

Treatment of radioiodine-negative bone metastasis from papillary thyroid carcinoma with percutaneous ethanol injection therapy

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A 62-year-old woman with metastatic papillary thyroid carcinoma in the sternum was successfully treated with percutaneous ethanol injection therapy (PEIT) when previous radioiodine therapy and external irradiation were ineffective. The patient tolerated the treatment well and the refractory pain in the anterior chest wall that was alleviated with morphine prior to PEIT completely disappeared. No severe complications were observed. PEIT was performed 4 times (2 times with ultrasound guidance and 2 times with CT guidance). The posttreatment CT scan and ^{201}Tl scintigraphy demonstrated significant decrease in the tumor volume. The serum thyroglobulin level fell to less than one-twentieth of the pretreatment value. It is suggested that PEIT has a value in treating bone metastasis from thyroid carcinoma which do not respond to radioiodine.

Key words: thyroid carcinoma, bone metastasis, radioiodine, percutaneous ethanol injection therapy

INTRODUCTION

ALTHOUGH MOST PATIENTS with differentiated thyroid cancer have a good prognosis, the presence of bone metastasis predicts a poor one.¹⁻⁴ If the tumor could not concentrate radioiodine and if there were bony pain and/or neurological complications, the quality of life of such patients would be miserable.

Recent reports that have suggested the usefulness of percutaneous injection therapy (PEIT) in treating recurrence of thyroid cancer were encouraging.⁵⁻⁷ This is a report on a successful PEIT on a female patient with metastatic bone tumor in the sternum from papillary thyroid carcinoma.

CASE REPORT

The patient was a 62 year old female whose chief complaints were growing tumors in the right neck (that she had

been aware of) and a painful hard mass in the upper anterior chest wall. She had received left thyroid lobectomy (pathology unknown) about 30 years ago. The surgical probe revealed that the neck tumors were metastatic lymph nodes from papillary thyroid carcinoma. The chest wall mass was diagnosed to be bone metastasis in the sternum. Total thyroidectomy and surgical resection of the sternum was proposed to the patient but was refused. Right hemithyroidectomy was performed in September, 1994. It confirmed the incidental existence of a small papillary carcinoma in the right lobe. It was followed by the administration of 5.55 GBq ^{131}I in October, 1994. Whole body and spot scintigrams were obtained by using a gamma camera (Sigma-410S, Ohio Nuclear, USA) equipped with a high energy collimator 6 days after administration. Although the serum TSH level before treatment was high (120.1 $\mu\text{U/ml}$), the tumor showed only partial and equivocal radioiodine uptake on the scintigram (Fig. 1) and further growth. Then external radiotherapy (30 Gy) was added but there was significant change in the tumor volume and the pain persisted. She was given morphine for pain control. Considering the encouraging preliminary results of PEIT in treating recurrent thyroid cancer, we proposed PEIT to the patient as an additional

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Fig. 1 Anterior whole body image 6 days after 5.55 GBq ^{131}I . The radioiodine uptake in the metastatic tumor is poor (arrow).

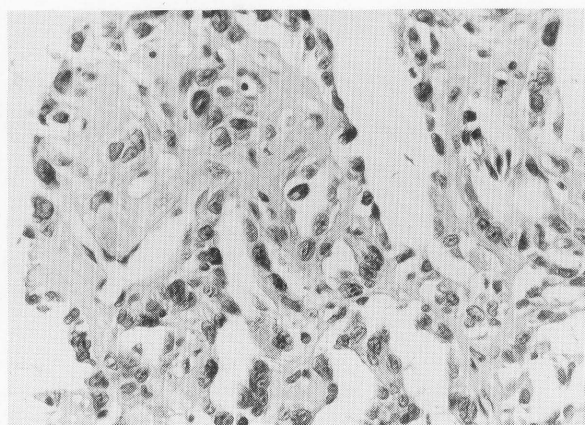


Fig. 2 Microscopic findings of biopsy specimen from metastatic tumor ($\times 400$).

