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CASE REPORT

Follicular Thyroid Carcinoma with Extensive Pulmonary and Mediastinal Metastases: Long-Term Symptom Control through Sequential High-Dose IMRT in a Patient Declining Systemic Therapy

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Abstract

Background: Follicular thyroid carcinoma (FTC) has a greater tendency for hematogenous spread compared with other differentiated thyroid cancers, and distant metastases may become refractory to radioactive iodine (RAI). When systemic therapy is declined or not tolerated, management becomes challenging. External beam radiation therapy (EBRT) with intensity-modulated radiotherapy (IMRT) may offer meaningful symptom control and local disease management. **Case Presentation:** A 51-year-old man with metastatic FTC underwent total thyroidectomy and high-dose RAI, followed by radiologic progression with extensive pulmonary and mediastinal metastases causing dyspnea and dysphagia. The patient refused systemic therapy. High-dose mediastinal IMRT (6000 cGy/30 fractions) led to rapid symptom improvement and an 18-month symptom-free interval. Later, orbital pain and diplopia caused by a posterolateral orbital lesion were treated with IMRT (6000 cGy/30 fractions), resulting in marked relief. One year later, a painful scapular metastasis was treated with IMRT (5000 cGy/20 fractions), providing effective pain control. A follow-up whole-body staging CT performed months later during evaluation for cabozantinib initiation unexpectedly confirmed sustained thoracic response, with the largest pulmonary nodule decreasing from 45 mm to 26 mm and subcarinal lymphadenopathy shrinking from 50 × 70 mm to 38 × 21 mm. The patient remains clinically stable under cabozantinib therapy. **Conclusion:** Sequential IMRT provided durable symptom control, preserved performance status, and delayed systemic therapy in this patient with RAI-refractory metastatic FTC who repeatedly declined drug treatment. IMRT may serve as a practical therapeutic strategy when systemic therapy is not feasible.

Keywords: Follicular thyroid carcinoma, RAI-refractory, IMRT, metastatic disease, external beam radiation therapy

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Introduction

Thyroid cancer (TC) has shown a significant global increase over the past three decades [1]. While it affects both men and women, it remains more common among women. Despite the rising incidence, mortality rates have remained relatively stable, emphasizing the importance of accurate classification and tailored management strategies for this malignancy [2].

Differentiated thyroid carcinoma (DTC), mainly comprising the follicular thyroid carcinoma (FTC) subtype, represents the majority of thyroid cancers [3]. Among patients with DTC, approximately 7–23% develop distant metastases (DM), which markedly worsen prognosis and reduce overall survival [4, 5]. The lungs and bones are the most common sites for distant spread [6]. For over seven decades, radioactive iodine (^{131}I) therapy has remained the cornerstone treatment for iodine-avid metastatic DTC [7]. Management typically includes TSH suppression (TSH < 0.1 μU/L) and repeated RAI therapy [8]. However, therapeutic options become limited once the disease becomes refractory to RAI. Conventional

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chemotherapy has shown limited efficacy and considerable toxicity [9]. In such patients, local treatment modalities including external beam radiation therapy (EBRT) and percutaneous ablation can provide effective tumor control, palliate symptoms, and defer the need for systemic therapy [10].

In the present report, we describe a patient with RAI-refractory FTC who developed extensive pulmonary and mediastinal metastases, later followed by orbital and scapular lesions. The patient repeatedly declined systemic therapy; thus, sequential high-dose EBRT with intensity-modulated radiotherapy (IMRT) was employed to achieve local control and durable symptom relief.

Case Presentation

A 51-year-old man with a history of thyroid cancer underwent total thyroidectomy in 2014 for a thyroid mass. Histopathological examination confirmed follicular thyroid carcinoma (FTC), and he subsequently received 150 mCi of radioactive iodine (RAI). The patient remained asymptomatic until 2018, when he presented with progressive dyspnea, dysphagia, and weight loss.

