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Case Report

Diagnostic and therapeutic implications of asymptomatic parathyroid adenoma co-existing with papillary thyroid carcinoma; a rare case report

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Abstract

Asymptomatic parathyroid adenoma (PA) co-existing with a papillary thyroid carcinoma (PTC) is rare. Pre-operative diagnosis of the PA based on routine investigations is challenging. Ultrasound is a poor diagnostic tool for central compartment evaluation and pre-operative serum calcium estimation is not routinely performed in non-medullary thyroid cancers (NMTCs). Intra-operatively a PA can mimic a metastatic central compartment node. A 28 years old lady presented with a large right sided thyroid nodule with no other associated symptoms which was diagnosed as PTC on fine needle aspiration cytology (FNAC). Ultrasound did not reveal any suspicious central compartment lymph nodes. Intra-operatively, a right sided central compartment nodule separate from the thyroid gland was found. The lesion clinically mimicked a metastatic node based on which central compartment nodal clearance was performed. All parathyroids except the right superior parathyroid (which could not be identified intra-operatively) were preserved. Postoperatively, she developed severe transient hypocalcemia. The suspicious metastatic node on histopathology was incidentally found to be a PA. An asymptomatic PA can rarely co-exist with a non-medullary thyroid carcinoma (NMTC) and we recommend pre-operative routine serum calcium evaluation and intra-operative frozen section of suspicious central compartment nodes to pre-empt and diagnose such associations.

Keywords: Asymptomatic parathyroid adenoma, Papillary thyroid carcinoma, Hypocalcemia, Non-medullary thyroid carcinoma

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Introduction

The association of primary hyperparathyroidism with medullary thyroid carcinoma (MTC) is well established in patients with multiple endocrine neoplasia (MEN) syndrome type 2A (1). A thorough clinical evaluation for signs and symptoms of hyperparathyroidism and assessment of serum calcium levels are mandatory in the pre-operative work up of all patients of MTC. The co-existence of primary hyperparathyroidism (PHPT) with non-medullary thyroid carcinoma (NMTC) is rare and literature is limited to few case reports (1). Most commonly these patients present with primary hyperparathyroidism and thyroid carcinoma is diagnosed either during the pre-operative work up or during pathological evaluation of the resected specimen (2-4). Incidentally discovered asymptomatic PA in a known patient of NMTC is extremely uncommon (5,6). However, this entity carries immense clinical significance both in the intra-operative and the post-operative period. Here we report the case of a 28-year-old lady with a papillary thyroid carcinoma (PTC) who had a co-existing asymptomatic undiagnosed PA which intra-operatively mimicked a metastatic central compartment node.

Case Report

A 28-year-old lady presented to our head and neck surgical oncology unit with a progressively increasing right sided thyroid swelling since last four months. She was clinically euthyroid with no other associated symptoms. On clinical examination, there was a firm solitary thyroid nodule involving almost the entire right lobe measuring about 5×4 cm without any clinically evident retrosternal or extra-thyroid extension. There were no palpable neck nodes. She had no past history of irradiation or contributory

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Implication for health policy/practice/research/ medical education

Asymptomatic parathyroid adenoma (PA) co-existing with non-medullary thyroid carcinoma (NMTC) is not common and routine pre operative investigations for NMTC are insufficient for diagnosing such associations. Intra-operatively PA can resemble a metastatic central compartment node which is far more common in NMTC. Diagnosis of such co-existance not only helps in planning the extent of surgery but also pre-empts immediate post operative transient hypocalcemia even when other parathyroids are preserved. We recommend routine pre operative serum calcium evaluation and intra operative frozen section analysis of suspicious central compartment nodes in patients of NMTC to diagnose such rare but possible association.

family history.

Diagnostic assessment

Ultrasound neck revealed a large (2.6 × 5.2 × 5.4 cm) isoechoic to hypoechoic, wider than taller right sided thyroid nodule with few micro-calcifications and central and peripheral vascularity. Extra-thyroid extension was not evident. The left lobe was normal. The nodule was classified sonologically by thyroid image reporting and data system (TI-RADS) as TI-RADS 4 (suspicious for malignancy). There were no suspicious nodes either in the central or the lateral neck. Fine needle aspiration cytology (FNAC) from the right thyroid nodule was suggestive of Bethesda category VI-papillary carcinoma thyroid. Pre-operative laboratory investigations were normal and confirmatory of an euthyroid status.

