Advancing the Management of Anaplastic Thyroid Carcinoma: A Case Study of Multimodal Therapy and the Role of Emerging Nuclear Medicine Infrastructure in Bangladesh

[1]Priyanka Podder, [1]Fatema Tuz Zohra, [2]Samiul Alim, [3]Abul Hasnat, [3]Rayhan Alam, [4]Sanchoy Chandra Biswasarma, [5]M A Mannan, [6]M Monjur Ahsan

[1]Senior Medical Officer, [2]Experimental Officer, [3]Senior Scientific Officer,
Institute of Nuclear Medical Physics (INMP), AERE, Savar
[4]Scientific Officer, National Institute of Nuclear Medicine and Allied Sciences (NINMAS), BSMMU
[5]Associate Professor, Labaid Cancer Hospital, Dhaka
[6]Chief Scientific Officer, Atomic Energy Center (AEC), Dhaka.

Correspondence Address : Dr. Dr. Priyanka Podder, Senior Medical Officer, INMP, AERE, Savar. Email: priyankaszmc25@gmail.com

ABSTRACT

Anaplastic thyroid carcinoma (ATC) is an aggressive and rare form of thyroid cancer, representing 1-2% of thyroid malignancies but accounting for the majority of thyroid cancer-related deaths due to its rapid progression, invasiveness, and resistance to standard therapies. This report highlights the case of a 60-year-old male histopathologically diagnosed with ATC stage IV as there were lymph node metastases. The patient was managed with a multidisciplinary team approach and had total thyroidectomy followed by systemic chemotherapy and three-dimensional conformal radiotherapy. The reported case highlights the importance of aggressive, integrated therapeutic approaches in managing ATC, emphasizing personalized, multidisciplinary care, advanced radiotherapy techniques, and molecular-targeted therapies for improved outcomes.

Keywords: Anaplastic thyroid carcinoma, Lymph nodes, Chemotherapy, 3D-CRT, PET-CT.

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INTRODUCTION

Anaplastic thyroid carcinoma (ATC) is a rare but extremely aggressive form of thyroid cancer, accounting for only 1-2% of all thyroid malignancies yet responsible for a disproportionately high number of thyroid cancer-related deaths. Its rapid progression, local invasiveness, and resistance to conventional therapies make ATC one of the deadliest thyroid cancers, with a median survival of three to nine months and a one-year survival rate below 20%. Typically affecting older adults, ATC shows a slight female predominance and is most commonly diagnosed in the sixth and seventh decades of life. Patients often present with a rapidly enlarging neck mass accompanied by compressive symptoms such as hoarseness, difficulty swallowing (dysphagia), and breathing difficulties (dyspnea). The tumour often invades local structures, including the trachea and oesophagus, and metastasizes to distant organs such as the lungs, bones, and brain.

Histologically, ATC is marked by poorly differentiated or undifferentiated cells with diverse morphologies, including squamous, spindle, and giant cell patterns. Immunohistochemical analysis has revealed the presence of key mutations and molecular markers that contribute to the tumour's aggressive behaviour and resistance to therapy. Immune checkpoint inhibitors and molecularly targeted therapies targeting actionable mutations, such as BRAF inhibitors, are emerging as potential game-changers in managing ATC. (4, 9). The reported case of a 60-year-old man diagnosed with ATC and treated with 3D-CRT combined with chemotherapy after thyroidectomy highlighted the potential of integrated therapeutic strategies to extend survival and improve the quality of life.

CASE REPORT

Patient Background and Initial Diagnosis

A 60-year-old man noticed a rapidly growing anterior neck mass and hoarseness in February 2021, accompanied by significant weight loss and exhaustion over three months. A firm, immobile mass in the thyroid

region was found on physical examination. High-resolution ultrasound (HRUS) of the neck revealed a large, irregular, hypoechoic thyroid mass with invasion into soft tissues and tracheal compression, leading to the suspicion of anaplastic thyroid cancer.

