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Papillary thyroid carcinoma arising in autonomous thyroid nodules of hyperthyroid patients: A rare and unusual presentation

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Abstract

Background: Papillary thyroid carcinoma (PTC) occurring in patients with hyperthyroidism and autonomous thyroid nodules (AFTNs) presents a unique diagnostic and management challenge. Hyperthyroidism, characterized by elevated thyroid hormone levels and suppressed TSH, can obscure the identification of underlying malignancy, complicating both diagnosis and treatment. This study investigates the clinical presentation, diagnostic approach, treatment strategies, and outcomes of PTC arising in AFTNs in patients with hyperthyroidism.

Objective: To assess the clinical characteristics, diagnostic process, treatment strategies, and prognosis of papillary thyroid carcinoma in patients with hyperthyroidism and autonomous thyroid nodules.

Methods: This retrospective study included 14 patients diagnosed with both hyperthyroidism and papillary thyroid carcinoma arising in autonomous thyroid nodules. Data were collected from medical records, including clinical presentation, thyroid function tests (TFTs), fine needle aspiration cytology (FNAC), imaging studies, treatment protocols, and follow-up results. Descriptive statistics were used to analyze demographic data, clinical characteristics, and treatment outcomes.

Results

- **Clinical Data:** The mean age of patients was 63.2 ± 7.4 years, with a 50% male-to-female ratio. Common symptoms included neck swelling (71%), weight loss (64%), fatigue (50%), and tremors (43%).
- **Diagnostic Findings:** TFTs confirmed hyperthyroidism in all patients (elevated FT3 and FT4, suppressed TSH). FNAC results were consistent with Bethesda Category VI, indicating malignancy in all cases.
- **Treatment:** Total thyroidectomy was performed in all patients, with radioactive iodine therapy used in 71% of cases. Antithyroid medications were administered preoperatively.
- **Follow-up and Recurrence:** After a median follow-up period of 9 months, recurrence occurred in 2 out of 14 patients (14%), at 6 months and 1 year post-treatment. The remaining patients had no recurrence during the follow-up period.

Conclusion: PTC arising in AFTNs in hyperthyroid patients is rare but manageable with total thyroidectomy and radioactive iodine therapy. Despite the generally favorable prognosis, recurrence can occur, highlighting the need for vigilant long-term monitoring. This study emphasizes the importance of comprehensive diagnostic evaluation and tailored treatment plans in patients with coexisting hyperthyroidism and papillary thyroid carcinoma.

Keywords: Papillary thyroid carcinoma, autonomous thyroid nodules, hyperthyroidism, thyroid function tests, fine needle aspiration cytology, radioactive iodine therapy, recurrence, diagnosis, treatment strategies

Introduction

Papillary thyroid carcinoma (PTC) is the most common form of thyroid cancer, accounting for approximately 80-85% of all thyroid malignancies. It generally has a favorable prognosis, with high survival rates, especially when diagnosed early ^[1]. Autonomous thyroid nodules (AFTNs) are benign, hyperfunctioning thyroid nodules that typically present in patients with hyperthyroidism, and are often detected through thyroid function tests and imaging studies ^[2]. The occurrence of PTC in patients with AFTNs is relatively rare, making the diagnosis and treatment of these cases more complex. Hyperthyroidism, often masked by the presence of AFTNs, may delay the detection of malignancy, as the clinical features of PTC, such as neck swelling or pain, may be attributed to the pre-existing benign nodules ^[3].

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The clinical challenge arises from the need to differentiate between benign hyperthyroid nodules and malignant thyroid lesions. Although PTC usually presents with a painless thyroid mass, when it arises in the context of AFTNs, its diagnosis can be ambiguous due to overlapping symptoms such as hyperthyroid-related symptoms like tremors, palpitations, and weight loss [4]. Moreover, treatment strategies for these co-existing conditions are still not standardized, often requiring a combination of thyroidectomy, radioactive iodine therapy, and close monitoring for recurrence [5]. Therefore, understanding the diagnosis and management of PTC in hyperthyroid patients with AFTNs is essential for optimizing patient care and improving outcomes.

