International Clinical and Medical Case Reports Journal
Case Report (ISSN: 2832-5788)

Fastly Progressive Tall Cell Variant Papillary Thyroid Carcinoma with Radioactive Iodine Refractoriness and Fatal Outcome

Dr. Tariq Nasser Tabbakh Sr., MD*

College of Medicine, King Saud bin Abdulaziz University for Health Sciences, Department of Medicine/Endocrinology, King Abdullah International Medical Research Center, Jeddah, Saudi Arabia

Citation: *Tabbakh TN. Fastly Progressive Tall Cell Variant Papillary Thyroid Carcinoma with Radioactive Iodine Refractoriness and Fatal Outcome. Int Clinc Med Case Rep Jour. 2026;5(6):1-5.*

Received Date: 07 June, 2026; **Accepted Date:** 10 June, 2026; **Published Date:** 12 June, 2026

***Corresponding author:** Dr. Tariq Tabbakh, College of Medicine, King Saud bin Abdulaziz University for Health Sciences, Department of Medicine/Endocrinology, King Abdullah International Medical Research Center, Jeddah, Saudi Arabia

ABSTRACT

Papillary thyroid carcinoma (PTC) generally has a good prognosis. Still, more aggressive types, such as the tall cell variant (TCV-PTC), seem resistant to treatment in some cases and progress rapidly. In the case we present, we report on a 58-year-old man with TCV-PTC who developed distant metastases and radioactive iodine refractoriness and died from respiratory failure at a young age of 38 years. This underscores the complexity associated with TCV-PTC and the need to consider novel treatment options at a young age of 38 years. This underscores the complexity associated with TCV-PTC and the need to consider novel treatment options.

Keywords: Papillary thyroid carcinoma; Tall cell variant; Prognosis; Metastasis

INTRODUCTION

Papillary thyroid carcinoma accounts for 80% of thyroid malignancies and has a 10-year survival greater than 90%[1]. TCV-PTC accounts for 5% of cases and is characterized by long columnar cells, extrathyroidal extension and higher rates of metastasis[2,3], Radioactive iodine (RAI) refractoriness occurs in 5%-15% of differentiated thyroid cancer (DTC) cases, increasing to approximately 50% in metastatic cases. This decrease in iodine sensitivity results from tumor dedifferentiation and is commonly associated with older age, larger metastases and specific molecular mutations, such as BRAF or TERT gene mutations[4].

CASE PRESENTATION

A 58-year-old man with hypertension presented with a 3-month history of dyspnea, dry cough, and pleuritic chest pain. Physical examination showed tachypnea (24 breaths/min), hypoxemia (SpO: 88%), and right-sided dullness to percussion. Imaging confirmed a large right pleural effusion **(Figure 1)**. Thoracentesis drained 1.2 L

of exudative fluid, and cytology was positive for adenocarcinoma. CT scan identified pleural thickening, bilateral pulmonary nodules, and a 3.5 cm irregular thyroid mass **(Figure 2)**. Serum thyroglobulin was elevated (>1,000 ng/mL). Neck ultrasound revealed a hypoechoic right thyroid nodule and abnormal cervical lymph nodes. Fine-needle aspiration confirmed TCV-PTC (Bethesda VI) with tall cells showing eosinophilic cytoplasm and nuclear pseudoinclusions. Total thyroidectomy with central and lateral neck dissection confirmed TCV-PTC (pT3bN1b) with extra thyroid extension and 8/15 metastatic lymph nodes **(Figure 3)**. Postoperatively, he received radioiodine (I-131) 150 mCi, and the post-ablation whole-body scan showed weak uptake at metastatic sites (non-avid on the whole-body scan) **(Figure 4)**. Two months after surgery, he developed recurrent pleural effusion, lymphangitic carcinomatosis, and hypoxemia requiring mechanical ventilation. Sorafenib (400 mg BID) was initiated but discontinued after 4 weeks due to clinical deterioration. The patient died of multi-organ failure.