Therapeutic intervention

A treatment plan of total thyroidectomy with central compartment inspection with or without clearance (based on intra-operative findings for suspicious nodes) followed by radioactive iodine therapy was made and discussed accordingly with the patient. Intraoperatively, during mobilization of the right thyroid lobe, a 2×1 cm firm nodule separate from the thyroid lobe and located in a posterior-superior relation to the gland was encountered. It was clinically suspected as a metastatic node and a complete central and lateral compartment nodal clearance was done along with a total thyroidectomy. The right superior parathyroid could not be identified intra-operatively. All the other three parathyroids were identified, preserved and found viable.

In the post-operative period, the patient developed clinical and biochemical hypocalcemia on the second post-operative day. She was initially managed with oral calcium and calcitriol supplementation. However, her symptoms worsened and she was started on slow intravenous infusion of calcium gluconate (2 grams thrice daily) supplemented with calcitriol tablets (0.5 mg three times daily). Her clinical hypocalcemia further worsened and serum calcium dropped progressively up to less than 5 mg/dL. Serum parathormone was found to be 3 pg/ml. Calcium supplementation was further intensified to 24-hour continuous calcium gluconate infusion (6 ampoules in 500 mL of 5% dextrose infused at a rate of 20 mL/h) with cardiac monitoring. The patient's symptoms started improving on 14th post-operative day and the biochemical reports started showing an upward trend of serum calcium. The dose of calcium gluconate infusion was gradually reduced and the patient was weaned off parenteral calcium supplementation on 18th post-operative day. She was discharged in a stable condition on oral calcium and calcitriol supplementation at a serum calcium level of 8.7 mg/dL. Enteral calcium support was completely withdrawn after one week of discharge.

Treatment outcome

The histopathology report was confirmatory of a solid variant of papillary thyroid carcinoma (5.5×5×4 cm) (Figures 1, 2a, 2b) with no extra thyroid extension. Right central compartment tissue on gross examination measured 4×3×1 cm and yielded five nodes largest measuring 1.8×1 cm. On microscopic examination, the largest node was incidentally found to be a PA (Figure 3a-c). All other nodes in both the right and left central compartments were reactive.

Post-operative ultrasound revealed no suspicious lesions in the operated thyroid bed. Serum parathyroid levels (40 pg/mL) and calcium levels (8.8 mg/dL) were normal at one-month post-surgery.

Discussion

Primary hyperparathyroidism (PHPT) is a rare disorder and is found in up to 0.1% of the general population (1). In majority of the cases the condition is asymptomatic and patients can remain so for 6 to 8 years before being clinically evident (1). When symptomatic, PHPT patients commonly present with bone pain, osteoporosis and renal stones. The most common cause of PHPT is a single gland adenoma (75%–85% of the cases) (1). Multiple adenomas although rare can occur in 15%-25% of the cases. Initial diagnostic work up includes estimation of serum calcium, serum parathormone and neck imaging. Our patient primarily presented with a solitary thyroid nodule and did not have any symptom of PHPT at presentation.

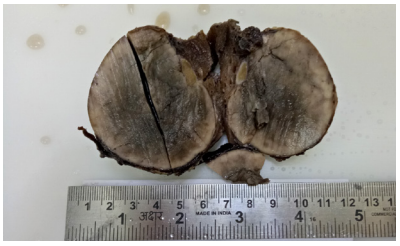

Figure 1. Total thyroidectomy specimen- cut section shows right of lobe of thyroid replaced by solid grey white tumor.

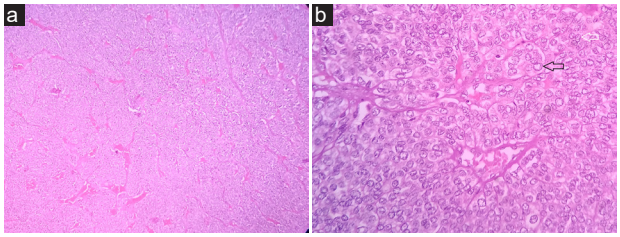

Figure 2. (a) Papillary Thyroid Carcinoma (10x) shows tumor arranged in papillary architecture with central thin fibro vascular core. (b) Papillary Thyroid Carcinoma (40x) shows characteristic nuclear clearing (black arrow) and grooving (white arrow).

Thus only routine pre-operative laboratory investigations were performed which did not include serum calcium estimation. However, in view of this rare but possible co-existence, we intend to highlight the importance of pre-operative serum calcium evaluation as a routine work up, even for non-medullary thyroid cancer patients.

