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Short Communication



# Anaplastic Thyroid Cancer Successfully Treated With Paclitaxel and Radiation: A Case Report

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## ABSTRACT

Anaplastic thyroid cancer (ATC) is rare and aggressive, with an extremely low cure rate and poor prognosis. Here, we report a case of treating patients with ATC through multimodal treatment and review the related literature. We report the case of a 56-year-old woman who was referred to our hospital for getting treated for ATC, which extended to the external right tracheal wall and muscular layer of the esophagus, with lateral lymph node metastasis. The patient underwent concurrent chemoradiotherapy. Three cycles of weekly paclitaxel administration were conducted, along with intensity-modulated radiotherapy. In response evaluation after three cycles of paclitaxel treatment, the main mass showed a partial response, and 2 additional cycles of paclitaxel administration were included in the treatment regimen. After the 5 cycles, the patient showed a partial response and was considered operable. The patient underwent bilateral total thyroidectomy with central compartment neck dissection and bilateral modified radical neck dissection. More than 43 months following diagnosis, the patient is still alive without evidence of local recurrence or distant metastases. Paclitaxel-based concurrent chemoradiation therapy has demonstrated potential as an alternative and effective treatment option in patients with unresectable ATC, with a durable response of 43 months and mild toxicity.

**Keywords:** Anaplastic thyroid carcinoma; Paclitaxel; Radiation therapy; Intensity-modulated radiotherapy

## INTRODUCTION

Anaplastic thyroid cancer (ATC) is rare and aggressive, comprising 1. 7% of all thyroid cancers (1). It has the worst prognosis among all thyroid malignancies due to a very low curative rate, with a median survival duration of 3–9 months, a 3-year overall survival (OS) rate of 10%, and most patients are not alive one year from the time of diagnosis (2).

In recent years, the prognosis of ATC has improved with the development of novel treatment methods. The MD Anderson Cancer Center analyzed the OS of ATC patients from 2000 to

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2019 and divided them into three groups (2000–2013, 2014–2016, and 2017–2019) according to the date of publication and OS for all three cohorts combined. The median overall survival rate was 9.5 months (3). These studies generally agreed to consider ATC as a systemic disease after diagnosis due to the rapid hematogenous dissemination of cancer cells resistant to standard chemotherapy drugs. Therefore, American Thyroid Association guidelines strongly recommend a multimodal approach (4).

Here, we report a case of treating patients with ATC using multimodal treatment and review relevant literature.

## CASE REPORT

A 56-year-old woman approached our hospital with a right thyroid nodule and bilateral cervical mass that were revealed during medical examination. The patient had no relevant medical history. At the first examination, the patient appeared physically active and could perform all pre-disease activities without restriction. Therefore, according to the Eastern Cooperative Oncology Group (ECOG) performance status score, the patient was classified as having ECOG grade 0.

Subsequently, the patient underwent staging examinations. Ultrasonography (US) revealed a 2.7 cm nodule in the right thyroid gland that originated from the posterior of the gland, extended along the tracheoesophageal groove, and invaded the trachea and esophagus. In addition, metastatic lymph node (LN) findings were confirmed at levels VI and IV (**Fig. 1**). US-guided fine-needle aspiration biopsy revealed highly atypical cells with markedly pleomorphic nuclei, favoring anaplastic carcinoma. Neck computed tomography (CT) was performed to confirm extrathyroidal extension and the extent of LN metastasis, and multiple LN metastases in the central compartment and bilateral level IV (<2 cm) were confirmed. Positron emission tomography-computed tomography (PET-CT) revealed no distant metastases (**Fig. 2**).

In the first operation, strongly invaded the internal carotid artery, and resection was attempted, but the operation was unsuccessful due to the possibility of damage to the surrounding major structures. Therefore, a frozen biopsy was performed on the central LN, showed poorly differentiated metastatic carcinoma and adenocarcinoma originating from other organs. The surgery was completed with only an excisional biopsy. Definitive pathologic examination confirmed metastatic anaplastic thyroid carcinoma with cytokeratin 7, HBME-1, TTF-1, PAX-8, and WT1 positivity and cytokeratin 20, thyroglobulin, napsin A,