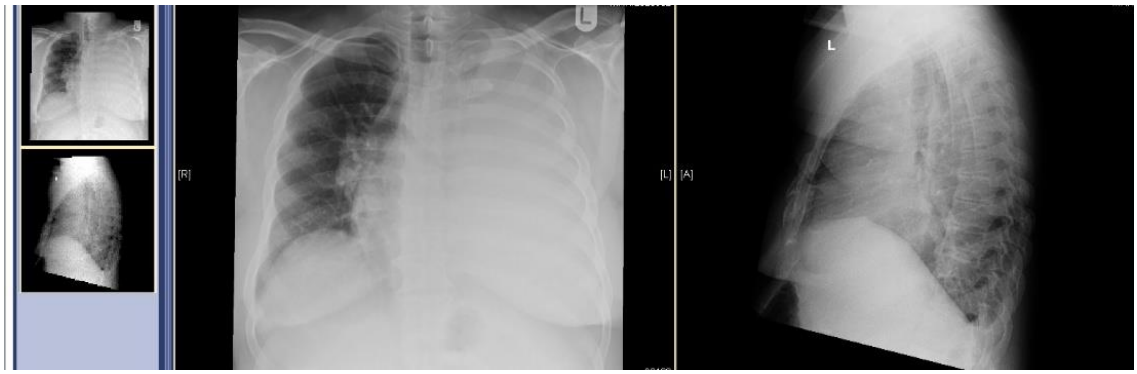

Figure 1: Chest imaging demonstrating a large right-sided pleural effusion at presentation, associated with respiratory symptoms and hypoxemia

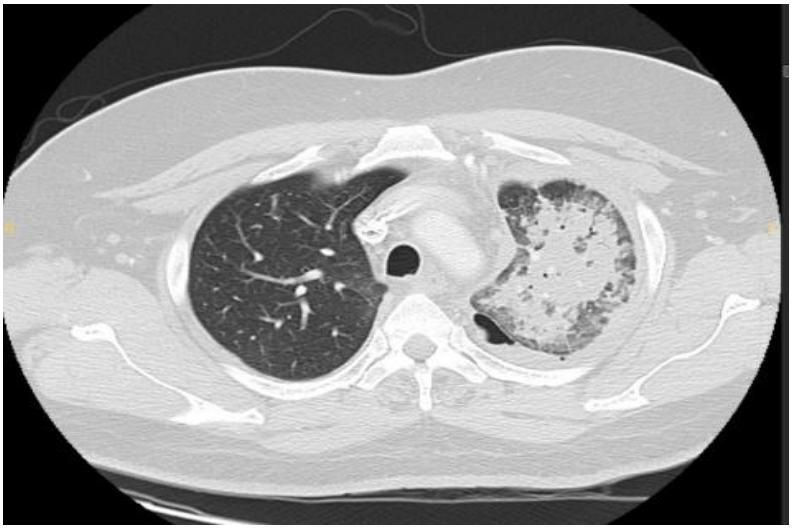

Figure 2: Computed tomography (CT) scan showing pleural thickening, bilateral pulmonary nodules, and a 3.5 cm irregular thyroid mass suggestive of advanced thyroid malignancy

