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Subcutaneous Metastasis Following Percutaneous Ethanol Injection Therapy for Hepatocellular Carcinoma

Sir,

Percutaneous ethanol injection therapy (PEIT) was first reported by Sugiura et al. in 1983 (1) and has been widely used for the treatment of hepatocellular carcinomas (HCC) (2, 3). Recently, PEIT has also been performed in the treatment of other tumors (4–6). Histopathologic examinations of tumors after therapy have revealed that PEIT can completely destroy the tumor in most cases (7).

Minor complications of PEIT, such as pain, fever and transient alcohol intoxication, have been reported (2, 3). However, a few reports have described of subcutaneous or pleural needle track seedings of tumor cells after PEIT (8–10). Here we describe two cases of metastatic subcutaneous tumors along the needle track for PEIT.

CASE REPORTS

The characteristics of the two patients are summarized in Table I. Briefly, the first patient, a 72-year-old female, had undergone two sessions of PEIT for three HCCs measuring < 20 mm in diameter, but a subcutaneous nodule was noticed 5 months after performance of PEIT in the epigastric region (Fig. 1a). The tumor, which seemed to develop as a result of needle track seeding, was resected. The pathological findings of the tumor revealed a non-capsuled solid lesion in the lower dermis through fatty tissue, and the lesion consisted of mainly α -fetoprotein (AFP)-positive, moderately differentiated HCC by immunohistochemical examination (Figs. 1b, c).

The second patient, a 69-year-old male, had undergone 10 sessions of PEIT for one HCC measuring 18 × 20 mm in diameter. He noticed a subcutaneous nodule in the epigastric region 2 months after under-

going PEIT. The tumor was resected. The pathological findings revealed a non-capsuled solid lesion in the lower dermis and fatty tissue consisting of moderately differentiated HCC (not shown).

DISCUSSION

The first case of needle track seeding following PEIT for the treatment of HCC was reported by Saito et al. (11) in 1989, in Japan. Since then, there have only been 32 cases, including ours, reported in the literature. In Japan, where PEIT was initially started, 17 cases have been reported. Of note, 28 cases (87.5%) were reported in the past 5 years (1995–1999) after PEIT became a more common procedure.

The clinical features of HCC seeding have been described as solid tumors in the abdominal wall (8, 10), pleural lesion (9), peritoneal lesion (12), intercostal muscle (13), or subcutaneous tissue (10, 11, 13). The incidence of HCC seeding in the subcutaneous tissue after a fine-needle biopsy is below 0.005% (14). Di Stasi et al. (15) reported that tumoral seeding occurred following PEIT in 0.66% of the patients. Saito et al. (11) described the tumor as a black or brown subcutaneous mass protruding from the liver. The interval for the emergence of the tumor following PEIT ranges from 2 months to 4 years (mean 16 months). Our patients developed brown-colored subcutaneous nodules in the epigastric region. The mechanism of needle track seeding is considered to be complex, and several causes have been discussed. The diameter and type of needle, the number of needle passes, extent of tumor aggressiveness, and the immune status of the patient are all considered (10). However, according to the literature, patients developing seeding show no significant clinical differences from the other non-seeding patients. Many reports emphasize the correct therapeutic application and good technique of PEIT. Similarly, in our two patients, PEIT was carried out correctly by doctors experienced in PEIT. Therefore, needle track seeding can occur indiscriminately and accidentally, although the probability seems small.

The prognosis for needle track seeding is usually not bad, which is the same as that for the other non-seeding patients. The systemic condition of the patient is most important. The

Table I. Clinical features of two patients with subcutaneous nodules after performing percutaneous ethanol injection therapy (PEIT)

Age/ gender	HCV	HBs	Child	AFP	PEIT	Interval (months)
72/F	+	–	A	29	Twice	5
69/M	+	–	A	50	10 times	2

HCV = hepatitis C virus; HBs = hepatitis B virus; Child = the stage of liver cirrhosis (A = good, B = moderate, C = poor); AFP: α -fetoprotein.

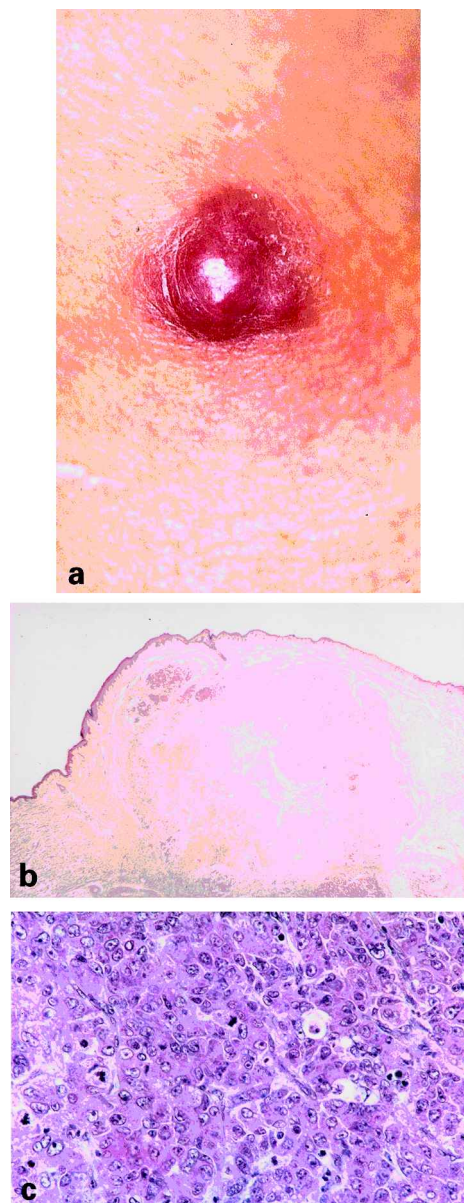


Fig. 1. Clinical and histopathological appearance of the skin tumor in the epigastric region (the first case). (a) A brownish, small and solid nodule in the epigastric area and (b) an excisional biopsy specimen showing a solitary hepatocellular nodule in the subcutaneous tissue (hematoxylin and eosin (HE); original magnification, $\times 10$). (c) α -Fetoprotein staining showing a well-differentiated hepatocellular carcinoma (original magnification, $\times 400$).

implanted tumors are mostly well or moderately differentiated and rarely invade. Thus, resection of the metastatic tumor will be very effective and will also help to distinguish between needle track seeding and a hematoma.

In summary, when subcutaneous tumors adjacent to the place of the PEIT are found, needle track seeding should be taken into consideration, and an excisional biopsy of the tumor is desirable for its diagnosis and therapy.

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