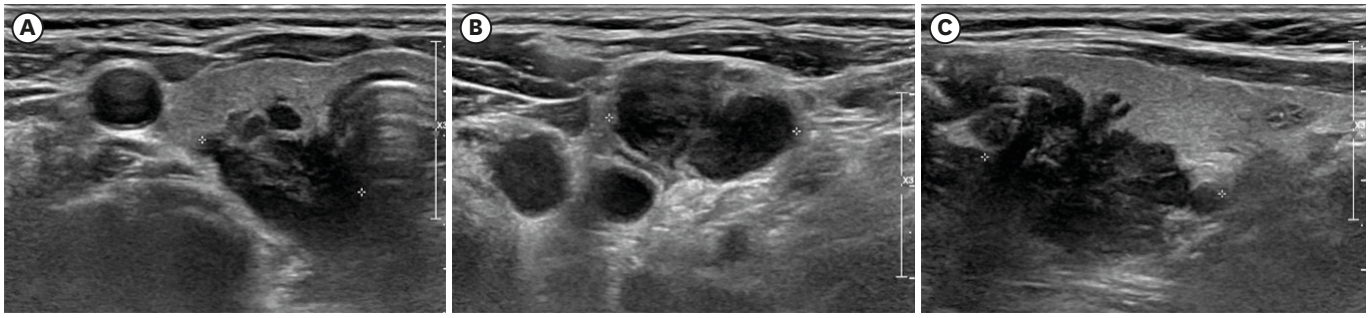


**Fig. 1.** Preoperative neck ultrasonography. (A) Right thyroid cancer with tracheal and esophageal involvement. (B) Left level IV lymph node. (C) Longitudinal view of right thyroid cancer.


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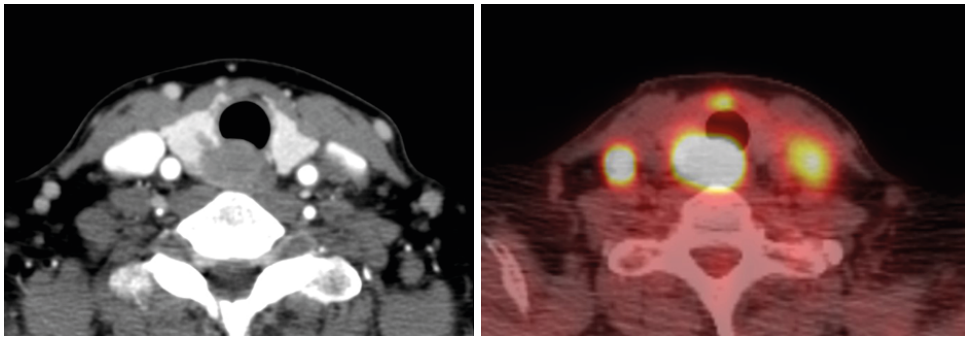

**Fig. 2.** Preoperative cervical CT and PET-CT. Multiple LN metastases in both the lateral neck.
CT = computed tomography; PET-CT = positron emission tomography-computed tomography; LN = lymph node.

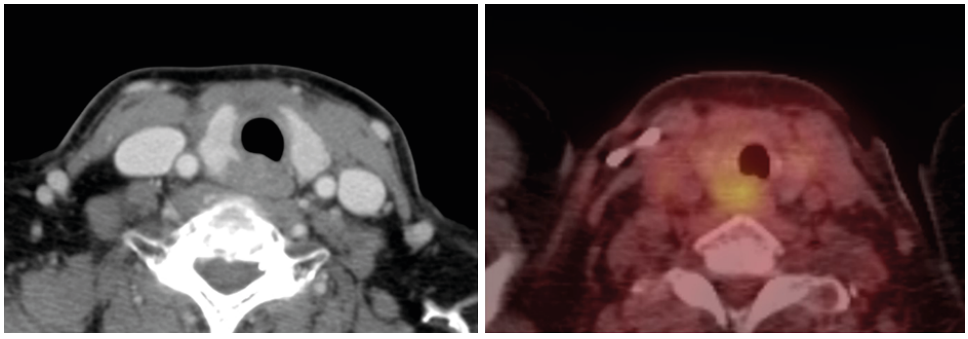

**Fig. 3.** CT and PET-CT images at the time of response evaluation after CCRT. Partial response of the main mass and lateral LN confirmed.
CT = computed tomography; PET-CT = positron emission tomography-computed tomography; CCRT = concurrent chemoradiation therapy; LN = lymph node.

p53, CEA, ER, and PR negativity. Based on these observations, we planned a concurrent chemoradiation therapy (CCRT).

Paclitaxel-based CCRT was administered as a chemotherapeutic regimen. Three cycles of weekly paclitaxel administration (70 mg/m$^2$) were conducted, along with intensity-modulated radiotherapy (RT) (66 Gy, 30 fractions). In the response evaluation following three cycles of paclitaxel administration, the main tumor was reduced to 1.8 cm, and the size of the lateral metastatic LN was also reduced, showing partial remission. Next, another two cycles of paclitaxel therapy were added to the regimen. According to the Common Toxicity Criteria Adverts Events Toxicity scale (CTCAE v. 4.0), the patient experienced mild acute toxicity during radiochemotherapy, with grade 2 dysphagia and dermatitis.

