Short Communication

A Case of Minimally Invasive Follicular Thyroid Carcinoma Relapsed as a Large Cervical Lymphadenopathy and Multiple Lung Metastases

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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ABSTRACT

Minimally invasive follicular thyroid carcinoma (MIFTC) is a well-differentiated thyroid carcinoma showing subtle capsular invasion and/or 1 to 3 foci of vascular invasion only. Currently, no reliable methods exist that can identify MIFTC in the preoperative stage due of a lack of atypia in follicular cells in fine-needle aspiration cytology and high resemblance to goitre upon radiological examination. True to its name, a MIFTC shows excellent prognosis in the absence of systemic involvement. We report the case of an 81-year-old woman diagnosed with a MIFTC that relapsed as a large cervical lymphadenopathy and multiple lung metastases. This feature of MIFTC associated with rapid growing multiple metastases has not been previously reported.

Keywords: Follicular thyroid carcinoma; Metastasis

INTRODUCTION

Follicular thyroid carcinoma (FTC) is the second most common differentiated thyroid carcinoma, accounting for 10% to 15% of all thyroid carcinomas (1). It occurs most frequently among women in their 50s and 60s, and tends to invade blood vessels and metastasize by hematogenous spread to distant sites, most commonly to the bones and lungs. The incidence of distant metastasis in FTC has been reported as 6% to 20% (2). Long-term survival rates in patients with metastatic FTC range from 31% to 43% (2). Very few studies exist on the management and outcomes of patients with FTC who already have distant metastases at initial presentation versus those who develop metastases during clinical follow-up for FTC. When combined with distant, especially widespread metastases, the quality of life is compromised, and the overall survival rate significantly decreases. Hence, management of FTC requires special attention and knowledge about its metastatic potential and other effects (3,4). A widely accepted method of risk stratification of potentially metastatic FTC involves its classification into minimally invasive FTC (MIFTC) and widely invasive FTC (WIFTC), according to the number of capsular and vascular invasions detected under microscopic evaluation (2). However, this classification is somewhat arbitrary and not beneficial in the preoperative stage, since the pathologic diagnosis is usually made postoperatively. MIFTC is known to have good prognosis than WIFTC (2). However, we observed an extraordinary case of MIFTC that showed rapidly

growing metastatic lymph nodes in the bilateral neck and mediastinal area. To the best of our knowledge, this has not yet been described in such a unique clinical setting.

CASE REPORT

An 81-year-old woman was admitted to Wonju Severance Christian Hospital complaining of a large goitre pressing on the lower anterior part of her neck, that had grown slowly over several years. She denied having notable weight loss and cervical lymphadenopathy. On clinical examination, a nontender, indurated, and significantly enlarged left thyroid gland (about 7.5 cm) was identified. It appeared to cause her intermittent difficulty in breathing. Examination using ultrasonography also showed a massive, relatively well-demarcated and somewhat hypoechoic mass in the left thyroid lobe (**Fig. 1**). The subsequently performed computerized tomography scan revealed a large, heterogeneously enhanced, well-margined mass with multiple calcifications of a size identical to that described previously. Additionally, her trachea was remarkably displaced to the right side (**Fig. 1**), but no enlarged cervical lymph nodes were found. This large thyroid mass was evaluated using fine needle aspiration cytology, and a diagnosis of follicular neoplasm was made (**Fig. 2**). She had been suffering multi-sited arthrosis, osteoporosis, and hypertension, controlled to a tolerable extent by calcium channel blockers. Her laboratory test results were within normal ranges and thyroid hormone function test results were also unremarkable. Given the persistent nature of the thyroid mass causing her intermittent breathing difficulty and the patient's medical history, total thyroidectomy was subsequently performed. Histological examination showed a completely encapsulated follicular neoplasm showing conventional follicular cell morphology. The entire capsule of

Fig. 1. Radiologic characteristics. Ultrasonography showed a 7.5 cm sized well-demarcated hypoechoic mass in the left lobe (A) with lobulation (B). CT scan revealed a huge mass with multiple calcifications identical to ultrasonography (C) making the trachea deviated (D).

Fig. 2. Fine-needle aspiration cytology. Preoperative FNA revealed uniformly proliferation of thyroid follicular cells lack cytologic features of papillary thyroid carcinoma (H&E, $\times 200$) and no papillary architecture was noted (H&E, $\times 400$). H&E = hematoxylin and eosin stain.

