A Case of Intrathyroidal Parathyroid Carcinoma in a Patient with End-Stage Renal Failure: A Rare Case Report and Diagnostic Challenge

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Keywords:

ABSTRACT

Parathyroid carcinoma is an uncommon malignancy of the endocrine system which can closely mimic as severe secondary or tertiary hyperparathyroidism in patients with chronic kidney disease. It often presents with marked hypercalcemia and significantly elevated parathyroid hormone (PTH) levels. Its diagnosis is challenging due to clinical overlap with other benign parathyroid disorders. The likelihood of an intrathyroidal location is low, estimated at approximately 0.2%, which poses a challenge for pre-operative suspicion as well as diagnosis. Fewer than 20 cases of intrathyroidal parathyroid carcinoma coexisting with end-stage renal failure have been reported in the literature. Here, we describe a case of 36-years gentleman, ECOG-0 with an End-stage renal failure (ESRF) since 20-years of age on regular dialysis with an intrathyroidal parathyroid carcinoma manage with right hemithyroidectomy. Surgical excision of a suspicious right thyroid nodule revealed parathyroid carcinoma on histopathology. This case emphasizes the diagnostic challenges and importance of considering parathyroid carcinoma in patients with refractory hyperparathyroidism in ESRF patient.

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INTRODUCTION

Parathyroid carcinoma is rare neoplasm originating from parathyroid glands, with an estimated prevalence of just 0.0005% among all malignancies. Similarly uncommon is the occurrence of an intrathyroidal parathyroid gland (0.2%), resulting from abnormal migration of parathyroid tissue from the third and fourth branchial pouch [1]. The coexistence of parathyroid carcinoma is even more uncommon, with only 3% of cases are linked to an ESRF [2]. The first documented case of parathyroid carcinoma in the context of renal hyperparathyroidism was reported by Bertland et al in 1982 [3]. Thus, differentiating a benign from malignant parathyroid disease in ESRF patient is critical, as treatment approaches differ substantially.

CASE REPORT

The patient is a 36-years gentleman with ESRF secondary to long-standing hypertension, in which he has been on renal replacement therapy for the past 16-years. He had a history of subtotal parathyroidectomy in July 2023 for renal hyperparathyroidism in which intraoperatively the superior right parathyroid gland could not be identified. There was a distinct right thyroid nodule over the superior pole and was excised along with the other parathyroid glands.

Histopathological examination of all the samples showed evidence of parathyroid hyperplasia. The patient was subsequently referred for evaluation and consideration of parathyroidectomy due to persistently elevated levels of PTH complicated by hypercalcemia. His serum intact parathyroid hormone (PTH) was elevated ranging 690-780 pmol/L (normal range; 1.6-6.8 pmol/L) and serum calcium ranging 2.3-2.6 mmol/L (normal range; 2.1-2.5 mmol/L).

Ultrasonography scan (USG) of the thyroid showed a solid enlarged and highly suspicious right thyroid lesion with punctate echogenic foci within the exophytic component approximately 2.6cm x 2.8cm x 2.7cm (TIRADS-5) as shown in Figure 1. Subsequently, an Ultrasound-guided fine-needle aspiration cytology (FNAC) was carried out and the result consistent with benign follicular nodule. Repeated FNAC was performed which resulted as suspicious of a follicular neoplasm, Thus the patient was counselled for a right hemithyroidectomy in considerations of the radiological as well as the pathological findings.

