

CASE REPORT

Simultaneous medullary carcinoma, occult papillary carcinoma and lymphocytic thyroiditis

Abdulla Darwish, MRCPPath, Ali A. Satir, FRCPath, *Tariq Hameed, FRCSI, *Syed Malik, MS and **Nayef Aqel, MRCPPath

Department of Pathology and *Surgery, Arabian Gulf University and BDF Hospital, Bahrain and **Department of Histopathology, Charing Cross Medical School, London, United Kingdom.

Abstract

A 55-year-old female underwent total thyroidectomy for medullary carcinoma of the left lobe of the thyroid. The right lobe showed an incidental occult papillary carcinoma. There was also diffuse lymphocytic thyroiditis. Immunohistochemistry for calcitonin and thyroglobin confirmed the separate histogenesis for both carcinomas. The coexistence of medullary and papillary carcinoma of the thyroid is rare and the literature usually documents mixed tumours with features of both carcinomas, rather than independent tumours, as in our case.

Key words: Medullary carcinoma, papillary carcinoma, thyroiditis.

INTRODUCTION

Medullary carcinoma of the thyroid gland is a rare neoplasm and represents 5-10% of all thyroid cancers. The simultaneous occurrence of medullary carcinoma (i.e. neuroendocrine derived) with another epithelial-derived type cancer is even more rare. Most of the published cases document single tumours with mixed patterns, some of which are considered as new variants of thyroid carcinoma. The presence of medullary carcinoma and papillary carcinoma as geographically separate tumours in the same thyroid gland has been described by Gonzalez-Campora *et al.*' The association of Hashimoto's thyroiditis or lymphocytic thyroiditis with medullary carcinoma is also rare. We report a patient with rheumatoid arthritis who developed two separate medullary and papillary carcinomas of the thyroid. The surrounding thyroid showed features of lymphocytic thyroiditis.

CASE REPORT

A 55-year-old female, a known case of rheumatoid arthritis, presented with generalised body aches and lethargy for 4 months. She was on non-steroidal anti-inflammatory drugs for treatment of rheumatoid arthritis. On examination, a mass about 5 cm in maximum diameter was found in the left lobe of the thyroid. Fine needle aspiration cytology was suggestive of medullary carcinoma, and total

thyroidectomy was undertaken. The level of serum T3, T4 and catecholamines were normal before surgery. The level of calcitonin had not been checked before surgery due to technical errors, but was normal after surgery. Routine thyroid scanning was not done because it had no diagnostic role in medullary carcinoma.

PATHOLOGICAL FINDINGS

Macroscopical examination: The thyroid lobes were received separately. The left lobe measured 5.5×3.0×2.5 cm and weighed 40.9 gm. It was almost totally replaced by a homogenous creamy yellow tumour about 5 cm in maximum diameter. The right lobe measured 4.5×2.0×0.5 cm and weighed 8.2 gm. The cut surface showed a central stellate nodule 1 cm across surrounded by multiple ill-defined white foci involving the whole lobe (Fig. 1).

Microscopical examination: The left lobe showed medullary carcinoma. It consisted of sheets of polyhedral, round and spindle cells having light eosinophilic and granular cytoplasm (Fig. 2). Amyloid material (Congo red-positive) was seen in the stroma. Immunohistochemical stains for calcitonin and chromogranin were positive. The carcinoma cells were negative for thyroglobin. The white stellate lesion, found in the right lobe, proved to represent papillary carcinoma with the characteristic nuclear morphology. The nuclei of papillary carcinoma



FIG. 1: Note the homogenous appearance of the medullary carcinoma on the right side of the figure, which has almost totally replaced the left lobe of the thyroid. Also note on the left side of the figure, the **stellate** macroscopical appearance of the occult papillary carcinoma involving the upper third of the right lobe and the white specks of the lymphoid follicles in the background.

