CASE REPORT

Two separate malignancies in a multinodular goiter: A case report

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Abstract

Multinodular goiters are common benign lesions removed primarily for cosmetic reasons. The incidence of malignancy in a multinodular goiter is 4 to 14%. The commonest malignancy encountered is a papillary carcinoma. Medullary carcinoma accounts for 1 to 5% of thyroid malignancy but is responsible for approximately 13% of all thyroid cancer-related mortality.

We present the case of a 43-year-old female with a multinodular goiter having a TIRADS 3 nodule in the left lobe with no cervical lymphadenopathy. Cytology of this nodule revealed a Bethesda category 3 lesion, warranting a repeat FNAC. The repeat smear revealed similar cytology and was also reported as Bethesda category 3. Ideally, in such instances where the lesion is indeterminate, molecular testing should be done to guide clinical decision making. However, molecular testing is not routinely available in resource-limited settings such as Sri Lanka. Therefore, in keeping with the current guidelines for management of multinodular goiter, a total thyroidectomy was done. Histology showed a spindle cell tumour in the left lobe and a micropapillary carcinoma in the right lobe. The spindle cell tumour was strongly positive for calcitonin, thereby confirming a medullary carcinoma.

This case reinforces the current guideline for the management of multinodular goiter with total thyroidectomy, especially in resource-limited settings such as Sri Lanka, where molecular testing is not freely available.

Keywords: Multinodular goiter, papillary carcinoma, medullary carcinoma

Background

Multinodular goiters (MNGs) are a commonly encountered clinical problem. The majority of MNGs arise due to iodine deficiency.[1] They usually present with an anterior neck lump but can rarely produce pressure symptoms such as hoarseness of voice, dyspnea, and dysphagia.[1,2] Long-standing MNGs may present with hyperthyroidism.[1,2]

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Papillary carcinomas (PC) are the commonest thyroid malignancy. They also account for the majority of malignancies detected in MNGs.[3] PCs arise from the epithelial cells that surround the thyroid follicles. If these carcinomas are less than 10mm in diameter, they are categorized as microcarcinomas. The prognosis and management of microcarcinomas and carcinomas over 10mm in diameter are different.[4]

Medullary carcinomas (MC) are neuroendocrine tumours and arise from the thyroid parafollicular C cells, which are responsible for producing calcitonin.[5] They may occur sporadically or be a part of the hereditary cancer syndromes.[5] MCs account for 1 to 5% of all thyroid malignancies but are responsible for approximately 13% of all thyroid cancer-related mortality.[5] This increased mortality is partially due to delayed detection as well as a higher tendency for metastasis.[5]

The occurrence of two morphologically and histologically distinct malignancies in an organ is referred to as a collision tumour.[6,7] Collision tumours are extremely rare and account for less than 1% of all thyroid tumours.[6,7] The commonest collision tumour seen in the thyroid consists of PC and MC.[6,7]

Case presentation

A 43-year-old female presented to the surgical clinic with a goiter. She had no other comorbidities nor a history of exposure to ionizing radiation or a family history of thyroid carcinoma. She was clinically euthyroid. Her TSH values were within the normal range. Ultrasound scan of the thyroid showed an early multinodular goiter with a TIRADS III nodule in the left lobe. The cervical lymph nodes were not enlarged. FNAC of the left lobe nodule was done. Cytology revealed a Bethesda category 3 lesion showing 'atypia of undetermined significance', warranting a repeat FNAC. The repeat smear revealed similar cytology. Molecular testing was not done due to financial constraints. In keeping with the guidelines for management of multinodular goiter, a total thyroidectomy was done, and the sample was sent for histopathology.

Grossing of the specimen revealed an irregular tan coloured lesion measuring 5mm in diameter in the right lobe and a well-defined nodule measuring 27 × 12 × 17mm with a gray-tan cut surface and foci of haemorrhage in the left lobe. The rest of the thyroid gland showed colloid nodules.

Microscopy of the lesion in the right lobe revealed a PC comprising infiltrating follicular structures filled with thick colloid and lined by a columnar epithelium showing crowded, pale nuclei with irregular nuclear membranes and nuclear grooves. Occasional cells showed nuclear inclusions.

Sections from the nodule on the left lobe revealed a diffuse arrangement of spindle-shaped cells with oval nuclei, finely stippled chromatin, indistinct nucleoli, and eosinophilic, granular cytoplasm. Occasional pleomorphic cells were present. Mitoses were scanty. Amyloid was not seen.

Neither lesion showed thyroid capsular invasion, extra-thyroidal extension of tumour, or lympho-vascular invasion. Immunohistochemistry for calcitonin showed strong diffuse positivity of spindle-shaped cells in the left lobe.

A diagnosis of a multinodular goiter with a papillary microcarcinoma of the right lobe and a MC of the left lobe was made.

