OPEN ACCESS

Saudi Journal of Medicine
Abbreviated Key Title: Saudi J Med
ISSN 2518-3389 (Print) | ISSN 2518-3397 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Case Report

Simultaneous Papillary Thyroid Carcinoma and Primary Hyperparathyroidism: Unusual Presentation

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DOI: 10.36348/sjm.2024.v09i01.003 | **Received:** 21.12.2023 | **Accepted:** 25.01.2024 | **Published:** 30.01.2024

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Abstract

The coexistence of Primary Hyperparathyroidism (PHPT) with Papillary Thyroid Carcinoma (PTC) is a rare clinical occurrence. Thyroid pathology is reported in 20% to 84% of Primary Hyperparathyroidism (PHPT) cases, with malignancies identified in 2% to 20% of instances. We report a case of a 49-year-old woman referred for evaluation of left iliac wing and hip pain with elevated parathyroid hormone levels. Imaging revealed a toxic multinodular goiter with a parathyroid adenoma. The patient underwent total thyroidectomy with parathyroid adenoma excision. Subsequent histological examination unexpectedly identified a papillary thyroid microcarcinoma associated with the parathyroid adenoma. The association between PHPT and PTC is complex, influenced by shared embryological origins and genetic factors. Elevated PTH levels in PHPT may contribute to thyroid cell proliferation, and hypercalcemia is suggested to promote thyroid carcinogenesis. Molecular analyses suggest the involvement of pathways like MAPK and Wnt/β-catenin. The coexistence of PHPT and PTC highlights the necessity for thorough preoperative assessment and the ongoing need for research. While minimally invasive parathyroid surgery is favored, the risks associated with coexisting thyroid pathology should be carefully considered. Routine thyroid ultrasonography in PHPT patients is crucial to exclude nodular thyroid disease, emphasizing the role of research in guiding clinical practices. A balanced approach integrating technical advancements and thoughtful risk assessment is essential in navigating this complex clinical scenario.

Keywords: primary hyperparathyroidism, papillary thyroid cancer, hypercalcemia, parathormone, parathyroid surgery, thyroid ultrasonography.

INTRODUCTION

The association of parathyroid adenoma in Primary Hyperparathyroidism (PHPT) with papillary thyroid cancer represents a rare clinical occurrence [2]. PHPT is characterized by elevated serum calcium levels resulting from inappropriate parathyroid hormone (PTH) secretion, with a prevalence ranging from one to seven cases per 1,000 adults [1].

Papillary thyroid carcinoma (PTC) constitutes 70% to 90% of thyroid tumors, with known risk factors including radiation exposure and genetics [2,4].

The concurrent occurrence of thyroid and parathyroid carcinoma is notably infrequent, as initially documented by Kissin *et al.*, in 1947 [2]. The coexistence of parathyroid adenoma and incidental PTC is reported to be rare. In most case reports discussing the coexistence of these two diseases, PHPT was usually the primary pathology and was diagnosed before the identification of thyroid carcinoma, typically found incidentally in pathology specimens [5].

Thyroid pathology is reported in 20% to 84% of Primary Hyperparathyroidism (PHPT) cases, with malignancies identified in 2% to 20% of instances [3]. The presence of these two pathologies can complicate patient management due to untreated hypercalcemia, unrecognized thyroid cancer, and the potential need for a second surgery if not carefully screened for both diseases [5].

This unique case emphasizes a rare situation where both thyroid cancer and primary hyperparathyroidism occur together, highlighting how uncommon this clinical scenario is. It calls for a thorough investigation into how these two conditions interact,

providing valuable insights for improving clinical diagnosis and treatment strategies.

CASE REPORT

A 49-year-old woman was referred to our department due to elevated parathyroid hormone at 789.40 pg/ml, discovered during the evaluation of disabling pain in the left iliac wing and hip. She had no significant medical history but reported recurrent and debilitating right sciatic pain for the past 10 months. A hip X-ray revealed an osteolytic image resembling a geographical map in the metaphyseal-diaphyseal region of the greater trochanter. Pelvic MRI confirmed osteolytic involvement of the left iliac wings, acetabulum, and cervicodiaphyseal region without extension into soft tissues.

