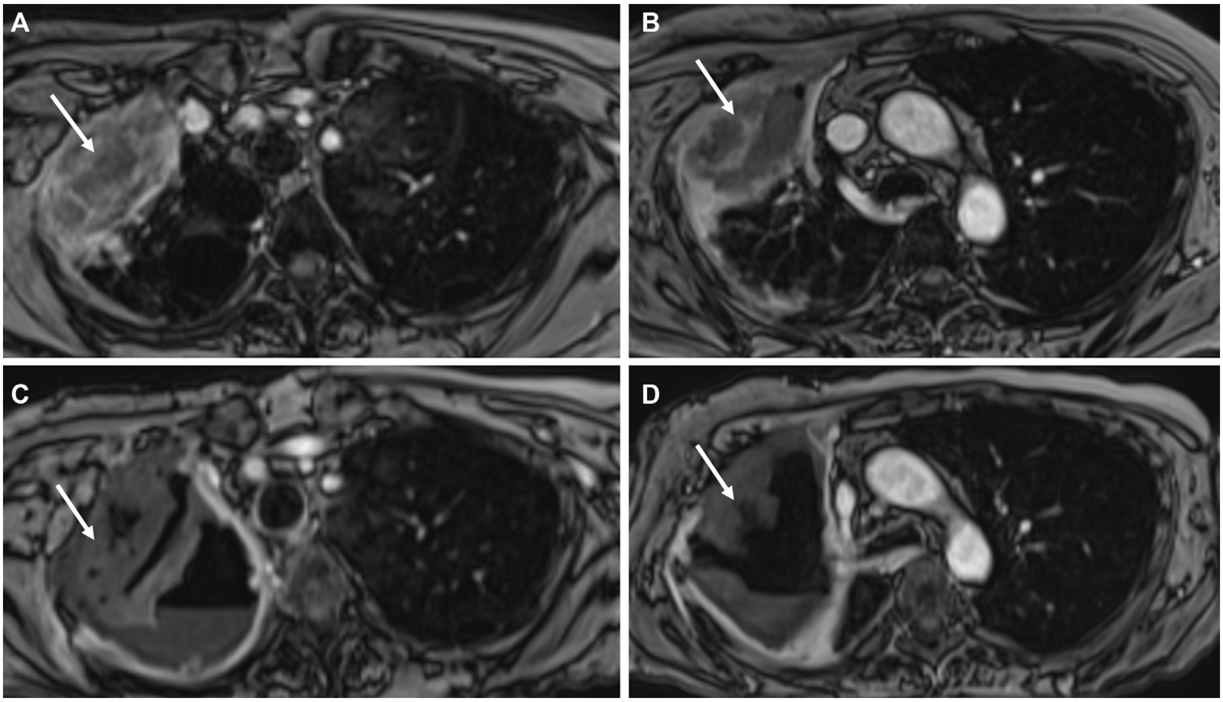

Fig. 4 – Imaging evaluation with MRI (A, B) before cryoablation showing heterogenous enhancement inside the mass, and (C, D) 6 months after cryoablation showing no enhancement at all in the ablated region, indicating complete ablation and no recurrence of the cancer.

pain was caused by compression of brachial plexus located near the apical segment of the lung, and ablating the apical tumor was expected to relieve the nerve compression. However, care was taken not to damage the brachial plexus itself during the treatment.

Cryoablation causes cytotoxic cell destruction at freezing temperatures below −20 °C, and a thawing phase will follow afterwards. The freezing-thawing cycle will repeat until effective ablation is achieved. In this way, structures containing collagenous matrix, such as blood vessels, are preserved [1,5]. Therefore, cryoablation is less likely to cause nerve damage compared to other ablation methods and was thus more suitable for our patient. Another advantage of cryoablation is stimulation of the antitumor antibody production, which may help to prevent recurrence [5].

