

# Anaplastic Thyroid Cancer with Uncommon Long-term Survival

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In general, most thyroid cancers are indolent and have a slowly progressive course. The exception is anaplastic thyroid cancer. It is one of the most fatal neoplasms in humans, with median survival of 4–12 months. Here, we present a patient with anaplastic thyroid cancer who survived for more than 10 years after diagnosis. A 68-year-old man was incidentally found to have anaplastic thyroid cancer during operation for follicular neoplasm. Total thyroidectomy was performed and hyperfractionated radiotherapy was carried out. After operation, annual follow-up examinations were negative for residual tumor or metastatic lesions. The patient also had chronic obstructive pulmonary disease and unfortunately died of pneumonia in a local hospital 10 years after thyroid operation. [*J Chin Med Assoc* 2006;69(10):489–491]

**Key Words:** anaplastic thyroid cancer, hyperfractionated radiotherapy, thyroidectomy

## Introduction

Anaplastic thyroid cancer (ATC) is rare, representing 2–14% of all thyroid cancers.<sup>1</sup> It has very poor prognosis, with the 5-year survival rate ranging from 1.0% to 7.1% and median survival of 4–12 months.<sup>1,2</sup> Nearly all the patients are elderly; peak incidence is in the seventh decade of life.<sup>3</sup> The male-to-female ratio is 1:1.5. The most common presentation in patients with ATC is rapidly enlarging neck mass with a long-standing history of goiter. Compressive symptoms, such as hoarseness, dyspnea, cough and dysphagia, are common, and 1-third of such patients have neck pain. On examination, most patients have a dominant mass measuring 5–10 cm in diameter, multiple other nodules and enlarged cervical lymph nodes. Local extension of tumor growth can be detected on sonography, computed tomography, magnetic resonance imaging or scintigraphy. Diagnosis is established by fine-needle aspiration cytology (FNAC) or by histopathologic examination of the tumor after surgery. ATC is very aggressive, such that cervical lymph nodes and adjacent organs are frequently involved early. About

20–50% of patients have distant metastases, mostly to the lung, bones, brain and liver.

## Case Report

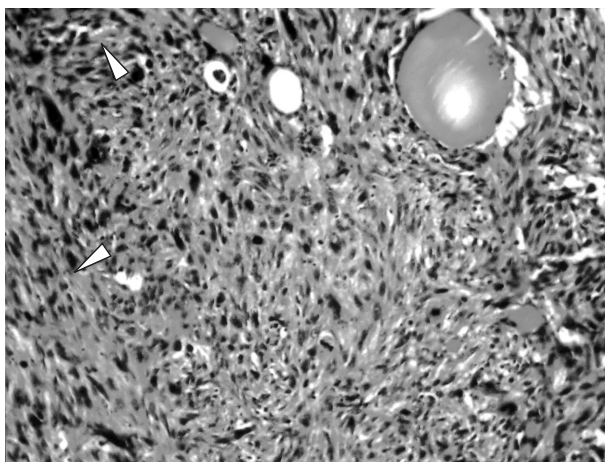
In 1989, a 68-year-old man visited our hospital because he had an anterior neck mass which resulted in compressive sensation over his throat and difficulty in breathing. FNAC on the mass in another hospital had shown normal thyroid follicular cells with lymphocytes. Thyroid function tests were within normal limits. Except for mild elevation of thyroid stimulating hormone receptor antibody (11%; normal, <10% with TBII-I), the thyroid antibodies were non-reactive. There was no fever or leukocytosis. On physical examination, a nodule 2 × 2 cm in size was palpable over the left lobe of the thyroid gland. It was stony hard, smooth-surfaced, movable and non-tender. No lymph node was found on the neck.

The patient received thyroid operation in April 1989. A large nodule about 5 × 3 × 4 cm in size, with sternothyroid muscle invasion and 2 other small nodules

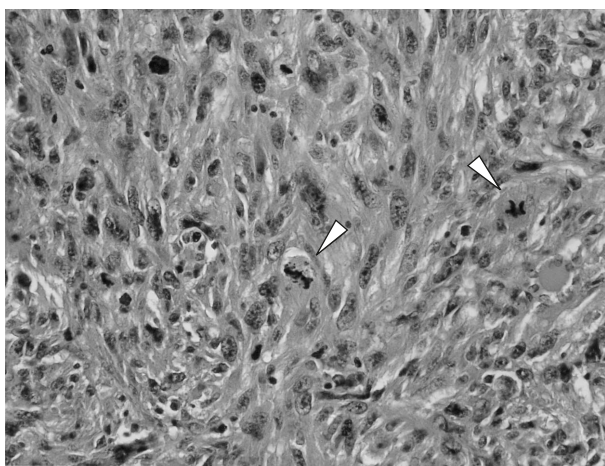
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were found in the left lobe of the thyroid. Frozen section of enlarged lymph nodes in the neck showed benign picture, but the specimen from the large thyroid nodule was reported as ATC. Total thyroidectomy was performed. Microscopic examination showed typical findings of ATC (Figures 1 and 2). No lymph node involvement was noted, and the right lobe was uninvolved.