An abdominopelvic CT scan showed multiple likely secondary multifocal bone lesions and a heterogeneous goiter. On physical examination, the patient had a stable condition, normotension, WHO grade 3 goiter, and a lateral swelling of the left femur with perilesional edema. Laboratory results indicated hypercalcemia at 129 mg/l, hypophosphoremia at 23 mg/l, and a high PTH level at 1176 pg/ml. Peripheral hyperthyroidism was also detected with a TSH of 0.01 mUI/L and free T4 of 22.2 pmol/L.

Cervical ultrasound revealed a multi-heteronodular goiter. A sestaMIBI scan showed two tissue nodules with uptake: one retrolobar inferiorly on the right, suggesting a pathological parathyroid gland, and one intrathyroidal inferiorly on the left, capturing both free technetium and MIBI. This rare configuration could be observed in both parathyroid adenoma and hyperfunctional thyroid nodule.

The patient was prescribed thyrozol 20 mg/day and referred for surgery. She underwent total thyroidectomy with excision of the parathyroid adenoma. Histological examination revealed an unencapsulated papillary thyroid microcarcinoma without capsular extraction or extra-thyroidal extension, classified as PT1A. The parathyroid parenchyma exhibited nodular hyperplasia indicative of a parathyroid adenoma.

Postoperatively, serum parathormone and calcium levels returned to normal. The patient received levothyroxine for replacement and suppressive therapy. Additional tests, including thyroglobulin and anti-thyroglobulin antibody levels, along with cervical ultrasound, showed an excellent therapeutic response. Notably, there was significant clinical and biological improvement during follow-up.

DISCUSSION

The association between PHPT and PTC is reported, occurring in 2% to 20% of patients undergoing neck surgery for PHPT. Benign thyroid pathologies are prevalent in 17% to 40% of PHPT cases, with this coexistence observed in both women and men [5]. Moreover, patients with Multiple Endocrine Neoplasia (MEN) syndromes more often exhibit overall thyroid and parathyroid pathologies. Genetic relationships result in well-documented cases of Medullary Thyroid Carcinoma (MTC) associated with PHPT in MEN type 2 [2,6]. Despite these associations, the exact pathogenic relationship between PHPT and PTC remains unclear.