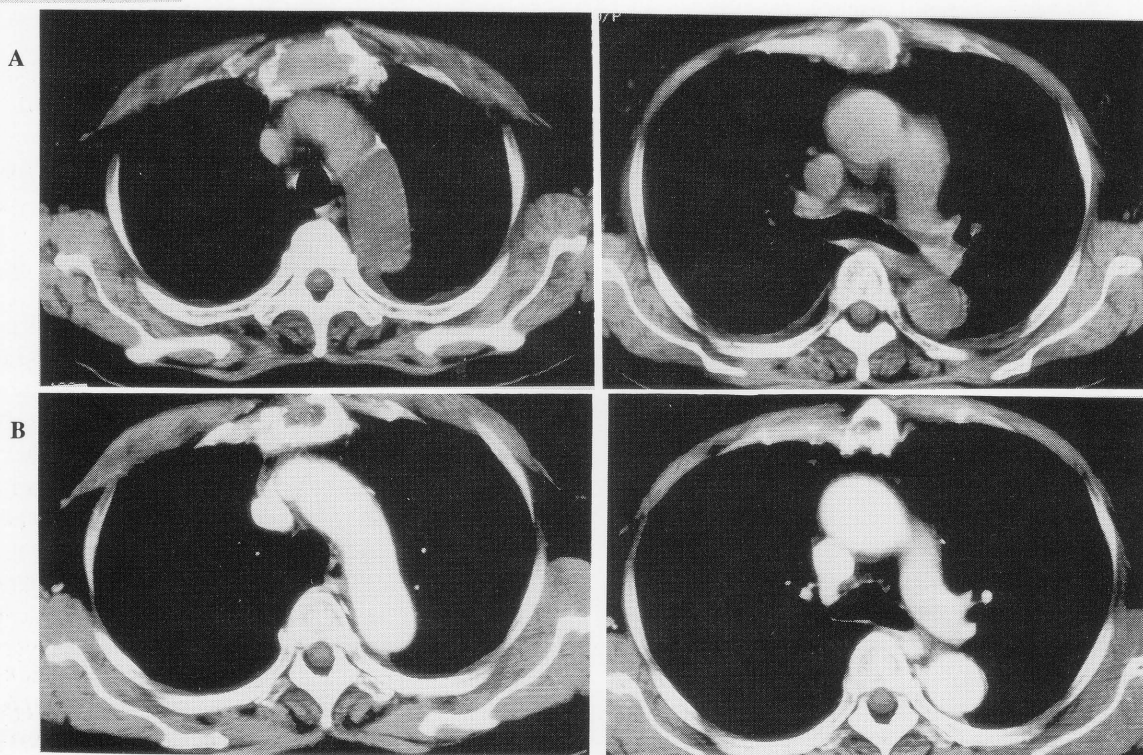


Fig. 3 Selected CT scan images of the chest. (right: upper level; left: lower level). A) before PEIT, B) 3 months after the final session.

treatment and she gave her informed consent to undergo it.

PEIT was performed according to our treatment regimen.^{7,9} The baseline nodular volume (Vb) was calculated by means of CT. Vb was 28 ml. The total dose of ethanol to be given was tentatively determined as 120% of Vb. Needle biopsy of the sternum was performed to rule out

possible anaplastic transformation. The histopathological diagnosis was well differentiated papillary carcinoma (Fig. 2). PEIT was started in late March, 1995 and was performed in four fractionated sessions once a week. It was finished in the middle of April, 1995. The first two sessions were performed under guidance with an echo camera (SSD-1200CV, Aloka) and the last 2 sessions

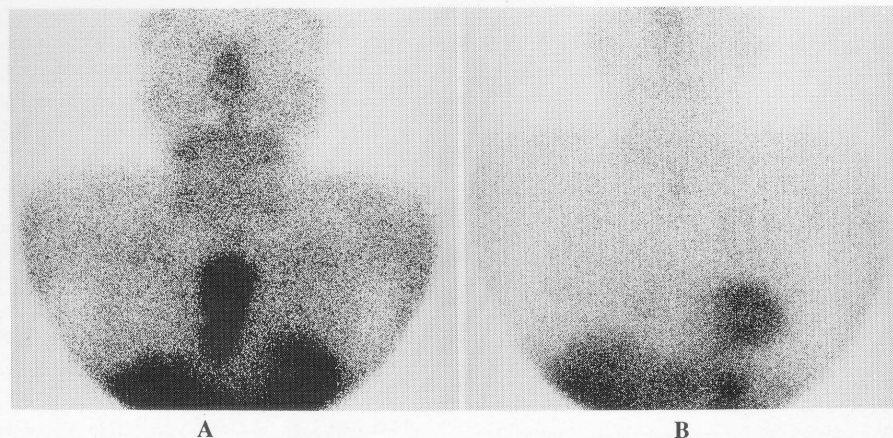


Fig. 4 Anterior image of ^{201}Tl late scan. A) before PEIT, B) 3 months after the final session.

were done under the guidance of CT (SCT-2500T, Shimadzu, Japan). A venous line was maintained and injection of midazolam (10 mg/body) for sedation was given prior to the treatment. The 99% ethanol was selectively injected within the tumor with a 23 or 25 gauge injection needle (Top, Japan) or a 22 gauge Biosuc C-7 needle (Hakko, Japan). The total dose of ethanol actually injected was 36 ml. The injection sites were cooled with ice for several hours.

