Singapore Med J 2012; 53(3) : e49

Follicular thyroid carcinoma with insular component: a retrospective case study, immunohistochemical analysis and literature review

Htwe TT[1], MBBS, MSc, *Karim N*[2], MBBS, FRCPath, *Lam AKY*[3], MBBS, FRCPath

ABSTRACT This is a retrospective case study of a 61-year-old woman diagnosed with follicular thyroid carcinoma. The patient underwent thyroidectomy for the treatment of goitre after being admitted for shortness of breath. Microscopic and immunohistochemical studies were performed, which confirmed follicular carcinoma of the thyroid with an insular component. We also conducted a review of the literature on this uncommon entity.

Keywords: follicular thyroid carcinoma, immunohistochemistry, insular
Singapore Med J 2012; 53(3): e49–e51

INTRODUCTION

Malignant tumours of the thyroid follicular cells are traditionally classified as either well-differentiated (composed of papillary and follicular carcinoma) or undifferentiated (anaplastic). There exists a group of tumours that fall in-between these two types, in terms of morphologic appearance and biologic behaviour. These tumours are a separate entity and are grouped as poorly differentiated carcinoma (or insular carcinoma). Biologically, they behave in an intermediate manner between well-differentiated and anaplastic carcinomas.[1-4] Insular carcinoma was first described in 1907 by Langhans, who referred to it as "wuchernde struma" due to its characteristic nesting pattern, formation of small follicular lumina leading to a cribriform configuration, small size, uniform cells and 'peritheliomatous' cell nests.[5] In 1984, Carcangui et al defined this group of tumours as having characteristic microscopic features in the formation of solid clusters (insulae) of uniform tumour cells, together with the presence of mitotic activity, necrotic foci, and capsular and vessel invasions.[6]

In this report, we present an uncommon case of mixed follicular thyroid carcinoma with an insular component. A series of immunohistochemical studies were performed, followed by a literature review and discussion of the case.

CASE REPORT

A 61-year-old Malay woman presented with shortness of breath of three months' duration. She was noted to have had thyroid swelling for over 20 years. At presentation, she was having tracheal obstruction, and immediate intubation was done. Previous fine needle aspiration cytology showed colloid material only. The clinical diagnosis was multinodular goitre. A near total thyroidectomy was performed, and a thyroid measuring 25 cm × 15 cm × 5 cm was received from the histopathology laboratory.

Macroscopically, there was a firm rounded nodular thyroid mass measuring 13 cm × 10 cm × 5 cm in the thyroid, with numerous dilated vessels on its outer surface. Cut section showed a variegated appearance with solid, cystic, mucoid and calcified areas. There was no obvious breach in the capsule. Microscopic sections revealed a fairly circumscribed lesion composed of solid areas and round to polygonal cells with granular amphophilic cytoplasm. These cells were arranged in tightly packed lobular, trabecular and carcinoid-like pattern (Fig. 1a). Some areas showed follicular and microfollicular patterns. Tumour emboli were present within the vascular channels (Fig. 1b). In some areas, the lobules were widely separated by highly vascularised, hyalinised and myxomatous stroma (Figs. 1c & d). Foci of calcification and haemorrhage were also observed. Occasional mitotic figures were noted. Areas of tumour necrosis were seen at the resected margins. The relative proportion of the follicular pattern and solid pattern was 40:60 (or > 50% insular component). A year later, the patient was re-admitted for cervical lymphadenopathy. Biopsy revealed poorly differentiated follicular carcinoma. Unfortunately, the patient died after a year of radiotherapy.

In addition to routine histopathologic sections, immuno-histochemical study using a panel of antibodies for thyroglobulin (TGB) (1:800), calcitonin (1:200), chromogranin, synaptophysin, Galectin-3, neuron-specific enolase (NSE), epithelial membrane antigen (EMA) (1:300), cytokeratin 7 (CK7) (1:100), cytokeratin 20 (CK20) (1:100), CD30 and reticulin (all from DAKO, Carpinteria, CA, USA) was applied to the formalin-fixed paraffin-embedded tissue slides after antigen retrieval. The immunostaining procedure was performed on a Lab Vision Autostainer 480. Immunohistochemimistry revealed that tumour cells in the

[1]Discipline of Pathology, UniKL-RCMP, Ipoh, Malaysia, [2]Department of Pathology, Hospital Raja Permaisuri Bainun, Ipoh, Malaysia,[3]Department of Pathology, Griffith Medical School, Gold Coast, Australia.
Correspondence: Dr Than Than Htwe, Associate Professor, Universiti Kuala Lumpur – Royal College of Medicine Perak, 3 Jalan Greentown, Ipoh 30450, Perak, Malaysia. ththan@rcmp.unikl.edu.my.