The disadvantage of cryoablation is that it needs multiple cycles of freezing-thawing to achieve an effective ablation; this makes treatment times longer than with radiofrequency or microwave ablation. The cryoablation protocol in previous studies varied between two or three freeze-thaw cycles. In the 2-cycle protocol, the duration of each freeze was between 12 and 15 minutes. In the 3-cycle protocol, the freezing time was 3-5 minutes for the first cycle, 7-10 minutes for the second cycle, and 8-10 minutes for the third cycle [1,3,6–8]. Animal studies by Izumi et al. [9] and Nakatsuka et al. [10] showed that in the first freeze-thaw cycle, the infiltration of blood from the frozen region into the aerated lung parenchyma would obliterate the air spaces, creating optimal environment for thermal conduction. As a result, the second cycle produced a significantly larger frozen area. In the third cycle, there is no significant difference in the size of the frozen area (ice ball), but it could be necessary for more effective cytotoxicity [1,7].

The cryotherapy probe creates a limited ablation zone in lung, meaning multiple probes are needed to create larger treatment zones. The current literature suggests to apply a tip-to-tip distance of 2 cm between the probes so that a slight overlap of the ice balls created seamless cryoablation coverage [1,7]. However, recent *in vitro* study showed that the optimum temperature of −20 °C degrees was achieved only at 0.5 cm from the cryoprobe, and not always achieved at 1 cm from the cryoprobe [11]. Although this study used a different cryoprobe from our procedure, the results indicated that triple phase protocol with tip-to-tip distance of 2 cm may not always create a consistent size of optimum frozen area. Based on the cryoprobe characteristics used in our department, we have developed local department protocol utilizing four-phase cryoablation protocol to further consolidate the ice ball and applying tip-to-tip distance of 1.5 cm between the probes to aim for −40°C ablation zone.

After cryoablation, pneumothorax is a common complication which occurs in up to 60% procedures, 25% of which required drain insertion [4]. Our patient did not experience pneumothorax despite long procedure time. This may be because the tumor had already infiltrated the pleura and the ribs, anchoring it to the chest wall and preventing the formation of pneumothorax. Additionally, the previous radiotherapy may have induced pulmonary fibrosis [12], thereby further decreasing the risk of pneumothorax.

Imaging follow-up to evaluate tumor recurrence relied on postcontrast enhancement. The lesion size was not reliable, because initial increase in size could happen due to thermal injury in the adjacent lung tissue. No enhancement in the ablation zone indicated successful ablation. Irregular focal soft-tissue enhancement (>15 HU) in the vicinity of the old ablation zone suggested residual or recurrent cancer. Areas with local enhancement (>15 HU) also indicated recurrence. On the other hand, low-density areas with circular enhancement at the edge of ablation zone were not considered as recurrence [13,14]. In our case, we used MRI for follow-up because it was easier to appreciate the enhancement in the ablation zone. The disadvantage of using MRI is that we could not measure the enhancement quantitatively as in CT scan. However, in our case we could see the complete lack of enhancement in the ablated tumor, indicating a successful ablation.

Previous studies showed that the only significant predictors for local progression were tumor diameter of more than 3 cm or 2 cm, and presence of a thick vessel (diameter more than 3 mm) close to the tumor [7,15]. To our knowledge, our case is the largest malignant lung tumor treated successfully with cryoablation. Previous clinical studies using cryoablation treated lesions with largest diameter of less than 8 cm [8,13–16]. A recent clinical study by Nomori et al. [17] which treated early-stage NSCLC with cryoablation, had largest tumor diameter of 3.5 cm, and found most of the recurrence occurred in patients with tumor diameter >1.8 cm. Recent clinical review showed that the largest average diameter of advanced NSCLC treated with cryoablation was 1.6 cm [5]. To the authors' knowledge, this is the first case of successful cryoablation for an exceptionally large lesion.

Conclusion

CT-guided percutaneous cryoablation is an effective, safe, and less invasive procedure to treat lung malignancies, especially for tumor located close to the nerves. It can also be used for larger tumor and significantly improved patient's quality of life.

Patient consent

Written informed consent was obtained from the patient of this case report.

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