Case Report of a Rare Collision Tumour of Papillary and Follicular Thyroid Carcinoma

Prasad Mothayapan
University of Malaya
Diana BL Ong
University of Malaya
Khoon Leong Ng (ngkl@um.edu.my)
University of Malaya

Case Report

Keywords: Thyroid Malignancy, Papillary Thyroid Carcinoma, Follicular Thyroid Carcinoma, Collision Tumours, Case Report

Posted Date: May 5th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1613682/v1

Abstract

Introduction

Papillary and follicular thyroid carcinomas account for 90–95% of all thyroid cancers. The co-existence of these two cancers is extremely rare and have only been described in case reports. We report a rare case of a collision tumour of papillary and follicular thyroid carcinoma in the same thyroid lobe.

Case Presentation

A 43-year-old woman presented with an anterior neck mass. A right thyroid nodule was clinically palpable. Ultrasonography revealed bilateral thyroid nodules. Fine needle aspiration (FNA) of the right nodule revealed cyst content, while FNA of the left nodule demonstrated atypia of undetermined significance. The patient was counselled for a left hemithyroidectomy but opted for removal of the enlarged right thyroid nodule. A right hemithyroidectomy was performed and histopathology revealed follicular carcinoma as well as a nodule consisting of papillary carcinoma. These two malignant nodules were separated by a section of normal thyroid tissue. A completion left hemithyroidectomy subsequently revealed papillary carcinoma in the left thyroid lobe. The patient was subsequently treated with radioiodine (131I) and thyroxine suppression therapy.

Conclusion

Collision tumours have been described as two independent tumours with distinct morphology which occur concurrently at the same site but having a distinct border. They are extremely rare entities. Clinical, radiological and cyto-histopathological evaluation is fundamental in investigating thyroid nodules but may miss a collision tumour. A number of theories and genetic mutations have been implicated in this collision phenomenon, but none have been proven so far. Management of collision tumours need to be individualised.

1. Introduction

Papillary thyroid cancers (PTC) and follicular thyroid cancers (FTC) are the two commonest thyroid cancers reported to date [1]. The co-existence of these two distinct malignancies is extremely rare despite the rising incidence of thyroid cancers globally [2]. The pathogenesis of this entity is poorly established owing to its rarity and scarcity of available literature – mainly in the form of case reports. [3–8]. Herein, we report a case of collision tumour of PTC and FTC in the same anatomical lobe and PTC in the opposite lobe in a patient with a background of Hashimoto's thyroiditis.

2. Case Report/case Presentation

A 43-year-old woman with no prior medical illness was referred to our Endocrine Surgery clinic for an anterior neck mass detected on routine health check-up. The patient had no risk factors associated with thyroid malignancies such as prior radiation exposure, family history or genetic diseases. She was also not a resident of an iodine-deficient geographical area. Clinical examination revealed a firm right thyroid nodule which was prominent on deglutition. Cervical lymphadenopathy was absent and systemic examination was unremarkable. Serum thyroid function tests were within the normal range [TSH: 2.02 mIU/L (range: 0.55–4.78 mIU/L) and Free T4: 17.8 pmol/L (range: 11.5–22.7 pmol/L)]. Neck ultrasonography (USG) revealed multiple solid cystic nodules in both thyroid lobes. The largest nodule in the right lobe measured: 1.2 X 1.6 X 1.9cm while in the left lobe, the largest nodule measured: 0.7 X 0.6 X 1.0cm. None of the nodules demonstrated calcifications or increased intra-lesional vascularity (shown in Fig. 1a-d).

As per recommended guidelines the patient was subjected to an ultrasound-guided Fine Needle Aspiration (FNA) of the largest left and right thyroid nodules. FNA of the right nodule was consistent with *cyst content*, which was non-diagnostic and FNA of the left nodule demonstrated *atypia of undetermined significance (AUS)*. A left hemithyroidectomy was recommended based on the FNA findings. However, the patient opted for resection of the enlarged right nodule instead. A right hemithyroidectomy was subsequently performed and histopathological examination (HPE) revealed the co-existence of FTC and PTC - a “collision tumour” (shown in Fig. 2a).