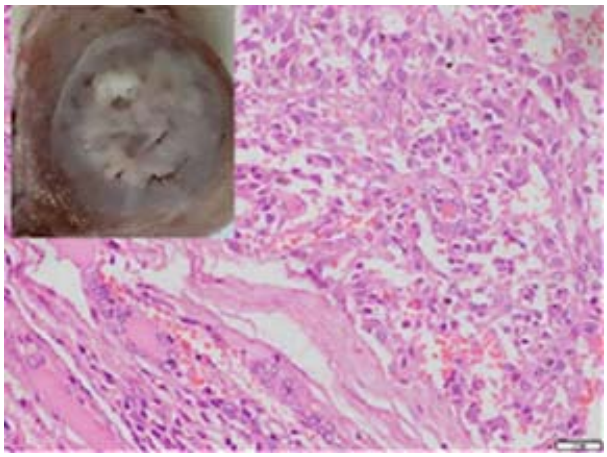

Figure 1. H&E (× 100) Histology of left lobe nodule. Lower left showing normal thyroid tissue. The upper right shows the spindle cells of the medullary carcinoma. Inset: Corresponding macroscopic image of nodule.

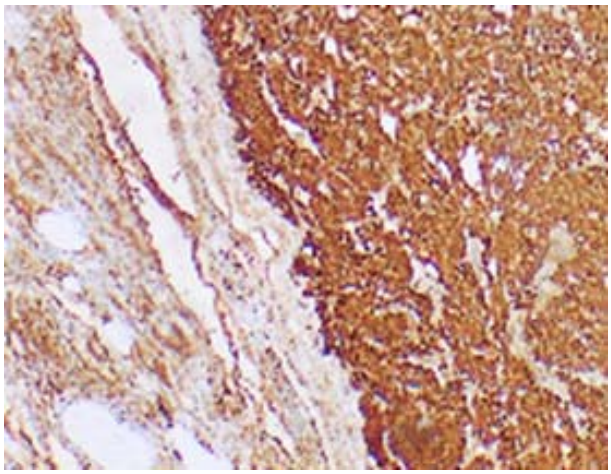

Figure 2. Immunohistochemistry for calcitonin (×100). Strong positivity is seen in the tumour cells on the right-hand side. The normal thyroid follicles on the left show negative staining.

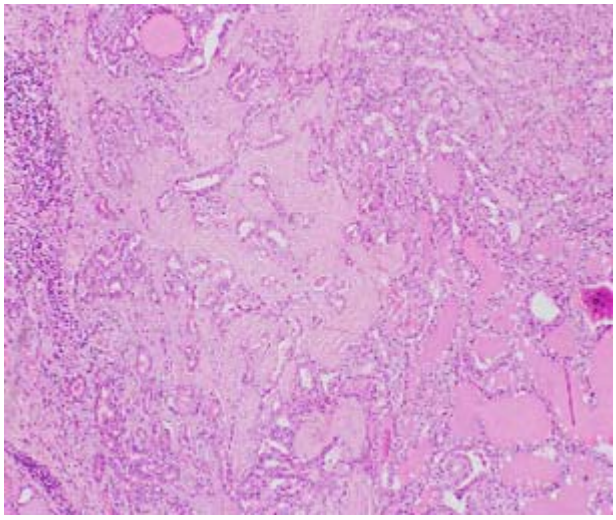

Figure 3. H&E (× 40). Histology of papillary carcinoma in the left lobe.

The patient is currently doing well. She is on thyroxine replacement and is followed up in the oncology clinic with three monthly serum calcitonin levels and ultrasound scans of the neck and thyroid bed to monitor for metastases and recurrences.

Discussion

A goiter is an enlarged thyroid gland. This enlargement may be diffuse or nodular. Functionally, a goiter may be toxic or non-toxic. A non-toxic goiter usually arises due to a deficiency of iodine or an abnormality in its metabolism. These goiters are initially diffuse and, with time, become nodular. Nodule formation is due to hyperplasia of the thyroid follicular epithelial cells due to chronic, low-grade, intermittent stimulation by TSH.[1,2]

Long-standing multinodular goiters can show features of hyperthyroidism or toxicity, except ophthalmopathy.[1,2] The incidence of hyperthyroidism in a multinodular goiter is related to the duration of the goiter.[1] Rarely, goiters can cause pressure on the larynx, trachea, and oesophagus, giving rise to pressure symptoms such as hoarseness of voice, dyspnea, and dysphagia.

Our patient presented with a multinodular goiter. She did not complain of any pressure symptoms. She was clinically euthyroid. Her only concern was the cosmetic appearance.

Diagnostic evaluation of a multinodular goiter consists of biochemical testing, imaging, and FNAC. Serum TSH level is considered a sensitive and reliable marker of thyroid function and is the first line of assessment.[1,8] If serum TSH is abnormal, serum free T4 and free T3 levels are done to assess for subclinical hyper or hypothyroidism. As our patient's TSH value was normal, serum T4 and T3 levels were not done. Serum calcitonin levels were not warranted in this patient at presentation.

