

Case Report

Papillary Thyroid Carcinoma with Lung Metastasis after 31 Years: A Case Report

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Abstract: Thyroid cancers are the most common endocrine malignant tumors. Papillary thyroid cancer (PTC) is the most common histological type of differentiated thyroid cancer (DTC), accounting for 90% of thyroid cancers. PTC commonly metastasizes to regional lymph nodes. However, distant metastasis may rarely occur and accounts for 5% of the patients. The lungs and the bones are the most common sites for distant metastasis. Major risk factors for PTC include radiation exposure, insufficient or excess dietary iodine, Cowden's disease, Gardner's syndrome and dysmorphogenetic goiter. The serum thyroglobulin (Tg) level is the most sensitive and reliable marker indicating persistent or recurrent disease during follow-up after total or near-total thyroidectomy and I¹³¹ remnant ablation in patients with DTC.

Keywords: Papillary carcinoma thyroid, metastasis, malignancy.

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INTRODUCTION

Well differentiated thyroid carcinoma (WDTC) is the most common endocrine malignancy regardless of ethnicity or of geographic location. Incidence of WDTC has been increasing in most areas over the world during the recent 3 decades. Many doctors believe that such increase is mainly due to increased detection which might have been caused by widespread use of medical imaging including thyroid ultrasonography, by increase in thyroid surgery revealing occult cancers or by more deliberate examination of surgical specimen obtained by thyroid surgery and so on [1]. In United States, incidence of thyroid cancer has been increasing continuously from 1980's and such increase was observed regardless of ethnicity. In Korea, incidence of thyroid cancer increased rapidly from year 2000. By the year of 2010, age-adjusted rate of thyroid cancer was over 80 per 100,000 of population in women and it was around 20 per 100,000 in men showing the highest incidence in the world. The main histological subtype which has been contributing to surge in thyroid cancer is papillary thyroid carcinoma (PTC) both in Korea and United States [2].

Papillary thyroid cancer (PTC) is the most common histological type of differentiated thyroid

cancer (DTC), accounting for 90% of thyroid cancers. PTC has a good prognosis, and it is one of the best treatable cancers, leading to a survival rate of 93% at 10 years. PTC commonly metastasizes to regional lymph nodes [3]. However, distant metastasis may rarely occur and accounts for 5% of the patients. The lungs and the bones are the most common sites for distant metastasis. Major risk factors for PTC include radiation exposure, insufficient or excess dietary iodine, Cowden's disease, Gardner's syndrome and dysmorphogenetic goiter [4].

CASE REPORT

The patient was a 61 year-old male who was admitted to the department of pulmonary medicine with complaints of dyspnoea, cough and hemoptysis. The patient had a past history of right thyroid lobectomy and isthmusectomy performed for papillary thyroid carcinoma at the age of 30 years. On physical examination, there was decrease in bilateral respiratory sounds. Thyroid function tests were as follows: Free T3: 4.18 (2.5–3.9) pg/mL, free T4: 0.76 (0.61–1.12) ng/dL and TSH: 3.69 (0.34–5.60) uIU/mL. Thyroglobulin level – 7077 ng/ml (3.5 - 77). In the chest radiography, bilateral nodular opacities were detected (Figure 1 and 2). CT Thorax showed multiple nodule formations that were atypically scattered along bilateral lungs (Figure 3). The neck ultrasound revealed

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multiple hypoechoic and isoechoic nodules that have the greatest size of 13 × 12 mm in the thyroid gland. A diagnostic bronchoscopy was done and biopsy was taken. The result of biopsy was consistent with thyroid papillary carcinoma (Figures 4 and 5). IHC was done for confirmation and the tumour cells were thyroglobulin and TTF 1 positive and CK 20 negative. IHC was consistent with metastasis from papillary carcinoma thyroid. Then, he was referred to General Surgery department followed by completion thyroidectomy and radioactive iodine treatment.

