

A Case of needle-tract implantation of hepatocellular carcinoma in the ovary after radiofrequency ablation

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Radiofrequency ablation (RFA), a local ablative modality, is gaining acceptance for the treatment of liver malignancies. Despite a relatively low complication rate, tumor seeding resulting from RFA in hepatocellular carcinoma (HCC) treatment can occur. A 44-year-old woman was diagnosed with HCC. Spiral computed tomography (CT) revealed a 2.3 × 2.0-cm mass in the S5 segment, which was treated with RFA on May, 2005. Follow-up imaging, performed at 6-month intervals after RFA, showed complete tumor necrosis. In October 2009, CT revealed a heterogeneous mass, 5.7 cm in diameter, in the right ovary. Since the lesion was limited to the right ovary without evidence of spread, bilateral salpingo-oophorectomy was performed. Histopathology indicated that the metastatic spread from the HCC to the ovary was positive for hepatocyte-specific antigen on immunohistochemistry. The ovary is a rare site for HCC metastasis. Moreover, needle tract implantation of HCC in the ovary is very rare.

Key Words: Hepatocellular carcinoma, Metastasis, Neoplasm seeding, Radiofrequency ablation

Radiofrequency ablation (RFA), one of several local ablative modalities gaining acceptance in the treatment of liver malignancies, is based on the induction of coagulative necrosis by delivering electrical energy to tissue using a shielded needle electrode.^{1,2} Though uncommon, complications may result from the percutaneous application of RFA, including tumor seeding associated with the needle tract.³ The seeding risk after percutaneous RFA for hepatocellular carcinoma (HCC) is approximately 0.6%.⁴ In general, the rate of tumor seeding resulting from RFA for HCC is 0%-2.8%.⁴⁻¹¹ In Korea,

omental and skin metastases,^{12,13} along the needle tract have been reported after RFA of HCC. However, tumor implantation in the ovaries after percutaneous RFA of HCC is rarely reported.¹⁶ We describe the first reported case of needle tract implantation of HCC in the ovary after percutaneous RFA.

