A very unusual thyroid tumor: a nodule with mature fat papillary hyperplasia and focal atypia

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Abstract

Fat-containing lesions of the thyroid are rare, encompassing several clinical-pathological conditions such as adenolipomas, thyrolipomatosis and lipomatous tissue in case of amyloidosis. Furthermore, cases of papillary thyroid carcinoma have been identified in association with thyrolipomatosis. We report a case of 51 years old man referred to surgery for a multinodular goiter, showing multiple cystic and hemorrhagic nodules of up to 3 cm. One of these lesions showed features of papillary hyperplasia with focal cytological atypia and mature fat. Here, we describe and discuss the histological and immunophenotypical features of this rare lesion.

Introduction

Papillary architecture in thyroid pathology can be seen in several conditions including nodular goiter, papillary carcinomas (PTC), hyperfunctioning (toxic) adenoma, and follicular adenoma with papillary hyperplasia (FAPH).1 Although each of the above-mentioned conditions has defined clinical and histological features, cytological and architectural features simulating a PTC can be detected in some benign lesions. On the other hand, detection of mature fat tissue in thyroid gland is not a common finding. It can be diffuse (thyreolipomatosis), limited to a follicular adenoma (thyrolipoma) or it can involve both follicular adenomas and the surrounding thyroid tissue.2-4

It is important to note that the presence of fat in thyroid lesions does not always imply benignity, in fact cases of FTC harbouring mature fat in the stroma have been reported in the literature.2,3 Here we describe a peculiar thyroid lesion containing fat and mimicking a PTC.

Case Report

A 51-years old man presented with a clinical diagnosis of multinodular goiter. The patient did not show evidence of autoimmune disorders or thyroiditis and the thyroid function was normal. He was referred to surgery and complete thyroidectomy with intraoperative histological examination was performed. The thyroid was enlarged with a weight of 55 g, measuring 5×4.5×4.5 cm in the right lobe and 5×3×3 cm in the left lobe. Macroscopically, the right lobe harboured a cystic-colloid hemorrhagic nodule 2.5 cm diameter while two colloid nodules of 2 cm and 3 cm respectively, were found in the left lobe. All of the aforementioned nodular lesions were examined intraoperatively. The cystic nodule in the right lobe showed a diffuse papillary architecture with slight overlapping and enlarged nuclei; as a consequence an intraoperative histological diagnosis of suspicious papillary thyroid carcinoma/papillary hyperplasia with atypia, was posed. The two nodules in the left lobe were considered benign, although one of them also showed cystic aspects with papillary architecture. The lesions were finally sampled, formalin fixed and paraffin embedded for the final histological evaluation. Microscopically two colloid-cystic nodules showed papillary structures with a delicate stroma and prominent intranodular mature fat (Figure 1A). Furthermore, the nodule in the right thyroid lobe showed cytological features suspicious for FTC. The nuclei in fact were sometimes enlarged, with scattered grooves, overlapping and clearing, but no nuclear pseudoinclusion or psamomabodies were found (Figure 1B).

The lesion did not show a complete capsule and merged with the surrounding thyroid tissue. Neither mitotic figures nor necrosis were found. In the left nodule the nuclei were basally located with dark chromatin without atypical features. To exclude the diagnosis of a FTC and to better categorize these lesions, the expression of two well known thyroid cancer associated antigens namely Galectin-3 (Gal-3) and HBME-1 was evaluated by using immunohistochemical procedures. A biotin-free immuneroxidase detection system was applied, and foamy macrophages were considered as internal positive control for Gal-3 immuno-staining.6 The left nodule showed a faint and merged with the surrounding thyroid tissue. However the larger part of the papillary lesion was unreactive with both Galectin-3 and HBME-1. On the basis of the morphological and immunophenotypical analysis we classified the lesion as an adenomatous nodule with fat-rich stroma and papillary atypical hyperplasia, with focal expression of Galectin-3 and HBME-1 reflecting an incipient transformation in FTC. To exclude the presence of a FTC, we carefully examined the rest of the thyroid for a total of 28 slides.

