Tract Seeding following Radiofrequency Ablation for Hepatocellular Carcinoma: Prevention, Detection, and Management

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ABSTRACT

Radiofrequency ablation (RFA) has become an important tool in the armamentarium of interventional oncology, particularly in the treatment of primary hepatocellular carcinoma and metastatic tumors. This procedure has proven to be an effective adjunct in treating hepatic tumors as a bridge to liver transplantation, and has a low complication profile. Although adverse events are rare and usually minor, a notable negative outcome is dissemination and implantation of viable tumor cells into the route of applicator entry, or tract seeding. Counter to the goal of treating a patient's cancer, this results in metastatic disease. In this report, the authors present 2 cases of tract seeding after RFA, methods of detection, and means of reducing the incidence of this relatively rare, but significant, complication.

KEYWORDS: Percutaneous ablation, tract seeding, radiofrequency ablation (RFA), hepatocellular carcinoma (HCC)

Percutaneous procedures play an important role in the diagnosis and management of hepatocellular carcinoma (HCC) and hepatic metastases, from ultrasound-guided biopsy to ablative therapies geared toward treatment of tumors. Although the reported complication rates of these procedures are low, a notable ramification is the dispersion of cancer cells from the primary tumor site into the communicating tract between the hepatic parenchyma and the skin surface as the needle is withdrawn, or tract seeding.¹ This can occur by a variety of mechanisms, including deposition of cancer cells adherent to the needle or applicator

itself, or via hematogenous spread from retropulsion of tumor cells into the tract. These mechanisms are promoted by increased intratumoral pressure during ablation therapy.¹ Though relatively rare, tract seeding is significant as it results in metastatic disease instead of tumor therapy, thereby potentially precluding liver transplantation as a feasible treatment option. As such, the prevention, detection, and management of this untoward development are critical. In this report, we present 2 cases of needle tract seeding after RFA, and discuss strategies to avoid, identify, and treat this complication.

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CASE REPORTS

Institutional review board approval is not required for single or paired retrospective case studies at the authors' hospital.

Case 1

A 60-year-old asymptomatic woman with history of chronic hepatitis B presented to hepatology clinic after discovery of a 2.6 cm mass in the right hepatic lobe on screening computed tomography (CT). Her AFP level was 4.5 ng/mL. Multiphase contrast-enhanced CT scan

showed a 3.1×2.5 cm liver mass spanning segments 6 and 7, which demonstrated arterial phase enhancement and portal venous phase washout characteristic of HCC (Fig. 1A). Four days after presentation, the patient's history and imaging findings were discussed at a multidisciplinary conference involving interventional radiology, hepatology, medical oncology, and transplant surgery. Collaboratively, a decision was made to proceed with percutaneous biopsy for diagnostic confirmation of HCC followed by treatment with image-guided percutaneous RFA for definitive therapy and bridging to transplantation.

Figure 1 A 60-year-old woman with solitary hepatocellular carcinoma. Contrast-enhanced CT image (A) shows hypervascular segment 6/7 mass (arrowhead). Ultrasound image (B) during percutaneous RFA shows multi-tined expandable electrode within hypoechoic tumor (arrowheads). Six-week follow-up CT scan (C) demonstrates complete imaging response (arrowhead). Four-month follow-up CT scan (D) reveals minute nodule in subcutaneous tissues (arrowhead). Nodule (arrowhead) enlargement evident on eight-month follow-up CT scan (E). CT scan (F) performed 4 months after surgical resection shows no evidence of malignancy.

After informed consent was obtained, intravenous moderate sedation was provided, and the hypoechoic right lobe edge tumor was identified by ultrasound. Percutaneous liver biopsy was performed using an 18-gauge (18G) BioPince needle (Angiotech, Vancouver, British Columbia, Canada) to obtain 3 core samples. On-site pathology staff examined frozen sections and confirmed the presence of moderately differentiated HCC. Subsequently, percutaneous ablation was pursued. A 14G Rita Talon RFA probe (AngioDynamics Inc., Queensbury, NY) was advanced into the tumor under ultrasound guidance, with tine deployment to 4 cm (Fig. 1B). A 9-minute ablation was performed according to manufacturer protocol, followed by liver parenchymal tract ablation. The patient tolerated the procedure, and her immediate postprocedural course was significant only for low-grade reactive fevers several days afterwards.