Chest CT revealed numerous bilateral pulmonary metastases, multiple hilar lymphadenopathies up to 45 mm, and a bulky subcarinal lymph node measuring 50 × 70 mm. Bronchoscopic biopsy confirmed metastatic FTC (Figure 1).

Because of symptomatic mediastinal disease and poor response to RAI (cumulative dose 1000 mCi), external beam radiotherapy with intensity-modulated radiotherapy (IMRT) was initiated. The mediastinal and hilar regions received 6000 cGy in 30 fractions over 6 weeks. Symptoms including dysphagia, cough, and dyspnea markedly improved during therapy. Treatment was completed without significant acute toxicity, and follow-up imaging months later demonstrated a reduction of the largest pulmonary nodule (from 45 mm to 26 mm) and shrinkage of the subcarinal lymph node (from 50 × 70mm).

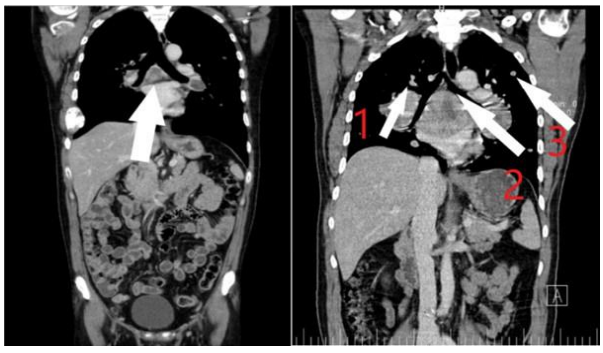

Figure 1. Chest CT images demonstrating radiologic response to mediastinal IMRT in metastatic FTC. Right: Pre-treatment CT showing numerous bilateral pulmonary metastatic nodules (largest approximately 45 mm) and a bulky subcarinal lymph node measuring 50 × 70 mm. Left: Follow-up whole-body CT performed months after scapular metastasis work-up reveals interval regression of thoracic metastatic disease, with the largest pulmonary nodule reduced to 26 mm and the subcarinal lymph node reduced to 38 × 21 mm, confirming durable radiologic response.

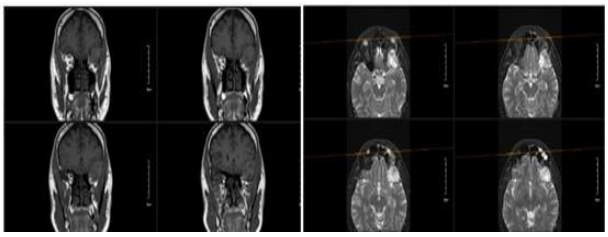

Figure 2. Orbital MRI before radiotherapy showing a 39 × 33 mm lobulated enhancing mass in the posterolateral left orbit along the sphenoid ridge, exerting significant pressure on the optic nerve and displacing the superior and lateral rectus muscles, corresponding to the patient's diplopia and orbital pain.

The patient remained symptom-free for 18 months. In January 2023, he developed left eye pain, swelling, diplopia, and blurred vision. Brain MRI demonstrated a 39 × 33 mm lobulated enhancing mass in the posterolateral wall of the left orbit compressing the optic nerve and extraocular muscles. Biopsy confirmed metastatic FTC based on immunohistochemical staining. Because systemic therapy was again declined, radical orbital IMRT was delivered (6000 cGy in 30 fractions). Diplopia and orbital pain significantly improved after treatment, with no acute adverse effects (Figure 2)

In February 2024, the patient reported severe left shoulder pain and restricted motion. MRI revealed a 74 × 68 mm scapular lesion with extraosseous extension. Restaging demonstrated stable pulmonary and orbital metastases but additional asymptomatic bone lesions. Palliative IMRT (5000 cGy in 20 fractions) was delivered to the scapular site, achieving rapid pain relief. After completion, systemic therapy with cabozantinib was initiated.

Follow-up whole-body CT performed several months after scapular irradiation during baseline assessment for cabozantinib showed sustained reduction of pulmonary and mediastinal lesions, confirming prolonged local control. The patient remains clinically stable and under ongoing systemic therapy.