There were indications of local invasion, including the compression of nearby structures. During the initial evaluation, there was no indication of distant metastases. A big, irregular, hypoechoic thyroid mass with invasion into surrounding soft tissues and tracheal compression was discovered during the patient's ultrasound imaging study. Anaplastic thyroid cancer was suspected after fine-needle aspiration cytology (FNAC) revealed poorly differentiated malignancy. Total thyroidectomy was done in February, 2021 and histopathology reported ATC with squamous cell pattern, and immunohistochemical staining was positive for p53, which was consistent with the characteristics of ATC. Post thyroidectomy whole-body radioactive iodine (^{131}I) scan (WBS) showed negligible iodine uptake, confirming lack of differentiation of tumor cells.

Treatment approach

a. Initial Chemotherapy

Following total thyroidectomy in February 2021, the patient underwent systemic chemotherapy using doxorubicin and cisplatin, targeting residual disease and potential micrometastases, administered over seven cycles from March to September 2021.

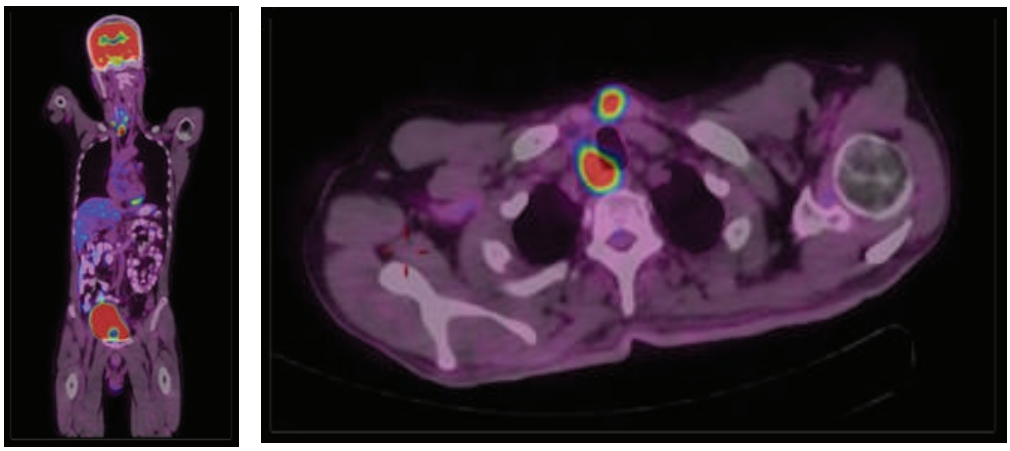

Figure 1: ^{18}F-FDG Uptake in Thyroid Bed, Supraclavicular Nodes, and Suprasternal Nodule

A follow-up PET-CT scan in September 2021 found hypermetabolic areas in the right thyroid bed, supraclavicular lymph nodes, and a subcutaneous nodule in the suprasternal region, which suggested progression of the disease.

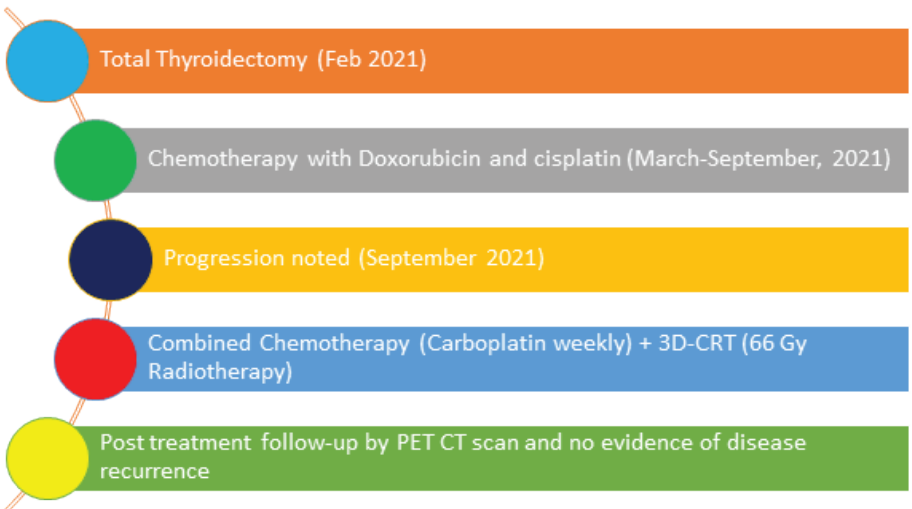

Figure 2: A flowchart outlining the chemotherapy protocol, including drugs and treatment cycles.

b. Combined Chemotherapy and Radiotherapy

To combat disease progression, combined concurrent chemotherapy and three-dimensional conformal radiotherapy (3D-CRT) was started in September 2021 to target residual disease in the thyroid bed and involved lymph nodes while treating micro metastases as well.

