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ORIGINAL ARTICLE

Radiofrequency ablation (RFA) for palliative treatment of painful non-small cell lung cancer (NSCLC) rib metastasis: Experience in 12 patients

Mu Hu, Xiuyi Zhi & Jian Zhang

Thoracic Surgery Department, Xuanwu Hospital Capital Medical University, Beijing, China

Keywords
Non-small cell lung cancer, painful rib metastasis, radiofrequency ablation.

Correspondence
Jian Zhang, Thoracic Surgery Department, Xuanwu Hospital Capital Medical University, Beijing 100053, China.
Tel: +86 139 10086960
Fax: +86 010 63027064
Email: zhangjianxw2008@163.com

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Abstract

Background: Painful rib metastasis is common in non-small cell lung cancer (NSCLC). Pain is often partially or totally refractory to analgesic medications or the side effects of medication are unacceptable. We report the safety and efficacy of a new method: radiofrequency ablation (RFA) in treating painful NSCLC rib metastasis.
Methods: RFA procedures were completed in 12 patients with painful rib metastasis. Patient age ranged from 66–83 years (mean 74.8 years, standard deviation (SD) = 5.3). There were four cases of squamous-carcinoma, seven adenocarcinomas, and one case of large cell carcinoma. Pain caused by neoplasm size, pain levels pre-procedure and post-procedure (as assessed using the visual analog scale, VAS), time length, and target temperature of RFA treatments were documented.
Results: RFA procedures were performed with 100% technical success. The mean pre-procedure and post-procedure pain, as measured by the VAS, was 7.9 (SD = 0.90) and 3.4 (SD = 0.99), respectively. No symptomatic complications occurred. Non-symptomatic complications included one case of pneumothorax and one case of hemoptysis.
Conclusion: RFA appears to be a safe, practical, and effective method for the palliative treatment of painful NSCLC chest wall metastasis.

Introduction

Lung cancer is one of the most common cancers in the world and pain is its most common symptom. Pain can be brought about by several different causes including local effects and regional or distant spread of the tumor, such as rib metastasis.[1] Historically, treatment for inoperative painful bone metastases has been conservative, utilizing radiotherapy, chemotherapy, and analgesics.[2] More recently, minimally invasive techniques have been introduced for treating painful bone lesions including microwave, cryoablation, and radiofrequency ablation (RFA).[3–5] The first reported use of RFA in the musculoskeletal system was for the treatment of osteoid osteoma.[6] Some cases of successful RFA for the palliation of painful osteolytic bone metastasis have been reported.[7,8] In non-small cell lung cancer (NSCLC), bone metastasis occurs in stage IV, and rib metastasis is a common development. Symptoms, such as severe pain when the tumor invades the intercostal nerve may be associated with the worsening of other symptoms affecting quality of life. Patients in this stage receiving RFA are in palliative care, and the goal of therapy is the timely control of pain, while minimizing treatment complications, including side effects of pharmacological methods, thus, providing a better quality of life. We present 12 cases of RFA for palliative treatment of painful NSCLC rib metastasis. This method allows for the quick and effective control of pain. To our knowledge, this is the first report describing this method specifically for painful NSCLC rib metastasis.

Patients and methods

Hospital ethics board approval was obtained prior to the initiation of this trial. From June 2012 to October 2014, the painful rib metastases of 12 NSCLC patients were treated in our department. Patients ranged in age from 66–83 years (mean 74.8 years, standard deviation [SD] = 5.3). For inclusion in the study, a patients' pain was required to be clinically localized to a region with intercostal nerve and rib involvement. Patients were required to have pain that was considered partially or totally refractory to analgesic medications; the side effects experienced or anticipated of additional

medication were deemed unacceptable. Patients with purely osteosclerotic metastases were excluded as these would preclude RFA probe deployment. Other exclusion criteria included platelet counts less than 50 000 and any local or systemic infection. Four cases of squamous-carcinoma, seven adenocarcinomas, and one large cell carcinoma were included in the study.

