CLINICAL NOTE

Cholangitis and multiple liver abscesses after percutaneous ethanol injection (PEI) for recurrent hepatocellular carcinoma (HCC)

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ABSTRACT

Percutaneous ablation procedures are minimally invasive treatments for unresectable early stage hepatocellular carcinoma (HCC). These techniques are usually safe, but rare and even fatal complications have been described. We present a fatal result after percutaneous ethanol injection (PEI) for the treatment of a recurrent HCC in a non-cirrhotic liver, with subsequent development of diffuse cholangitis and multiple liver abscesses. Although percutaneous drainage and intensive antibiotic treatment were employed, the patient finally died. We discuss about the etiology and the physiopathology of this rare complication in which the therapeutic options are limited and usually unsuccessful.

Key words: Liver. Hepatocellular carcinoma (HCC). Percutaneous ethanol injection (PEI). Ablative percutaneous therapy. Cholangitis.

INTRODUCTION

Percutaneous ablation procedures (radiofrequency and ethanol injection) are effective and minimally invasive treatments for unresectable early stage hepatocellular carcinoma (HCC). Safety profile of ablation procedures is excellent (1). Nevertheless, major complications, even with fatal

course, may occur. In this setting, post-ablation infections such as cholangitis and liver abscess are rare but potentially severe complications (2). It has been previously estimated that an infectious complication could be present up to 1.5 % of PEI sessions (3).

CASE REPORT

We report the case of a 76-year-old male, with a past history of ischemic arterial coronary, peripheral, and carotid disease, which underwent surgery for coronary by-pass, appendectomy, and partial gastrectomy with Billroth II type gastroenteroanastomosis because of a perforated duodenal ulcer. At 1995, he was diagnosed of a 36 mm in diameter single HCC at segment VI in a non-cirrhotic liver, and segmentectomy was performed. Four years later, the patient underwent further surgery (right hepatectomy) because of 50 mm in diameter single HCC recurrence. After 10 years of follow-up, two nodules less than 30 mm in diameter at segments III and IV, with typical dynamic HCC pattern in magnetic resonance imaging (MRI), were detected. Percutaneous radiofrequency ablation of the lesion localized at segment IV, and percutaneous ethanol injection (PEI) of the subcapsular nodule localized at segment III were made without complications. Contrast-enhanced computed tomography (CT) four weeks after ablation showed great areas of necrosis in both lesions, but viable neoplastic tissue remained. Two additional cycles of PEI were performed, but no complete response was achieved.

A few days after the third session of the last cycle of PEI, the patient was admitted at hospital because of fever, jaundice and right upper quadrant abdominal pain. Laboratory tests revealed the presence of increased levels of transaminases, cholestasis, and moderate hyperbilirubinemia (total bilirubin 8.4 mg/dL, conjugated bilirubin 6.3 mg/dL, AST 138 UI/L, ALT 213 UI/L, GGT 486 UI/L, alkaline phos-

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phatases 1,082 UI/L), elevated white blood cells count (16,850/ μ L), elevation of C-reactive protein (11.3 mg/dL), and procalcitonin (2.7 ng/mL). Abdominal contrast-enhanced CT showed a diffuse alteration of the bile ducts compatible with cholangitis, and the presence of several focal liver lesions suggestive of abscesses (Fig. 1A). These findings were confirmed by a liver MRI, which also showed tumor viability of the HCC located at segment IV (Fig. 1B). Magnetic resonance cholangiography excluded the presence of any stenosis in the main bile duct (Fig. 2). Empirical antibiotic therapy was prescribed, which was subsequently modified according to the isolation of *Enterobacter cloacae* in blood cultures. Ultrasound-guided percutaneous aspiration of fluid of the two larger abscesses was performed. The microbiological culture of these samples was negative.

Initial clinical and analytical improvement was observed, but complete resolution of the abscesses was not achieved, and jaundice remained. During the outpatient follow-up, progressive deterioration of the performance status occurred subsequently to recurrence of the cholangitis and the persistence of residual liver abscesses, despite maintenance of the antibiotic treatment. Finally, the patient died 4 months after the ablation procedure.

DISCUSSION

HCC occurs mainly in the context of liver cirrhosis, but it may arise in non-cirrhotic liver in 15-20 % of cases (4). Despite the possibility of application of more aggressive treatment in these patients, the overall and disease-free survival are impaired by a high rate of recurrence (5).

Patients with early stage HCC who are not candidates for surgical treatment or liver transplantation must be evaluated for ablative percutaneous therapy. The most frequent complications of PEI are abdominal pain and self-limited fever (6). Although infrequent, major complications, includ-

ing intraperitoneal hemorrhage, hemobilia, right pleural effusion, portal thrombosis, liver infarction, arterio-portal shunt, pneumothorax, perforation of abdominal organs, neoplastic seeding and shock, have been previously reported (7-10). Infectious complications are rare but potentially severe complications (2), with an estimated incidence up to 1.5 % of PEI sessions (3). Although these infectious complications may be fatal, most of patients recover with antibiotic therapy alone or in combination with percutaneous drainage. Given the fact that the majority of HCC occur on cirrhotic livers the development of the complication reported here could be even more unexpected.

Previous studies have shown that the presence of any biliary abnormality may predispose to infectious complications after percutaneous ablation (2,11). In this setting, the presence of a bilioenteric anastomosis has been strongly correlated with the development of cholangitis and/or liver abscess after PEI (3). In our case, we believe that the morphological changes caused by the previous liver resection surgery may have played a role in the occurrence of post-procedure infectious complication. No other alteration in the bile ducts was observed by the magnetic resonance cholangiography in our case.

The physiopathology of abscess development after PEI is not clearly established. Bacterial contamination of ablated necrotic lesions leading to abscess formation is one of the suspected hypothesis. The bacteria can be inoculated from the outside during the percutaneous ablative procedure, but the enteric bacterial translocation seems to be more frequent (i.e., *Escherichia coli*, *Enterococcus spp*, *Enterobacter cloacae*). Direct damage induced by ethanol on the bile duct can also cause chemical cholangitis, which subsequently leads to the formation of the liver abscesses. In the presented case the precipitating factor could be the development of diffuse chemical cholangitis caused by ethanol, or ischemic injury secondary to direct injection into a left hepatic artery branch, with subsequent enteric bacterial translocation to the necrotic tissue that led to the abscess formation. In this setting, several studies have provided conflicting results

Fig. 1. Radiological findings after percutaneous ethanol injection showing diffuse cholangitis and multiple liver abscesses. A. Contrast-enhanced coronal reformatted CT image acquired in the portal phase evidences status post-right hepatectomy and the presence of multiple focal hypodense lesions that mainly represents abscess. B. Coronal magnetic resonance cholangiography image demonstrates multiple cystic lesions in liver parenchyma corresponding to foci of abscess. Biliary ducts show a normal caliber (CT: Computed tomography).

Fig. 2. Magnetic resonance processed images. A. Contrast-enhanced coronal reformatted 3D gradient echo T1-weighted MR image acquired in the portal phase evidences multiple abscesses. B. Fused image superimposing axial T2-weighted MR image and color-coded map derived from high-b-value diffusion-weighted image clearly demonstrates restricted water diffusion in both hepatocellular carcinoma and abscesses (MR: Magnetic resonance).

regarding to antibiotic prophylaxis previously to perform percutaneous ablative therapies (12). Nowadays, prophylactic administration of antibiotics previously or following a percutaneous ablation procedure seems to have not a significant impact on the post-ablation efficacy or on incidence of infectious complications (13).

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