The enlarged right thyroid lobe specimen revealed two solid tumours of which the larger was capsulated measuring 2.5 x 2 x 2cm with the smaller solid tan coloured tumour without capsule measuring 0.5 x 0.5 x 0.5cm. These two tumours were interposed by normal thyroid parenchyma. Microscopy of the capsulated tumour revealed variable appearance, ranging from well-formed follicles, trabeculae patterns and solid growth pattern (shown in Fig. 3a-d). The neoplastic cells exhibited mildly pleomorphic round nuclei, dispersed chromatin and inconspicuous nucleoli with occasional mitotic figures. There were no papillary nuclear features observed. Follicular carcinoma was defined by the presence of invasion of the capsule and blood vessels (shown in Fig. 3c-f). The smaller solid thyroid lesion had dissimilar features. Microscopically, the tumour was unencapsulated exhibiting true papillae with multiple branching (shown in Fig. 3g, h). These papillae are lined by pleomorphic epithelium with Orphan Annie eye nuclei which are optically clear with thick nuclear outline. Pseudonuclear inclusions and grooves were also present (shown in Fig. 3i, j). These morphological features are consistent with papillary thyroid carcinoma.

Subsequent completion left hemithyroidectomy was performed (shown in Fig. 2b). The left thyroid lobe revealed a tan-coloured solid nodule measuring 0.7 x 0.6 x 0.5 cm. This nodule exhibited papillary thyroid carcinoma (shown in Fig. 4a, b). Post-surgery, the patient was treated with radioiodine (131I) and thyroxine suppression therapy.

3. Discussion

Papillary and follicular thyroid carcinomas are recognized entities of differentiated thyroid carcinomas (DTC's) which are derived from thyroglobulin-secreting follicular cells [9]. Collectively, they make up 80–95% of all thyroid cancers, the remaining variants being, poorly differentiated thyroid carcinoma, anaplastic carcinoma (AC) and medullary thyroid carcinoma (MTC) [10–12]. The simultaneous occurrences of these different histological thyroid cancers have been reported previously but mainly of PTC and MTC or a combination with other forms of cancers [13–18]. Despite the first reporting of a collision tumour of PTC and FTC almost a decade ago by *Plauche et.al*, data on this phenomenon is still lacking. [4, 5, 7].

The terms "collision tumours", "synchronous tumours", "mixed tumours" and "composite tumours" have been used to describe the simultaneous existence of different forms of malignant cells in an organ. Collision tumours are described as two independent tumours with distinct morphology which occur concurrently at the same site but having a distinct border [19, 20], whereas in synchronous tumours, these primaries are anatomically separated [6]. The term "mixed tumours" is used when there is histological admixture of two tumours in the same organ with the same precursor cells while in "composite tumours", the tumour contains two discrete cell populations [21].

A simultaneous occurrence of tumours pose a diagnostic challenge as FNA could miss the more sinister locus harboring malignancy as demonstrated in our case where the cytology of the right gland revealed cyst content while AUS was seen in the left gland. AUS carries a 6–18% risk of malignancy and the customary management is either a repeat FNA after an appropriate time interval, molecular studies or a surgical lobectomy, which was the initial proposed management in this case [22]. Surprisingly, HPE of the right thyroid lobe in our case revealed a nodule of follicular neoplastic cells with capsular and vascular invasion – indicating FTC and another adjacent nodule with malignant cells arranged in papillary architecture exhibiting dispersed chromatin nuclei, ground glass appearance, nuclear pseudoinclusions and nuclear grooves consistent with PTC. These two nodules occurring in the same thyroid lobe, each with different malignant cells and having a distinct border allows its categorization as a "collision tumour". In addition to that, the histopathological specimen of the left thyroid lobe also revealed PTC, further adding a concern on the potential aggressive nature of collision tumours. As per consensus with the oncologist, the patient was treated with radioiodine (131I) and was also subjected to thyroxine suppression therapy to treat both the PTC and FTC.

A number of theories have been proposed concerning the pathogenesis of these tumours but none could completely explain this phenomenon. In their retrospective review of 53 patients, *Kim et al* proposed that concurrent occurrences of thyroid carcinomas could simply be coincidental but did recognize the various theories related to this event which includes – stem cell theory, collision theory, hostage theory, tumourigenic stimulus and divergent differentiation theory [7, 23–26]. Genetic mutations were detected in studies of collision tumours and several genes have been implicated, namely BRAF, RAS and RET protooncogenes [27–29]. The use of molecular markers have shown promising results in the detection, prognostication and guidance of the therapeutic regime [30]. Fundamentally, the concept of triple assessment by clinical examination, radiological imaging and cyto-histopathological confirmation that is

usually performed for the investigation of thyroid lesions may miss these “collision tumours”. The addition of molecular markers as an investigative tool may be useful in selected cases.