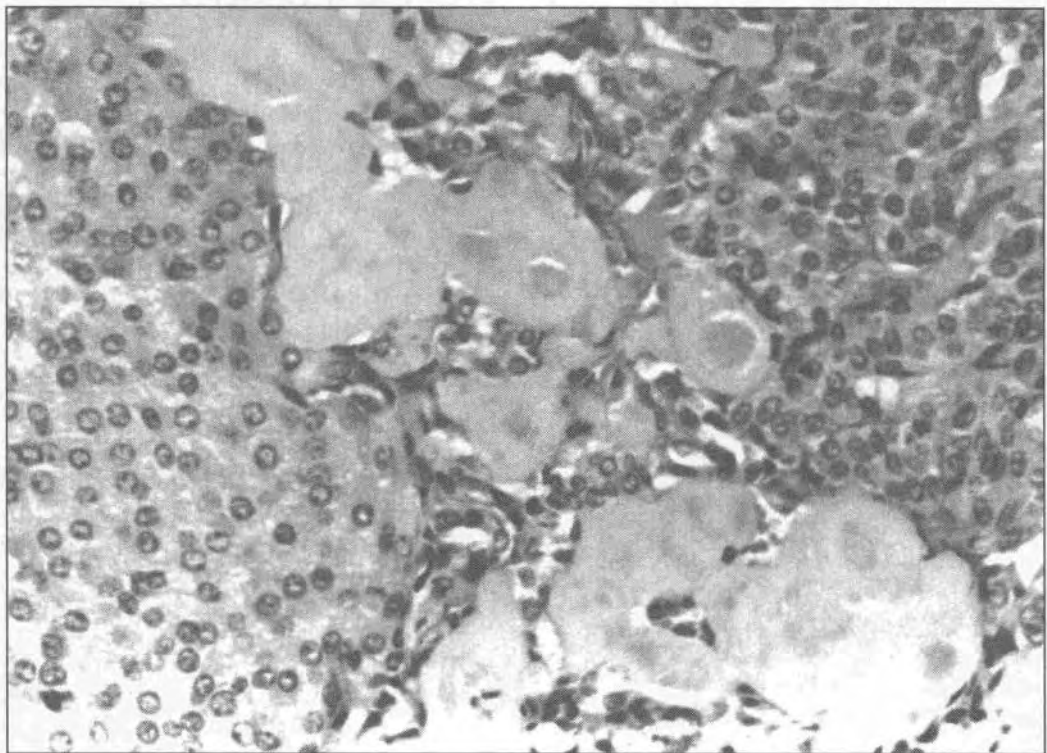


FIG. 2: High power view of medullary carcinoma showing round and polygonal tumour cells with abundant intercellular amyloid **stroma**.