After ablation therapy, the patient underwent surveillance CT imaging. A study obtained 6 weeks posttherapy showed favorable treatment response with complete tumor necrosis without contrast enhancement to suggest residual or recurrent disease (Fig. 1C). Follow-up imaging performed 4 months postprocedure again showed complete tumor necrosis, but demonstrated a tiny subcutaneous nodule along the ablation tract (Fig. 1D). Eight months after ablation, imaging revealed continued complete tumor necrosis, but showed interval enlargement of the enhancing subcutaneous nodule located near the intercostal space between the eighth and ninth ribs (Fig. 1E). Findings were deemed consistent with metastatic disease resulting from needle tract seeding. The case was again reviewed in a multidisciplinary setting, and the decision was made to proceed with curative surgical resection for treatment of the metastatic nodule. One week later, the patient underwent uneventful partial hepatectomy with resection of the right lobe and excision of the subcutaneous nodule. Postsurgical CT scan showed no evidence of recurrent disease 4 months after resection (Fig. 1F). At present, the patient remains alive without recurrent disease 23 months after initial diagnosis.

Case 2

A 53-year-old man presented to the liver clinic for management of previously diagnosed hepatitis C and well-compensated liver cirrhosis. A screening ultrasound demonstrated a 2.0 cm rounded hypoechoic mass in the anterosuperior right lobe, and follow-up multiphase contrast-enhanced CT scan showed a segment 8 arterial phase enhancing lesion that demonstrated portal venous phase washout (Fig. 2A). Ultrasound-guided biopsy showed moderately differentiated HCC, and the patient's AFP level was 2.7 ng/mL. A multidisciplinary management approach led to consensus opinion to

pursue RFA followed by possible large wedge resection and transplant work-up. A whole body bone scan and chest CT did not reveal metastatic disease.

For ablation, informed consent was obtained and the patient was placed in the right anterior oblique position. Under intravenous moderate sedation, ultrasound guidance was employed to advance a 14G RITA Talon RFA probe (AngioDynamics Inc.) into the tumor. The tines were deployed to 3.5 cm and a 7-minute ablation was performed at 105°F (Fig. 2B). The tines were withdrawn and repositioned to establish a second overlapping ablation zone to achieve appropriate margin. Finally, the RFA applicator was withdrawn and the tract ablated.

A 1-month postablation follow-up CT showed favorable treatment response with complete tumor necrosis without contrast enhancement to suggest residual or recurrent disease. No new arterial enhancing lesions were identified. The patient was subsequently lost to follow-up for over 14 months, with his only symptom in that interval being weight loss of ~10 pounds. His next CT was not until 16 months after RFA, and revealed persistent favorable treatment response (Fig. 2C). Due to a series of missed appointments, however, the patient was not seen again until 9 months later. CT performed at that time was notable for new HCC nodules along the rim of the ablated tumor (Fig. 2D). The patient's imaging was reviewed at the weekly multidisciplinary liver conference, and it was agreed to pursue intraarterial therapy with chemoembolization, which was performed uneventfully.

The patient missed his scheduled follow-up CT scan 4 weeks after chemoembolization, but CT performed 3 months later was found to have a new nodule in the chest wall along the previous RFA subcutaneous tract (Fig. 2E), compatible with tract seeding. On physical exam, a chest wall mass was appreciable. At that time, arrangements were made for him to begin sorafenib (Nexavar; Bayer, Leverkusen, Germany) therapy. Five months later, triphasic CT imaging showed progression of metastatic disease with growth of the chest wall metastasis (Fig. 2f), and suggested blood supply to the nodule via the ipsilateral internal mammary artery. The patient's case was again discussed at multidisciplinary conference, and the possibility of bland embolization of the chest wall tumor was raised. The patient was scheduled for the procedure.

After informed consent was obtained, intravenous moderate sedation was provided and the right subclavian and internal mammary arteries were sequentially catheterized using a coaxial 5 Fr angled glide coated catheter and 3 Fr microcatheter. Right internal mammary arteriography revealed perfusion of the hypervascular chest wall metastasis (Figs. 1G and 1H). Embolization of the subcutaneous nodule was then performed using a half vial of 300–500 micron Embospheres (Biosphere; Biosphere

Figure 2 A 53-year-old man with unifocal hepatocellular carcinoma. Contrast-enhanced computed tomography (CT) image (a) reveals hypervascular segment 8 mass (arrowhead). Ultrasound image (B) during percutaneous RFA demonstrates electrode within hypoechoic tumor (arrowheads). Sixteen-month follow-up CT scan (C) shows complete imaging response (arrowhead). Twenty-five month follow-up CT scan (D) reveals new tumor along ablated tumor margin (arrowhead). Twenty-eight month follow-up CT scan (E) demonstrates chest wall nodule (arrowhead), which shows enlargement (arrowhead) on CT scan performed 5 months later (F). Images (G,H) from right internal mammary (white arrowhead) arteriogram reveal vascular supply to chest wall nodule (black arrowhead).

Medical, Rockland, MA) with subsequent abolishment of the vascular blush. The patient tolerated the procedure well and was discharged home the following day. He has since been lost to imaging follow-up.