Discussion

High-dose external beam radiation therapy (EBRT) and stereotactic body radiation therapy (SBRT) have demonstrated considerable efficacy in achieving local control and extending survival among patients with differentiated thyroid carcinoma (DTC), even in those presenting with recurrent or metastatic lesions [11, 12]. Evidence from randomized clinical trials in other metastatic cancers, such as prostate cancer, suggests that directed local radiotherapy to the primary tumor may improve overall survival in patients with a limited metastatic burden [13]. Metastatic DTC, several prognostic indicators have been recognized irrespective of iodine avidity. These include younger age (<40 years), limited metastatic distribution (particularly when confined to lungs and lymph nodes), and smaller pulmonary lesions (<1 cm) [14]. Although DTC has historically

been considered relatively radioresistant, accumulating evidence indicates that high-dose radiation can achieve meaningful local control. Doses ≥50 Gy with curative intent have produced five-year local recurrence rates as low as 15% [11]. Similarly, SBRT has achieved high local control rates for metastatic lung lesions derived from DTC [12]. Given the indolent biological behavior and generally favorable long-term prognosis of many DTC cases, individualized case selection remains essential, especially for patients with good performance status and limited systemic disease [15]. In the present case, EBRT was chosen as a local therapy because of symptomatic mediastinal involvement and the patient's repeated refusal of systemic therapy.

The prognosis of metastatic DTC varies widely between slow-progressing and aggressive subtypes [16] Patients with iodine-avid disease often achieve long-term survival exceeding 90% at ten years, whereas those with RAI-refractory disease face much poorer outcomes, with ten-year survival rates near 10% [17]. Approximately two-thirds of DTC patients have iodine-avid distant metastases, and one-third of them achieve remission after repeated RAI courses [6]. However, 15–20% of patients particularly those with Hürthle or follicular variants remain unresponsive, with overall survival ranging between 2.5 and 4.5 years [6]. Approximately 15%–20% of patients with metastatic DTC and most with Hürthle cell thyroid cancer do not respond to radioiodine treatment. The overall survival for these patients ranges between 2.5 and 4.5 years [6, 18]. For these patients, ablative local modalities such as surgery, vertebroplasty, EBRT, or thermal ablation can effectively relieve symptoms and delay systemic therapy [19]. In our case, considering the patient's stable pulmonary lesions, good performance status, and the availability of IMRT, sequential EBRT was an appropriate and well-tolerated approach. Notably, IMRT provided precise dose conformity to mediastinal targets while minimizing exposure to critical structures such as the heart and lungs, resulting in symptom relief and no significant acute toxicities such as pneumonitis or esophagitis.

When the orbital lesion developed 18 months later, a similar IMRT protocol (60 Gy in 30 fractions) achieved excellent local control and symptomatic improvement. Subsequent scapular metastasis was managed with palliative IMRT (50 Gy in 20 fractions), achieving pain relief and maintaining local stability until the initiation of systemic therapy with cabozantinib.

For patients with progressive RAI-refractory disease, multikinase inhibitors (e.g., lenvatinib, sorafenib, vandetanib, cabozantinib, vemurafenib, dabrafenib/ trametinib) provide temporary disease stabilization in 50–70% of cases, with median progression-free survival of 2–3 years [9, 20, 21]. However, these agents rarely achieve durable remission and are often limited by toxicity.

In our patient, the use of sequential high-dose IMRT not only achieved sustained local control and prolonged symptom-free intervals but also deferred the initiation of systemic therapy for nearly two years. This experience supports IMRT as an effective therapeutic option for selected patients with RAI-refractory metastatic FTC, particularly those who decline or cannot tolerate systemic treatment.

Funding

None declared.

Conflict of Interest

The authors declare that there is no conflict of interest.

Ethical Approval

Mazandaran University of Medical Sciences Ethics Committee IR.MAZUMS.REC.1404.091.

Patient Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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