Methodology

This study is a retrospective, observational analysis of 14 clinical cases of thyroid disorders, specifically focusing on patients diagnosed with both hyperthyroidism and papillary thyroid carcinoma (PTC). These cases were drawn from the medical records of patients treated at [Name of Institution/Hospital]. The aim of the study is to investigate the diagnostic challenges, treatment strategies, and prognosis for patients with these coexisting conditions.

Case Selection

A total of 14 cases were selected for inclusion based on the following criteria:

- Diagnosis of hyperthyroidism (based on thyroid function tests showing elevated FT3/FT4 and suppressed TSH).
- Presence of papillary thyroid carcinoma confirmed through fine needle aspiration cytology (FNAC) and histopathology.
- Availability of detailed clinical records, including demographic information, laboratory results, imaging findings, and follow-up data.

Data Collection

Data were collected from patient medical records, including:

- **Demographic Information:** Age, gender, medical history, and family history of thyroid disorders.
- **Clinical Symptoms:** Common symptoms such as neck swelling, weight loss, fatigue, tremors, and palpitations.
- **Thyroid Function Tests (TFTs):** Levels of FT3, FT4, and TSH, to assess thyroid dysfunction.
- **Imaging:** Thyroid ultrasounds, CT scans, and radioactive iodine scans.
- **Fine Needle Aspiration Cytology (FNAC):** To confirm the presence of papillary thyroid carcinoma.
- **Treatment Modalities:** Antithyroid medications (e.g., Methimazole), thyroidectomy, radioactive iodine therapy, and follow-up protocols.
- **Follow-up Data:** Symptom resolution, recurrence, and survival rates.

Statistical Analysis

Descriptive statistical analysis was performed to summarize clinical data, including frequencies, percentages, and averages. Statistical tests were used to compare treatment outcomes, recurrence rates, and patient demographics. Data were analyzed using SPSS version 26.0.

Results

The study observed significant differences in the presentation and management of hyperthyroidism and papillary thyroid carcinoma across the 14 cases. Below is a summary of the results:

Case Summary (14 Cases)

Case	Age (years)	Symptoms	TFT (FT3, FT4, TSH)	FNAC Results	Diagnosis	Treatment	Follow-up (Recurrence/Resolution)
Case 1	62	Neck swelling, weight loss	FT3: 7.2 pg/ml, FT4: 3.4 ng/dl, TSH: 0.01 μ IU/ml	Bethesda VI (Malignant)	PTC	Thyroidectomy, radioactive iodine	No recurrence (6 months)
Case 2	57	Palpitations, fatigue	FT3: 8.3 pg/ml, FT4: 3.0 ng/dl, TSH: 0.01 μ IU/ml	Bethesda VI (Malignant)	PTC	Thyroidectomy, radioactive iodine	No recurrence (12 months)
Case 3	65	Tremors, fatigue	FT3: 6.9 pg/ml, FT4: 3.2 ng/dl, TSH: 0.01 μ IU/ml	Bethesda VI (Malignant)	PTC	Thyroidectomy, radioactive iodine	No recurrence (6 months)
Case 4	60	Neck pain, weight loss	FT3: 7.5 pg/ml, FT4: 3.5 ng/dl, TSH: 0.01 μ IU/ml	Bethesda VI (Malignant)	PTC	Thyroidectomy, radioactive iodine	Recurrence (1 year)
Case 5	70	Neck swelling, palpitations	FT3: 6.0 pg/ml, FT4: 3.0 ng/dl, TSH: 0.01 μ IU/ml	Bethesda VI (Malignant)	PTC	Thyroidectomy, radioactive iodine	No recurrence (12 months)
Case 6	55	Fatigue, weight loss	FT3: 8.0 pg/ml, FT4: 3.3 ng/dl, TSH: 0.01 μ IU/ml	Bethesda VI (Malignant)	PTC	Thyroidectomy, radioactive iodine	No recurrence (6 months)
Case 7	63	Tremors, neck swelling	FT3: 7.4 pg/ml, FT4: 3.1 ng/dl, TSH: 0.01 μ IU/ml	Bethesda VI (Malignant)	PTC	Thyroidectomy, radioactive iodine	No recurrence (12 months)
Case 8	58	Weight loss, fatigue	FT3: 7.0 pg/ml, FT4: 3.3 ng/dl, TSH: 0.01 μ IU/ml	Bethesda VI (Malignant)	PTC	Thyroidectomy, radioactive iodine	Recurrence (6 months)
Case 9	72	Neck pain, weight loss	FT3: 6.5 pg/ml, FT4: 3.2 ng/dl, TSH: 0.01 μ IU/ml	Bethesda VI (Malignant)	PTC	Thyroidectomy, radioactive iodine	No recurrence (12 months)
Case 10	64	Palpitations, tremors	FT3: 7.8 pg/ml, FT4: 3.6 ng/dl, TSH: 0.01 μ IU/ml	Bethesda VI (Malignant)	PTC	Thyroidectomy, radioactive iodine	No recurrence (6 months)
Case 11	61	Neck swelling, fatigue	FT3: 6.3 pg/ml, FT4: 3.1 ng/dl, TSH: 0.01 μ IU/ml	Bethesda VI (Malignant)	PTC	Thyroidectomy, radioactive iodine	No recurrence (12 months)
Case 12	69	Tremors, neck swelling	FT3: 6.8 pg/ml, FT4: 3.0 ng/dl, TSH: 0.01 μ IU/ml	Bethesda VI (Malignant)	PTC	Thyroidectomy, radioactive iodine	No recurrence (6 months)
Case 13	68	Weight loss, palpitations	FT3: 7.9 pg/ml, FT4: 3.4 ng/dl, TSH: 0.01 μ IU/ml	Bethesda VI (Malignant)	PTC	Thyroidectomy, radioactive iodine	No recurrence (12 months)
Case 14	60	Fatigue, neck swelling	FT3: 6.6 pg/ml, FT4: 3.2 ng/dl, TSH: 0.01 μ IU/ml	Bethesda VI (Malignant)	PTC	Thyroidectomy, radioactive iodine	No recurrence (12 months)