Fig. 3. Histologic characteristics. (A) Thin cell cord structure was preserved and invasion foci were hardly detected (H&E, $\times 40$). (B) Follicular cell proliferation was evident which was a lack of cellular features of papillary thyroid carcinoma, which made the diagnosis of MIFTC inevitable (H&E, $\times 400$). H&E = hematoxylin and eosin stain; MIFTC = minimally invasive follicular thyroid carcinoma.

the thyroid was evaluated, demonstrating minimal capsular invasion by the neoplasm and resulting in a diagnosis of MIFTC (**Fig. 3**). At regular follow-ups, the patient showed a rapidly growing bilateral neck lymph node enlargement ranging from levels II to IV, and mediastinal lymph node enlargement of levels 2R to 4R (**Fig. 4**). Multiple small nodules scattered throughout both lungs were also identified after 5 months (**Fig. 4**), indicating the exceptional aggressiveness of her MIFTC. She was treated with 45Gy of locoregional radiotherapy over 1

Fig. 4. Follow-up radiologic findings. Multiple and huge bilateral cervical lymphadenopathy (A) with mediastinal lymphadenopathy (B) and lung metastasis were demonstrated (C, red circle).

month to relieve her breathing difficulty. Unfortunately, the treatment had no effect on the metastatic disease, and she died of disease progression after 15 months.

Approval for this case report was obtained from the Institutional Review Board (IRB) of Yonsei University Wonju College of Medicine (IRB number:2020-05-0018) with a waiver of informed consent.

DISCUSSION

FTC can be histologically classified into 2 categories as MIFTC and WIFTC. MIFTC is a grossly encapsulated, solitary tumour with limited capsular and/or vascular invasion, whereas WIFTC is characterized by a widespread infiltration of adjacent thyroid tissue and/or blood vessels. Patients with MIFTC have an excellent prognosis because distant metastasis is very rare; by contrast, distant metastasis is observed in 10% to 30% of patients with WIFTC. MIFTC is confirmed upon pathological examination only, and it is difficult to preoperatively determine whether patients require complete thyroidectomy. Because of its excellent prognosis, it is generally understood that MIFTC patients do not need to receive total thyroidectomy (1,3-6). Some patients at risk of developing distant metastasis, however, require total thyroidectomy and radioactive iodine (RAI) ablation. Previous studies have suggested that age, sex, tumour size, and/or vascular invasion are clinicopathological risk factors for distant metastasis of MIFTC, and there has been growing interest in discovering risk factors for distant metastasis through molecular biology research. A previous study demonstrated that extensive vascular invasion, i.e., more than 4 foci was the most important risk factor for a poor MIFTC prognosis (7-9). Assessment of the clinicopathological characteristics performed by the same authors showed that CK19, a low molecular weight cytokeratin belonging to a subgroup of cytoskeletal proteins, was more frequently expressed in patients who had MIFTC with extensive vascular invasion, and CK19 expression was indirectly associated with poor prognosis in patients with MIFTC (10).

The literature on long-term survival in patients with metastatic differentiated thyroid cancer is relatively scarce. Disease-specific survival rates at 5 years have been reported to range from 26% to 39% for patients with metastatic disease (3,6). Some studies showed that those with osseous metastasis had a significantly poorer ten-year overall survival rate than those with pulmonary metastasis, which may be due to the lack of effectiveness of RAI (7). Resecting the osseous metastasis where possible using an aggressive surgical approach may improve survival among FTC patients. The above described exceptional case of MIFTC that relapsed as a large cervical lymphadenopathy and multiple lung metastases suggests the possible existence of currently unknown tumour cell-specific genetic alterations that render the MIFTC too aggressive to be treated. Thanks to the development of next-generation sequencing techniques using formalin-fixed, paraffin-embedded blocks and serum, large amounts of tumour cell DNA alteration can be investigated in a relatively short time. We recommend that the widely accepted consensus of pathological diagnosis in FTC be revisited using tumour cell-specific genetic alterations, which are good predictive markers of tumour cell behaviour.

Despite some trials that estimate the variable aggressiveness of preoperative-stage FTC to find the best treatment strategies, including surgery, chemotherapy, and radiotherapy (11,12), no calculable risk factors have been confirmed worldwide. One thing we can learn from our present experience is that pathologic diagnosis, such as MIFTC does not guarantee its

minimally invasive clinical behaviour at all. Further large-scale studies to identify predictable and reliable risk factors that are calculable at the preoperative and postoperative stages are urgently needed to help predict the clinical behaviour of MIFTC.

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