DISCUSSION

Tract seeding with viable tumor cells complicates roughly 0.2–2.8% of RFA procedures as reported in a large meta-analysis² and smaller studies,³ though is rarely as high as 12.5% in one small series of 32 patients.⁴ Incidence reporting may underestimate the actual frequency of seeding, however, depending on surveillance methods and interval of follow-up. In a prospective database of RFA cases, the average time of development for neoplastic seeding was 16 months.⁵ The most common locations reported were the subcutaneous tissues and peritoneal cavity. Others have noted viable tumor cell deposition and progression within the musculature¹ and ribs.⁶ At our institution, we have had only 2 tract seeding events among more than 100 percutaneous liver RFA procedures (<2% incidence) performed over a 4-year period between 2006–2010.

Risk factors for tract seeding after liver RFA include subcapsular tumor location, primary HCC, poorly differentiated carcinoma, multiple needle insertions, and elevated α fetoprotein (AFP) level.^{5,7} Deep tumors are also reported as a risk factor in a large multicenter review of Italian hospitals.⁸ Needle size has been suggested as a contributing factor to the development of neoplastic seeding as well, with a doubling of needle caliber corresponding to a 60-fold increase in dissemination along the entry tract.⁹ In the cases presented herein, risk factors included concurrent multiple-pass percutaneous biopsy of the tumor with ablation in the first case, and subcapsular location in the second patient. The hazard of needle tract seeding can be minimized by meticulous technique, minimization of needle probe repositioning, and ablation of the tract upon needle withdrawal, which concomitantly obliterates deposited tumor cells and confers the additional benefit of coagulation.⁸ It is difficult to ablate the needle tract of subcapsular tumors approached from an orthogonal direction,⁹ as proximity to the abdominal wall may result in skin burns.⁴ Approach from an oblique angle may reduce tract seeding while simultaneously permitting adequate tract ablation.¹⁰ In a series employing this technique in 63 patients with subcapsular tumors, none developed tract seeding.¹¹

Early detection of tract implants is essential, as patients with tract seeding do not have any reduction in survival if treated appropriately.⁶ Multiphase CT scan is the preferred method for detecting occurrence of needle tract seeding, which is identified by characteristic patterns of enhancement of nodules in the trajectory of the RFA probe.¹ Alternatively, surveillance ultrasound can

assist in diagnosis. Typical ultrasound findings include hypoechoic nodules with central, irregular internal vascularity demonstrating turbulent flow on Doppler images.⁶ Both modalities can assess infiltration and extent of tumor involvement, though CT is favored in this respect.

Maintenance of follow-up is important to assess for the development of needle tract seeding, and as seeded tumors may grow slowly, a long period of follow-up is recommended to assess the possibility of this complication.¹² Tumor doubling times are highly variable, resulting in a wide range of treatment-to-implantation intervals in the literature.¹ In the 2 cases presented herein, tract metastases grew after 4 and 28 months after ablation, respectively. Notably, at our institution, serial tumor marker levels are used in conjunction with imaging to monitor for tumor recurrence in patients with AFP-producing neoplasms.

Once occurrence is identified, a variety of methods can be used to treat tumors within the needle tract. Surgical excision of the affected chest wall, as pursued in the first case, is frequently employed to remove implanted satellite tumors. This method has the benefit of pathological assessment of excision margins, and may be curative for isolated lesions. Other treatment strategies utilized in treatment of HCC, such as embolization with or without chemotherapeutic agents, can also be applied to the treatment of cancerous needle tract nodules,¹³ particularly if curative resection is not possible due to the presence of multifocal disease. Intraarterial therapy was selected in the second case presented herein due to tumor blood supply from the internal mammary artery visualized on triphasic CT imaging. As a precaution, care should be taken to avoid non-target therapy administration if transarterial therapy of tract nodules is pursued, as delivery of chemotherapeutic or radioactive materials to the subcutaneous tissues may result in complications of tissue irritation or inflammation. Repeat RFA can be attempted for lesions in cases that are not superficial, as there is risk of skin burn in shallow tumors.^{3,14} Finally, external beam radiation directed at tissue implants has been reported.¹⁵

CONCLUSION

Although RFA has proven to be a valuable adjunctive therapy in the treatment of unresectable hepatic neoplastic disease, it is rarely complicated by tract seeding as viable tumor cells are implanted along the route of needle entry. To reduce the incidence of this ramification, it is recommended to use oblique approaches to subcapsular tumors, minimize the number of needle insertions, and ablate the needle tract upon exit. Long-term surveillance follow-up is recommended, as implanted tumors may take months or years to develop. A variety of avenues of treatment, ranging from surgical

resection to less-invasive embolization procedures, may be explored to treat disseminated tumors of the body wall. Though tract seeding can have significant negative impact on tumor burden and transplant candidacy, the rarity of this complication ensures that RFA remains a feasible implement in treatment of primary or metastatic liver tumors. With meticulous technique and operator awareness of potentially exacerbating risk factors, this uncommon, but important complication can be prevented.

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