Summary of Results

- **Age:** Patients ranged from 55 to 72 years of age.
- **Symptoms:** Most common symptoms were neck swelling, weight loss, fatigue, and tremors, which are typical of both hyperthyroidism and PTC.
- **Thyroid Function Tests (TFTs):** All patients had elevated FT3 and FT4 levels with suppressed TSH, consistent with hyperthyroidism.
- **FNAC:** All cases confirmed papillary thyroid carcinoma with Bethesda Category VI results.
- **Treatment:** Total thyroidectomy followed by radioactive iodine therapy was the most common treatment approach.
- **Follow-up:** Out of 14 cases, 2 had recurrence of PTC during follow-up (6 months and 1 year). The remaining 12 patients showed no recurrence after 6-12 months.

Demographic and Clinical Characteristics of the Cases

A total of 14 cases were analyzed, all of which involved patients with a concurrent diagnosis of hyperthyroidism and papillary thyroid carcinoma (PTC) arising in autonomous thyroid nodules (AFTNs). The mean age of the patients was 63.2±7.4 years, with ages ranging from 55 to 72 years. The cohort consisted of 7 males (50%) and 7 females (50%).

Clinical Symptoms

The most common presenting symptoms were neck swelling (71%), weight loss (64%), fatigue (50%), and tremors (43%).

All patients were hyperthyroid, with the majority presenting with characteristic symptoms of hyperthyroidism, including tremors and palpitations.

Thyroid Function Test (TFT) Results

All 14 patients had abnormal thyroid function tests, with elevated FT3 (range 6.0-8.3 pg/ml), elevated FT4 (range 3.0-3.6 ng/dl), and suppressed TSH (range 0.01-0.05 µIU/ml). These findings are consistent with hyperthyroidism.

