

## Anaplastic Cancer and Papillary Thyroid Cancer in the same Patient: Is it a Co-Incidence or a Process of Transformation? A Case Report

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### Abstract

Anaplastic carcinoma of the thyroid gland is rare, but very aggressive, and the median survival is 3–5 months after establishing the diagnosis. The annual incidence in the USA is 1-2 cases per million populations. However, its incidence appears to be decreasing, while that of well-differentiated thyroid cancer is increasing. This report presents a patient with anaplastic thyroid cancer together with papillary carcinoma. A 62-year-old male visited our endocrinology clinic with a lump on the neck, palpable lymph nodes, and symptoms of compression. Fine-needle aspiration biopsies were inconclusive and he underwent surgery. Histopathology revealed intrathyroidal anaplastic carcinoma and papillary carcinoma in two distinct foci. Given the aggressive nature of the disease, there are few data on the tumor biology of anaplastic cancers; nevertheless, it is known that well-differentiated cancers of the thyroid gland can transform into anaplastic cancer. This results from point mutations in tumor suppressor genes due to previous radioactive iodine treatment or radiation exposure. It is not known whether de novo anaplastic cancers behave differently than those that evolved from differentiated cancers. By understanding the underlying pathophysiology of the disease, we can develop new therapies.

**Keywords:** Anaplastic thyroid; Intrathyroidal; Hypoechoic; Tumorigenesis; Dysphagia

### Introduction

Anaplastic carcinoma of the thyroid (ATC) gland is rare, but highly aggressive, with a median survival of 3-5 months after diagnosis [1,2]. The 10-year survival rate is less than 5%. It usually affects the elderly. In one study of 5583 thyroid cancers, 67% of anaplastic cancer patients were older than 70 years [3]. The annual incidence in the USA is one to two cases per million populations [4]. Although less than 1-3% of all thyroid cancers are anaplastic tumors, it contributes 14-50% of the annual mortality associated with thyroid cancer.

However, its incidence has been decreasing, while that of well-differentiated thyroid cancer has been increasing [4]. Some authors explain the decreased incidence of anaplastic thyroid cancer as resulting from aggressive treatment of well-differentiated cancers with surgery and radioactive iodine (RAI) [1]. Patients with anaplastic cancer usually present with local symptoms, such as hoarseness, a large neck mass, dysphagia, stridor, and less frequently neck pain. Lymph nodes are usually palpable at the time of diagnosis. Anaplastic thyroid cancer requires multi-modal treatment, consisting of surgery combined with radiotherapy or chemotherapy in appropriate cases. Surgery is useful for local control of the disease and confers short-term palliative and survival benefits [5,6]. It reduces the tumor burden.

However, many patients present with inoperable disease, and complete resection is possible for only up to one-third of patients at presentation. Postoperatively, radiotherapy or chemotherapy or both is performed to prevent tumor progression and further distant metastasis. The outcome of chemotherapy is usually poor [7]. Weekly low-dose doxorubicin concurrently with radiation therapy showed acceptable toxicity and might be a therapeutic option for patients with ATC. The 2-year local control rate is 68%, and the median survival time is 1 year [8]. Combination chemotherapy with bleomycin, doxorubicin, and cisplatin resulted in a response rate of 40% in advanced thyroid cancer, producing considerable palliative effects [8].

Here, we present a case of anaplastic thyroid cancer concomitant with papillary carcinoma. The co-existence of well and poorly differentiated tumors within the thyroid gland is extremely rare, and some data suggest that anaplastic carcinoma can evolve from papillary thyroid carcinoma.

### Case Presentation

A 62-year-old male presented to our clinic complaining of a neck lump, hoarseness, and dysphagia for a few months. The symptoms had progressed and become disturbing. He had no history of radiation exposure or family history of thyroid cancer. In the physical examination, we palpated 4-cm mass and cervical lymph nodes the largest was 1.5 cm on the left hand side of the neck. Unilateral vocal cord paralysis was detected by laryngoscopy.

Thyroid ultrasonography showed a hypoechoic 41.5-mm nodule in the left thyroid lobe, with cystic degeneration together with micro- and macro-calcifications. Color flow Doppler revealed increased vascularity. Two preoperative fine-needle aspiration biopsies (FNAB) were reported as non-diagnostic. His thyroid function tests were within the normal range. He underwent a total thyroidectomy and left extended lymph node dissection. The final postoperative pathology report was a 3-cm anaplastic carcinoma in the left lobe (Figure 1) that was intrathyroidal

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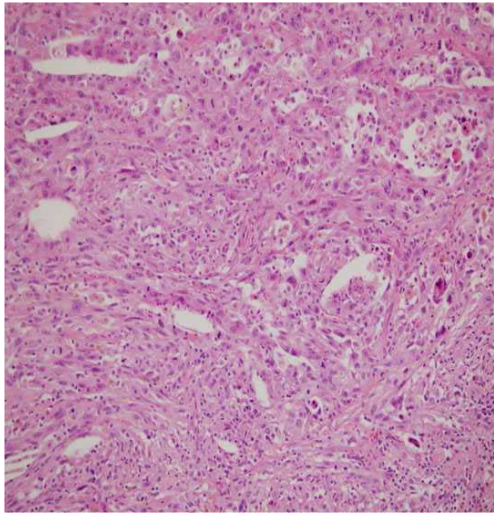


Figure 1: Anaplastic cancer.

