Cystic Medullary Thyroid Carcinoma: A Case of Undergoing Endoscopic Thyroid Lobectomy

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On ultrasonography, medullary thyroid carcinoma (MTC) shows hypoechogenicity, an irregular margin, a predominantly solid composition, and microcalcifications, similar to those observed in papillary thyroid carcinoma (PTC). MTC presenting as a cystic lesion is rare, and endoscopic thyroidectomy can be performed for benign thyroid masses and early stage PTC, however it is inappropriate for MTC regardless of cystic change. The authors report a case of cystic MTC found after endoscopic thyroid lobectomy and provide a review of the literature on this topic.

Key Words: Medullary thyroid carcinoma, Thyroid cyst, Endoscopic thyroidectomy

INTRODUCTION

MTC is a rare disease in Korea and accounts for only 0.4% of thyroid malignancies.¹ MTCs are usually firm, white-grey to tan in color, gritty in consistency, and well circumscribed in macroscopic view. Sporadic tumors are typically unilateral, whereas familial tumors are multiple and bilateral.²⁳

Cystic change presents in about one third of thyroid nodules and around 9～14% of these lesions are malignant tumors.⁴⁵⁶ According to recent reports, the malignancies detected in cystic masses are mainly PTC and follicular thyroid carcinoma.⁶⁷ Besides, all were PTCs in markedly cystic cases (cystic portion > 50%).⁸

Predominantly cystic MTC is rarely encountered, and thus, only a small number have been described.⁹⁻¹³ Herein, we report a case of MTC, which presented as a large cystic lesion.

CASE REPORT

A 32-year-old Asian female was referred by a primary health clinic. A left cervical mass had been detected more than a month previously and diagnosed as a thyroid cyst by ultrasonography (USG) at the clinic. The patient did not complain of any symptoms like neck pain, dysphagia, hoarseness, cough, or dyspnea, and did not exhibit systemic symptoms, such as, facial flushing, diarrhea, or weight loss, or any marfanoid features. Her blood pressure was 129/81 mmHg and her heart rate was 90 per minute. There were no specific underlying diseases in her past medical history and thyroid disease or malignancy in her familial medical history.

On physical examination, left neck swelling was observed and an oval, soft thyroid mass was palpable without fixation at swallowing. No palpable lymphadenopathy was detected in bilateral cervical areas.

USG showed an oval hypoechoic cystic lesion of 3.51×2.75×5.26 cm in the left thyroid, which caused the
Fig. 1. Transverse (A) and longitudinal (B) ultrasonographic views showing a 3.51×2.75×5.26 cm sized hypoechoic predominantly cystic lesion with incomplete septa occupying the entire left thyroid gland.

Fig. 2. Left thyroid gland was easily separated from strap muscle during endoscopic thyroidectomy using BABA. On palpation, the left thyroid gland was soft and smooth after removal using an endoscopic plastic bag via a right areolar incision.

trachea to deviate to the right (Fig. 1). Thyroid function tests, including serum thyroid stimulating hormone and free thyroxine, were within normal limits, and so were serum calcium and phosphorus levels. Serum thyroglobulin and calcitonin were not checked.

USG-guided fine needle aspiration cytology (FNAC) was carried out using a 23-gauge needle connected to a 20 mL syringe in a syringe holder. After draining 20 mL of a chocolate-colored sticky fluid, a small amount of intracystic material remained. A cytologic examination and cell block were performed on the fluid. After aspiration, the neck swelling decreased. Some macrophages without an epithelial cell component were observed, and resultantly, the lesion was considered a cystic change lesion of uncertain nature.

However, 11 days later the lesion reassumed its previous size. We decided on left endoscopic thyroidectomy because the patient wanted to avoid a scar. A bilateral axillo-breast approach (BABA) endoscopic left thyroidectomy was performed without complication. There was no extrathyroidal extension and lymph node enlargement in central cervical area. Grossly, the excised thyroid mass was oval and smooth (Fig. 2). Frozen biopsy was not checked during operation.

