CASE REPORT

Medullary Thyroid Carcinoma with Multiple Hepatic Metastases: Treatment with Transcatheter Arterial Embolization and Percutaneous Ethanol Injection

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A 54-year-old man with medullary thyroid carcinoma in the thyroid gland was unable to undergo total thyroidectomy because the tumor had invaded the mediastinum. Radiation therapy and chemotherapy were given. Seven years later, intractable diarrhea and abdominal pain appeared, and computed tomography demonstrated hypervascular tumors in the thyroid gland and in the liver. The tumors were successfully treated with percutaneous ethanol injection to a lesion in the thyroid gland and transcatheter arterial embolization followed by percutaneous ethanol injection to tumors in the liver. Transcatheter arterial embolization and percutaneous ethanol injection may be valuable in treating medullary thyroid carcinoma.

(Key words: liver metastasis, carcinoid syndrome, combination therapy)

Introduction

Medullary thyroid carcinoma is a tumor of the parafollicular or C cells of the thyroid. These cells are derived from the neural crest and have amine precursor uptake and decarboxylation characteristics (1). Medullary thyroid carcinoma releases not only calcitonin and carcinoembryonic antigen (CEA), but also, occasionally, other peptides (serotonin, chromogranin, gastrin-releasing peptide, substance P, pro-opiomelanocortin-derived products, and somatostatin). Medullary thyroid carcinoma accounts for 5 to 10% of all thyroid neoplasms (2). This cancer arises in both a sporadic form and a familial form, with the latter characterized as multiple endocrine neoplasia (MEN) syndrome; 80% of medullary thyroid carcinoma is sporadic and 20% occurs as part of the MEN syndrome (1, 3).

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The treatment of medullary thyroid carcinoma consists of total thyroidectomy in combination with lymph node dissection, followed by surgical excision of any recurrences, detected using ultrasonography, computed tomography, 131-I-methiodobenzyl guanidine, 99-mTc dimercaptosuccinic acid and selective venous catheterization (1). Recurrence occurs in about 50% of patients, and is often preceded by high serum calcitonin and/or CEA concentrations. The success of re-operation derives from early detection of secondary disease (4). Chemotherapy results in almost no curative responses and few partial responses. External beam radiotherapy is indicated only as palliation for those patients with brain metastases, symptomatic hepatic metastases, mediastinal metastases with upper vena cava syndrome, or for those patients with compression of vital organs. The medical treatment of advanced medullary thyroid carcinoma, however, is still controversial (3).

The therapeutic approaches for hepatocellular carcinoma have progressed markedly in recent years through the development of transcatheter arterial embolization (TAE) (5, 6) and percutaneous ethanol injection (PEI) (7, 8). TAE is a powerful nonsurgical treatment for hepatocellular carcinoma (9). Because the effect of TAE mainly depends upon the occlusion of the feeding artery with small particles of gelatin, tumor necrosis can be extensive. PEI has recently attracted a great deal of attention in the treatment of liver neoplasms (7, 8). The intratumoural injection of ethyl alcohol causes dehydration and intracellular coagulation leading to necrosis and ultimately to vascular occlusion and fibrosis. Combination therapy with TAE and PEI for hepatocellular carcinoma significantly prolonged the 3-year survival rate and significantly reduced the
rate of local recurrence during the follow-up period, compared with TAE alone (10). Recent reports suggesting that PEI can also be used to treat recurrent thyroid cancer have been encouraging (11). This is the first report of a successful TAE and PEI combination approach for treating a patient with medullary thyroid carcinoma and hepatic metastases.

