Papillary Thyroid Carcinoma with Anaplastic Transformation:A Case Report

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Abstract

Anaplastic thyroid carcinoma (ATC) is one of the most aggressive malignancies with poor prognosis. Approximately 20 % of patients with ATC have a history of differentiated thyroid carcinoma, and 20 to 30 % have a coexisting differentiated thyroid carcinoma. We report a case of papillary thyroid carcinoma (PTC) with anaplastic transformation after follow-up for 17 years. Patient presented with an ulcerative mass over the previous surgical wound. Further examination revealed lung metastasis. Patient expired within half a year after ATC was diagnosed. Conventional therapies provide little aid in treating ATC. Multiple molecular abnormalities have been disclosed with the progression of normal follicular thyroid cells to ATC. This should provoke the development of innovative strategies beyond the conventional methods to overcome the lethal disease. (J Intern Med Taiwan 2009; 20: 167-170)

Key Words：Papillary thyroid carcinoma, Anaplastic thyroid carcinoma, Anaplastic transformation

Introduction

Anaplastic thyroid carcinoma (ATC) is one of the most aggressive malignancies with poor prognosis. Although ATC accounts for only 1% to 2% of the thyroid cancers[1], it is responsible for more than half of the death attributed to the thyroid cancers[2]. Patients with ATC have median survival time of 3 to 12 months from the time of diagnosis[2-4]. Approximately 20 % of patients with ATC have a history of differentiated thyroid carcinoma, and 20 to 30 % have a coexisting differentiated thyroid carcinoma[2,3,5-8]. Here we report a case of papillary thyroid carcinoma (PTC) with anaplastic transformation after follow-up for 17 years.

Case Report

A 40-year-old man visited our clinic in July, 1988 with a right neck mass persisting for 2 months. PTC in the right lobe (2.5 x 2 x 1.5 cm) with right internal jugular vein and paratracheal space lymph nodes metastasis was discovered during surgical exploration (Figure 1A). Extrathyroidal and extranodal invasions were also described.

After surgery, physical examination revealed one palpable nodule (1x1 cm) over the left lower neck. Thereafter, the patient received I-131 ablation

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therapy for 4 times (80 mCi, 80 mCi, 100 mCi, 100 mCi) from October, 1988 to November, 1990. The lesion still persisted after I-131 ablation therapy, thereafter he received external radiotherapy from December, 1990 to Febuary, 1991. The nodule became nonpalpable and thyroglobulin (TG) level decreased from detectable (6.9 μg/L) to undetectable (less than 0.5 μg/L) after external radiotherapy.

High TG antibody levels had appeared since May, 1995 without other clinical evidence of recurrence. In June, 1998, Tc-99m-MIBI scan showed two focal areas of increased uptake of radioactivity in the left lower neck and the right upper neck. Further surgical intervention was not performed at that time due to the fear that previous external radiotherapy might delay wound healing.

In April 2004, rapid enlargement of the right upper neck lymph node occurred. Thyroid echo showed the palpable mass to be a well-defined hypoechoic nodule with cystic change and uneven margin in right upper neck, lateral to sternocleidomastoid muscle. Aspiration cytology showed high cellularity and mild anisonucleosis pattern suggesting thyroid malignancy. Magnetic resonant imaging (MRI) of neck showed an irregular nodule (2.1 x 2.5 cm) in the right upper neck. Thus, the patient received resection of the right neck lymph node and partial resection of the sternocleidomastoid muscle. Pathology showed PTC metastases to the lymph node with focal extension beyond the capsule (Figure 1B). Post-operation I-131 radiotherapy (150 mCi) was given and the whole body scan showed negative findings (Figure 2A).