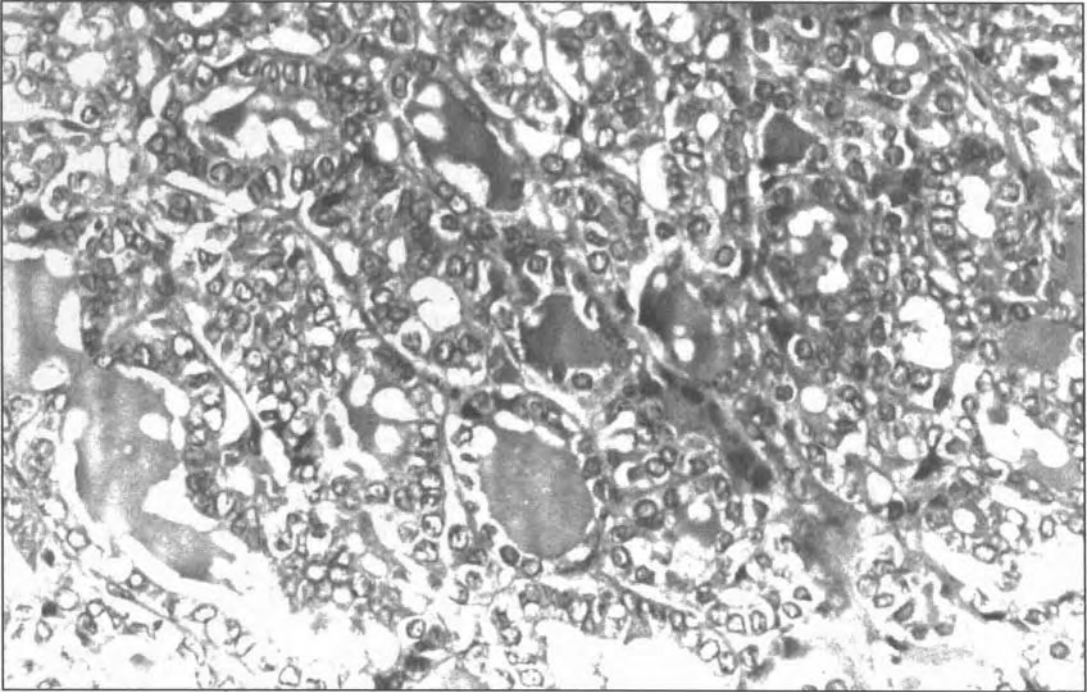


FIG. 3: High power view of papillary carcinoma showing the characteristic nuclear morphology. Note overlapping and ground glass appearance of the nuclei.

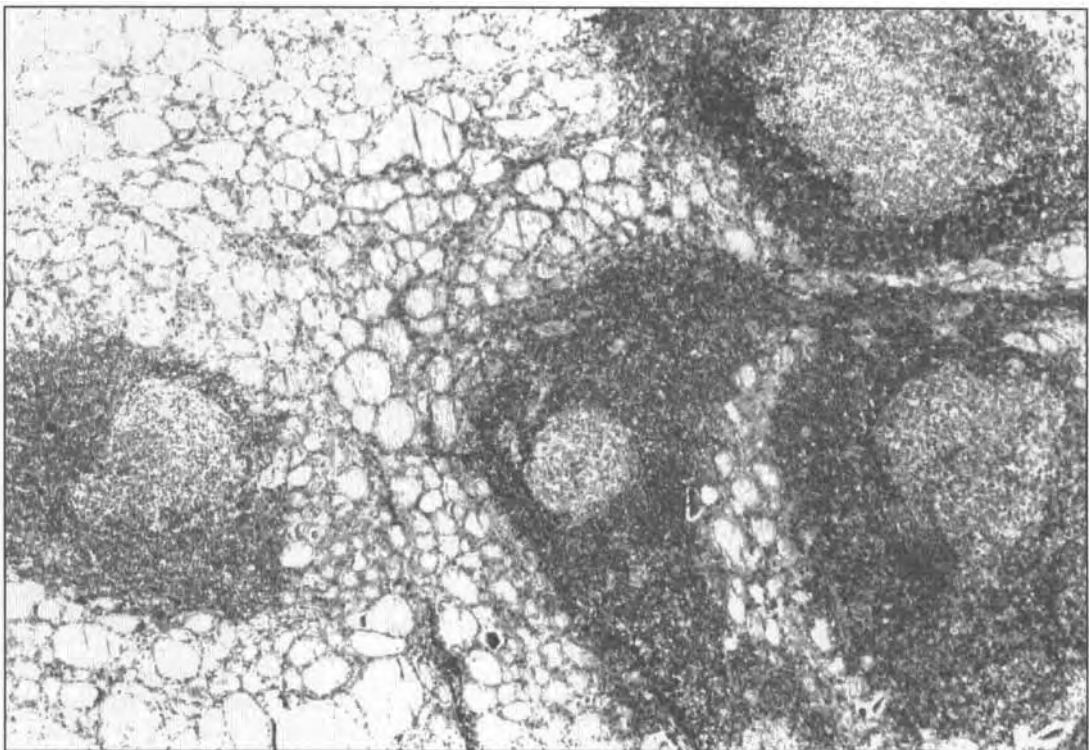


FIG.4: The background of right thyroid lobe showing diffuse prominent lymphoid follicles with active germinal centres.

cells were grooved, overlapping and had clear ground glass appearance (Fig. 3). Immunohistochemistry showed these carcinoma cells to be positive for thyroglobin and negative for calcitonin and chromogranin. Thyroid parenchyma in both lobes away from the carcinomas showed diffuse lymphocytic infiltration with many germinal centre formation (Fig. 4), corresponding to the small white foci seen on gross examination. There was no evidence of C-cell hyperplasia in the non-neoplastic part of the thyroid.