Case Report

The patient was a 54 year-old male whose chief complaints were growing left neck tumors and diarrhea. He was admitted to the Yokohama City University Hospital for the first time in 1990 when he was 47 years old and with a complaint of masses in the left neck. Microscopic examination of the needle biopsy specimen revealed organoid rounded tumor cells divided by fibrous septa and vascular channels in nested patterns, with amyloid deposition between tumor cells. The tumor was diagnosed as a medullary thyroid carcinoma. Because the tumor invaded the upper mediastinum, the patient received systemic chemotherapy twice (1st adriamycin (ADR) 80 mg/m², 2nd ADR 100 mg/m²) and radiation therapy to the neck and upper mediastinum (total 66.6 Gy). But the size of the tumor never changed, and there was radiological evidence of incomplete necrosis. In January 1996, he started to complain of diarrhea. Despite various attempts to pharmacologically control the diarrhea over the following year, the diarrhea never stopped. Abdominal ultrasonography was carried out in March 1997. It demonstrated 2 large hepatic tumors, 2 small hepatic tumors (in S7.8 79×67 mm, S6 40×31 mm and 10×9 mm, S5 10×9 mm in diameter, respectively) and many small hepatic tumors which were less than 5 mm in diameter. He was admitted again to our hospital in March 1997. Many hypervascular hepatic tumors were disclosed by abdominal computed tomography and abdominal arteriography. Needle biopsy revealed that the tumors were metastases from medullary thyroid carcinoma. We speculated that the extensive medullary thyroid carcinoma metastases in the liver were causing diarrhea as a symptom of carcinoid syndrome. CEA level was 50 ng/ml (normal range, 0–5 ng/ml) and calcitonin level was more than 1,600 pg/ml (normal range, 0–100 pg/ml). Among other hormones, gastrin level was 350 pg/ml (normal range, 30–100 pg/ml), somatostatin level was 15 pg/ml (normal range, 1.0–12 pg/ml), and 5-HIAA level was 11.6 ng/ml in blood (normal range, 1.8–6.1 ng/ml). These high concentrations of hormones were one cause of the patient’s intractable diarrhea. We proposed PEI to the patient as a treatment of the thyroid gland tumors and TAE and/or PEI as a treatment of the hepatic tumors. We received his informed consent to undergo these treatments.

In the thyroid gland region, we administered PEI to the lesion in the left neck in order to palliate against tracheal compression. Pretreatment computed tomography (CT) showed a soft tissue mass extending from the left lobe of thyroid gland (Fig. 1A). PEI was started in May 1997 and was performed twice a week. PEI was performed 12 times (total volume of the injected ethanol, 78.4 ml; average volume of single PEI, 6.53 ml) to the lesion in the thyroid gland with ultrasound guidance. The post-treatment CT scan demonstrated that the enhancing area in the main tumor had disappeared (Fig. 1B).

On the other hand, to treat the hepatic metastases, TAE was initially administered to the right lobe of liver and then PEI was delivered 11 times (total volume of injected ethanol, 1188.1 ml; average volume of single PEI, 108 ml) to the 4 large hepatic tumors. Hepatic arteriogram demonstrated 2 large and 2 small tumors (at S7.8 79×67 mm, S6 40×31 mm, S6 10×9 mm, and S5 10×9 mm in diameter, respectively) and many small tumors (less than 5 mm in diameter) (Fig. 2A). Enhanced CT obtained before these treatments demonstrated 2 large and 2 small hypervascular tumors and many tiny nodules in the same location as seen in the hepatic arteriogram (Fig. 2B). After injection of homogeneous suspension of 6 mg of styrene maleic-acrylonitrile copolymer, PEI was delivered to the tumors.
Figure 2. Helical CT and arteriogram of the multiple hepatic metastases from medullary thyroid carcinoma. A) Before transcatheter arterial embolization and percutaneous ethanol injection therapy, hepatic arteriogram demonstrated that hypervascular tumors were located in the S7,8 79×67 mm, S6 40×31 mm, S6 10×9 mm, and S5 10×9 mm. B) Contrast-enhanced CT scan obtained before these treatments shows that hypervascular hepatic metastases from medullary thyroid carcinoma (arrows) were located in the liver (S7,8). C and D) Post-treatment contrast-enhanced CT (C) and arteriography (D) shows that the hypervascular areas had disappeared.