A computed tomography (CT) scan of each patient was taken within four weeks of treatment for procedural planning and inclusion criteria. Prior to RFA, each patient was assessed using a visual analog scale (VAS) to determine patient pain. Using the VAS, patients are asked to rate their current level of pain on a scale from 0–10 (0 = no pain, 10 = agonizing pain). This score was recorded just prior to intervention. Informed consent was obtained from all patients. Procedures were performed with local anesthesia, by one of four thoracic surgeons experienced in interventional procedures. CT (Siemens 64-slice Somatom Sensation, Erlangen, Germany) was utilized for lesion localization. Local anesthetic (1% lidocaine) was introduced from the skin to the ablation site. RFA was performed with RITA therapeutics probes StarBurst Talon and RITA type 1500X Radiofrequency generator host (Mountain View, CA, USA). Radiofrequency target temperature was maintained at a maximum of 90°C (range 80–90) and ablation was performed in 20–25 minutes. The diameter of ablation sites were designed 5 mm bigger than the maximum axis of the tumor. All patients received a CT scan immediately following treatment to capture intra-procedure complications, such as pneumothorax or hemorrhage in the lung. Patients were instructed to maintain normal use of any basal analgesic medication following RFA. Patients were asked to rank their pain again via VAS 24 hours post-RFA. A biopsy was routinely obtained for gene analysis, including epidermal growth factor receptor, Kirsten rat sarcoma viral oncogene homolog, anaplastic lymphoma kinase, and ROS proto-oncogene 1 receptor tyrosine kinase, for future systematic treatment after the RFA procedure.

Statistics

This study was a retrospective, single arm, paired comparison observational study with patients serving as their own control. The end-point was the average amount of pain reduction 24 hours post RFA, evaluated by VAS. Analysis was performed using paired *t*-tests. A difference of $P < 0.05$ was considered statistically significant.

Results

A 100% technical success rate was achieved in all patients. Table 1 summarizes the collected data. The lesion size was recorded by maximum axis length (mm); the average value was 27.0 mm (range 20–35; SD = 5.3); the average ablation time was 22.1 minutes (range 20–25; SD = 2.6); and the average target ablation temperature was 87.1°C (range 80–90; SD = 4.5). The mean immediate pre-procedure VAS pain score of all treated patients was 7.9 (range 7–9; SD = 0.90), while the mean post-procedure VAS pain score was 3.4 (range 2–5; SD = 0.99). There was a statistically significant decrease in pain score with a *P* value of <0.001 (Fig. 1). No symptomatic complications occurred. Non-symptomatic complications included one case of pneumothorax and one case of hemoptysis. No further treatment for complications was required, and the patients recovered quickly. For patients who suffered severe pain in the intercostal nerve area, particular

Table 1 Patient characteristics

Patient number	Age	Pathology diagnosis	Lesion size (maximum axis mm)	Ablation time (minutes)	Target temperature (°C)	Preoperative pain	Postoperative pain	Complications
1	76	Squamous-carcinoma	22	20	90	8	3	None
2	73	Squamous-carcinoma	34	25	90	8	2	None
3	66	Adenocarcinoma	25	20	90	9	4	Pneumothorax
4	81	Adenocarcinoma	33	25	85	7	3	None
5	76	Squamous-carcinoma	20	20	90	7	4	None
6	69	Adenocarcinoma	30	25	90	9	5	None
7	72	Large cell carcinoma	25	20	90	7	2	None
8	83	Squamous-carcinoma	25	20	80	8	3	None
9	74	Large cell carcinoma	20	20	90	9	3	None
10	77	Adenocarcinoma	35	25	80	9	3	Hemoptysis
11	69	Adenocarcinoma	25	20	80	7	4	None
12	81	Adenocarcinoma	30	25	90	7	5	None
Total 12	Average 74.8 (SD =5.4)		Average 27 (SD = 5.3)	Average 22.1 (SD = 2.6)	Average 87.1 (SD = 4.5)	Average 7.9 (SD = 0.90)	Average 3.4 (SD = 0.99)	None

SD, standard deviation.

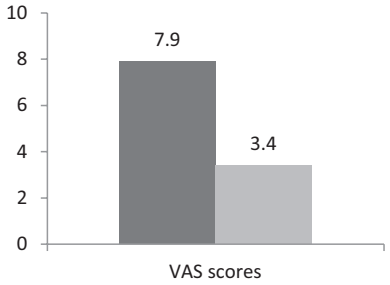

Figure 1 Pre-radiofrequency ablation (RFA) and post-RFA pain was measured using a visual analog scale (VAS). An average pre-RFA VAS pain score of 7.9 (standard deviation [SD] = 0.90) was reduced to a mean score of 3.4 (SD = 0.99) after RFA. There was a statistically significant decrease in pain $P < 0.001$. ■ Preoperative pain, ■ Postoperative pain.

attention was paid to ensure the invaded nerve was ablated (Fig. 2).