4. Conclusion

Collision tumours occur infrequently and a combination of PTC and FTC is a rare occurrence with only a handful of cases reported to date. With the paucity of data and good quality evidence, management of these tumours have proven to be challenging to the physician. Individually, PTC and FTC have excellent 5-year survival rates. In combination however, collision tumours are unpredictable due to their unascertained biological behaviour. Triple assessment of thyroid lesions by clinical examination, radiological imaging and cyto-histopathological confirmation may have missed the second malignancy in this patient. It is fortuitous that the adjuvant treatment required is similar for both cancers. Management of these tumours therefore need to be individualized.

Declarations

Author Contributions

Prasad Mothayapan performed literature review, collected clinical data and created the initial manuscript draft. Diana BL Ong participated in writing and revision of the manuscript. Khoon Leong Ng was involved in clinical care of the patient, conceptualized the paper and performed critical review of the manuscript. All authors approved the final version to be published.

Statement of Ethics

All procedures and investigations performed in this case were done in accordance with the ethical standards of our institution and available clinical practice guidelines. This case report conforms to the Declaration of Helsinki (as revised in 2013). Ethical approval was obtained from our institution and written informed consent was obtained from the patient for the publication of the case and the accompanying images.

Funding Sources

There were no funding sources received to assist in preparation of this manuscript.

Conflict of Interest Statement

The authors have no competing interests to declare that are relevant to the content of this article.

References

1. Lloyd R, Osamura R, Klöppel G, Rosai J. WHO Classification of Tumours of Endocrine Organs, 4th edn IARC Press. Lyon; 2017.

2. Brito JP, Morris JC, Montori VM. Thyroid cancer: zealous imaging has increased detection and treatment of low risk tumours. Bmj. 2013;347:f4706.
3. Thomas V, George R. Collision tumors of the thyroid: Review of literature and report of a case of papillary&Follicular collision tumor. Thyroid Research and Practice. 2018;15(2):60–4.
4. Plauche V, Dewenter T, Walvekar RR. Follicular and papillary carcinoma: a thyroid collision tumor. Indian J Otolaryngol Head Neck Surg. 2013;65(Suppl 1):182–4.
5. Feng JW, Ye J, Hu J, Liu SY, Jiang Y, Hong LZ. Synchronous papillary thyroid carcinoma and follicular thyroid carcinoma: case report and review of literature. Int J Clin Exp Pathol. 2020;13(11):2767–71.
6. Cracolici V, Mujacic I, Kadri S, Alikhan M, Niu N, Segal JP, et al. Synchronous and Metastatic Papillary and Follicular Thyroid Carcinomas with Unique Molecular Signatures. Endocr Pathol. 2018;29(1):9–14.
7. Abdelaal A, El Ansari W, Abusabeib A, Farghaly H, Tabeb AAM. Simultaneous occurrence of follicular and papillary thyroid carcinomas in same thyroid lobe: A case series of six patients from Qatar. Int J Surg Case Rep. 2020;73:65–70.
8. Pishdad R, Cespedes L, Boutin R, Jaloudi M, Raghuwanshi M. Coexistence of Two Different Thyroid Malignancies: A Collision Phenomenon. Cureus. 2020;12(4):e7539-e.
9. Siegel R, Ma J, Zou Z, Jemal A. Cancer statistics, 2014. CA: A Cancer Journal for Clinicians. 2014;64(1):9–29.
10. Fagin JA, Wells SA, Jr. Biologic and Clinical Perspectives on Thyroid Cancer. N Engl J Med. 2016;375(11):1054–67.
11. Katoh H, Yamashita K, Enomoto T, Watanabe M. Classification and General Considerations of Thyroid Cancer. Annals of Clinical Pathology. 2015;2.
12. Chmielik E, Rusinek D, Oczko-Wojciechowska M, Jarzab M, Krajewska J, Czarniecka A, et al. Heterogeneity of Thyroid Cancer. Pathobiology. 2018;85(1–2):117–29.
13. Guerreiro V, Costa C, Oliveira J, Santos AP, Farinha M, Jácome M, et al. Mixed medullary-papillary thyroid carcinoma with mixed lymph node metastases: A case report. Clin Case Rep. 2021;9(5):e04165.
14. Thewjitcharoen Y, Krittiyawong S, Butadej S, Nakasatien S, Polchart S, Junyangdikul P, et al. De-differentiation of papillary thyroid carcinoma into squamous cell carcinoma in an elderly patient: A case report. Medicine (Baltimore). 2020;99(16):e19892.
15. Gadong LC, Crisostomo T. Simultaneous Occurrence of Papillary Carcinoma and Medullary Carcinoma. J ASEAN Fed Endocr Soc. 2019;34(2):226–8.
16. Samiee-Rad F, Farajee S, Torabi E. Concurrence of Papillary Thyroid Carcinoma and Hürthle Cell Carcinoma in an Iranian Woman with Hashimoto's Thyroiditis. Iran J Pathol. 2019;14(4):342–6.
17. Dikbas O, Duman AA, Guvendi GF. Medullary Thyroid Carcinoma and Papillary Thyroid Carcinoma in the Same Patient as a Collision Tumour. Case Rep Endocrinol. 2019;2019:4038628.