acid neocarzinostatin (SMANCS; Yamamouchi Pharmaceutical, Tokyo) in 6 ml of Lipiodol (Lipiodol Ultrafluide, Laboratoire Guerbet, Aulnay-sous-Bois, France), small fragments of gelatin sponge were also infused into the right and the left hepatic arteries supplying tumors. Two weeks after TAE, PEI was performed 11 times on the hepatic metastases. The post-treatment CT scan demonstrated that the hepatic metastases were no longer enhancing (Fig. 2C), and on hepatic arteriogram, tumor stains indicating the presence of large tumors had disappeared (Fig. 2D).

The patient had a mild feeling of compression at the injection point during the PEI procedure. The feeling disappeared after therapy. He also had a mild fever following every PEI that lasted 1 day. After six months of follow-up, there have been no signs of tumor regrowth or worsening of diarrhea.
Discussion

In this case, we were able to successfully treat the patient with medullary thyroid carcinoma using PEI only in the neck lesion and by combination therapy with TAE and PEI for the multiple hepatic metastases. Nakada et al (11) recently reported a similar case in which the patient had a painful sternal metastasis of papillary thyroid carcinoma which was treated with PEI. In that case, previous radioiodine therapy and external irradiation were ineffective. After PEI, the 201-Tl uptake disappeared, suggesting that the tumor had necrosed (11). Unlike papillary thyroid carcinoma, medullary thyroid carcinoma accounts for only 5 to 10% of thyroid cancers. This is the first report of a patient who had medullary thyroid carcinoma with multiple hepatic metastases who was treated using TAE and PEI.

When it is possible, radical surgical resection has therapeutic value and the prognosis of medullary thyroid carcinoma is generally favorable; however, there have been no effective strategies for unresectable medullary thyroid carcinoma. Recently, PEI has been used for the treatment of recurrent thyroid cancer and autonomously functioning thyroid nodules (12). The present case report suggests that TAE and/or PEI are valuable in attacking medullary thyroid carcinoma and hepatic metastases from medullary thyroid carcinoma. The histopathological change induced by intratumoral ethanol injection is one type of direct necrosis of the ethanol-perfused area. Although we did not confirm the post-treatment histopathological findings, we speculate that the disappearance of the hypervascular area on CT suggests that most of the tumor had necrosed. Indications for PEI are limited to certain tumors which are not close to the spinal cord or internal organs. But in the present case, PEI was effective for selected medullary thyroid carcinoma tumors in the left thyroid gland and for hepatic metastases. In the neck, chemotherapy and radiation therapy resulted in infiltration of ethanol throughout the entire tumor, which facilitates the diffusion of ethanol and enables a large volume of ethanol to be injected into the lesion and there is less wash-out of ethanol out of the tumor, resulting in infiltration of ethanol throughout the entire tumor (13). Medullary thyroid carcinoma is one of the endocrine tumors; therefore, we speculated that PEI was a good choice for therapy of hepatic metastases from medullary thyroid carcinoma. However, because the greatest diameter of the hepatic metastases was greater than 3 cm, TAE was initially carried out. After this therapy, most of the hypervascular tumors were completely necrotic. Injection of sufficient ethanol throughout the entire tumor resulted in complete necrosis of any remaining viable tumor. After combination therapy with TAE and PEI, hepatic metastases from medullary thyroid carcinoma were therefore completely necrosed.

It is reported that radiotherapy has little effect on medullary thyroid carcinoma (16) and combination chemotherapy does not offer a sufficient effect (17, 18). On the other hand PEI as a treatment of autonomous thyroid nodules is effective and very safe in a large series of patient and with a long-term follow-up (19, 20). In conclusion, this case report suggests that the combination of TAE and PEI is an effective and safe therapy for medullary thyroid carcinoma with hepatic metastases. TAE and PEI could be the first choice treatment for advanced medullary thyroid carcinoma.

References