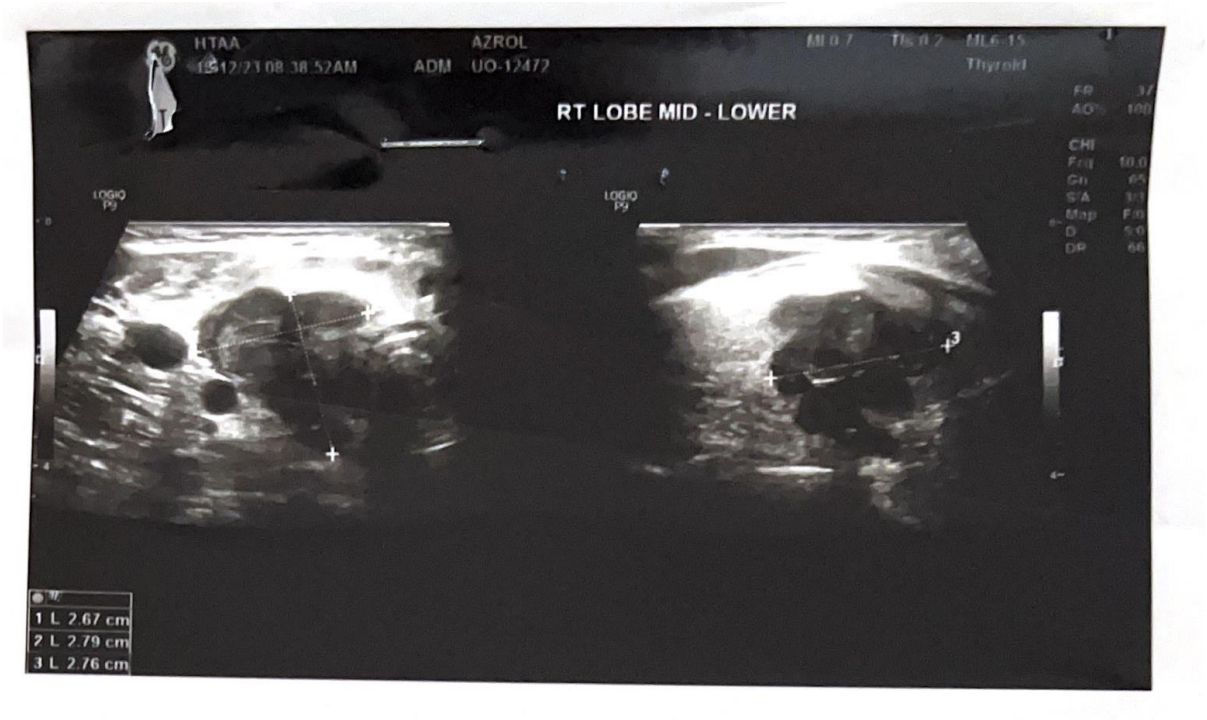

Fig. 1. Shows hypoechoic, solid lesion with punctate echogenic foci at the right thyroid lobe.

Intraoperative exploration revealed that there was a palpable nodule over the posterior superior aspect of right thyroid gland measuring 2cm x 2cm suspicious of parathyroid gland. The patient had an uneventful post-operative recovery and was discharged home on post-operative day 5. Histopathological examination of the right hemithyroidectomy specimen was consistent with a diagnosis of parathyroid carcinoma (shown in Figure 2 and Figure 3). The tumor cells show mild to moderately pleomorphic cells with multiple foci of lymphovascular invasion as well as capsular invasion.

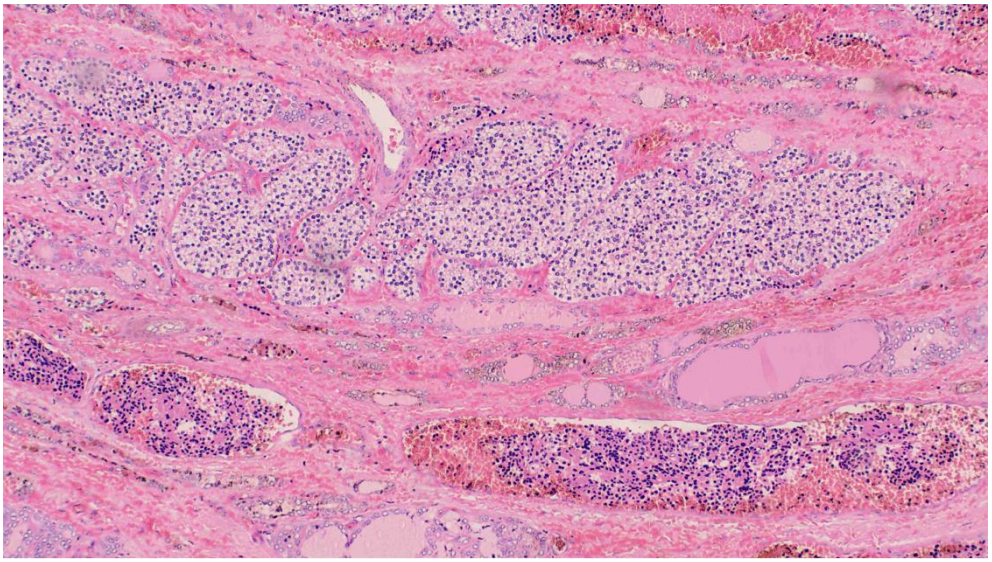

Fig. 2. Shows mild to moderately pleomorphic tumor cells (top) with multiple foci of lymphovascular invasion (below).