18. M AAH, Albisher HM, Al Saeed WR, Almumtin AT, Allabbad FM, M AS. BRAF gene mutations in synchronous papillary thyroid carcinoma and Langerhans cell histiocytosis co-existing in the thyroid gland: a case report and literature review. BMC Cancer. 2019;19(1):170.
19. Bulte CA, Hoegler KM, Khachemoune A. Collision tumors: A review of their types, pathogenesis, and diagnostic challenges. Dermatol Ther. 2020;33(6):e14236.
20. Siraj F, Shruti S, Jain S, Bhatnagar A, Agrawal U. Collision of Malignant Melanoma and Squamous Cell Carcinoma in Rectum: First Report of a Rare Tumor. Turk Patoloji Derg. 2019;35(3):237–41.
21. Baloch ZW, Mandel S, LiVolsi VA. Combined tall cell carcinoma and Hürthle cell carcinoma (collision tumor) of the thyroid. Arch Pathol Lab Med. 2001;125(4):541–3.
22. Cibas ES, Ali SZ. The 2017 Bethesda System for Reporting Thyroid Cytopathology. Thyroid. 2017;27(11):1341–6.
23. Kim WG, Gong G, Kim EY, Kim TY, Hong SJ, Kim WB, et al. Concurrent occurrence of medullary thyroid carcinoma and papillary thyroid carcinoma in the same thyroid should be considered as coincidental. Clin Endocrinol (Oxf). 2010;72(2):256–63.
24. Polat ŞB, Arpacı D, Yazgan A, Başer H, Kılıç M, Ersoy R, et al. Simultaneous Occurrence of Different Follicular Neoplasms within the Same Thyroid Gland. Turkish Journal of Endocrinology and Metabolism. 2016;20(2):31–5.
25. Matias-Guiu X, Caixas A, Costa I, Cabezas R, Prat J. Compound medullary-papillary carcinoma of the thyroid: true mixed versus collision tumour [corrected]. Histopathology. 1994;25(2):183–5.
26. Ljungberg O, Ericsson UB, Bondeson L, Thorell J. A compound follicular-parafollicular cell carcinoma of the thyroid: a new tumor entity? Cancer. 1983;52(6):1053–61.
27. Appetecchia M, Lauretta R, Barnabei A, Pieruzzi L, Terrenato I, Cavedon E, et al. Epidemiology of Simultaneous Medullary and Papillary Thyroid Carcinomas (MTC/PTC): An Italian Multicenter Study. Cancers (Basel). 2019;11(10).
28. Castellone MD, Santoro M. Dysregulated RET Signaling in Thyroid Cancer. Endocrinology and Metabolism Clinics of North America. 2008;37(2):363–74.
29. Liu LP, Hao JY, Pan H, Wang C, Yue P. [Mutation of RAS gene in follicular-differentiated thyroid tumors and its significance]. Zhonghua Bing Li Xue Za Zhi. 2020;49(3):256–61.
30. Hsiao SJ, Nikiforov YE. Molecular approaches to thyroid cancer diagnosis. Endocrine-Related Cancer. 2014;21(5):T301-T13.