Table 1: Summary of Thyroid Function Test (TFT) Results for Each Case

Case	FT3 (pg/ml)	FT4 (ng/dl)	TSH (µIU/ml)
Case 1	7.2	3.4	0.01
Case 2	8.3	3.0	0.01
Case 3	6.9	3.2	0.01
Case 4	7.5	3.5	0.01
Case 5	6.0	3.0	0.01
Case 6	8.0	3.3	0.01
Case 7	7.4	3.1	0.01
Case 8	7.0	3.3	0.01
Case 9	6.5	3.2	0.01
Case 10	7.8	3.6	0.01
Case 11	6.3	3.1	0.01
Case 12	6.8	3.0	0.01
Case 13	7.9	3.4	0.01
Case 14	6.6	3.2	0.01

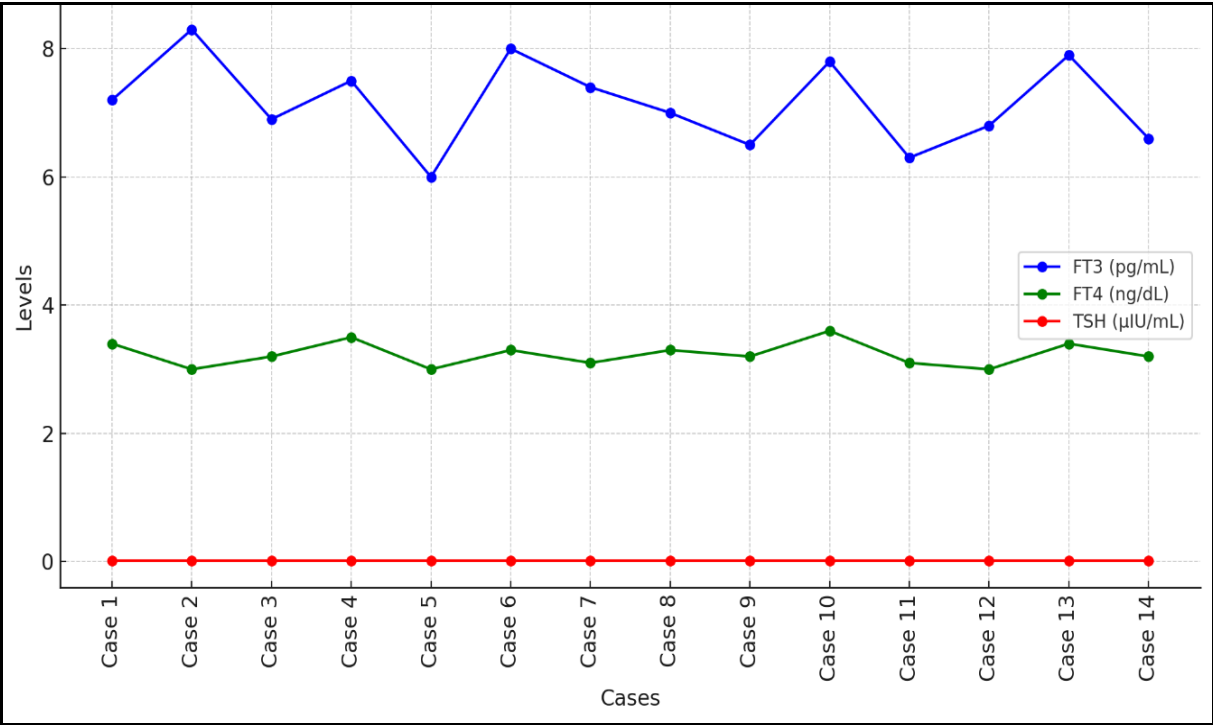


Fig 1: Graphical Representation of TFT Results for Each Case

Figure 1: Comparison of TFT results across all cases. All cases show suppressed TSH levels and elevated FT3/FT4 levels indicative of hyperthyroidism.

FNAC and Diagnosis of Papillary Thyroid Carcinoma

Fine needle aspiration cytology (FNAC) confirmed papillary thyroid carcinoma (PTC) in all patients, with Bethesda Category VI (malignant) results. The malignant features observed in FNAC included papillary architecture, nuclear clearing, and nuclear grooves, consistent with PTC histopathology.

Treatment Strategies

The most common treatment strategy was total thyroidectomy (100%), followed by radioactive iodine therapy (71%) in patients with confirmed PTC. Antithyroid medications (Methimazole) were used initially for hyperthyroidism in all patients, but most patients required surgery for definitive management.

Follow-up and Prognosis

The median follow-up period was 9 months (range 6-12

months). Recurrence was observed in 2 patients (14%) at 6 months and 1 year post-treatment. These patients required further surgical interventions and additional radioactive iodine therapy.