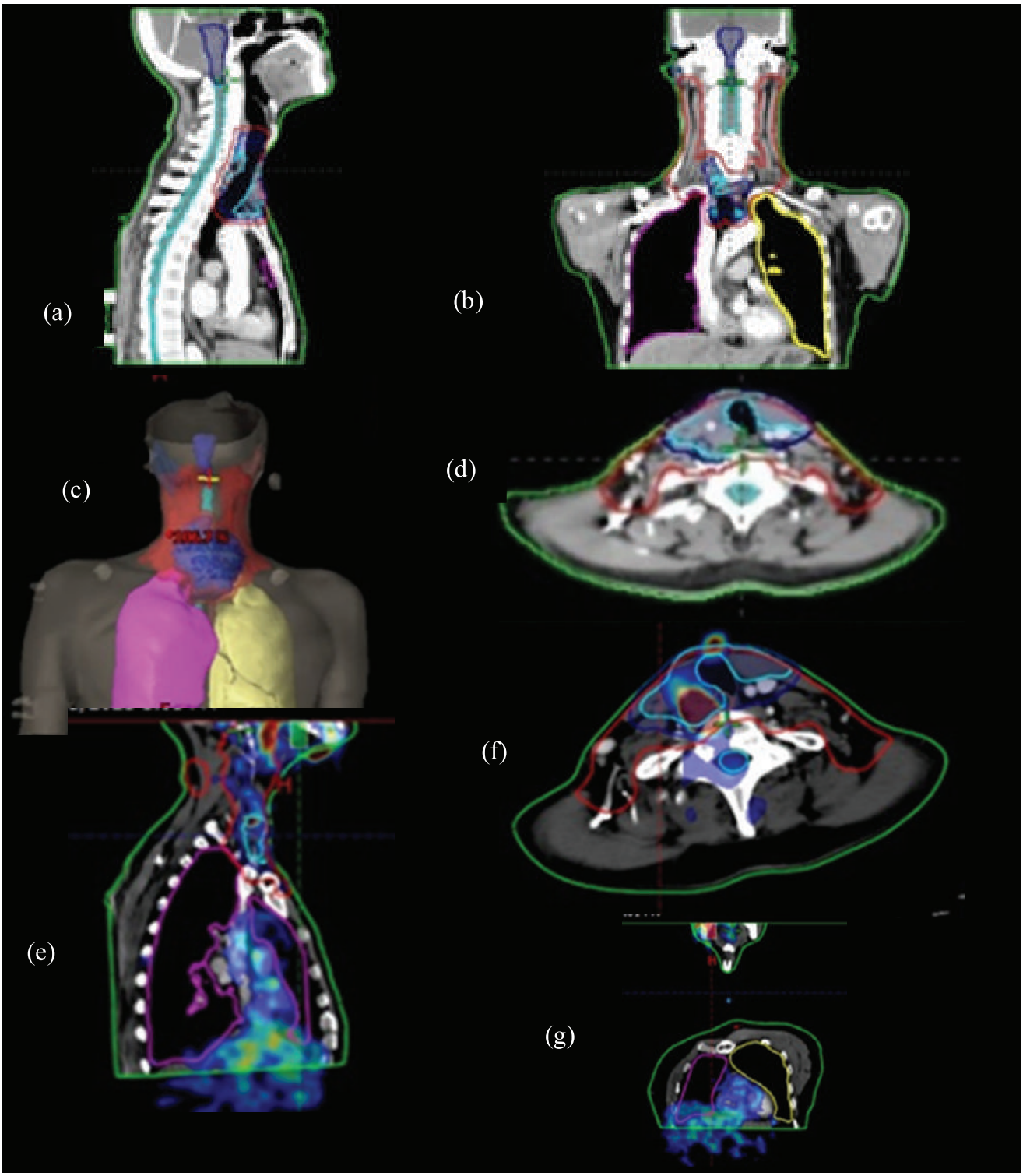

Figure 3: PET-based images showing (a) & (b) Organ at Risk, (c) 3D image of the contoured area, (d),(e), (f)& (g) CTV and PTV area.