In May 2005, recurrence of an ulcerative mass (5 x 5 cm) over the previous surgical wound occurred. Hemoptysis and fever were also described. Laboratory examination showed elevated C-reactive protein level with normal white blood cell count. Chest radiography showed

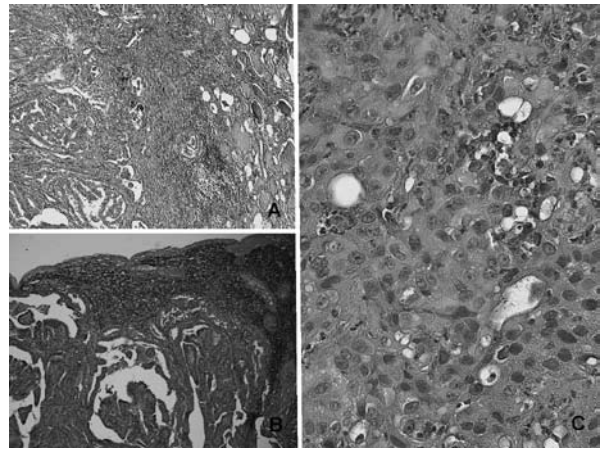

Fig.1. A: The pathology in June, 1988 showed neoplastic epithelial cells arranged in papillary structure infiltrating in thyroid follicles (H&E stain 40X).
B: The pathology in May, 2004 showed neoplastic epithelial cells having ground-glass nuclei in lymphoid tissue. They are arranged in papillary structure (H&E stain 100X).
C: The pathology in May, 2005 showed solid nests of neoplastic cells, bearing vesicular and pleomorphic nuclei and eosinophilic cytoplasm. Some tumor cells contained prominent nucleoli (H&E stain 400X).

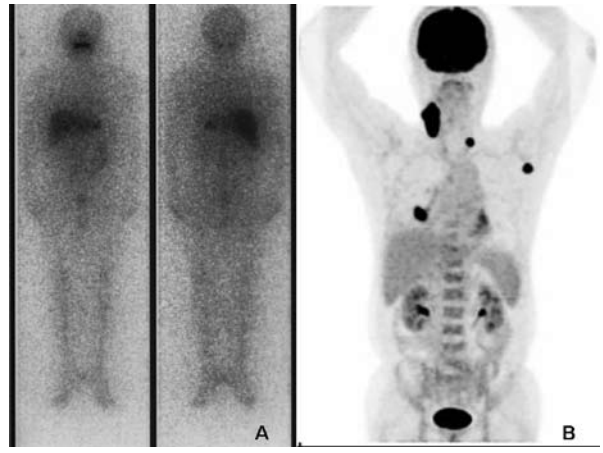

Fig.2. A: I-131 whole body scan showed no focal area of abnormally increased radioactivity uptake.
B: PET scan showed multiple 18F-FDG avid lesions in the neck, left axilla, right lower lung, and left lower lung.

nodular densities in the lower lung area. Computed tomography (CT) of chest revealed multiple tiny nodules in the right upper lobe, lingular segment

and bilateral lower lobe. Neck MRI showed one mass over right lower neck area. The fluorine-18 2-fluoro-2-deoxy-D-glucose-positron emission tomography (18F-FDG PET) scan showed multiple intensive uptake in the neck, left axilla, right lower lung, and left lower lung (Figure 2B). Incision biopsy of right neck mass showed anaplastic carcinoma (Figure 1C) with focal positive thyroid transcription factor-1 (TTF-1), positive cytokeratin 7 (CK7), negative TG, and negative cytokeratin 20 (CK20) stain in immunohistochemistry study. Under the diagnosis of ATC with lung metastasis, he received palliative chemotherapy. In October 2005, the man expired in spite of chemotherapy.

Discussion

Most patients with ATC present with a rapidly enlarging mass with mean size 8 cm (3 to 20 cm)[2,3,7,9]. Symptoms are related to mechanical compression, such as dyspnea, stridor, dysphagia, neck pain, and hoarseness[3,4,6,7]. Involvement of the cervical lymph nodes (40%) and surrounding structures (70%), such as muscle (65%), trachea (46%), esophagus (44%), and larynx (13%) are frequent[3,5,7]. Evidence of metastatic disease is seen in 50% of the patients at presentation, and another 25% develop metastasis during the course of the illness. The lung is the most common site (80%), followed by bone (6%-15%) and brain (5%-13%)[2,3,5,7]. Advanced stage, male gender, older age, leukocytosis, hypoalbuminemia, and hypothyroidemia were described as poor prognostic factors in previous reports[1,2,4,9]. In our case, male gender, and lung metastasis were poor prognostic factors.