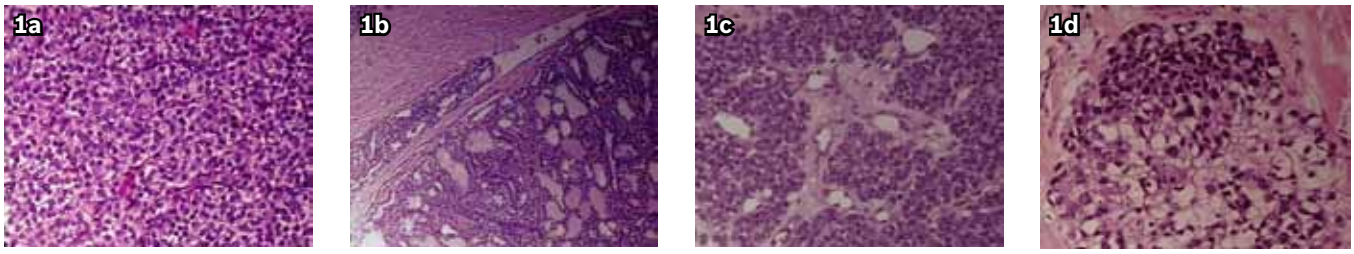

Fig. 1 Photomicrographs show (a) thyroid follicular cells arranged in a tightly packed lobular pattern; (b) tumour emboli within the vascular channel; (c) the foci where lobules were separated widely by highly vascularised stroma; and (d) the hyalinised and myxomatous stroma (Haematoxylin & eosin, × 100).

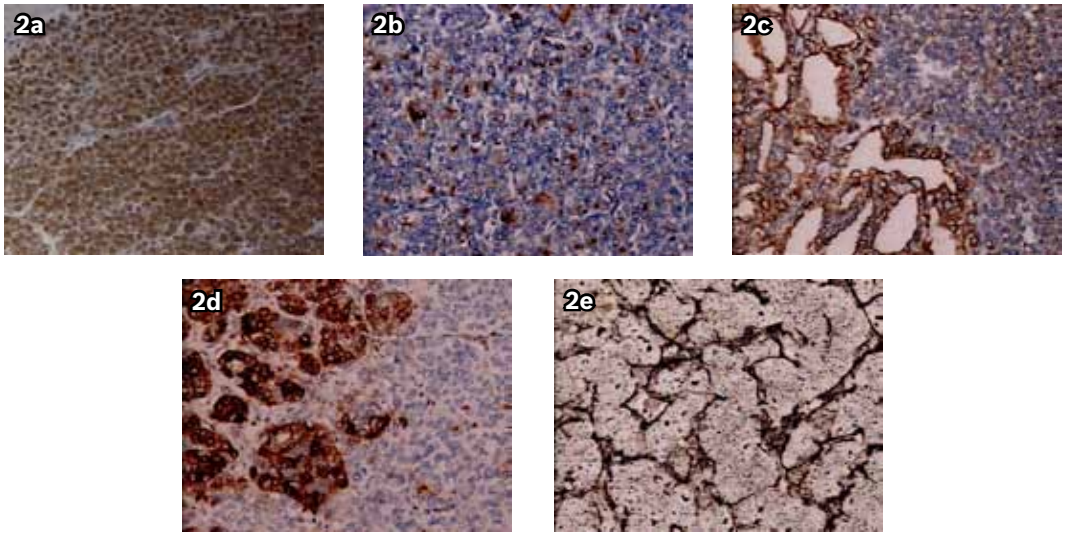

Fig. 2 Photomicrographs show (a) positive staining for neuron-specific enolase and (b) negative staining for thyroglobulin in the solid areas; (c) positive staining for cytokeratin 7 and (d) Galectin-3 in areas with follicular patterns (all IHC stain, × 100); (e) positive reticulin stain highlighting the tightly packed lobular and trabecular pattern (Reticulin stain, × 100).

solid areas were positive for NSE but negative for thyroglobulin, calcitonin, chromogranin, synaptophysin, Galectin-3, EMA, CK7, CK20 and CD30 (Figs. 1a–d). On the other hand, the follicular areas exhibited immunopositivity to TGB, EMA, CK7 and Galectin-3 (Figs. 2a–d). A positive reticulin stain highlighted the tightly packed lobular and trabecular pattern (Fig. 2e).