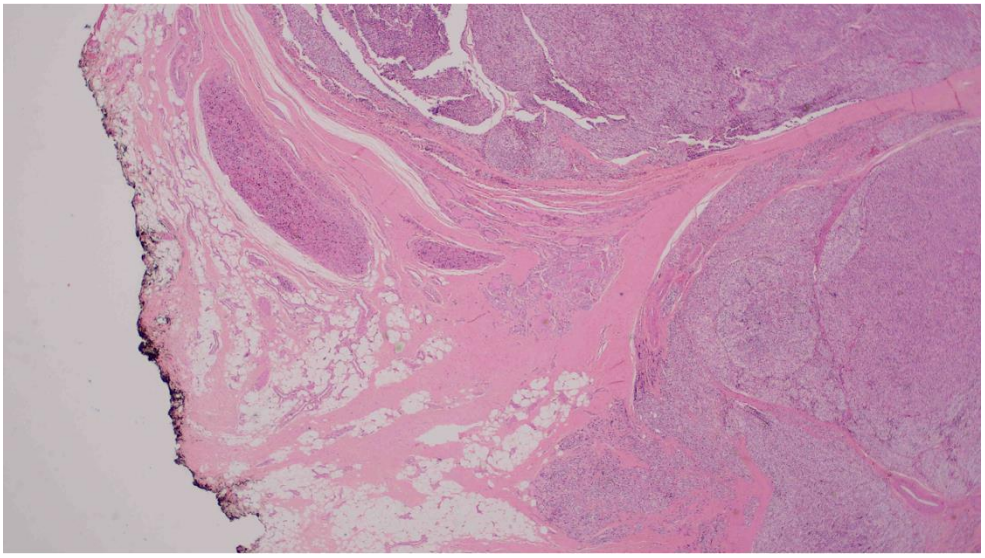

Fig. 3. Shows area of capsular invasion into adjacent thyroid tissue and surrounding adipose tissue.

DISCUSSION

Parathyroid carcinoma is a highly rare endocrine malignancy, representing fewer than 1% of all primary hyperparathyroidism cases [4,5]. Its incidence in patients with ESRF is uncommon and complex to diagnose. In ESRF, parathyroid dysfunction is frequently encountered in the form of secondary or tertiary hyperparathyroidism, where condition characterized by parathyroid gland hyperplasia due to chronic hypocalcemia, hyperphosphatemia as well as altered vitamin D metabolism. These benign disorders can often masquerade the biochemical and clinical presentation of parathyroid carcinoma, making an early diagnosis extremely difficult. Therefore, this condition often diagnosed after surgery via histopathologic examination as there is no definitive diagnostic test available for the pre-operative identification of parathyroid carcinoma.

In most cases of secondary hyperparathyroidism, serum PTH levels are elevated, however rarely exceed 1000 pg/mL. Some studies stated that when the PTH levels are disproportionately high especially when accompanied with hypercalcemia despite adequate medical therapy, thus tertiary hyperparathyroidism or more rarely, parathyroid carcinoma should be considered [6]. The classic features of parathyroid carcinoma include a single large parathyroid mass, markedly elevated serum PTH, serum calcium levels above 14 mg/dL and end-organ damage such as nephrolithiasis, osteoporosis, neuropsychiatric symptoms or cardiac dysfunction [6]. Despite such findings, many of these features is non-specific in an ESRF patient that may be incorrectly attributed to chronic renal dysfunction or tertiary hyperparathyroidism. It should be highlighted that both serum calcium & serum PTH levels are not reliable indicators for diagnosing parathyroid carcinoma in patients with long-standing ESRF as the kidney may develop autonomous parathyroid function over time as well as hypercalcemia.