After the 5 cycles of therapy, the size of the main tumor decreased, and that of the lateral LN was also reduced. The expansion into the surrounding tissues also decreased, showing a partial remission; therefore, it was deemed operable (**Fig. 3**). Bilateral total thyroidectomy with central compartment neck dissection and bilateral modified radical neck dissection were performed 5 months after the diagnosis. During surgery, the right thyroid tumor severely invaded the tracheal wall and esophagus but relatively easily identified the border upon resection. The recurrent laryngeal nerve on the ipsilateral side of the tumor was entrapped, and the nerve was resected by shaving. The right recurrent laryngeal nerve signal was inspected during intraoperative nerve monitoring and nerve shaving was performed. This patient did not have vocal cord paralysis before surgery. After nerve shaving during the


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operation, the nerve signal was clearly captured and maintained the nerve function without any side effects after the operation.

Final pathological examination revealed a residual anaplastic carcinoma of 0.5 cm with no lymphovascular invasion, microscopic perithyroidal soft tissue extension, or skeletal muscle involvement. Metastatic LNs were found in one central compartment and in one right IV LN. Thus, according to TNM staging (8th ed., 2016) and the American Joint Committee on Cancer System (AJCC), the patient was classified as pathological T4a N1b (stage IVA). Immunohistochemical staining showed that PAX-8, HBME-1, and TTF-1 were positive with no BRAF mutations.

Levothyroxine and calcium carbonate were administered as replacement therapies after thyroidectomy. Patient follow-up was done continuously. Endocrinological evaluation (including thyroid function examinations) was performed at each visit. Neck US and contrast-enhanced CT of the head, neck, and chest were regularly conducted. Four years after diagnosis, the patient is still alive, without evidence of locoregional recurrence or distant metastases, and maintains a good quality of life.

## DISCUSSION

ATC is an extremely rare undifferentiated cancer with a high mortality rate (5). Complete surgical resection combined with adjuvant therapy (RT and chemotherapy) is key to its treatment. However, it is mainly ineffective, since despite these treatments, the mortality rate remains high (4). Approximately 85%–95% of ATC patients have invasive primary tumors (6,7). In addition, 32%–69% of the patients exhibit tracheal involvement, 37%–55% esophageal involvement, and 24%–39% carotid artery involvement (8,9).

Although there is no consensus on standard treatment, past studies report improved outcomes with combination therapy involving surgery, radiation, and chemotherapy compared with that of monotherapy. Several studies have reported that surgery is the cornerstone of treatment. It has been associated with better clinical outcomes than radiation or radiochemotherapy (44 vs. 4 months, P<0. 01) (10).

The extent of surgical resection should be considered in the context of morbidity that may arise from the resection of adjacent related structures. Approximately 38% of primary thyroidectomies for ATC treatment require an extended resection (11). Extensive tumor progression in the thoracic inlet and upper mediastinum may presuppose involvement of the mediastinal vasculature if emergency sternotomy is performed to control the bleeding. Ultimately, preoperative staging and assessment of the local tumor extent should be performed with the surgeon's experience, judgment, and technical expertise to determine whether primary tumor resection should be attempted with acceptable morbidity and risk.

If the primary tumor is considered unresectable, alternative neoadjuvant approaches may be appropriate in carefully selected patients. External beam RT may be followed by primary surgical resection. These therapies may be as effective as early primary resection (12).

Paclitaxel is known to exert a radiosensitizing effect on a variety of tumors. A study indicated that in patients with ATC, IV docetaxel administration at a dose of 60 mg/m$^2$ every three


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weeks may produce complete response in some cases, but more commonly, it stabilizes the disease for a period of time (13). The induction mechanisms of radiosensitization in adenocarcinoma cell lines may act by inhibiting DNA repair, cell cycle redistribution, and apoptosis (14,15). The level of apoptosis after paclitaxel treatment may be predicted by paclitaxel-induced radiosensitisation. In treating patients with non-small cell lung cancer, the administration of low-dose paclitaxel with RT as a radiosensitizer is more effective than chemotherapy and RT alone (16). When paclitaxel is used as a cytotoxic drug and radiosensitizer, the radiation dose can be reduced to avoid radiation toxicity (17).

Paclitaxel has been reported to produce encouraging results in ATC, especially when combined with radiation therapy. In a study of 10 consecutively treated ATC patients with local disease, 5 patients were survived and cancer-free, having been followed >32 months with a median overall Kaplan-Meier survival of 60 months in response to intensity-modulated RT combined with adjuvant and radiosensitizing chemotherapy (18). However, there have also been reports of a rather disappointing response rate of only 14% in response to docetaxel monotherapy in advanced ATC (13).

In conclusion, paclitaxel-based CCRT has demonstrated potential as an alternative and effective treatment option in patients with unresectable ATC, with a durable response of 43 months and mild toxicity. In the future, it will be necessary to study whether it can be used as a neoadjuvant treatment before surgery or as long-term maintenance therapy.

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