Mature Fat Containing Thyroid Lesions
Report of Five Cases and Review of The Literature

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ABSTRACT
Mature fat tissue can be found in both benign lesions and neoplasms of the thyroid gland. The pathophysiology of adipose tissue infiltration in the thyroid gland is not clear. Three cases of diffuse lipomatosis and two cases of thyroid papillary microcarcinoma containing mature fat in their stroma were diagnosed between 2002 and 2009 years. These five cases are presented in this report with a review of lipomatous lesions in the literature.

Key words: Thyroid, papillary carcinoma, fat, lipomatosis

INTRODUCTION
Thyroid lesions containing fat cells are uncommon (1, 2). They have been divided into two groups: fat containing thyroid neoplasms, including papillary carcinoma, follicular carcinoma and follicular adenoma, and nonneoplastic conditions with fat tissue such as amyloid goitre, diffuse lipomatosis, lymphocytic thyroiditis, adenolipoma, heterotopic adipocyte nests, intrathyroid timic or parathyroid lipoma, thyroid atrophy, dishormonogenetic goitre and Graves’ disease (1-5). Herein, it is aimed to report five cases; three cases of diffuse lipomatosis represented nonneoplastic conditions and two cases of papillary microcarcinoma counted in neoplastic lesions.

CASE
Five patients are reported those ranged in age from 25 to 63 years (mean age 40 years). Three patients were female and two patients were male. Data from these patients is summarized in the table 1. Patients with papillary microcarcinomas were female and clinically euthyroid. Two cases with diffuse lipomatosis were male. One of them was clinically euthyroid and the other case was hypothyroid. The last patient with diffuse lipomatosis was female and exhibited hypothyroidism.

The amount and distribution of fat in the lesions varied. In cases of papillary microcarcinomas, mature fat was found within tumor stroma and papillary structures lined by cells with overlapping ground glass nuclei including nuclear groove and inclusions (Figure 1). No fat was detected in adjacent nontumoral thyroid parenchyma. Cases with diffuse lipomatosis revealed varying distribution of fat. In the cases, mature fat tissue was scattered between the follicles varying in size and shape, lined by cuboidal cells and contained colloid. In one of the cases, abundance of fat cells between follicles was observed. A few thyroid follicles were preserved. No lymphocytic infiltration, malignancy, adenoma or amyloid deposition was demonstrated in the cases.
DISCUSSION

The presence of adipose tissue in the thyroid gland is rare (3). Few adipocytes may be found within normal thyroid gland near the capsule, in the perivascular location or in connective tissue septa (5). In the literature, there are reports documented cases of fat within neoplastic and nonneoplastic lesions of thyroid including papillary carcinoma (1,6), follicular carcinoma (1,2), follicular adenoma (7,8), amyloid goitre (1,9), diffuse lipomatosis (3,10), lymphocytic thyroiditis (3,4), adenolipoma (1,2,4,5), heterotopic adipocyte nests (11), intrathyroid timic or parathyroid lipoma (3,4), thyroid atrophy (1), Graves disease (4) and dishormonogenetic goitre (1). Primary liposarcoma of thyroid has also been reported (12,13).