The clinical presentation of parathyroid in patients undergoing hemodialysis is highly variable and remains inadequately characterized. Imaging modalities, including ultrasound of the neck and Tc-99m MIBI scans, are beneficent in localizing hyperfunctioning glands however it does not reliably differentiate between a benign from malignant lesion. These modalities may assist in detecting suspicious lesion, definitive diagnosis still relies on histopathological evaluation of tumor tissue obtained after surgical resection. Some suggest that ultrasound findings that suggest of malignancy include parathyroid gland larger than 2cm, with a lobulated or irregular contour, presence of calcification, invasion to surrounding tissue and presence of suspicious lymph nodes; however, this is not definitive [7].

This case highlights the challenges involved in diagnosing parathyroid carcinoma in the context of tertiary hyperparathyroidism with intrathyroidal manifestation. Both pre-operative and intraoperative identification of parathyroid carcinoma can be difficult. According to the American Association of Endocrine Surgeons' guidelines, pre-operative FNAC is not advised when parathyroid carcinoma is suspected, due to the risk of tumor seeding along the biopsy tract and potential hematoma or abscess formation [8]. Based on the overall imaging and pathology findings, the parathyroid carcinoma was misidentified as a thyroid nodule on ultrasound, thus FNAC was subsequently performed as a part of the thyroid nodule evaluation. The cytological similarities between both the

parathyroid carcinoma and follicular thyroid lesions posed a significant diagnostic challenge when interpreting the FNAC results. Both entities may exhibit overlapping features, such as epithelial cells arranged in microfollicular pattern and the presence of colloid-like material in the background. In our case, both the FNAC results suggested of a follicular lesion of benign and neoplasm. Ultimately, the definitive histopathological examination confirmed the diagnosis of parathyroid carcinoma.

An intra-parathyroidal carcinoma is believed to arise from an ectopic intrathyroidal parathyroid tissue, a phenomenon observed in approximately 0.2% of the population. The parathyroid glands develop from the third and fourth pharyngeal pouches and complete their migration by the seventh week of gestation. Variations during this migratory process are thought to contribute to the ectopic parathyroid gland localization [9]. Technetium-99m sestamibi (Tc-99m MIBI) scintigraphy is generally regarded as more sensitive modality for detecting parathyroid adenomas compared to high-resolution ultrasonography, with reported sensitivity and specificity ranging from 56% to 100% and 83& to 99% respectively. However, due to rarity of parathyroid carcinoma, the diagnostic performance of Tc-99m MIBI imaging for this malignancy has been assessed in only limited number of studies. In this case, the parathyroid lesion was mistakenly presumed as thyroid lesion. Thus, the investigations were tailored to the evaluation of thyroid lesion compared to parathyroid lesion.

Tumor resection with negative surgical margins offer the most favorable survival outcomes. Although resection of the ipsilateral thyroid lobe or the uninvolved ipsilateral parathyroid gland may be required to achieved clear margins, current evidence does not demonstrate a survival benefit from these additional procedures in patients with parathyroid carcinoma [10]. Chemotherapy has not demonstrated a clear therapeutic role in the management of parathyroid carcinoma [11,12]. While some studies have reported partial effectiveness or dacarbazine monotherapy or combination chemotherapy regime with 5-fluorouracil and cyclophosphamide, other investigations have shown no significant response [13,14]. Decisions regarding the use of adjuvant chemotherapy should be individualized, with comprehensive counselling regarding the limited evidence supporting its efficacy. Similarly, adjuvant radiotherapy has not been shown to provide a survival benefit in patients with parathyroid carcinoma [15]. As with chemotherapy, the consideration of adjuvant radiotherapy should be tailored to the individual patient and discussed within multidisciplinary teams setting [16]. For our patient, adjuvant therapy was not offered after comprehensive discussion with Oncology team, instead he was scheduled for regular surveillance.

CONCLUSION

Parathyroid carcinoma is a rare entity that presents significant diagnostic challenges. Inpatient with end-stage renal failure (ESRF), the presence of hypercalcemia and markedly elevated parathyroid hormone (PTH) levels may obscure suspicion for parathyroid malignancy, as these abnormalities are often attributed to the underlying renal disease. Furthermore, parathyroid carcinoma may be an incidental finding, however most patients achieve favorable outcomes when surgical resection is performed early in the absence of distant metastases.

CONFLICT OF INTEREST

None

ACKNOWLEDGEMENT

We would like to express our gratitude to the patient that gave their permission for this case report.

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