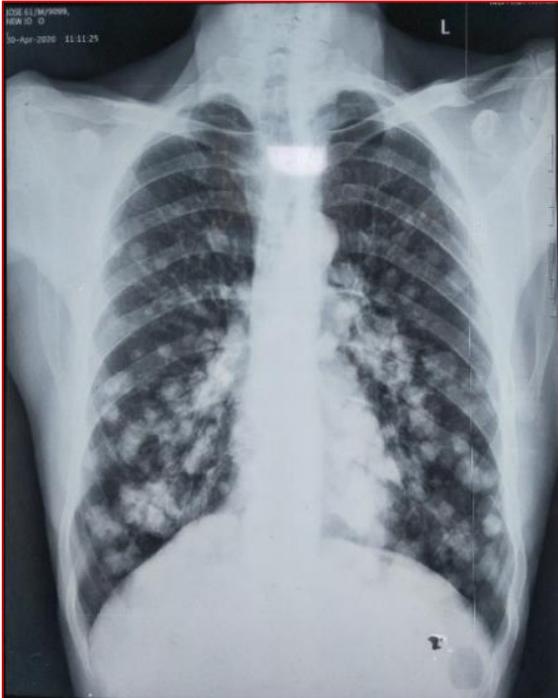


Figure 1: Chest X ray AP view



Figure 2: Chest X ray lateral view



Figure 3: C T chest

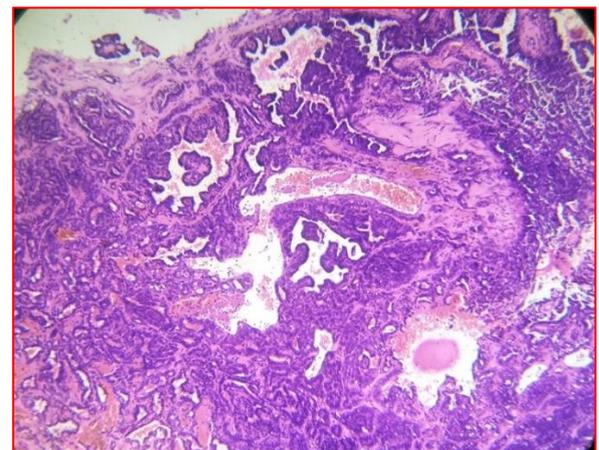


Figure 4: H&E (10X) showing papillary pattern

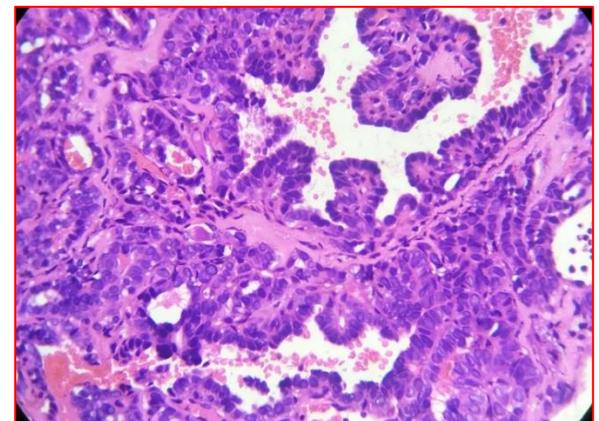


Figure 5: H&E (40X) showing nuclear crowding, grooving and clearing

DISCUSSION

According to the National Cancer Center, PTC is one of the fastest growing malignant tumors in China, especially in women under 30 years of age and has become the most commonly diagnosed cancer. The dramatic rise in thyroid cancer among younger women is similar to the situation in Western countries. Despite the increased incidence, patients with PTC usually have a good prognosis with a 5-years overall survival (OS)

rate of >98.1% and 10-years OS rate of >85% to 90% from the initial diagnosis. However, patients with PTC have a worse prognosis in the presence of distant metastases and/or local recurrence, which seriously affect quality of life and survival time of the patient. Distant metastatic lesions from DTC are usually seen in the lungs, followed by the bones. During the past 70 years, radioactive iodine (I^{131}) therapy has been the mainstream and routine treatment strategy for patients with DTC with lung metastasis. Several independent prognostic factors associated with a poor prognosis in patients with DTC with lung metastases have been reported, such as age at the initial diagnosis of lung metastases, I^{131} avidity, timing of diagnosis of lung metastases, maximal size of lung metastasis at diagnosis, pathological type and the presence of extrapulmonary distant metastasis [1].

A long follow-up interval is required to assess treatment for well-differentiated thyroid carcinoma because of its prolonged course and very slow growth rate. McConahey and colleagues, in a retrospective study of 859 patients with papillary thyroid cancer, found distant metastatic lesions in 40 (5%). The lungs were the leading site of involvement (76%), followed by the mediastinum (24%), bone (23%) and brain (15%). Compared with patients with cervical lymph node recurrence, patients with distant spread carry a poorer prognosis. Among 32 patients whose first postoperative recurrence occurred in cervical nodes, none died of thyroid cancer. However, the mortality rate in patients with a distant metastatic site was 36% by 5 years and 65% by 20 years, with the most common cause of thyroid cancer death being pulmonary metastatic disease. The presentation of lung metastases has been reported to be from 5 to 30 years after the initial diagnosis of thyroid cancer. Approximately 25% of first relapses occurred after 20 years of complete remission. It has been repeatedly documented that chest radiography does not detect all pulmonary metastases and that scintigraphy with I^{131} may demonstrate tumor that is not radiographically detectable. Neither I^{131} scintigraphy nor routine chest x-ray film alone will reveal all cases of pulmonary metastases. In addition, unlike most lung nodules, nodular lung metastases from papillary thyroid carcinoma may demonstrate no change in size on the chest x-ray film for 25 years [2].