The mechanism by which adipose tissue is included in thyroid parenchyma and thyroid lesions remains unknown and several theories have been proposed (3,4). Mature adipose tissue in the thyroid has been revealed in patients with congenital or acquired goitres (8,14). In most cases, it is suggested that the goitre is due mainly to the presence of adipose tissue in the gland rather than being secondary to proliferation of the thyroid epithelium. Adenolipoma of thyroid is also named ‘thyrolipoma’ or ‘thyroid hamartoma’, and is an encapsulated tumor composed of a variable proportion of thyroid glandular tissue and fat (2-4). Diffuse lipomatosis, also called ‘choristomatous adiposity’ demonstrates massive fatty infiltration rather than a single nodule (2,3). In the cases with diffuse lipomatosis reported here, mature fat tissue was scattered between the thyroid follicles in varying amounts. Abundance of fat cells and a few preserved follicles were detected in one case. The adenolipomas and diffuse lipomatosis of thyroid have a similar histological appearance of adipose tissue mixed with thyroid acini. Perhaps this suggests a similar etiology for these conditions. Hjorth et al. (7) suggested both conditions might represent true neoplastic diseases with proliferation of fatty tissue. Schröder and Böcker (10) argued that diffuse lipomatosis and adenolipoma of the thyroid are most likely to be derived from heterotopic islands of fat cells included in the gland during embryogenesis. Some authors believe that fatty tissue is included in thyroid in the same way as striated muscle during embryological development (4) and such a process could explain the presence of adipose tissue in congenital goitres (diffuse lipomatosis); however, it does not explain the presence of fat in acquired thyroid lesions, especially when the fat is limited to the lesion itself and does not involve the adjacent thyroid parenchyma.

To account for fat in hyperplastic or neoplastic thyroid

<table>
<thead>
<tr>
<th>Case no</th>
<th>Age/Sex</th>
<th>Thyroid lesion containing fat tissue</th>
<th>Thyroid hormone status</th>
<th>Fat tissue distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40/F</td>
<td>Papillary microcarcinoma (occult)</td>
<td>Euthyroid</td>
<td>Fat within papillary structures and tumor stroma</td>
</tr>
<tr>
<td>2</td>
<td>53/F</td>
<td>Papillary microcarcinoma (occult)</td>
<td>Euthyroid</td>
<td>Fat within papillary structures and tumor stroma</td>
</tr>
<tr>
<td>3</td>
<td>25/M</td>
<td>Diffuse lipomatosis</td>
<td>Hypothyroid</td>
<td>Fat scattered between the follicles varying in size and shape</td>
</tr>
<tr>
<td>4</td>
<td>19/F</td>
<td>Diffuse lipomatosis</td>
<td>Hypothyroid</td>
<td>Fat scattered between the follicles varying in size and shape</td>
</tr>
<tr>
<td>5</td>
<td>63/M</td>
<td>Diffuse lipomatosis</td>
<td>Euthyroid</td>
<td>Abundant fat between follicles, a few preserved follicles</td>
</tr>
</tbody>
</table>

Table 1. Clinicopathologic characteristics of patients
tumors or in amyloid goitres, some authors have postulated a metaplastic process from stromal fibroblasts due to chronic tissue hypoxia or to the phenomenon of senile involution demonstrated in other organs (1,10). Finally, one group of authors believes that fat in thyroid tumors is an integral neoplastic component of the tumor (1,15, 16). In the literature, Gnepp et al. (1) documented adipose tissue in seven papillary carcinomas and one follicular carcinoma out of seventeen fat containing thyroid lesions. Suggestion in that study was the varying degree of adiposity in the cases of carcinoma. They found only a few fat cells in some cases, whereas other tumors had extensive replacement of their stroma or fibrovascular cores by adipose tissue. Infiltration of adjacent non-neoplastic thyroid parenchyma by adipose tissue was observed in three cases. They also presented a multifocal occult papillary microcarcinoma in one case of amyloid goitre and pointed out that scattered fat cells were present within a small focus of the papillary carcinoma in addition to the characteristic distribution of mature adipose tissue within the amyloid stroma. The cases with papillary microcarcinomas presented in our report have similar properties to the reported cases in the literature. In our cases with papillary carcinomas, mature fat was found within tumor stroma and papillary structures lined by cells with overlapping ground glass nuclei including nuclear groove and inclusions. Differently, no fat was detected in adjacent nontumoral thyroid parenchyma.

In the report, five cases of thyroid lesions containing mature fat in their stroma are presented. Probable mechanisms and suggested theories of presence of fat tissue in thyroid gland and its lesions are discussed in the light of literature.

REFERENCES