Figures

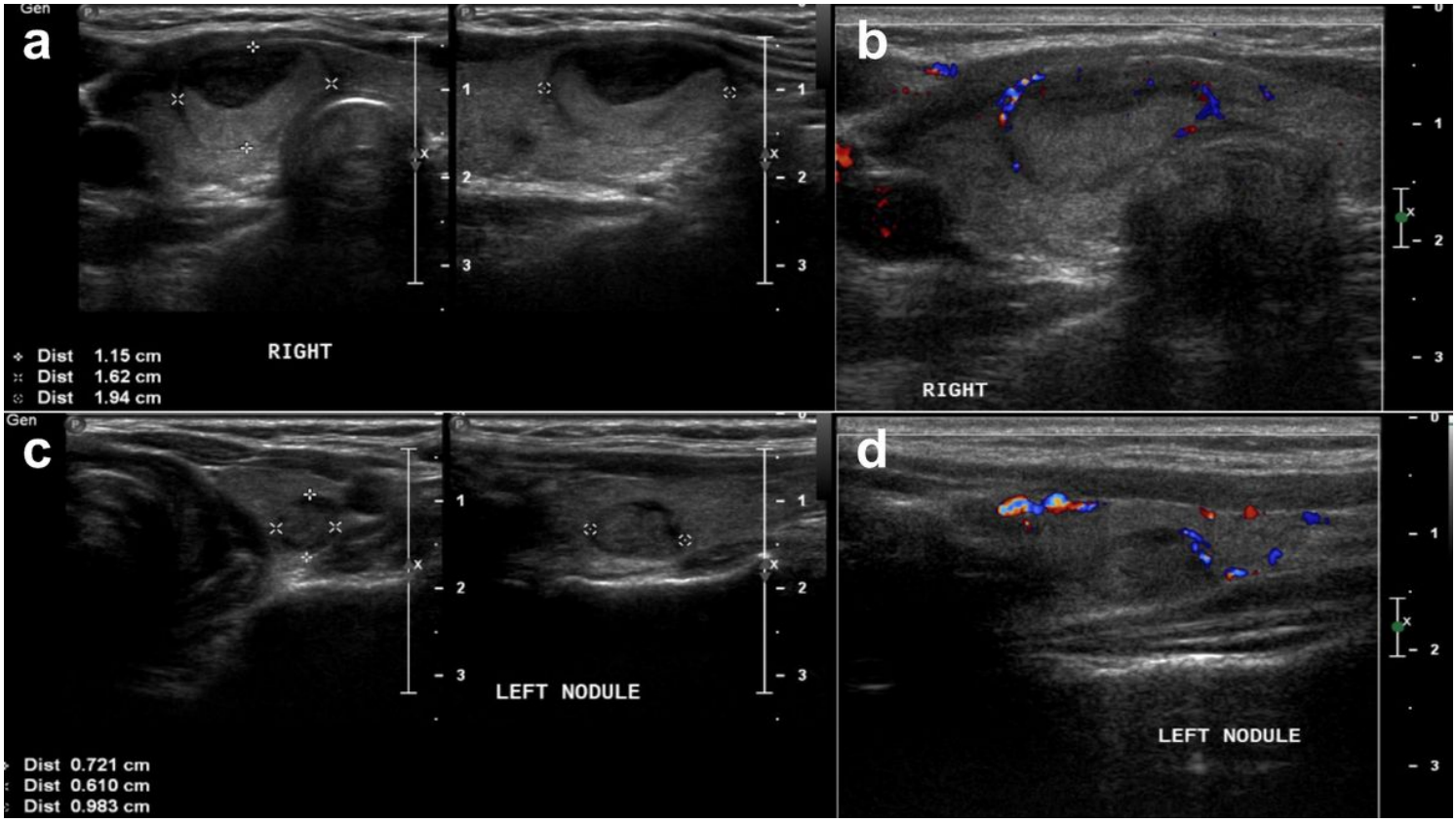

Figure 1

Pre-operative ultrasound imaging.

a, b. A well-defined, isoechoic, mixed solid-cystic nodule in the right lobe measuring 1.2 x 1.6 x 1.9cm. Peripheral vascularity was seen but no demonstrable internal vascularity, micro/macrocalcifications and no extra-thyroidal extension.

c, d. A similar appearing nodule measuring 0.7 X 0.6 X 1.0cm seen in the left thyroid lobe. The nodule was well-defined, isoechoic compared to the adjacent thyroid parenchyma and has a mixed solid-cystic appearance. There was no internal vascularity, micro/macrocalcifications and no extra-thyroidal extension seen in the left nodule.