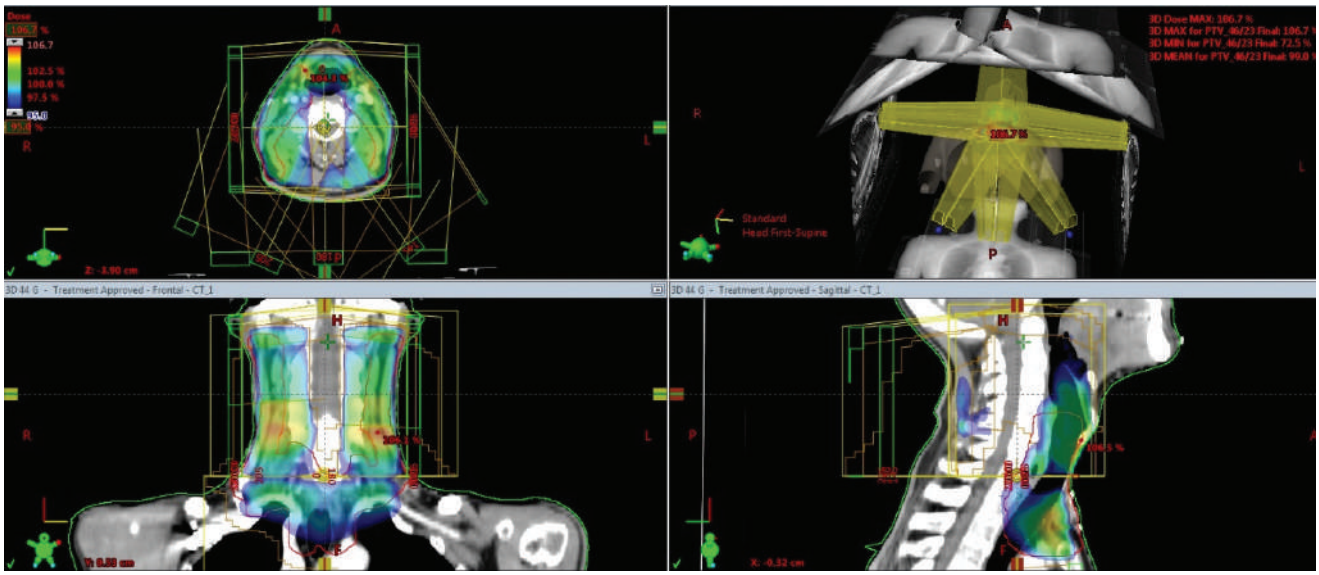

Figure 4: Illustration of the 3D-CRT process, highlighting the targeting of the thyroid bed and surrounding regions.

c. Radiotherapy Protocol

The patient underwent 3D-CRT, a highly conformal radiation therapy method, targeting specific regions like the thyroid bed, lymph nodes, and suprasternal nodules. The treatment, delivered over 6 weeks (a total dose of 66 Gy across 33 sessions using a standard fractionation strategy of 2 Gy each fraction) was proven to improve local control in anaplastic thyroid cancer while reducing radiation-induced toxicity to surrounding tissues. This approach is supported by evidence of improved survival outcomes.

d. Concurrent Chemotherapy

Carboplatin, a radio-sensitizing chemotherapy agent, was used alongside radiotherapy to enhance treatment effectiveness by disrupting DNA repair mechanisms and making cancer cells more susceptible to radiation-induced damage. The combination therapy was designed to optimize tumor response, minimize adverse effects, and efficiently target remaining cancer cells while managing metastatic spread.