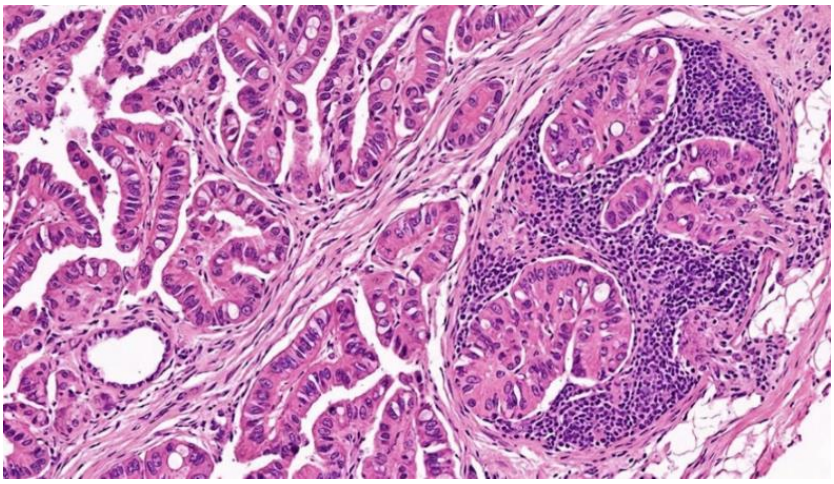

Figure 3: Histopathological examination of the thyroid specimen confirming Tall Cell Variant Papillary Thyroid Carcinoma (TCV-PTC) with characteristic tall columnar cells, eosinophilic cytoplasm, nuclear grooves, and intranuclear pseudoinclusions

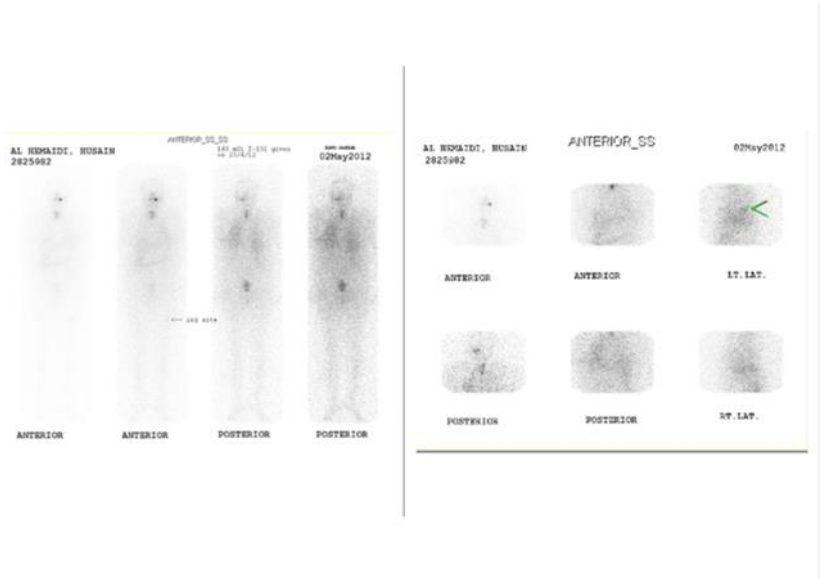

Figure 4: Post-radioiodine (I-131) whole-body scan demonstrating weak or absent uptake in metastatic lesions, consistent with radioactive iodine-refractory disease

DISCUSSION

The clinical history of our case underscores the complexity of TCV-PTC and the need for a thorough evaluation of patient parameters. Although papillary thyroid cancer is generally indolent, with 10-year survival rates above 90%, TCV-PTC cannot be ruled out and is therefore more likely to progress rapidly and require resistant treatment[2,3]. The patient presented with respiratory symptoms, including shortness of breath, dry cough and pleuritic pain. This contrasted with thyroid malignancy is a very good indication that, in many other cases, TCV-PTC could persist and not be recognized as a thyroid tumor until imaging revealed an irregular thyroid mass[3]. Cytology and histopathology established the diagnosis of TCV-PTC, with tall columnar cells containing eosinophilic cytoplasm (indicating a much deeper-than-thinner cell body), numerous grooves and even a few

pseudoinclusions (as is common in such tumors). The tumor's behavior was also telltale. Extrathyroidal growth and lymph node metastases at surgery indicated it was invasive and the rapid growth of pulmonary metastases and pleural effusion after surgery highlighted its destructive biology. For decades, thyroidectomy elevated thyroglobulin levels to over 1,000 ng/mL and served as a silent alarm, indicating that the disease was persistent and in need of aggressive treatment. The outcome was a significant failure when radioactive iodine (RAI) was not effective in treating cancer.