DISCUSSION

Thyroid tumour with a mixed histological component is uncommon and presents a great challenge for pathologists. There are approximately 50 reported cases of mixed medullary-follicular carcinoma (MMFC) of the thyroid[7] in the English literature. The histological features of the present case mimicked those of MMFC.[7,8] It is important to recognise the presence of an insular component in a follicular thyroid tumour, as it denotes the poorly differentiated nature of the tumour. It is also needed in order to differentiate the insular component from a medullary thyroid carcinoma, which tends to present as a mixed tumour together with follicular thyroid carcinoma. According to Lam et al's study, in which strict histopathological criteria were used, the incidence of insular carcinoma was reported to be 3% of all primary thyroid carcinomas and the ten-year survival rate was reported to be 42%.[9]

The presence of a predominant insular component is associated with a poor prognosis. It should be considered as a separate entity from not only classical papillary or follicular carcinoma but also focal insular tumour. The presence of an insular component together with typical follicular carcinoma could either be a coincident finding of a mixed tumour or a follicular thyroid carcinoma progressing into a poorly differentiated form, thus leading to a poorer prognosis compared to a pure classical follicular carcinoma. Careful immunohistochemical analysis and reporting of such cases are necessary for further prognosis and management by the attending clinician. The diagnosis of follicular carcinoma with an insular component could be confirmed by immunohistochemical study. Based on the panel of immunomarkers, including Galectin-3, we confirmed our diagnosis for this case as a mixed feature of follicular carcinoma with an insular component. We also found Galectin-3 to be a good marker for differentiating follicular and solid components.

In conclusion, follicular thyroid carcinoma with an insular component is a rare condition that could mimic mixed medullary and follicular carcinoma, both of which have a poorer prognosis than that of a pure follicular carcinoma. Although difficult, differentiation between the two conditions can be made with the aid of a series of immunohistochemical stains. Negative staining reactivity to calcitonin is the key to differentiating insular from medullary carcinoma, and positive immunoreactivity to thyroglobulin and Galectin-3 contributes the follicular component of thyroid carcinoma. Further studies with a larger number

of cases are required in order to determine the diagnostic criteria for follicular thyroid carcinoma presenting with mixed morphological features.

ACKNOWLEDGEMENT

This study is part of the research project performed under Universiti Kuala Lumpur short-term research grant UniKL/CRPGS/str06077.

REFERENCES

1. Rufini V, Salvatori M, Fadda G, et al. Thyroid carcinomas with a variable insular component: prognostic significance of histopathologic patterns. Cancer 2007; 110:1209-17.
2. Kirdak T, Saraydaroglu O, Duran C, Yerci O, Korun N. Thyroid carcinoma with insular component: report of three cases with different clinical pictures. Tumori 2006; 92:444-8.
3. Vanhaverbeke G. Follicular carcinoma of the thyroid with poorly differentiated component presenting with an ileal osteoblastic metastasis. Thyroid 2004; 14:858-61.
4. Patel KN, Shaha AR. Poorly differentiated and anaplastic thyroid cancer. Cancer Control 2006; 13:119-28.
5. Langhans TA. [On the epithelial structure of the malignant stroma]. Virchows Arch Pathol Anat 1907; 189:69-88. German.
6. Carcangui ML, Zampi G, Rosai J. Poorly differentiated ("insular") thyroid carcinoma. A reinterpretation of Langhans' "wuchernde Struma". Am L Surg Pathol 1984; 8:655-68.
7. Han Ö. Ünal T, Seçkin S, Kulaçoğlu S. Mixed medullary-follicular thyroid carcinoma: a report of two cases. Turk J Med Sci 2008; 38:359-63.
8. Matias-Guiu X. Mixed medullary and follicular carcinoma of the thyroid. On the search for its histogenesis. Am J Pathol 1999; 155:1413-8.
9. Lam KY, Lo CY, Chan KW, Wan KY. Insular and anaplastic carcinoma of the thyroid: a 45-year comparative study at a single institution and review of the significance of p53 and p21. Ann Surg 2000; 231:329-38.