The response of the tumor to PEIT was evaluated by CT scan, ^{201}Tl scintigraphy and serum Tg levels. These studies were performed within 2 weeks before the treatment and were repeated 2 to 3 months after the final session. CT scan of the anterior chest with intravenous contrast (slice thickness 1.0 cm) was obtained. Planar anterior chest images were acquired at 10 min (early scan) and 2 hour (late scan) after injection of 37 MBq ^{201}Tl by using LFOV (Searle, USA) equipped with a low energy all purpose parallel hole collimator. The serum levels of Tg (normal range; 0–35 ng/ml) and TSH (normal range; 0.3–4.0 $\mu\text{U}/\text{ml}$) were measured with a specific IRMA kit.

Pretreatment CT showed destruction of the sternum and soft tissue mass extending within the bone (Fig. 3-A). The late ^{201}Tl scan showed diffuse intense uptake over the sternum (Fig. 4-A). The serum levels of Tg and TSH were 382.5 (ng/ml), and 0.10 ($\mu\text{U}/\text{ml}$), respectively. TgAb titer was negative. Tumor regression became apparent during the treatment session. The posttreatment CT showed a significant decrease in the tumor size (Fig. 3-B). The estimated amount of reduction in the tumor volume was 88 (%). The posttreatment late ^{201}Tl scan showed that the abnormal uptake had almost disappeared (Fig. 4-B). The posttreatment Tg level fell to 16.4 (ng/ml) with a TSH value of 0.12 ($\mu\text{U}/\text{ml}$). Furthermore, because the refractory chest pain gradually became milder, the patient no longer needed analgesics. There has been no sign of tumor regrowth, increase in Tg, or worsening of chest pain to date (June, 1996). The patient had a mild feeling of compression at the injection point until the third session. Transient hypoproteinemia (total protein 5.7 g/dl) and

leucocytosis (WBC 9,000) were observed, but the former was improved 2 months after the final injection and the latter spontaneously recovered during the treatment session. No other uncomfortable or permanent complications were observed.

DISCUSSION

In spite of the generally favorable prognosis of differentiated thyroid carcinoma, bone metastasis is difficult to eradicate. Radioiodine therapy or surgical resection, if possible, has a therapeutic value. But there have been no effective strategies for unresectable or radioiodine-negative tumors. Although skeletal metastasis can be an indication for external irradiation and bone pain can be palliated in some cases, significant tumor volume reduction is hardly achieved.⁸

PEIT has been used for the treatment of recurrent thyroid cancer^{5–7} and for autonomously functioning thyroid nodules.^{9–12}

Although the role of PEIT is dominantly palliative, it is highly preferable for tumor shrinkage, for technical simplicity and for safety. Our case report suggests that PEIT is valuable in attacking metastatic bone metastasis from differentiated thyroid carcinoma. The histopathological change induced by intratumoral ethanol injection is direct necrosis of the ethanol-perfused area.^{7,9,13} Although we did not confirm the posttreatment histological findings, the disappearance of ^{201}Tl uptake in the tumor suggests that the majority of the tumor became necrotized. A small part of the tumor still remains viable, but it would be easy and safe to give additional injections for tumor regrowth.

Kanoh et al.⁶ recently reported on a similar case to ours in which the patient had painful sternum metastasis and was treated by PEIT. In this patient, the tumor was associated with cystic changes. The treatment was performed ultrasound guidance only. Although the whole tumor volume decreased and the pain was relieved after PEIT, the posttreatment CT scan showed that the bony part of the tumor had not shrunk. In contrast, the bony

mass significantly shrunk in our patient. This difference between Kanoh's patient and ours may be due to the performance of CT-guided PEIT, which could distribute the ethanol more accurately and diffusely even into the deeper part of the tumor.

Pain at injection has been a common complication in PEIT.^{5,6,7,9-12} But the use of midazolam was effective in protecting our patient from discomfort caused by ethanol injection. The side effects observed were transient and mild.

Indication for PEIT maybe somewhat limited to certain tumors that localize superficially or to those are not close to the spinal cord or internal organs. But our case report suggests that PEIT is effective for selected subjects with metastatic bone tumor from differentiated thyroid carcinoma which does not concentrate radioiodine.

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