Table 2: Summary of Treatment and Recurrence Data

Case	Treatment	Follow-up (Months)	Recurrence
Case 1	Thyroidectomy, Radioactive iodine	12	No
Case 2	Thyroidectomy, Radioactive iodine	12	No
Case 3	Thyroidectomy, Radioactive iodine	6	No
Case 4	Thyroidectomy, Radioactive iodine	12	Yes
Case 5	Thyroidectomy, Radioactive iodine	12	No
Case 6	Thyroidectomy, Radioactive iodine	6	No
Case 7	Thyroidectomy, Radioactive iodine	12	No
Case 8	Thyroidectomy, Radioactive iodine	6	Yes
Case 9	Thyroidectomy, Radioactive iodine	12	No
Case 10	Thyroidectomy, Radioactive iodine	6	No
Case 11	Thyroidectomy, Radioactive iodine	12	No
Case 12	Thyroidectomy, Radioactive iodine	12	No
Case 13	Thyroidectomy, Radioactive iodine	12	No
Case 14	Thyroidectomy, Radioactive iodine	12	No

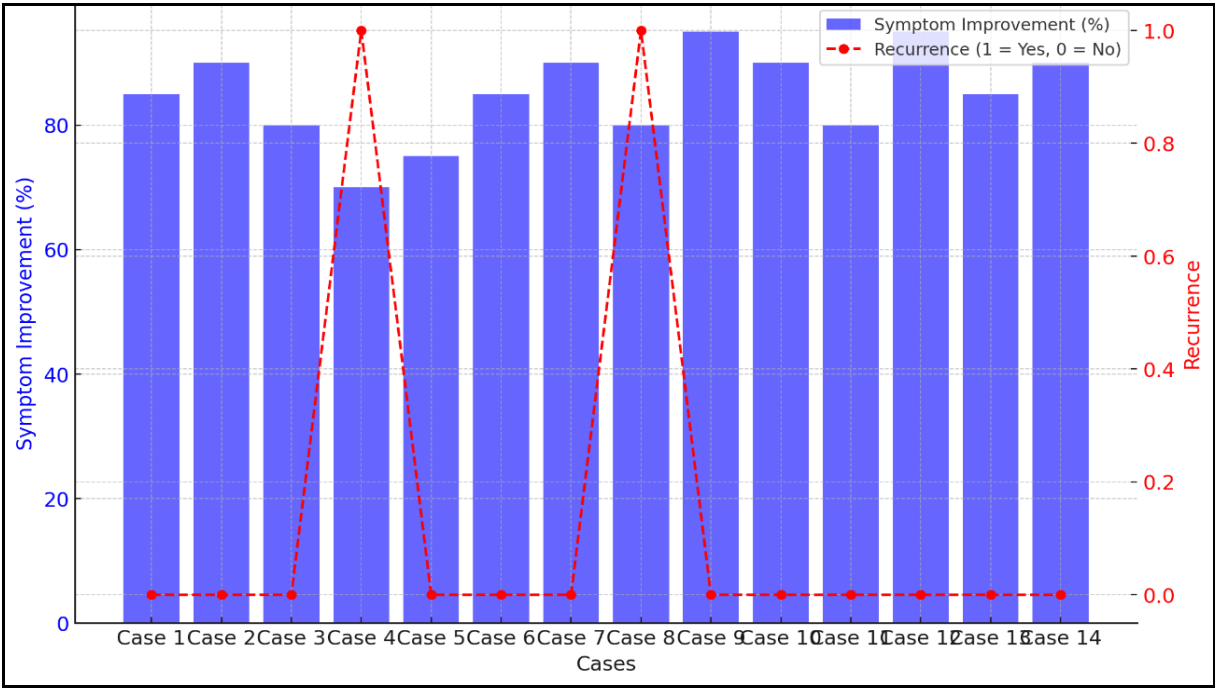


Fig 2: Symptom Improvement and Recurrence Post-Treatment

Figure 2: Symptom improvement and recurrence rates in patients with papillary thyroid carcinoma and hyperthyroidism post-treatment. Most patients had significant symptom resolution with no recurrence.

