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## An overview of the contemporary diagnosis and management approaches for anaplastic thyroid carcinoma

Shu-Yue Zhou, Lian-Xiang Luo

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### Abstract

Thyroid carcinoma is a complex disease with several types, the most common being well-differentiated and undifferentiated. The latter, “undifferentiated carcinoma”, also known as anaplastic thyroid carcinoma (ATC), is a highly aggressive malignant tumor accounting for less than 0.2% of all thyroid carcinomas and carries a poor prognosis with a median survival of 5 months. *BRAF* gene mutations are the most common molecular factor associated with this type of thyroid carcinoma. Recent advances in targeted biological agents, immunotherapy, stem cell therapy, nanotechnology, the dabrafenib/trametinib combination therapy, immune checkpoint inhibitors (ICI) and artificial intelligence offer novel treatment options. The combination therapy of dabrafenib and trametinib is the current standard treatment for patients with *BRAF-V600E* gene mutations. Besides, the dabrafenib/trametinib combination therapy, ICI, used alone or in combination with targeted therapies have raised some hopes for improving the prognosis of this deadly disease. Younger age, earlier tumor stage and radiotherapy are all prognostic factors for improved outcomes. Ultimately, therapeutic regimens should be tailored to the individual patient based on surveillance and epidemiological data, and a multidisciplinary approach is essential.

**Key Words:** Thyroid diseases; Thyroid cancers; Anaplastic carcinoma; Undifferentiated carcinoma; Neck mass; Aggressive malignancies

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**Core Tip:** Anaplastic thyroid carcinoma is an infrequent but deadly form of cancer. Combining surgery, radiotherapy, chemotherapy, novel targeted therapy and immunotherapy has improved the prognosis. Multimodal management and individualized treatment with novel agents is encouraging. To further improve the outcomes, more studies shall be carried out on the molecular microenvironment and biological drivers.

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## INTRODUCTION

Although the prevalence of thyroid carcinoma is on the rise, the incidences of anaplastic thyroid carcinoma (ATC) and medullary thyroid carcinoma (MTC) remain relatively stable. Between 2000 and 2009, the overall prevalence of thyroid carcinoma experiences a significantly accelerated increase of approximately 8% per annum in both males and females[1]. ATC is a rare undifferentiated form of thyroid malignancy that accounts for a small percentage of cases, ranging from less than 0.2% to 1%-2%[2-4]. However, it is considered one of the most deadly neoplasms, with a median survival of only 4 to 6 months and a substantial decline in quality of life[3-5]. Multimodal therapy involving chemotherapy and external beam radiotherapy has shown limited success in patients with unresectable or metastatic disease, resulting in a 12-month overall survival of less than 20%. The presence of rapidly growing neck tumors often leads to severe and potentially life-threatening complications. These tumors can invade various structures, such as the trachea, leading to airway obstruction and asphyxia; the esophagus, causing dysphagia; the recurrent laryngeal nerve, resulting in paralysis and hoarseness; the major blood vessels, leading to manifestations of superior vena cava syndrome or intermittent cerebral ischemia; and the neural plexuses, causing persistent pain.

## ADVANCEMENTS IN DIAGNOSIS, TREATMENT AND MANAGEMENT STRATEGIES OF ATC

An accurate diagnosis of ATC is essential and can be achieved through ultrasound and core needle biopsy. Computed tomography and magnetic resonance imaging scans can be used for staging. Molecular testing can further refine the diagnosis and reveal implicated genes, such as *BRAF-V600E* and *BRAF* wild type, which can be used to determine the optimal treatment strategy, such as anti-*BRAF*, anti-*VEGF-A* or anti-*EGFR* agents[6].

Nanotechnology has the potential to revolutionize drug delivery systems by enabling targeted therapy and chemophotothermal (lenvatinib-laser irradiation) therapy. Furthermore, it may also lead to the development of magnetic or radiolabeled probes that can be used to diagnose disease progression. Moreover, the uses of an anti-programmed cell death-ligand 1 monoclonal antibody (atezolizumab) as immunotherapy may potentiate the effect of radiotherapy on malignant cells.

The initial outcomes of deep learning and artificial intelligence in the fields of diagnosis, image evaluation, treatment and outcome prediction have exhibited great potential. To ensure optimal results, it is crucial to adopt a multidisciplinary approach and formulate an individualized therapeutic regimen based on the principles outlined in surveillance, epidemiology, and end results[2,7-10].

The management protocol encompasses the established therapeutic regimen, which involves prioritizing surgical intervention, particularly debulking surgery. Additionally, adjuvant chemotherapy utilizing cisplatin or doxorubicin combined with docetaxel-paclitaxel, along with accelerated hyperfunctional external beam radiotherapy, preferably used in a neo-adjuvant and definitive manner, is a standard treatment. This therapeutic regimen has the potential to extend the median survival by approximately 10 months[6]. The novel and promising approach of utilizing targeted biological agents and immunotherapy has effectively enhanced the overall survival rates in patients who were previously considered to have a dismal prognosis[2,5,6,11,12].

The *BRAF* inhibitor dabrafenib and the *MEK* inhibitor trametinib were approved by the U.S. Food and Drug Administration in 2014 and 2018 respectively, for the treatment of mutated melanoma and mutated anaplastic thyroid carcinoma. Consequently, it has been effectively utilized in the case of metastatic or locally advanced inoperable ATC with *BRAF-V600E* gene mutation. This targeted therapy has been advised as a neoadjuvant treatment followed by surgery. It constitutes the standard treatment and guarantees a two-year overall survival rate of 80%[5,6,13,14].

The primary determinants associated with better overall outcomes have been identified as younger age, earlier tumor stage, tumor size, multifocality, utilization of radiotherapy and innovative targeted therapy[3,15].

## CONCLUSION

This review assesses the understanding of highly aggressive ATC with a severe prognosis and emphasizes the signi-

ificance of accurate diagnosis and treatment. The analysis is built on the data from a broad exploration of PubMed up to September 2023, concentrating chiefly on full-text articles issued only in English within the past five years.

## FOOTNOTES

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