Discussion

Percutaneous thermal ablation of bone metastases has only developed over the past decade. The safety and effectiveness of RFA for the palliation of painful bone metastases has been demonstrated in two multicenter studies.[9,10] The pathophysiology of bone tumor pain appears to be multifactorial. Proton stimulation of nociceptors as a result of an acidic microenvironment created by increased osteoclast activity and tumor cell lysis is a likely component.[11] Mechanical stress and fracture trigger mechanosensitive sensory fibers.[12] Hyperalgesia and allodynia appear to be caused by tumor and/or macrophage release of nociceptive factors, including bradykinin, adenosine triphosphate, and nerve growth factor.[11,13,14] There may be a neuropathic component from the destruction of distal processes of sensory fibers that innervate tumor replaced mineralized bone and marrow.[14] Because of the complicated nature of bone tumor pain, individual pharmaceutical and radiopharmaceutical interventions are of limited utility. However, RFA may break multiple cancer-pain pathways. In an early feasibility study for RFA treatment of bone pain, it was hypothesized that mechanisms leading to successful analgesia include the ablation of nerves in the periosteum and cortex, decompression of nerves resulting from tumor volume reduction, destruction of cytokine-secreting tumor cells, and inhibition of osteoclast activity.[15] According to a recent report, RFA alone is theorized to reduce pain via local destruction of pain-sensitive nerves, as well as through decreased production of cytokines and growth factors via tumor necrosis.[5,15,16]

Ablation of intercostal nerves may play a role, particularly in eliminating the neuropathic pain component caused by the tumor-induced injury of sensory fibers, but such ablation could also be expected to produce a component of neuropathic pain itself. Given the apparent role of cytokine-induced hyperalgesia and allodynia, RFA denaturation of cytokines and destruction of cytokine-producing tumor cells and macrophages would eliminate a cause of nociceptor excitement and is a likely component of RFA analgesia. At the same time, the destruction of acid-producing osteoclasts and tumor cells with reduction in the acidity of the microenvironment is also a likely component.

There were several limitations to this study. Primarily, the sample size was small, with only 12 participants enrolled. In addition, the patients served as their own control; therefore, there was no randomized placebo control, no patient stratification based on further treatment for NSCLC, and a lack of long term follow-up.

Conclusion

In conclusion, this study demonstrates that RFA for NSCLC rib metastases can be safely performed and achieves a good

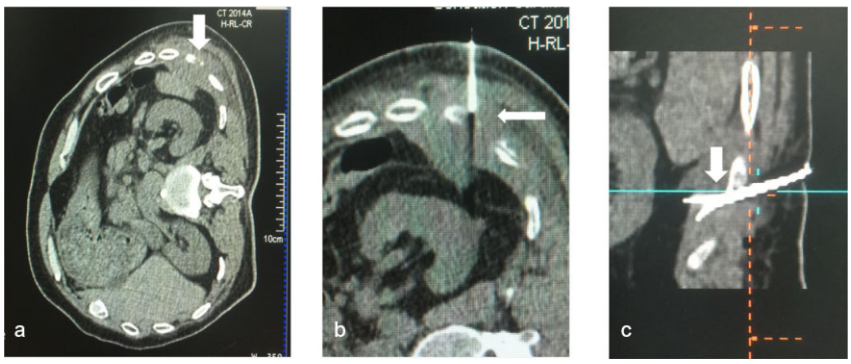

Figure 2 (**a**) A 73-year-old male patient, three years after a pneumonectomy for left upper lobe squamous carcinoma T3N0M0. A pre-procedural computed tomography scan was performed to locate the lesion (34 mm in maximum axis); the metastasis invaded the left 10th rib (arrow). (**b**) The needle tip (arrow) was accurately placed on the lesion to perform a biopsy for gene analysis. (**c**) An RFA needle was placed into the target lesion particularly aimed at the intercostal nerve area (arrow).

palliation effect for pain control. RFA represents a novel treatment option for patients with NSCLC that have painful rib metastasis. Further analysis in a randomized controlled trial is warranted, as well as an investigation of the pain causing-controlling mechanism.

Disclosure

No authors report any conflict of interest.

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