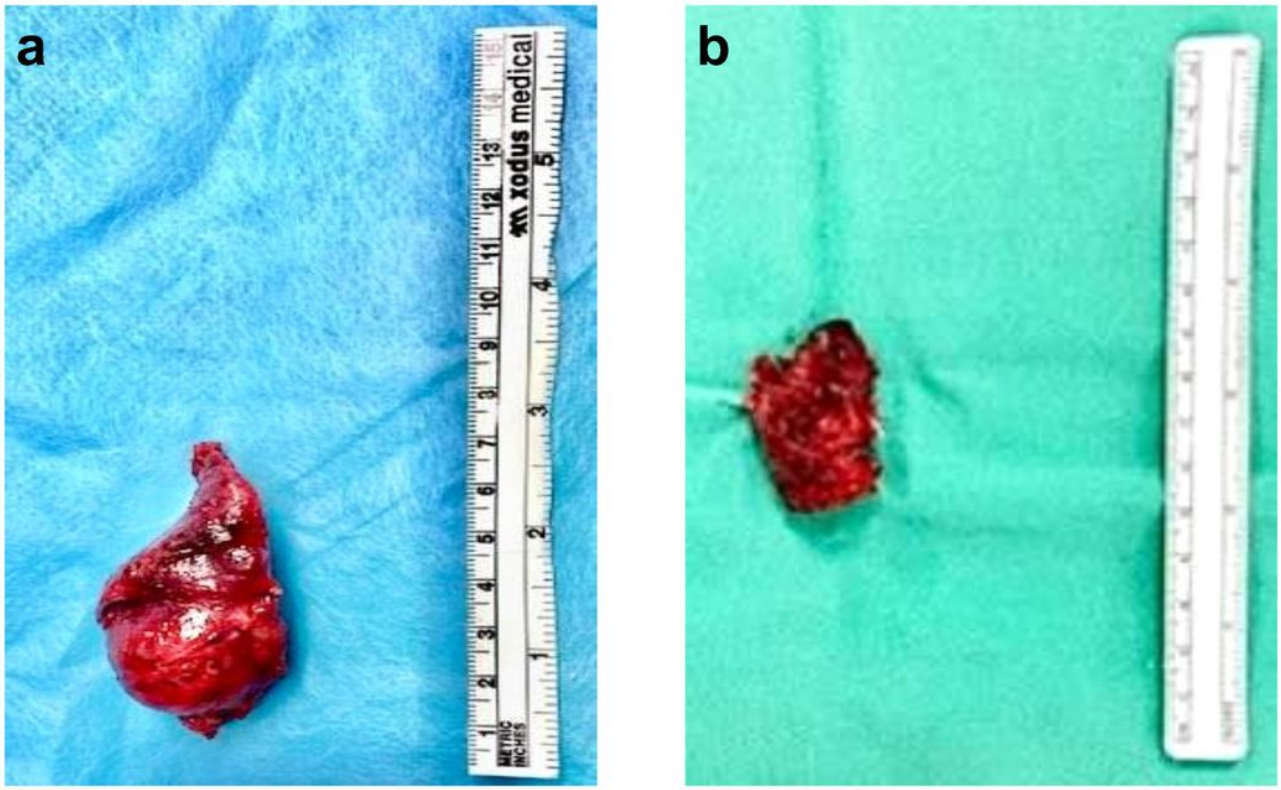

Figure 2

Thyroidectomy specimen.

a. Right hemithyroidectomy specimen

b. Left hemithyroidectomy specimen

Figure 3

Histological representative of the right thyroid lobe.

a, b. Encapsulated thyroid neoplasm with follicular differentiation. (a) Tumour is composed of closely packed follicles surrounded by fibrous capsule (arrow) (H&E, x10 magnification). (b) Well to poorly formed follicles with occasional absence of colloid lined by epithelium which are without papillary nuclear features (arrow) (H&E, x20 magnification).