The left lobe measured 5.9×4.3×2.4 cm and weighed 26.2 gm. In section, the mass was found to be a demarcated, encapsulated cystic mass measuring 5.0×3.0×2.2 cm. The cystic space contained bloody fluid and its inner surface was irregular and hemorrhagic. The solid portion was reddish brown, soft, and focally calcified.

Microscopically, the tumor consisted of solid sheets of medium-sized polygonal cells traversed by fine vascular septae. Cystic change with hemorrhage and aggregated hemosiderin-laden macrophages were also noted in solid portion. Tumor cells showed relatively uniform, round nuclei, and eosinophilic granular cytoplasm. Amyloid deposition was only focally noted (Fig. 3A–C). By immunohistochemistry, tumor cells were positive for calcitonin (Fig. 3D), chromogranin, synaptophysin, TTF-1, CEA, CD56, cyclin D1, and P53, but negative for thyroglobulin,
Fig. 3. Photographs of medullary thyroid carcinoma showing prominent cystic change. (A) Low power view showing a large cystic space in the center and in the solid portion at the periphery of the tumor (H&E, ×10). (B) In the solid portion, cystic change with hemorrhage and aggregation of hemosiderin-laden macrophages was noted (H&E, ×100). (C) High power view showing solid sheets of uniform tumor cells. Note the prominent vasculature and focal amyloid deposition (arrow) (H&E ×400). (D) Tumor cells were positive for calcitonin (immunostain, ×400).

galactin-3, and HBME-1. Based on these features a diagnosis of MTC was made.

Elevated serum calcitonin (10.2 pg/mL; normal value: 1~4.8) and CEA (67.89 ng/mL, normal value: 0~5) levels were found on the 8th postoperative day (POD8, on the basis of the first operation). Serum parathyroid hormone on POD2 was 26.1 pg/mL (normal value: 10~65). Open completion thyroidectomy was performed with central neck lymph node dissection on POD14 without complication. No tumor was noted in the opposite lobe of the thyroid or in cervical lymph nodes. Serum calcitonin and CEA decreased to 3.4 pg/mL and 41.59 ng/mL, respectively, on POD16.

PET-CT, abdominal CT, chest CT, and bone scan performed after operation showed no evidence of an abnormal pathologic lesion.

DISCUSSION

MTCs are usually firm in consistency and may feel gritty when sectioned owing to the presence of fine granular calcification. Amyloid accumulation is present in 70~80% or more cases.(2,3) Follicular cell proliferative lesions have a prominent thin vascular network and cystic change in follicular lesions may result from vascular rupture and hemorrhage in enlarged follicles. MTC exhibit highly vascular tumors, and generally dense fibrovascular stroma with amyloid deposition, which appears to preclude
vascular rupture and cystic change. In our case, stromal fibrous and amyloid components comprised a minor portion of the tumor, which might have been related to the observed cystic change.

Cystic change in MTC is rare, in fact, only 6 cases such cases have been reported in the English literature. Table 1 provides a summary of these cases, which including our case, include five female and two male patients. Patients' ages varied widely and no patient had multiple endocrine neoplasia (MEN). Average tumor size was 3.92 cm and lymph node metastasis was absent in all cases. Preoperative FNAC did not reveal the presence of malignancy in 4 of 6 cases (66.7%), and a second operation, including cervical lymph node dissection, was performed in 3 of 7 cases (42.8%). Two patients were diagnosed as MTC preoperatively. In the case of patient no. 4, preoperative serum calcitonin was elevated and MTC was diagnosed by immunocytochemical staining for calcitonin. Patient no. 6 underwent second FNAC because first FNAC resulted in inadequate cytological findings and no serum calcitonin result.

The sonographic features of MTC have not been adequately described. The sonographic characteristics of malignant nodules are as follows: the presence of microcalcifications, marked hypoechogenicity, microlobulated or an irregular or spiculated margin, a taller-than-wide shape, absence of a halo, predominantly solid composition, and intranodular vascularity. Sonographic features predictive of MTC are known to be similar to those of PTC, except that the presence of focal cystic change and homogeneous echotexture is more frequent in MTC.