The post-treatment report shows no iodine uptake in the metastatic lesions, which we believe represent RAI-refractory disease caused by tumor dedifferentiation and will be studied further. With loss of the sodium-iodide symporter, the molecular gateway for RAI, the therapy was no more and the only option was systemic treatment as previously explained by[5,6]. Sorafenib was introduced as a multikinase inhibitor targeting VEGF and BRAF, which could be treated with cautious optimism, but the patient experienced a rapid decline (with lymphangitic spread and a suffocating pleural response, along with failure of thyroid treatment with respect to the tumors at the same time), prompting criticism of how effective these treatments are for treating cancer, which has a broad spectrum of treatments (TCV-PTC)[3,7]. Could earlier molecular tracking have altered the trajectory? TCV-PTC, in particular, shows high rates of BRAF V600E mutations, both of which indicate dedifferentiation and RAI resistance[8]. While Sorafenib does not directly target BRAF, highly selective inhibitors such as dabrafenib, when combined with MEK inhibitors, have been demonstrated in BRAF-induced thyroid cancer[8]. However, the patient's decline did not allow for such research, highlighting a shortcoming in molecular diagnostics among critically ill patients[3,8]. The story also tells us why: It is the clinical challenge of being unable to be truly prepared for the disease's arrival without a clear clue about which patients will progress rapidly, yet you never see it happening, only the patients you encounter in your clinical case. TCV-PTC's reputation for aggression is well established, but its triggers tend to be lacking. Was it due to the patient's age or sex, as epidemiological work has indicated? Were genetic modifications beyond BRAF, such as DNA mutations and PI3K pathway alterations, involved? The answer lies in molecular science and exploration of those pathways can lead to personalized therapies, such as RET inhibitors or immune checkpoint blockers, that are evolving in the meantime[3,8]. This patient's case serves as a warning for thyroid cancer physicians, highlighting concerns about the potential presence of TCV-PTC in cancers with atypical patient presentations[2,3] and encourages rapid molecular profiling so we can work at these levels through surgery, minimally invasive interventions and palliative care and therapy as needed. Although his story was tragic, he illustrates the urgent need to undertake clinical trials on tumors with extremely aggressive variants[1,7] and to enable the health care system to rapidly accelerate genomic testing in the cancer setting[5,6]. Reflecting on past challenges in darkness, we hope future patients will benefit from therapies developed from his contributions. This includes children with TCV-PTC, transforming a generation of treatments into therapies that could potentially manage TCV-PTC in the future.

CONCLUSION

TCV-PTC is a lethal variant with a risk of metastasis and resistance to treatment. This case underscores the urgency of early molecular profiling, participation in clinical trials and personalized therapy to improve outcomes.

REFERENCES

1. Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association Management Guidelines for Adult patients with Thyroid nodules and Cancer. CA Cancer J Clin. 2013;63:373-394.
2. Lloyd RV, Osamura RY, Klöppel G, Rosai J. WHO classification of tumours of Endocrine organs. World Health Organisation (ed): International Agency for Research on Cancer. 2017.
3. Ghossein RA, Leboeuf R, Patel KN, et al. Tall cell variant of papillary thyroid carcinoma without extrathyroid extension: biologic behavior and clinical implications. Thyroid. 2007;17:655-61.
4. Lakhdar MB, Mouaden A, Zekri M, et al. Predictive Factors of Radioactive Iodine Therapy Refractoriness in Patients with Differentiated Thyroid Carcinoma. World J Nucl Med. 2024;14:185-190.
5. Rivera M, Ghossein RA, Schoder H, et al. Histopathologic characterization of radioactive iodine-refractory fluorodeoxyglucose-positron emission tomography-positive thyroid cancer. Cancer. 2008;113:48-56.
6. Durante C, Haddy N, Baudin E, et al. Long-term outcomes of 444 patients with distant metastases from papillary and follicular thyroid carcinoma: benefits and limits of radioiodine therapy. J Clin Endocrinol Metab. 2006;91:2892-2899.
7. Xing M, Alzahrani A, Carson K, et al. Association Between BRAF V600E Mutation and Mortality in Patients with Papillary Thyroid Cancer. JAMA. 2013;10:1493-501.
8. Durante C, Haddy N, Baudin E, et al. Long-Term Outcome of 444 Patients with Distant Metastases from Papillary and Follicular Thyroid Carcinoma: Benefits and Limits of Radioiodine Therapy. JCEM. 2006;91:2892-2899.