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NOTE

CT-Guided Acetic Acid Injection Therapy for Aldosterone-Producing Adrenocortical Adenoma: A Preliminary Report of Three Cases

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Abstract. We reported the preliminary outcomes of CT-guided percutaneous injection therapy for aldosterone-producing adrenocortical adenoma (APA). Five sessions of injection therapy, 4 percutaneous acetic acid injections (PAI) and 1 percutaneous ethanol injection (PEI) were performed in 3 patients with APA. A small amount of acetic acid or ethanol solution was injected via a needle placed precisely inside the tumor. The procedure was frequently monitored by repetitive CT scanning. The follow-up period ranged from 5 to 27 months.

After the treatment, hypertension was normalized or controlled by a low dose of conventional anti-hypertensive drug. In 2 of 3 cases the plasma aldosterone levels were normalized. Although temporary symptoms of alcoholic intoxication were observed in the single session of PEI, the 4 sessions of PAI were associated with no adverse symptoms or complications.

Although this study covers only short-term results in 3 patients, CT-guided PAI appears to be a safe and effective treatment and may be a promising alternative as a simple and far less invasive therapy for APA.

Key words: Percutaneous injection, Acetic acid, Aldosteronoma

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PERCUTANEOUS ethanol injection (PEI) has been commonly used as a simple and effective treatment for hepatocellular carcinomas measuring 3 cm or less in diameter [1–2]. Recently PEI has also been employed for the treatment of endocrine tumors of the thyroid and parathyroid [3–5]. In addition, the use of a high concentration of acetic acid, instead of ethanol, has achieved safer and more effective results [6–7].

With respect to percutaneous injection therapy for adrenocortical solid tumors, however, only 1 case with aldosterone-producing adenoma (APA) has ever been reported to be successfully treated by PEI in spite of associated massive leakage [8]. Here we present 3 cases with APA who have undergone computed tomography(CT)-guided percutaneous acetic acid injection (PAI) therapy.

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Subjects and Methods

Patients

Three patients with APA underwent the treatment between March 1997 and March 1999. They featured typical primary aldosteronism including hypertension, increased plasma aldosterone, reduced plasma renin and hypokalemia (Table 1). Also CT scan revealed a tumor of the adrenal gland, and an ^{131}I-adosterol scintiscan showed unilaterally increased

Table 1. Patient Characteristics

Case No.	Age, Sex	plasma aldosterone (pg/ml)	plasma renin (pg/ ml)	serum kalium (mEq/l)	tumor site, diameter (mm)
1	56, F	630	2.4*	2.5*	left, 20
2	37, M	770	<2.0*	3.0*	right, 19
3	45, M	480	2.1*	2.7*	right, 20
		(normal range: 30–180)	(normal range: 2.5–21.4)		

* The values of plasma renin and serum kalium were determined before the administration of spironolactone.

uptake, which was consistent with the tumor site. Before the treatment sessions, hypertension, hypokalemia and reduced plasma renin level had been normalized by spironolactone.

Methods

The patient was placed prone on the bed of a CT scanner. The scout scan confirmed the location of tumor, the appropriate puncture point on the skin, which should be positioned vertically above the tumor, and the distance from the puncture point to the tumor. We used a 21-gauge PEI puncture needle with 3 pores 4 mm from the tip (Hakko Shoji Co., Tokyo). This is the same type of needle used for treatment of hepatocellular carcinoma. The needle was inserted along the puncture line toward the adenoma with frequent CT scanning. The monitoring was repeated 4 to 6 times until we delivered the needle tip precisely inside the tumor. Puncturing adjacent vessels and penetrating the tumor with the needle were meticulously avoided. Then, an aliquot of 0.5 ml of 36% or 50% acetic acid mixed with approximately 10% contrast medium was injected and repeated. After every injection, the absence of leakage outside the tumor or into the vascular system was confirmed by CT scan. The patients were monitored carefully overnight after the treatment procedures.

This study was approved by the local ethical committee and conducted in accordance with the Helsinki Declaration. An informed written consent was obtained from the patient.

Results

Case 1: A 56-year-old woman received injection of

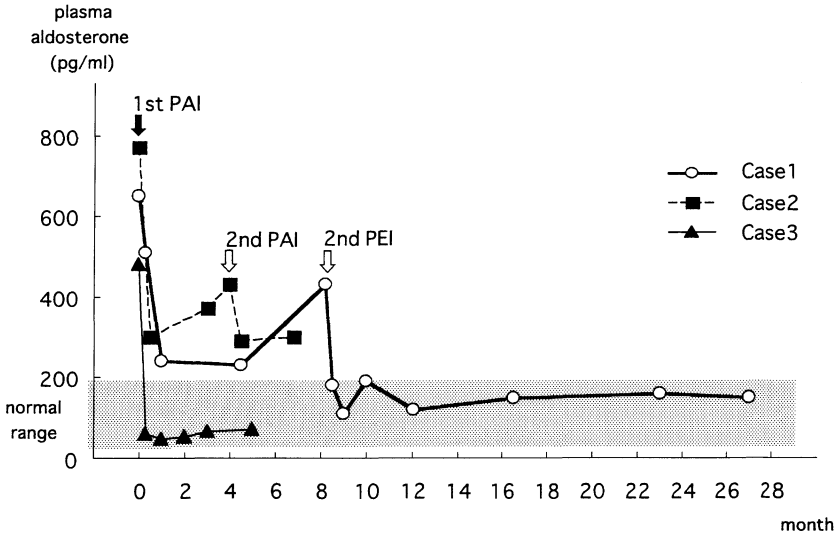

Fig. 1. Profiles of plasma aldosterone level. PAI: percutaneous acetic acid injection. PEI: percutaneous ethanol injection. See the text for details of treatment.