Normal findings on the chest x-ray film appear to confer a survival advantage in those patients with metastatic lung lesions. Schlumberger and associates presented data on 141 patients with lung metastases. They reported that the overall survival rate was 30% at 15 years in patients with distant metastases but 95% in patients with normal findings on the chest x-ray film and 55% in patients with micronodular lung metastases [5]. Serum thyroglobulin measurement should be performed routinely as part of the follow-up visit. This glycoprotein is a secretory product produced only by the thyroid tissue. A detectable thyroglobulin level

warrants further investigation, beginning with a total body scan. Negative findings on the total body scan do not preclude the existence of metastases and additional attempts to localize thyroid tissue should be made, including neck ultrasound, neck and thoracic computed tomographic scans, and a 100-mCi I^{131} whole-body scans. These modalities will help to identify those patients with lung metastases and normal chest x-ray findings. It should also be noted that a normal thyroglobulin level, does not exclude a metastatic focus. The treatment recommended is radioactive iodine. Samaan and colleagues reported a 5-year pulmonary metastatic survival rate of 61% for patients with positive radioactive uptake on the scan and 29% for patients with no uptake. The appearance of micronodular metastases on the chest x-ray film and the ability of the lesions to concentrate radioiodine confer improved prognosis when treated with radioactivity.⁶ Emphasis should therefore be placed on early detection and treatment. The cause of arrest of metastatic growth in papillary thyroid carcinoma is unknown. It may be due to long tumor doubling time or to phases of dormancy during the course of the cancer. The doubling time of pulmonary metastases of differentiated thyroid cancers is among the longest observed and growth arrest has occurred without irradiation or suppressive chemotherapy. The present case demonstrates one such occurrence after 31 years of initial diagnosis. Such patients must be followed up for their entire lifetime [7].

Young patients that have smaller tumors and do not present with invasion have better prognosis. Thyroid cancers are quite rare in children and an annual incidence of 0.52/100.000 is reported for the children under the age of 19 in the USA. In differentiated thyroid cancers, females have a twice higher incidence rate than males and the mean age of diagnosis is 45 years. In the regions with insufficient iodine, follicular carcinoma is more common than papillary carcinoma [1]. Prior radiation exposure, particularly in early childhood, is reported as a significant risk factor for papillary carcinoma. Differentiated carcinomas may be associated with Cowden's disease, Gardner's syndrome and familial adenomatous polyposis. Malignant transformation may occur in the children with congenital hypothyroidism if the risk of thyroid nodule is increased by the presence of dysmorphogenesis or iodine transport defect. Follicular carcinoma is the most common type among the cases of congenital hypothyroidism, while papillary carcinoma is very rare. A thyroid carcinoma may be associated with a high TSH stimulation. In a study conducted with the rats, it was reported that the presence of long-time elevated TSH levels results in thyroid carcinoma with lung metastasis [3].

The patient with PTC commonly presents with asymptomatic thyroid nodules. Symptoms including pain, respiratory insufficiency, stridor, vocal cord

paralysis and hemoptysis may also be seen. The current patient presented with cough, dyspnoea and hemoptysis. Kallel *et al.*, revealed the case of a PTC with lymph node metastasis resulting from dyshormonogenetic goiter in a 13-year-old boy who had total thyroidectomy due to voluminous goiter associated with hypothyroidism. Drut and Moreno reported the patient who was a 5-year-old girl with non goiter congenital dyshormonogenetic hypothyroidism. The specimens obtained from the thyroid nodule which was detected in the clinical followup during the appropriate treatment were diagnosed as PTC [2]. Yashiro *et al.*, reported a case of thyroid papillary carcinoma associated with dyshormonogenetic goiter who had been on thyroid hormone therapy since the age of three. In physical and ultrasonographic examinations, the case had a tumor in the right thyroid lobe, and PTC was detected following the total thyroidectomy. In all these cases, PTC was detected via the investigations of the findings related to thyroid gland. However, in our case, PTC was detected due to the symptoms related to distant metastasis [5].

In PTC, metastases primarily occur in regional lymph nodes. Systemic metastasis may rarely occur - most commonly in the lungs or bones and accounts for 5% of the patients. It rarely affects the skeletal muscle, ovaries, submandibular gland, sphenoidal sinus, brain, adrenal gland, and pancreas. In the present case, the metastasis were firstly defined in the lungs [4]. The lung metastases in PTC may develop as miliary or multiple or localized infiltration, widespread lymphadenopathy or pleural effusion. Our patient presented with bilateral widespread nodule formations in radiological examination. Risk factors for distant metastases include male gender, advanced age, histologic grade, completeness of surgical resection of the primary tumor and extrathyroidal invasion at initial examination. Treatment of metastatic PTC cases may include the sole use of radioactive iodine therapy, surgery, thyroid hormone, radiotherapy, and

chemotherapy or various combinations of these treatments [7].

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