Our patient underwent pre-operative neck ultrasonography (US) which was not able to identify the co-existing PA. Ultrasound neck is not a sensitive modality to image the central compartment especially in the presence of a large thyroid nodule (5). The reported intra-operative incidence of parathyroid incidentalomas is between 0.2% and 7.6%, (7,8) while the US incidence is <1%. (8,9). In our patient a small superior PA (1.8×1 cm) co-existed with a large thyroid nodule (2.6 × 5.2 × 5.4 cm) both on the right side. This may have been the reason for not being able to identify the PA on routine ultrasound especially with the radiologist not suspecting such a co-existing pathology.

PA/hyperplasia can be associated with medullary thyroid cancer (MTC) in 5-10% patients of MEN syndrome type 2A (2). Serum calcium estimation is mandatory in the pre-operative work up of all patients with MTC. However, PA associated with non-medullary thyroid cancer (NMTC) is rare (1-2%) (3,4). Based on the available literature, most NMTCs are diagnosed incidentally during work up of patients presenting with PHPT. However, co-existence of asymptomatic PA in a patient with NMTC with the PA being diagnosed post operatively is exceedingly rare. To our knowledge, similar finding was reported only in three patients in a series of seven cases of co-existing parathyroid disease with papillary thyroid cancer and in one case report (9, 10).

Central compartment clearance in differentiated thyroid cancers is indicated for advanced (T3, T4) stage cancers and in clinical radiological or cytological evidence of metastatic nodes in central or lateral compartments. However, central compartment dissection increases risk of transient and permanent hypoparathyroidism (11, 12). Identification and preservation of the parathyroids with their blood supply reduces the chances of such complications. Clinically differentiating a metastatic central compartment node from a PA per operatively is challenging as the former pathology is far more common. Furthermore, intra-operative diagnosis of a pathological

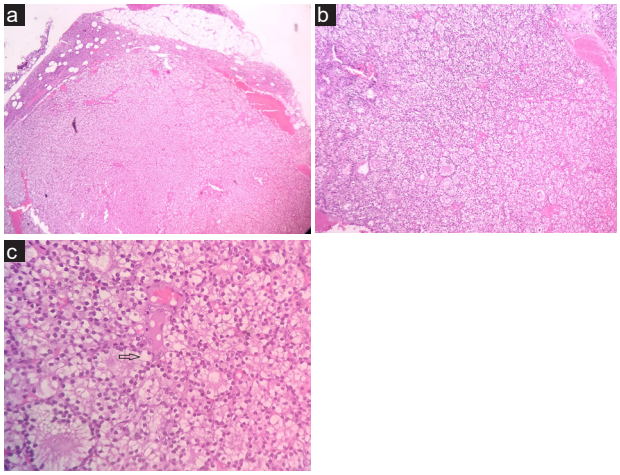

Figure 3. (a) Parathyroid adenoma (4x) shows cellular tumor composed of chief cells surrounded by thin fibrous capsule. Normal compressed parathyroid tissue and adipose tissue is seen at the periphery. (b) Parathyroid adenoma (10x) shows dense sheets of mostly chief cells arranged in lobules that are separated by fibrous septa. (c) Parathyroid adenoma (40x) shows predominantly chief cells (black arrow) with clear cytoplasm and round monomorphic nuclei arranged in follicular pattern.

parathyroid makes it mandatory to inspect all other parathyroids to rule out gland hyperplasia or multiple gland adenoma and also to preserve the normal glands to reduce chances of post-operative hypocalcemia. Similar to the other case report (9), we too misdiagnosed the adenoma as a metastatic node based on clinical suspicion. This highlights the importance of an intra-operative frozen section assessment of a suspicious node(s) in central compartment and if a pathological parathyroid is identified, intra-operative serum parathormone estimation provided the facilities are available. Post-operatively, our patient developed severe transient clinical and biochemical hypocalcemia (despite preserving three parathyroids during surgery) and required 24hour continuous high dose intravenous calcium infusion. The cause of such disparity was only evident on final histopathology. A per-operative diagnosis by frozen section could have intimated us of the possibility of severe post-operative transient hypocalcemia, as the preserved parathyroids remained dormant in presence of a functionally active adenoma.

Conclusion

This report depicts a rare case scenario of co-existing pathologies. A routine pre-operative serum calcium estimation even in NMTCs may point towards such an association which can be confirmed with further investigations. Routine intraoperative frozen section assessment of suspicious central compartment nodes in thyroid cancers can be both diagnostic and curative for a co-existing parathyroid pathology.

Authors' contribution

AP and SB prepared the manuscript. SG provided pathological inputs and photographs of the slides. AG

and TC did review of literature. SC did supervision and editing of the final draft and is the consultant in charge of the patient.

Conflicts of interest

The authors report no conflicts of interest.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors. The patient has given her informed consent regarding publication of this case report.

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