1.2 ml of 36% acetic acid in the left adrenal adenoma measuring 20 mm in diameter. The plasma aldosterone level was decreased from 630 pg/ml to 250 pg/ml (Fig. 1). Since the suppression of aldosterone was incomplete and the hormone level was rising steadily, 3.0 ml of pure ethanol was additionally injected 8 months after the first injection. On the second injection, symptoms of acute alcoholic intoxication such as feelings of drunkenness and palpitation transiently appeared. Soon after the treatment, the plasma aldosterone level was normalized, and blood pressure was controlled by a low dose of a Ca^{2+}-channel blocker. Six months after the second injection, CT scan revealed an irregularly diminished tumor with a higher density compared to the untreated APA.

Case 2: A 37-year-old man underwent PAI with 2.0 ml of 50% acetic acid to treat the right adrenal adenoma measuring 19 mm. The plasma aldosterone level was markedly decreased, but it still remained over 300 pg/ml. After the second PAI with 1.2 ml of 50% acetic acid, serum kalium was normalized and blood pressure was controlled by a low dose of anti-hypertensive drug, although the aldosterone level was still incompletely suppressed.

Case 3: A 45-year-old man had 1.5 ml of 50% acetic acid injected into the right adrenal adenoma measuring 20 mm with minimum leakage (Fig. 2). Six days after treatment, the plasma aldosterone level dramatically decreased to 61 pg/ml from the pretreatment level of 480 pg/ml. Blood pressure was also promptly normalized. CT scan showed a reduction of tumor size 3 months after the PAI. No adverse symptoms or complications were observed after the injection treatment.

Discussion

Open adrenalectomy has long been the standard treatment of adrenal tumor. Recently laparoscopic adrenalectomy has been employed for small adrenal lesions as a minimally invasive therapy [9–11]. However, laparoscopic surgery also has several disadvantages; learning the required technical skill is an important issue, and hemorrhages and various complications may develop during the initial induction phase of the treatment [11].

In our study 5 treatment sessions of PAI or PEI were performed in 3 cases with APA. Hypertension was normalized or controlled by a low dose of conventional anti-hypertensive drug in all cases. The plasma aldosterone levels were normalized in 2 of 3 cases after one or two percutaneous procedures (Fig. 1). The remaining one case is awaiting the third session of therapy. In treatment sessions no sporadic hypertensive episodes or complications were observed except for temporary symptoms of alco-

(a) (b) (c) (d)

Fig. 2. CT scan imaging during the PAI in Case 3. (a) The most appropriate insertion point was selected. (b) The needle was inserted and placed precisely within the tumor after repeated CT monitoring. (c) Acetic acid solution containing contrast medium was injected. (d) Total amount of injected 50% acetic acid solution was 1.5 ml.

holic intoxication in a case receiving PEI. CT-guided PAI or PEI appears to be a simple, cost-effective and far less invasive treatment for small, hyper-functioning adrenocortical tumors compared to open surgery and laparoscopic adrenalectomy.

Percutaneous injection of ethanol has been recognized as an alternative therapy for cystic or solid lesions in the liver, endocrine glands and various other organs. The mechanism of action of ethanol would be related to its sclerosing properties, which results in a direct coagulative necrosis and partial or complete vascular thrombosis and occlusion [1–5]. Acetic acid induces swelling in the fibers and promotes dissociation of the intermolecular cross-links of collagen in the tumor tissue owing to its low pH. The sclerosing effect of acetic acid at 15% was equal to or greater than absolute ethanol for hepatocyte necrosis in rats. Consequently, 50% acetic acid would have greater necrotizing effects than ethanol [6–7]. In addition, ethanol is not ideal as the injectable, since it may cause severe and/or persistent alcoholic intoxication due to the delayed metabolism in vivo, especially when directly mis-infused into the blood vessels. Acetic acid is rapidly metabolized in vivo, thus safer than alcohol.

The most important technical point of this therapy would be that the injection volume per shot should be minimized. An excessive dose to achieve complete ablation of tumor must definitely be avoided in a single session, since the therapy could be repeated at appropriate intervals.

A disadvantage of the injection therapy is the lack of histological confirmation of the lesions. However, we have so far experienced a large number of adrenocortical tumors including APA or incidentally discovered adrenal tumors [12–14]. Owing to various advanced diagnostic examinations such as endocrinological survey, CT scan, MRI and scintigraphy, accurate pretreatment diagnosis of APA is now feasible in almost all cases. Malignant lesions should be considered in tumors larger than 4-5 cm in diameter. To our knowledge, no aldosterone-producing cancers smaller than 3 cm have been reported.

While the follow-up period is insufficient in this study, we expect that PAI may be a promising alternative for the treatment of hyper-functioning adrenocortical adenomas in the near future. Further studies incorporating a larger number of patients with longer follow-up period would be mandatory.

Conclusion

Five sessions of CT-guided percutaneous injection therapy (4 PAI and 1 PEI) were performed in 3 patients with APA. The treatment yielded successful short-term effects without any serious complications. PAI is a simple, cost-effective and far less invasive alternative therapy for the management of selected patients with APA.

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