CASE

A 44-year-old woman with a 20-year history of

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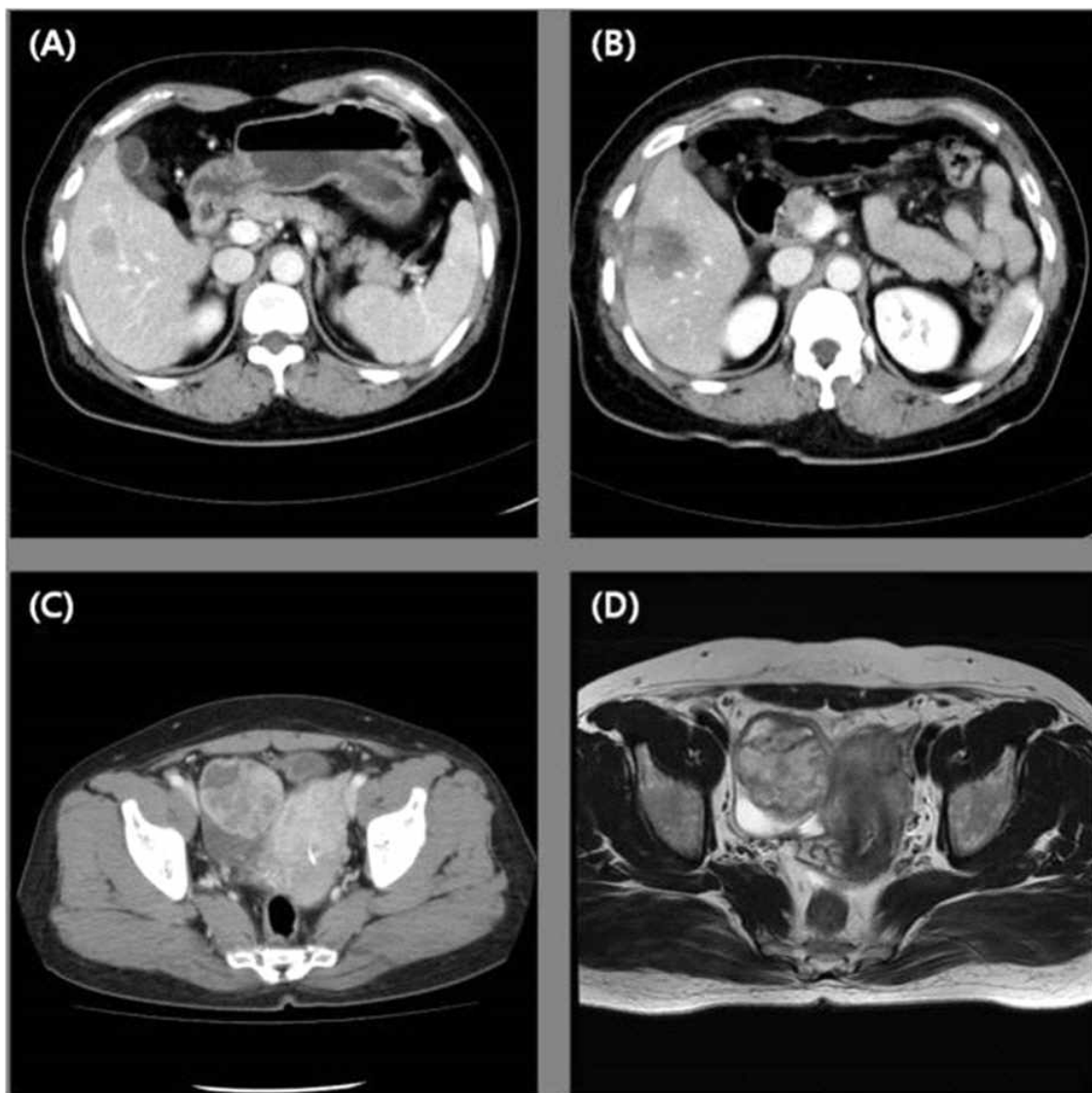


Fig.1. (A) Abdominopelvic computed tomography (CT) shows a low- density 2.3 cm mass (before radiofrequency ablation (RFA). (B) low-density lesion on the portal phase in S5 of the liver (post RFA). (C) Abdominopelvic CT reveals a 5.7 cm heterogeneous mass. (D) T2-weighted magnetic resonance image shows a high signal intensity mass in right ovary.

hepatitis B was diagnosed with HCC upon her half a year or annual physical examination. Spiral computed tomography (CT) revealed a 2.3×2.0 -cm mass in the S5 segment (Fig. 1A). Diagnostic testing revealed a 2.8 ng/mL (range, 0–20.0 ng/mL) serum alpha-fetoprotein (AFP), 71 m AU/mL (range, normal values: 0–40 mAU/mL) serum prothrombin induced by vitamin K absence or antagonist-II, and

4.5 g/dL (range, 3.8–5.2 g/dL) albumin. Hepatitis B viral DNA was present at < 0.5 pg/mL. Hepatitis B surface antigen (HBsAg), but not hepatitis B e antigen (HBeAg), was detected. Antibodies against HBsAg, HBeAg, and hepatitis B core antigen were not detected. Hepatic function was classified as Child-Pugh class A. Following written informed consent, Patients do not want surgery, RFA was