The diagnosis of ATC is usually suspected on clinical examination and confirmed by fine needle aspiration biopsy or core biopsy. Fine needle aspiration biopsy diagnosis has been shown to be accurate in 90% of patients with ATC[10]. There are three patterns of ATC—spindle cell (53%), giant cell (50%), and squamoid (19%). All of them carry the same prognosis[11]. In this case, the previous reported immunohistochemical profile of TTF-1, TG, CK7, and CK20 is useful to differentiate the origin of the metastatic tumor[12]. Virtually all thyroid tumors are positive for CK7 and negative against CK20[12,13]. TTF-1 and TG are demonstrable by immunohistochemistry in the majority of thyroid neoplasms, but they will be lost or reduced in expression during dedifferentiation. In previous reported studies, TG is absent in the ATC tumors and TTF-1 is present in a few ATC tumors. TTF-1 is a more sensitive marker than TG for poorly differentiated carcinomas[12]. The biopsy result in our case showed ATC with pleomorphic nuclei and esinophilic cytoplasm. The immunohistochemistry stain is compatible with the diagnosis of ATC.

Preoperative imaging is helpful in both staging and treatment planning[14]. PET scans are useful in detecting distant disease since ATC is highly metabolic[14]. In our case, negative I-131 whole body scan and positive PET scan represented the loss of sodium/iodine symporter expression and highly metabolic nature of the cancer.

The management of ATC has evolved over the decades[2,3,7]. However, complete resection of the tumor, combined preoperative and postoperative radiotherapy, hyperfractionated radiotherapy, combination chemotherapy, or multimodal therapy did not improve the lethal outcome of ATC prominently[2,3,7]. Due to ATC with lung metastasis, our patient received palliative chemotherapy. But the patient still expired within half a year in spite of chemotherapy.

Previous reports have suggested that previous or concurrent thyroid disorder (benign or well differentiated thyroid carcinoma) is a risk factor for the development of ATC[2,3,5-8], and it is likely that aggressive resection for well differentiated thyroid carcinoma might reduce its incidence by eliminating the risk of dedifferentiation of well differentiated thyroid carcinoma to ATC[6]. In our case, even

aggressive treatment of primary and recurrence disease of PTC was done, we could not eliminate dedifferentiation of PTC to ATC.

Multiple molecular abnormalities leading to uncontrolled cellular proliferation have been disclosed with the progression of normal follicular thyroid cells to benign adenomas, well-differentiated thyroid tumors, poorly differentiated thyroid tumors, and ultimately ATC[15]. The RTK/RAS/RAF/MAPK pathway and the PI3K/AKT pathway are associated with initial stage progression. The p53 inactivation is involved in late stage progression[15]. A large number of new compounds have been developed to target the critical pathways in thyroid tumorgenesis and progression[15]. We hope that these innovative strategies beyond conventional methods may change the uniformally lethal outcome of ATC in the near future.

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甲狀腺乳突癌變性爲甲狀腺分化不良癌：病例報告

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摘 要

甲狀腺分化不良癌是極惡性的癌症，預後極差。大約兩成的病人之前曾有甲狀腺分化癌的病史。另一方面，大約兩成至三成的病人併有甲狀腺分化癌。在此，我們提出一位甲狀腺乳突癌變性爲甲狀腺分化不良癌的病例。病人表現爲右頸腫瘤合併肺部轉移並於診斷後半年內死亡。多重基因的變異和甲狀腺分化癌轉變成甲狀腺分化不良癌相關。傳統治療方法對治療甲狀腺分化不良癌效果差。針對腫瘤致癌過程的治療方式是值得進一步研究的課題。