Hyperfractionated accelerated radiotherapy with a total dose of 6,000 cGy was given 30 times within 4 months. Human thyroglobulin (hTG) was <3 ng/mL after operation and radiotherapy. The patient was treated with supraphysiologic dose of thyroxine. After operation, annual imaging studies showed negative findings for residual disease. In serial follow-ups, hTG remained undetectable and carcinoembryonic antigen levels were



**Figure 1.** Anaplastic thyroid cancer with fascicular pattern of spindle neoplastic cells (arrowheads) growing in a diffuse fashion with follicular destruction (hematoxylin and eosin; 80 $\times$ ).



**Figure 2.** Anaplastic thyroid cancer with several giant tumor cells with frequent mitotic figures and hyperchromatic nuclei representing anaplastic change (arrowheads) (hematoxylin and eosin; 400 $\times$ ).

within normal limits for many years. Unfortunately, the patient died of pneumonia in a local hospital in February 2000, more than 10 years after he was diagnosed with ATC.

## Discussion

The prognosis of ATC depends on various factors, including age, tumor size, extent of disease, acute symptoms, resectability and presence or absence of distant metastases.<sup>4</sup> Tumor size >5 cm, distant metastases, the presence of acute symptoms and leukocytosis >10,000/ $\mu$ L were suggested to be significant risk factors in 1 study.<sup>5</sup> Complete tumor resection was the major favorable factor. Unfortunately, curative resection for most cases of ATC is unlikely because local extension has usually already occurred in most cases at the time of diagnosis. ATC cannot uptake iodine, so radioactive iodine ablation is not a helpful therapy. External radiation may have some efficacy in local disease control. Tennvall et al<sup>6</sup> and Pollinger and Duhmke<sup>7</sup> commented that patients suffering from ATC should receive combined treatment consisting of extensive surgery, external irradiation with total doses up to 60 Gy, and chemotherapy.

Most patients with ATC die within 1 year of diagnosis. Although it is rare to have long-term survival, Lam et al<sup>8</sup> reported a 10-year survival rate of ATC in Hong Kong Chinese of around 3%. In their report, treatment with surgery was adopted as the first-line treatment, followed by postoperative combination chemotherapy and radiotherapy in selected patients. Mellièrè et al<sup>9</sup> reported 3 out of 22 ATC patients who remained free of disease 10, 12 and 13 years, respectively, after aggressive therapy. It was suggested that complete tumor removal, followed by hyperfractionated radiotherapy and other multimodal therapy might result in long-term survival. In the case of our patient, long-term survival may be attributed to early diagnosis, little adjacent structure invasion, no distant metastasis, complete tumor resection and postoperative irradiation.

Rodriguez et al<sup>10</sup> reported a subgroup of ATC coexisting with differentiated thyroid cancer, with better prognosis than that for primary pure ATC. However, there was no histologic evidence of differentiated thyroid cancer in our case. Lam et al<sup>8</sup> found that the 10-year survival rate for patients with insular carcinoma was 42%, which was 14 times higher than that for ATC (3%). Insular carcinoma, a rare subtype of thyroid cancer, has morphologic and biological characteristics between well differentiated (papillary

and follicular) and undifferentiated thyroid carcinomas (anaplastic). Therefore, insular carcinoma is sometimes mislabeled as ATC. A typical feature of insular carcinoma is groups or islands of tumor cells (insulae) surrounded by hypocellular fibrous tissue. The cells are small and uniform in nature. On the other hand, ATC is typically composed of varying proportions of spindle, polygonal and giant cells. It usually has residual elements of more differentiated thyroid cancer. In our case, the histologic features were definitely diagnostic for ATC. However, a few thyroid follicular structures were found in the tumor, which implicates the possibility of the ATC in this case being metaplasia from thyroid follicular tissues.

Because of the dismal outcome of ATC, various new therapeutic methods have been tried recently. Some of them seemed to be effective in cellular experiments.<sup>11–14</sup> Wang et al<sup>11</sup> reported that a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor could induce apoptosis and differentiation in ATC cells. Tumor necrosis factor- $\alpha$  was also found to be able to induce differentiation of human ATC cells through activation of nuclear factor  $\kappa$ B.<sup>12</sup> These advances provide us with some insights into the pathophysiology of ATC and may be the dawning of a new era in the treatment of this uncommon and terrible thyroid cancer.

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