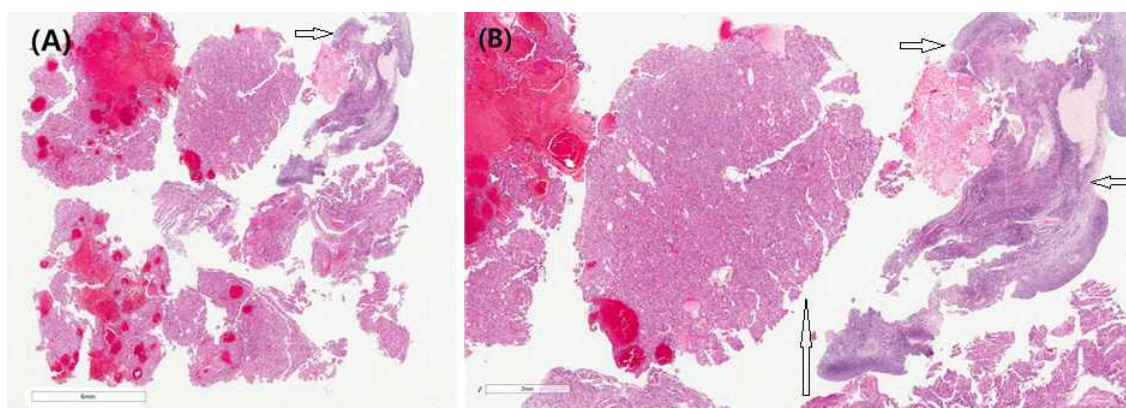


Fig. 2. (A) Tissue from ovarian mass (Hematoxylin and Eosin Staining (H&E) stain, x2). The ovarian mass compose of fragmented ovarian cortex, and tumor mass with hemorrhage. (B) Mid-magnification (H&E stain, x20). The ovarian mass is of hepatocellular carcinoma with hemorrhage. (Long arrow: HCC ,short arrow: Ovary)

performed on May 24, and 2005. The patient was sedated intravenously with 24 mg midazolam hydrochloride (Roche, Fontenaysous-Bois, France) and 100 mg fentanyl citrate (Hana Pharm. Co., Hwasung, Korea). Local analgesia with 2% lidocaine (Huons, Hwaseong) was administered in combination with intravenous analgesia. RFA was performed with a 200-W generator (Radionics, Burlington, MA, USA) and a single (with 3.0 cm tip) internally cooled electrode (Radionics, Burlington) with impedance-controlled pulsed current. The patient tolerated the procedure and experienced only a low-grade fever several days post-treatment. After ablation therapy, surveillance CT imaging showed a low-density lesion on the portal phase in the S5 segment (Fig. 1B). Follow-up imaging was performed at 6-month intervals after RFA and showed complete tumor necrosis. Later, CT was performed every 6-months, there were no specific finding. In September 2009, abdominopelvic CT revealed a 5.7-cm heterogeneous mass in the right ovary

(Fig. 1C). We performed positron emission tomography-computed tomography (PET-CT) and magnetic resonance imaging (MRI). T2-weighted MRI showed a mass with high signal intensity limited to the right ovary (Fig. 1D). Several studies, including PET-CT and MRI, showed that the lesion was limited to the right ovary and no evidence of tumor spread.

Accordingly, bilateral salpingo-oophorectomy was performed in October 2009. During the procedure, there was no evidence of metastases in the liver, left ovary, or peritoneum. The procedure was well tolerated, and the patient was discharged after a few days. The resected mass was 7 × 6 cm. The ovarian tissue was attached to a grayish granular mass-like lesion. Histopathology indicated that the ovarian mass was derived from HCC and composed of fragmented ovarian cortex and tumor mass with hemorrhaging (Fig. 2). A thick trabecular and occasionally pseudo-glandular architecture, clear cell type, and a nuclear grade of 2/3 (common/worst)