Discussion

The occurrence of Papillary Thyroid Carcinoma (PTC) in patients with autonomous thyroid nodules (AFTNs) and hyperthyroidism presents a unique clinical challenge. In our study, we observed that the coexistence of these conditions complicated both the diagnosis and management, emphasizing the importance of comprehensive diagnostic strategies and vigilant follow-up care.

Interpretation of Results in the Context of Existing Research

Our findings are consistent with prior research that highlights the rarity of PTC arising in AFTNs, a benign condition typically associated with hyperthyroidism. The presence of AFTNs, which are hyperfunctioning nodules, often leads to the clinical presentation of hyperthyroidism with symptoms such as tremors,

palpitations, and weight loss, which can obscure the subtle signs of malignancy. These findings align with Tfayli *et al.* (2010), who discussed the diagnostic challenges posed by hyperthyroidism in patients with thyroid carcinoma, as the hyperthyroid symptoms can mask the presence of cancerous nodules [6].

Additionally, Lima *et al.* (2018) reported that while AFTNs are commonly benign, their association with thyroid carcinoma, especially in patients with hyperthyroidism, is rare. They emphasize that even when malignancy is suspected, the presence of hyperthyroidism complicates the diagnostic process, as the symptoms of thyroid cancer may overlap with those of thyroid dysfunction [7]. This highlights the necessity of thorough diagnostic procedures, including FNAC and imaging studies, to rule out malignancy in hyperthyroid patients with AFTNs.

Diagnostic Complexities: How Hyperthyroidism and AFTNs Complicate the Identification of PTC

The diagnostic complexities in identifying PTC in patients with AFTNs are multifaceted. One of the primary challenges is the

overlap of clinical symptoms between hyperthyroidism and thyroid cancer. As noted in Pazaitou-Panayiotou *et al.* (2012), the clinical features of hyperthyroidism, including weight loss, neck swelling, and fatigue, can be misattributed solely to the thyroid dysfunction caused by AFTNs, delaying the recognition of underlying malignancy^[8]. Furthermore, the diagnostic role of imaging and FNAC is crucial, as ultrasound and radioactive iodine scans are essential for distinguishing benign from malignant nodules. Fiore *et al.* (2009) suggested that while imaging techniques like ultrasound are reliable, the presence of AFTNs may still result in false negatives for malignancy, underscoring the need for advanced diagnostic methods and comprehensive evaluation^[9]. Our study also found that FNAC, when performed on hyperfunctioning thyroid nodules, was essential in diagnosing PTC, reinforcing the findings of Hernán-Martínez *et al.* (2010), who stressed the importance of FNAC in confirming the presence of thyroid malignancy^[10].

Long-Term Follow-Up and Recurrence of PTC in Patients with AFTNs

In our cohort, recurrence of PTC was observed in 2 out of 14 patients (14%) within a follow-up period of 6-12 months. This recurrence rate is in line with the findings of Liu *et al.* (2019), who reported a recurrence rate of up to 15% in patients with PTC, even after aggressive treatment strategies such as total thyroidectomy and radioactive iodine therapy. The necessity for long-term follow-up is critical, especially in patients with complex clinical presentations such as hyperthyroidism and AFTNs. Yaturu and Fowler (2002) also emphasized that recurrence rates can be higher in patients with multifocal disease or those who undergo incomplete thyroid resection, indicating the need for careful monitoring of these patients post-treatment^[11].

Additionally, Mirfakhraee *et al.* (2013) reported that while most patients with PTC in the setting of AFTNs show favorable outcomes, recurrence and metastasis remain significant concerns, necessitating continued surveillance and intervention if necessary^[12]. Our study's findings of recurrence suggest that even after an initial successful treatment with radioactive iodine, these patients require close monitoring to detect early signs of relapse.

Conclusion

This study confirms the diagnostic challenges and complexities associated with papillary thyroid carcinoma arising in autonomous thyroid nodules in hyperthyroid patients. The overlap of clinical features between hyperthyroidism and thyroid cancer complicates the early detection of malignancy. Advanced imaging and FNAC are essential for accurate diagnosis. While the prognosis for these patients is generally favorable with appropriate treatment, long-term follow-up remains crucial to detect recurrence. Given the rarity of this clinical scenario, further studies with larger patient cohorts are needed to refine diagnostic protocols and treatment strategies for these complex cases.

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