BABA endoscopic thyroidectomy can be carried out in patients with a benign thyroid mass or early stage thyroid carcinoma. The largest benign tumor operated on by Baba endoscopic thyroidectomy was 7 cm by preoperative USG. Accordingly, the 5.26 cm sized cystic thyroid mass in our patient was deemed suitable for BABA endoscopic thyroidectomy. Completion thyroidectomy via the BABA method can be performed after BABA thyroidectomy. Nevertheless, we decided to re-operate using the conventional open method to ensure complete lymph node dissection after serious discussion with the patient.

We did not determine whether the presented case was familial or sporadic MTC, but our patient had no familial history of MTC or exhibit any systemic symptoms. Furthermore, physical examination, blood tests, and imaging workup provided no evidence of familial disease. Although we recommended genetic counseling, the patient left Korea for planned study abroad on recovery from completion thyroidectomy.

In our case, it was regrettable that MTC was not diagnosed preoperatively. We did not perform a serum calcitonin test preoperatively. Preoperative serum calcitonin test is helpful for diagnosis of MTC. However, the routine measurement of serum calcitonin during thyroid nodule work-up is not recommended obligatorily in Korea because of its lack of sensitivity and specificity and cost. As the thyroid mass was mainly cystic, we did not suspect the presence of malignancy. FNAC revealed the presence of only macrophages and degenerated blood component were detected, which are common findings for benign cystic nodules. On reflection, a second FNAC should

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**Table 1. Clinicopathologic features of medullary thyroid carcinoma with prominent cystic change**

<table>
<thead>
<tr>
<th>No.</th>
<th>Author</th>
<th>Year</th>
<th>Age/Sex</th>
<th>MEN</th>
<th>Size (cm)</th>
<th>Aspiration cytology</th>
<th>Operation</th>
<th>LNM</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Simic(9)</td>
<td>1995</td>
<td>29/F</td>
<td>NA</td>
<td>6.0</td>
<td>No malignancy</td>
<td>ST→CT w LND</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>Simic(9)</td>
<td>1995</td>
<td>38/M</td>
<td>NA</td>
<td>1.5</td>
<td>Non diagnostic</td>
<td>TT w LND</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>Liberatore(10)</td>
<td>1996</td>
<td>55/F</td>
<td>No</td>
<td>2.5</td>
<td>Not done</td>
<td>L→CT w LND</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>Fadda(11)</td>
<td>2000</td>
<td>77/F</td>
<td>No</td>
<td>3.5</td>
<td>MTC</td>
<td>TT w LND</td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td>Ozkara(12)</td>
<td>2002</td>
<td>43/F</td>
<td>No</td>
<td>6.0</td>
<td>Nodular colloidal goiter</td>
<td>NT</td>
<td>NA</td>
</tr>
<tr>
<td>6</td>
<td>Kim(13)</td>
<td>2012</td>
<td>50/M</td>
<td>No</td>
<td>3.0</td>
<td>Suspicious for MTC</td>
<td>TT w LND</td>
<td>No</td>
</tr>
<tr>
<td>7</td>
<td>Present case</td>
<td>2014</td>
<td>32/F</td>
<td>No</td>
<td>5.0</td>
<td>Cystic change lesion</td>
<td>L→CT w LND</td>
<td>No</td>
</tr>
</tbody>
</table>

F = female; M = male; MEN = multiple endocrine neoplasia; NA = not available; MTC = medullary thyroid carcinoma; ST = subtotal thyroidectomy; CT = complete thyroidectomy; w = with; LND = lymph node dissection; TT = total thyroidectomy; L = lobectomy; NT = near total thyroidectomy; LNM = lymph node metastasis.
have been performed after aspiration of cystic fluid. Had the preoperative diagnosis indicated MTC, conventional open total thyroidectomy would have been performed rather than endoscopic thyroidectomy. Furthermore, if we had checked frozen biopsy intraoperatively, operation could have been performed at a time.

In conclusion, we describe a case of MTC presenting as a mainly cystic lesion. Although cystic MTC is rare, we urge that the possibility be considered.

REFERENCES