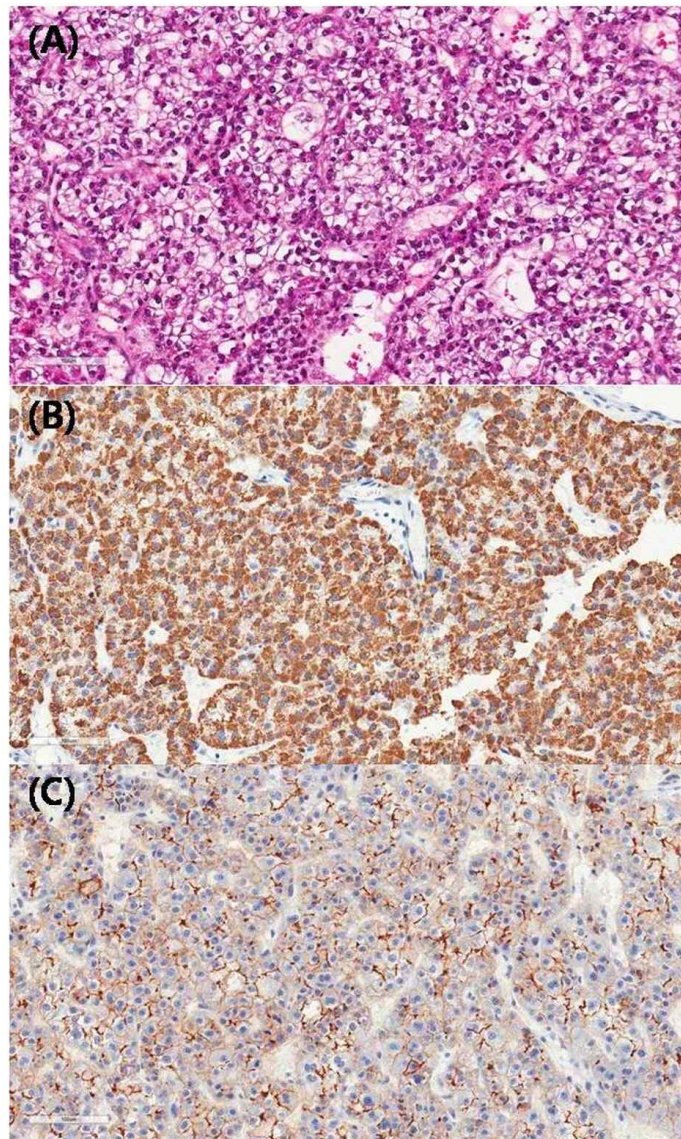


Fig. 3. Higher magnification (A, H&E; B, hepatocyte specific antigen immunohistochemistry (HSA) ; C, Carcinoembryonic Antigen immunohistochemistry (CEA), x200).

(A) The hepatocellular carcinoma metastatic to liver shows thick trabecular and occasionally pseudo glandular architecture, clear cell type and nuclear grade 2/3 (common/worst).

(B) Representing clear HSA (+) and (C) bile canalicular type of CEA.

were visible on higher magnification (Fig. 3A). Immunohistochemistry showed clear hepatocyte-specific antigen (HSA) positivity (Fig. 3B) and carcinoembryonic antigen (CEA)-positive bile canalicular structures (Fig. 3C). The patient is currently alive 4.5 years after resection, with no evidence of recurrence.

DISCUSSION

RFA is one of several loco-regional thermal ablation therapies for unresectable liver tumors. RFA kills both cancerous and normal cells by application of a heat-generating rapidly alternating radio-frequency current through probes inserted into the

tumor. Recently, RFA has been proposed as a promising alternative to conventional percutaneous ethanol injection and has been shown to be more effective locally.¹⁴

Complications are reported in approximately 7% of patients undergoing RFA of liver tumors, compared to up to 22% of patients undergoing open liver resection.¹⁵ The most common complications of percutaneous RFA are abdominal hemorrhaging, infection (abscess), biliary tract damage, and ground-pad burns. Despite a relatively low complication rate, the percutaneous application of RFA carries a potential risk of needle tract seeding. The use of RFA was recently questioned following the reported occurrence of neoplastic seeding in 12.5% of patients after such treatment for HCC.³ However, the overall rates of tumor seeding resulting from RFA for HCC are 0%–2.8%.^{4–11} Though the most common locations reported were the subcutaneous tissues and the peritoneal cavity, others have noted viable tumor cell deposition and progression within the musculature and ribs.