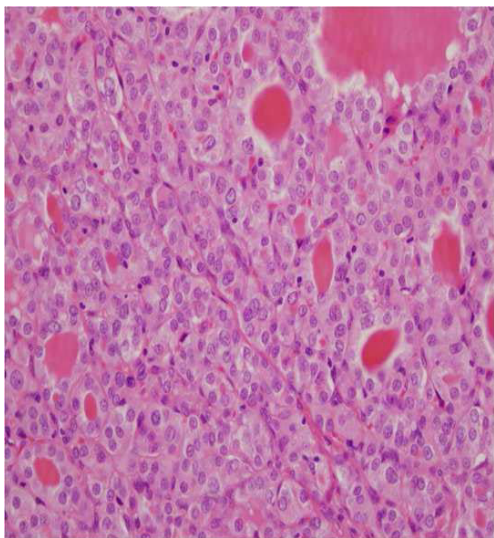


Figure 2: Papillary Cancer.

and had not invaded the thyroid capsule or lymphovascular structures. Histopathologically, the dissected lymph nodes were negative for cancer. Interestingly, the pathologists also detected a 5-mm papillary carcinoma in the right thyroid lobe specimen (Figure 2). He was given external beam radiation therapy postoperatively.

## Discussion

Given the extensive use of outpatient thyroid ultrasonography, the prevalence of incidental thyroid cancers has increased. These cancers are mostly well differentiated and the overall survival is excellent. Well-differentiated thyroid carcinomas originate from follicular epithelial cells derived from median endodermal structures. The risk factors for well differentiated thyroid cancers include iodine deficiency, radiation exposure to the neck, and a family history. Both patients and clinicians are concerned about the transformation of these well-behaving cancers into the more aggressive type called anaplastic cancer. Anaplastic tumors are aggressive and progress and disseminate rapidly. Microscopically, there are three patterns of ATC, spindle cell

(53%), giant cell (50%), and squamoid (19%), all of which have the same prognosis [9]. Unfortunately, almost half of the individuals have distant metastasis at the time of diagnosis [10,11]. Death in most cases is due to local invasion of the tumor into the vital structures, such as the trachea [12]. ATC is more common in regions where goiter is endemic, so with improved iodine supplementation, the incidence of this tumor should decline. Besic et al. reported that when the iodination of salt in Slovenia was increased from 10 mg of potassium iodide/kg from 1972-1997 to 25 mg of potassium iodide/kg in 1998, the mean incidence of ATC decreased from 6.2 (range 3-12) to 4 (range 2-10) [13]. Anaplastic transformation or intratumoral evolution of anaplastic carcinomas from pre-existing differentiated thyroid carcinomas is a recognized process, despite the limited understanding of the underlying mechanisms. A large proportion of ATC develops in elderly patients with long-standing goiter or previous malignant thyroid disease; this provides evidence for anaplastic transformation. In their series of ATC, Demeter et al. found that 76% of the patients had evidence of a previous thyroid disorder (benign or malignant), of which 46% had previous or concurrent well-differentiated cancer [14]. It is difficult to determine the underlying biology of this cancer because of its rarity and the fatal nature of the disease. No useful marker of the risk of anaplastic transformation has been identified. It was suggested that 2% of untreated well-differentiated thyroid carcinomas might evolve into anaplastic cancer during the course of the disease [15,16].

Some tumor suppressors or oncogenes that might be responsible for tumorigenesis and anaplastic transformation have been identified, including p53 [17], bcl-2 [18], and cyclin D1 [19]. The mechanism of transformation in patients with previously treated well differentiated cancers might be different. Postoperative radioactive iodine therapy should be used in high-risk patients with differentiated thyroid carcinoma to decrease both the recurrence and death rates, but a high cumulative dose of RAI does not confer any benefit [20]. The overall relative risk of secondary carcinoma or leukemia is increased in patients who received a cumulative dose of RAI > 500 mCi and external radiotherapy [21,22]. Inactivating point mutations of the tumor suppressor genes are frequently found in anaplastic thyroid carcinoma, in contrast to differentiated thyroid carcinoma [23]. Long-term RAI therapy might affect these genes and so contribute to anaplastic transformation.

In our case, the anaplastic cancer was concomitant with papillary carcinoma; whether they were independent of each other or the anaplastic carcinoma had evolved from a different focus of papillary carcinoma in the same gland was not known. One study suggested that the presence of a differentiated thyroid cancer component had no clinical value as a prognostic factor [24], while other studies reported a beneficial effect of differentiated thyroid cancer accompanying anaplastic cancer.

Anaplastic carcinoma of the thyroid gland is extremely aggressive and almost always fatal. By understanding its underlying pathophysiology, we can develop new therapies. The possibility of its emergence from a well-differentiated cancer indicates that papillary thyroid cancers should be treated carefully.

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