c, d. Areas of capsular invasions (arrow) and variable microscopic appearance of tumour with solid growth pattern and trabecular formation (H&E, x10 magnification).

e, f. (e) Complete penetration of tumour fibrous capsule. Capsular breach (short arrow) by infiltrating tumour cells (long arrow) (H&E, x10 magnification). (f) Tumour within vascular space (arrow) (H&E, x20

magnification).

g, h. Right thyroid lobe with separate solid tumour. Papillary thyroid carcinoma. Neoplastic thyroid cells are disposed in complex branching papillae (arrow) (H&E, x10 magnification).

i, j. (i) Papillary thyroid carcinoma (H&E, x20 magnification). (j) Nuclear features of papillary carcinoma. Optically clear nuclei (short arrow), nuclear pseudoinclusions (thick arrow) and nuclear groove (long arrow) (H&E, x40 magnification).

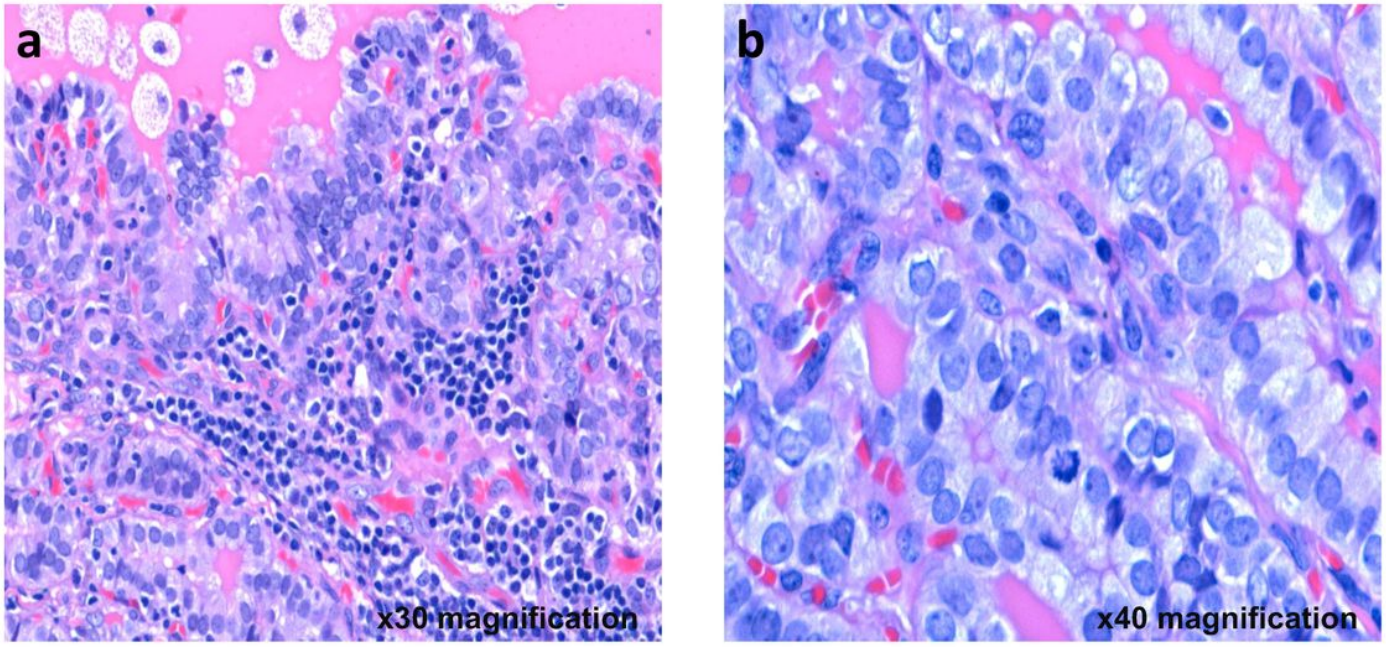

Figure 4

Histological representative of the left thyroid lobe.

a, b. (a) Solitary thyroid nodule. Papillary thyroid carcinoma (H&E, x30 magnification). (b) Nuclear features of papillary carcinoma (H&E, x40 magnification).