HCC rarely metastasizes to the ovary and needle tract implantation of HCC into the ovaries is also very rare.¹⁶ Metastatic HCC should be distinguished from a hepatoid yolk sac tumor and primary hepatoid carcinoma of the ovary. The former usually occur in women of reproductive age with germ cell neoplastic components or gonadal dysgenesis. Development of hepatoid carcinomas of the ovary is promoted by hepatoid carcinomas outside the ovary and tumor growth on the ovary surface. These carcinomas are usually metastases from the stom-

ach and leave a lesion on the surface. As hepatoid carcinoma and HCC cannot be differentiated purely by morphology, immunohistochemical characterization would be extremely helpful. The proportion of hepatoid carcinomas positive for CEA is high among both gastric (75%) and non-gastric hepatoid carcinomas (75%–100%). However, there are also CEA-positive HCCs and other metastatic liver adenocarcinomas arising from the colon, stomach, and pancreas. The proportions of hepatoid carcinomas positive for the epithelial markers AE1/AE3, CK18, and CK19 (92.3%, 100%, and 100%, respectively) are high, but the proportions of CK20 and CK7 positivity are low (25% and 15.4%, respectively).

In the case presented here, the patient had a history of HCC with no evidence of hepatoid carcinomas in other abdominal organs. Pathology suggested a diagnosis of HCC without any features of hepatoid yolk sac tumors, such as germ cells or gonadal dysgenesis. The HCC was positive for HSA and negative for CK19. We concluded that the ovarian mass developed not due to hematogenous spread but from needle tract implantation. There are three reasons for this. First, the mass was observed on the ovary surface and histopathology suggested that cancer cells invaded the ovary from the surface. Second, the lesion was limited to the right ovary without evidence of spread. Finally, the patient is currently alive 4.5 years after resection, with no evidence of recurrence.

Several mechanisms may contribute to needle tract implantation. Viable tumor cells may adhere

to the electrode during retraction. They may also be carried into the tract with slight bleeding. Alternatively, cells may be forced into the tract by the sudden intratumoral hyper pressure frequently encountered during RFA. Finally, cells may be washed in when saline is injected into the tumor before or during RFA.⁶

Llovet et al.³ found that tumor seeding was significantly associated with subcapsular tumor location, poor differentiation, and high baseline AFP levels. They concluded that RFA with a cooled-tip needle for HCC is associated with a high risk of neoplastic seeding (particularly in patients with the identified risk factors) and that this must be considered when selecting curative treatments for HCC or adjuvant therapies before liver transplantation. If this risk factor is present, treatment should proceed with caution. Several studies showed that risk can be minimized by meticulous technique, minimization of needle probe repositioning, and tract ablation upon needle withdrawal, which concomitantly obliterates deposited tumor cells and confers the additional benefit of coagulation.⁷ It is difficult to ablate the needle tract of subcapsular tumors approached from an orthogonal direction, as proximity to the abdominal wall may result in skin burns.³ Approach from an oblique angle may reduce tract seeding while simultaneously permitting adequate tract ablation.

Needle tract implantation may also occur in subcutaneous tissue, the chest wall, or muscle after percutaneous RFA. The mean interval of needle tract implantation after percutaneous RFA was re-

ported as 16 months. However, in this case, needle tract implantation of HCC into the ovary was observed after 50 months without evidence of liver cancer recurrence.

In conclusion, we report the first case of needle tract implantation of HCC in the ovary after percutaneous RFA. Though there has been no recurrence of liver cancer after percutaneous RFA, other organs should also be carefully examined during follow-up for signs of metastasis or needle track implantation, which may become evident even long after treatment. This is especially important for patients with certain risk factors.

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