DISCUSSION

Papillary carcinoma is the most common surgical thyroid neoplasm and can be found as an occult tumour in surgical and autopsy specimens. On the other hand, medullary carcinoma is a rare thyroid tumour and its presence in association with an epithelial thyroid tumour is even more rare. The recognition of both medullary and papillary carcinomas in this case was not difficult. Immunohistochemistry, however, was done for confirmation of diagnosis. However, mixed or compound thyroid tumours of neuroendocrine (i.e. medullary) and epithelial origin are rare. In the few published reports, such cases have been described as either true mixed tumours with both patterns seen in the same tumour or as geographically separate carcinoma, as in our

Albores-Saavedra *et al* described two cases of mixed medullary-papillary carcinoma.⁴ Each of their cases contained a single tumour with two admixed patterns (i.e. papillary or medullary areas) and are considered to be a distinctive variant of medullary carcinoma containing papillary areas with intracytoplasmic thyroglobin expression. Two other cases of mixed medullary and follicular carcinomas were reported by Kashima *et al*.⁵ It is believed that the most likely hypotheses of mixed tumours are that C cells and follicular cells are derived from a stem cell which able to differentiate in both directions.⁴ This hypothesis is supported by a study providing evidence that some follicular cells and C-cells arise from the ultimobranchial gland.⁶

Our patient is considered a sporadic case of medullary carcinoma because of her age, the absence of other endocrine tumours and a normal level of serum catecholamines. Her family history was not significant because she has no children, brothers or sisters and her parents died a long time ago without her knowing

their past medical history. In addition to the above findings, our patient, however, has autoimmune disease manifesting as long standing rheumatoid arthritis. Microscopic examination of the thyroid parenchyma revealed diffuse lymphocytic thyroiditis with prominent active germinal centres. The association of lymphocytic or Hashimoto's thyroiditis with papillary carcinoma is well known, but there is scanty documentation of associations between Hashimoto's thyroiditis and medullary carcinoma. Gaskin *et al* described three cases of medullary carcinoma associated with Hashimoto's thyroiditis in Canadian patients with family histories of multiple endocrine neoplasm type II.⁷ In recent years, C-cell hyperplasia has been shown to occur in cases of diffuse lymphocytic thyroiditis: but this has not been proved in our case.

In conclusion, the coexistence of these three conditions (medullary carcinoma, papillary carcinoma and lymphocytic thyroiditis) is a rare combination and might be purely coincidental. However, it remains possible that diffuse lymphocytic infiltration in the patient's thyroid may have a role in the pathogenesis of both carcinomas.

REFERENCES

1. Gonzalez-Campora R, Lopez-Garrido J, Martin-Lacave I, Mirallez-Sanchez E, Villar J. Concurrence of a symptomatic encapsulated follicular carcinoma, an occult papillary carcinoma and a medullary carcinoma in the same patient. *Histopathology* 1992; 21: 380-2.
2. Matias X, Caixas A, Costa I, Cabezas R, Prat J. Compound medullary-papillary carcinoma of the thyroid: true mixed tumour. *Histopathology* 1994; 25: 183-5.
3. Olinici CD, Vasiliu R. Mixed folliculo-papillary and squamous cell variant of medullary thyroid carcinoma. *Rom J Morphol Embryol* 1991, 37: 167-9.
4. Albores-Saavedra J, De La Mora T, De La Torre-Rendon F, Gould E. Mixed Medullary-Papillary Carcinoma of Thyroid: A previously unrecognized variant of thyroid carcinoma. *Human Pathol* 1990; 21: 1151-5.
5. Kashima K, Yokoyama S, Inoue S, Daa T, Kodama M, Nakayama I, Noguchi S. Mixed medullary and follicular carcinoma of the thyroid: report of two cases with an immunohistochemical study. *Acta Pathol Jpn* 1993; 43: 428-33.
6. Williams ED, Toyu CE, Harach HR. The ultimobranchial gland and congenital thyroid abnormality in man. *J Pathol* 1989, 159: 135-41.
7. Gaskin D, Parai SK, Parai MR. Hashimoto's thyroiditis with medullary carcinoma. *Can J Surg* 1992; 35: 528-30.

8. **Guyetant S, Wion-Barbot N, Rousselet MC, Franc B, Bigorgne JC, Saint-Andre JP. C-cell hyperplasia associated with chronic lymphocytic thyroiditis: a retrospective quantitative study of 112 cases. Hum Pathol 1994; 25: 514-21.**