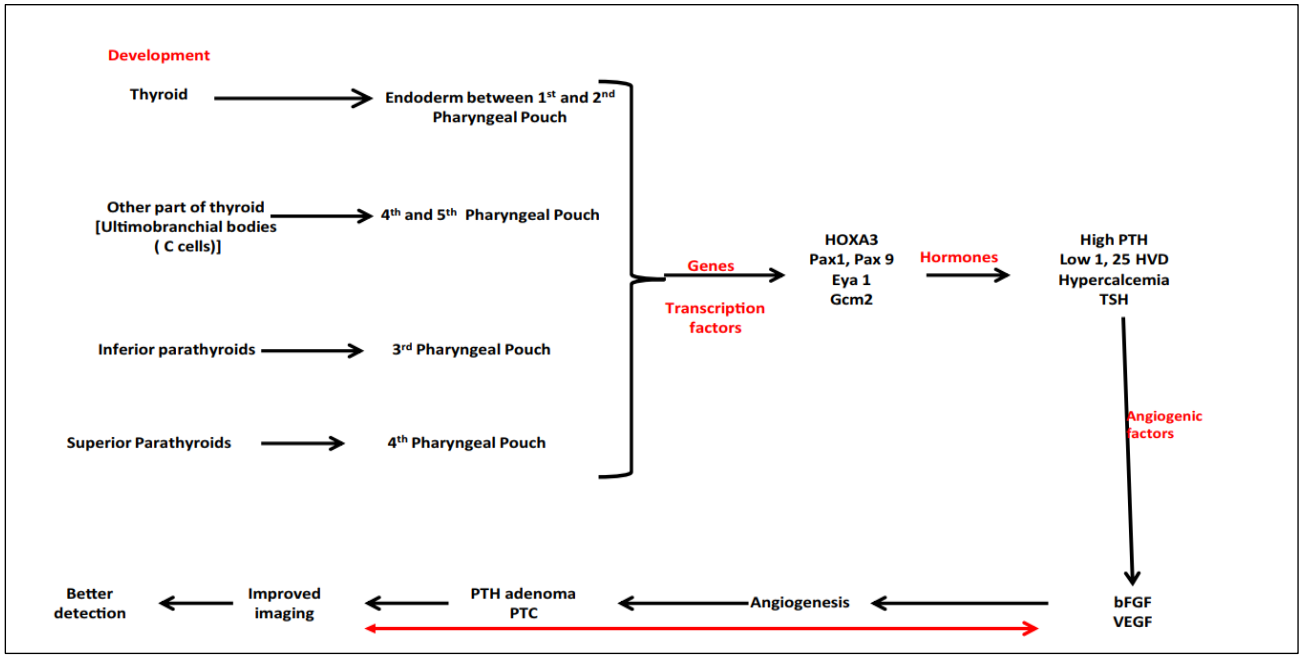

Figure 1: Suggested hypothesis for Primary hyperparathyroidism and papillary thyroid carcinoma coexistence [5]

The physiopathology underlying the association between PHPT and PTC is complex and not fully understood. Several factors contribute to this intricate relationship, including shared embryological origins and genetic factors (Figure 1). Elevated levels of Parathyroid Hormone (PTH) in PHPT patients may influence thyroid function, potentially contributing to thyroid cell proliferation. Hypercalcemia, a hallmark of PHPT, is suggested to contribute to thyroid carcinogenesis by promoting the release of growth factors. Low levels of 1,25-dihydroxyvitamin D3 (1,25D3) in PHPT patients may also influence PTC development [5, 6, 9].

The interplay of PTH, hypercalcemia, and low 1,25D3 levels may lead to the upregulation of angiogenic factors, promoting neovascularization in thyroid tissue. Molecular analyses suggest that the MAPK pathway's activation is crucial in initiating PTC, with PTH potentially potentiating this pathway. The Wnt/β-catenin signaling pathway is implicated in driving PTC development, with PTH contributing to its activation [5,8,10].

Despite these proposed mechanisms, the exact sequence of events and the relative importance of each factor in PTC development in the context of PHPT remain subjects of ongoing research. The relationship is likely multifactorial, influenced by both systemic hormonal changes and local molecular interactions within thyroid tissue [2,7].

The coexistence of HPT with thyroid disease emphasizes the importance of a thorough preoperative examination and imaging, especially when malignancy is suspected. Any thyroid nodule that appears suspicious should be assessed through fine needle aspiration (FNA). The majority of reported cases of thyroid cancer are the classical variant of PTC, typically measuring less than 1 cm. Multifocality with lymph node involvement is reported to be rare [3,9].

Improved imaging techniques contribute to the enhanced detection of both pathologies. However, preoperative challenges arise when dealing with concurrent thyroid nodules. Despite the absence of established guidelines, the management of Papillary Thyroid Carcinoma (PTC) in Primary Hyperparathyroidism (PHPT) patients often follows standard protocols [7,11].

The growing popularity of minimally invasive parathyroid surgery introduces complexity, given the potential oversights in coexisting thyroid pathology. Presently, there are no specific guidelines for the management of concurrent PHPT and PTC. PTC in these patients is typically handled similarly to cases of isolated PTC, following American Thyroid Association (ATA) guidelines [3,6,12].

While minimally invasive parathyroid surgery is gaining favor, the risk associated with coexisting thyroid pathology should be carefully considered. To mitigate this risk, thyroid ultrasonography should be routinely conducted in PHPT patients to exclude nodular thyroid disease.

In our case, the identification of a toxic multinodular goiter with a parathyroid adenoma prompted us to perform a total thyroidectomy with excision of the parathyroid adenoma. The histological examination revealed a surprising finding of a papillary thyroid microcarcinoma associated with the parathyroid adenoma.

CONCLUSION

The coexistence of Primary Hyperparathyroidism (PHPT) and Papillary Thyroid Carcinoma (PTC) underscores the need for thorough preoperative assessment. Enhanced imaging aids in detection, yet managing concurrent thyroid nodules poses challenges. While minimally invasive parathyroid surgery is favored, requiring careful consideration of associated risks, routine thyroid ultrasonography in PHPT patients is crucial to exclude nodular thyroid disease. The absence of specific guidelines for concurrent PHPT and PTC highlights the ongoing need for research. Navigating PHPT and PTC demands a balanced approach, integrating technical advancements with thoughtful risk assessment, emphasizing the continued role of research in guiding clinical practices.

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