Discussion and Conclusions

The presence of mature fat tissue in thyroid gland is an uncommon phenomenon, and in most of the cases adipose tissue can be found near blood vessels and/or in the perivascular location. Soda et al.7 reported two cases of heterotopic nests of fat cells in the thyroid gland in association with Graves’ disease and adenomatous hyperplasia. The fat cells were reported to be scattered among the thyroid follicles. Another condition, associated with intra-thyroid fat is the so-called amyloid goiter.11,12 There was no amyloid deposition in our cases and no follicular atrophy was observed. Multinodular goiter may show foci of adipose metaplasia, but the lesion is not distinct from the resting parenchyma, and the thyroid cells are not atypical. The diffuse permeation of thyroid gland by mature fat is known as thyreolipomatosis or lipomatosis.2,10 This condition can also occur as congenital swelling of the thyroid gland as reported by Chesky in 1953.13 Adenolipoma of the thyroid has both macroscopic and micro-
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Architecture. As previously mentioned, the lar structures, without a prominent papillary variable combination of mature fat and follicular yellow cut surface and is composed of a lipoma like appearance with a homogeneous differences with our case. It normally has not diagnostic implications because fat cells can be discovered in both benign and malignant thyroid conditions. Rarely, follicular adenomas, sometimes hyperfunctioning, are characterized by diffuse papillary features. These lesions may also have partial cystic degeneration, but the stroma is delicate and cells are cuboidal, with small basally located nuclei. PTC in follicular adenomas and/or hyperplasias may also occur. Apart the fat tissue, our case has indeed similarities with the latter type of lesions: for the presence of cystic changes and prominent papillary hyperplasia. However, detection of atypical follicular cells highlighted by focal immunostaining with Gal-3 and HBME-1, were clearly found in papillary structures with prominent fat infiltration. Because the classical variant of well-differentiated PTC is known to be strongly immunoreactive with both mAbs to Galectin-3 and HBME-1, the reaction pattern we observed excludes the presence of a frank malignancy. However, the cytromorphological and immunohistochemical features we observed in this unusual lesion, support an incipient transformation in PTC. Several theories have been proposed to explain the infiltration of the thyroid by adipose tissue. Gnepp and colleagues consider it as a developmental anomaly; other authors support the idea of an event connected with the inclusion of adipose nests during embryogenesis. De Rienzo et al. describe a case of thyrolipoma and a case of fat containing follicular carcinoma of the thyroid; two cases of thyrolipoma have been also reported by Schröder et al. They believe that thyrolipoma may represent a mixed neoplasm of both epithelial and displaced mesenchymal elements. On the other hand multino- dular goiter can harbor foci of adipose metaplasia, as marker of a regressive condition. Due to the prominent papillary pattern with diffuse fat cells infiltration, we believe that the thyroid lesion reported here, may be considered a hamartoma of thyroid gland with focal atypia suggesting a forma frustra of PTC. In conclusion, the presence of adipose tissue in the thyroid is rare but its presence does not exclude per se malignancy. For these reasons an accurate integration of morphology and ancillary tests such as immunohistochemistry are mandatory for correct diagnosis.

Figure 1. Histological and immunohistochemical features of thyroid nodule. A) Low power view of the nodule demonstrating the abundant mature adipose tissue. B) Higher magnification of lesion showing papillary architecture and nuclear overlapping. C) Immunostaining with Gal-3 showing the atypical positive cells (center of the field). D) Note the plasma membrane reaction with HBME-1 of atypical cells (right) compared with the negative immunoreaction of other bland cells (left).

References

1. Nikiforov YE, Biddinger PW, Thompson LDR, eds. diagnostic pathology and molecular genetics of the thyroid. 2nd ed. Philadelphia: Lippincot Williams & Wilkins; 2012, pp 129-30.