Treatment outcome

Short term outcome: After the end of the integrated treatment regimen, patient obtained full metabolic response, despite the aggressive nature of ATC, which was confirmed in a follow-up whole body 18F-FDG PET-CT scan done in April 2022. This outcome was achieved due to 3D-CRT's precise targeting and carboplatin's radio-sensitizing effects. Despite the intensity of the treatment protocol, the patient tolerated the therapy well, with no major adverse events like esophagitis, mucositis, and hematological complications reported.

Long-Term Outcome: While following up the patient, no local recurrence or metastatic involvement was found over last 16 months, suggesting good therapeutic response and a significant accomplishment compared to most ATC cases. Being asymptomatic and good quality of life was reported by the patient.

DISCUSSION

Historically, the prognosis for anaplastic thyroid carcinoma (ATC), a rare and aggressive form of thyroid cancer, has been disappointing. It is characterized histologically by poorly or undifferentiated cells, often lacking thyroid-specific markers like thyroglobulin and TTF-1 but sometimes expressing cytokeratin's and PAX8 (7). Its aggressive nature stems from genetic mutations in TP53, TERT promoter, BRAF, and other pathways, contributing to tumor dedifferentiation and treatment resistance. Traditional treatments, including

surgery, chemotherapy, and radiotherapy, have shown limited success, with median survival under six months (3). However, advancements like 3D-conformal radiotherapy with radiosensitizing agents and targeted therapies, including BRAF/MEK inhibitors and immune checkpoint inhibitors, are showing promise in improving outcomes for selected patients (8, 9). These recent developments in multimodal therapeutic approaches have demonstrated promise in enhancing patient outcomes, especially the combination of immunotherapy and targeted therapy. In contrast to patients getting limited treatment options, those receiving comprehensive multimodal therapy have much improved locoregional control and overall survival, according to new findings from retrospective cohort studies. These results highlight how crucial customized, multifaceted treatment programs are crucial to successfully control ATC (10,11). Determining prognostic variables is also essential to tailoring treatment plans to each patient's unique requirements. Additionally, the validation of survival prediction models for patients with anaplastic thyroid carcinoma (ATC) is crucial because it gives physicians the information they need to decide on the type and intensity of treatment based on evidence, which ultimately aims to improve patient outcomes and maximize resource allocation (12).

This study illustrates the potential of integrating advanced multimodal approaches in treating ATC and highlights the possibility of achieving long-term disease control, with no recurrence or metastasis observed over a 16-month follow-up period. Recent studies have reported similar success with multimodal approaches in ATC management. Combining radiosensitizing agents like carboplatin with 3D-CRT enhances treatment response while minimizing toxicity (13). Additionally, the role of targeted therapies such as BRAF/MEK inhibitors was established in improving outcomes for patients with actionable genetic mutations like BRAF V600E (14). While targeted therapies were not part of this case, their integration into treatment protocols has been shown to extend progression-free survival and improve quality of life in other ATC cases. The findings from retrospective studies further emphasize the importance of tailoring treatment plans to individual patient profiles. This underscores the importance of personalized, evidence-based strategies for optimizing therapeutic outcomes (15).

Lastly, the absence of major adverse effects in this case, such as esophagitis, mucositis, or hematological toxicity, supports the tolerability of advanced multimodal approaches. The combination of surgery, systemic therapy, and precision radiotherapy can significantly improve survival rates in ATC when tailored to prognostic factors such as tumour size, genetic mutations, and patient age (16). This case supports the use of integrated, multidisciplinary treatment strategies for ATC. Advanced approaches like 3D-CRT, radiosensitizing chemotherapy, and targeted therapies represent a shift towards more effective and individualized care. Further research and long-term follow-up are essential to refine these strategies and expand their applicability to broader patient populations.

CONCLUSION

Combining 3D-CRT with chemotherapy may provide long-lasting disease control in certain ATC cases. This supports the idea that vigorous multimodal therapy can improve ATC management when customized, leading to longer survival and higher quality of life. The case highlights the potential of aggressive, coordinated multimodal therapies for ATC management, indicating that further exploration of advanced radiotherapy techniques, chemotherapeutic agents, and molecular-targeted therapies could revolutionize the treatment.

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