All nodular goiters should be evaluated with an ultrasound scan.[8] Nodules showing hypoechogenicity, microcalcification, increased vascular flow, or irregular borders are associated with a higher risk of malignancy and should be assessed cytologically.[8] However, the absence of these features does not exclude the possibility of malignancy.[8] Our patient's ultrasound scan showed a dominant nodule in the left lobe with internal vascularity. There were no microcalcifications. The cervical lymph nodes were not enlarged. This nodule was subsequently categorized as a TIRADS 3 nodule. TIRADS (Thyroid Imaging Reporting And Data System) is a system used to determine the malignancy risk of thyroid nodules using ultrasound imaging features. TIRADS 3 nodules have benign features with approximately a 5% risk of malignancy.[9] The recommended management and follow-up of a TIRADS III nodule is active surveillance with ultrasound scans.[9] As the nodule in our patient was relatively large, an FNAC was done.

The cytology smears revealed regular thyroid follicular epithelial cells as well as oval to spindle-shaped cells. Due to the presence of the oval to spindle-shaped cells, this was categorized as a Bethesda category three nodule on cytology. The Bethesda system is used for classifying thyroid cytology with a view to further management. The suggested management for Bethesda III nodules is repeat FNAC. The repeat smear of this patient showed similar cytology.

Molecular testing for multiple mutations [BRAF, RAS, RET/PTC, PAX8/peroxisome proliferator-activated receptor (PPAR)γ] is recommended in the "2009 Revised American Thyroid Association (ATA) Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer" and can help guide clinical decision making when thyroid malignancy is suspected.[10] It can be done on FNAC samples that are indeterminate, as in this patient.[10] However, it is not routinely available in resource-limited settings such as Sri Lanka. Therefore, in keeping with the current guidelines for management of a multinodular goiter, a total thyroidectomy was done.

Grossing of the thyroid showed two lesions, one in each lobe. Histology of the lesion in the right lobe revealed a PC. As the lesion was less than 10mm, it was more accurately termed a micropapillary carcinoma.[11] Micro papillary thyroid carcinomas are usually not palpable but may be detected by the newer, high-resolution ultrasound scans.[11] However, the majority are incidental discoveries, seen in thyroids removed for benign lesions.[11] The clinical significance of papillary microcarcinoma is open to debate. Though they are not usually associated with recurrences or have any effect on survival, some researchers have found these lesions to behave aggressively, with up to 25% being associated with occult lymph node metastases.[11]

The left lobe of the thyroid showed a well-circumscribed tumour composed of spindle cells. Spindle cell tumours of the thyroid are rare. Depending on the features of histology, the possible differential diagnoses included medullary carcinoma, spindle cell variant of follicular carcinoma, and spindle cell variant of papillary carcinoma. Anaplastic carcinoma, though composed of spindle cells, was not considered in the initial differential diagnosis due to the lack of extensive cellular pleomorphism and the younger age of the patient. Immunohistochemistry for calcitonin showed strong positivity of the spindle cells, thereby confirming a diagnosis of MC.

MC is a relatively rare malignancy, especially when compared to PC. They may be sporadic or associated with hereditary syndromes such as multiple endocrine neoplasia type 2A and 2B.[5] Our patient did not give a significant family history and, therefore, most likely had sporadic MC.

The mortality seen in MC is mainly due to its late presentation.[5] Fortunately, in this patient, the malignancy was detected at an earlier stage, before lymph node involvement.

The National Comprehensive Cancer Network (NCCN) guidelines have recommended total thyroidectomy and level VI neck dissection for all patients with MTC larger than 10mm.

According to available literature, the commonest collision tumours seen comprise papillary and medullary carcinomas.[6,7] Due to its rarity, the management guidelines for collision tumours are poorly established.[6,7] Thomas et al (2021) did a retrospective study of MC and PC presenting as collision tumors of the thyroid in a tertiary care cancer centre between 2009 and 2019. Out of 21 patients with papillary and medullary collision tumours, five had undergone hemithyroidectomy at another institute. Therefore, a complete thyroidectomy with neck dissection was done. The rest of the patients underwent upfront total thyroidectomy with neck dissection. Radioactive iodine was given to 3 patients with PC with and without lymph node deposits. Seven patients with an advanced stage of MC were given radiotherapy. After a mean follow-up of 5.7 years, 15 of the 21 patients were free of the disease, 5 were alive with disease, and 1 had died due to an unrelated cause.

Our patient underwent a total thyroidectomy as it is the recommended management for a multinodular goiter. Therefore, lymph node dissection was not done initially. As the lymph nodes did not have deposits on the ultrasound scan, a lymph node dissection was not done after the detection of the medullary cancer either. She is currently on thyroxine replacement and is followed up in the oncology clinic with three monthly calcitonin levels and ultrasound scans of the neck and thyroid bed to identify metastases and recurrences.

Conclusion

This case reinforces the current guideline for the management of multinodular goiter with total thyroidectomy, especially in resource-limited settings such as Sri Lanka, where molecular testing for malignancy is not freely available.

Authors' Contributions

Concept and design: IK
Literature review: IK
Compilation of manuscript: IK, NP
Manuscript editing and proofreading: IK, NP

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