MEMOIRS HEALTH SCI. MED. KANAZAWA UNIV. Vol. 24 No. 2
183~187 2000

Follicular carcinoma of the thyroid gland showing an extensive papillary growth pattern

—A papillary variant of follicular thyroid carcinoma?—

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ABSTRACT

An unusual case of follicular carcinoma of the thyroid gland showing an extensive papillary growth pattern is reported. The tumor occurred in a 58-year-old woman, who died of lung metastases 5 years after surgery. The well-demarcated, nearly encapsulated tumor measured 5.5x4x3.5 cm and it completely replaced the left lobe of the thyroid gland. Microscopically the tumor was characterized by an extensive papillary proliferation of tall follicular epithelium with round to oval nuclei with stippled chromatin. Neither clear and ground-glass nuclei nor grooved nuclei, suggesting papillary thyroid carcinoma, were observed. The tumor showed a marked vascular invasion. The authors concluded that this thyroid tumor belongs to follicular thyroid carcinoma and carries a poor prognosis, and we tentatively designated it as "papillary variant of follicular thyroid carcinoma". It is important to distinguish this type of thyroid carcinoma from usual papillary carcinoma of the thyroid.

KEY WORDS

Follicular carcinoma, Thyroid gland, Extensive papillary proliferation

INTRODUCTION

Follicular carcinomas of the thyroid gland essentially show a follicular growth pattern. Nuclei of the follicular carcinoma cells are round to oval and hyperchromatic with stippled chromatin. Pseudopapillary structures may be occasionally found in the follicular carcinomas, but these pseudopapillae do not resemble papillae of papillary thyroid carcinomas[1,2].

We experienced a unique case of thyroid carcinoma that exhibited an extensive papillary growth pattern, similar to that of papillary thyroid carcinoma, but presented nuclear features of follicular thyroid carcinoma. We are not aware of any reports describing such a follicular carcinoma showing an extensive papillary growth pattern. We tentatively designated this thyroid tumor as "papillary variant of follicular thyroid carcinoma".

In the present article, the histopathologic features and aggressive behavior of this unique thyroid carcinoma are described.

CLINICAL SUMMARY

A 58-year-old woman presented with a progressively enlarging mass in the left side of the neck for the preceding 1 year. She complained of no other symptoms. Physical examination revealed a markedly enlarged neck mass, which involved the thyroid gland and measured 7 cm, in the left side of her neck. Enlarged lymph nodes were also palpable in the left neck. Thyroid function tests were normal. Suntigram with I-131 showed a defect corresponding to the left lobe of the thyroid gland. Chest X-ray examination

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lowed an enlargement of mediastinal lymph nodes nd multiple lung metastases of the tumor.

Total thyroidectomy and neck dissection were performed. The tumor completely replaced the left lobe of the thyroid gland, and it was grossly encapsulated and did not invade into the adjacent soft tissues or trachea. The left recurrent nerve was also uninvolved. Two enlarged lymph nodes were respected. The tumor was originally diagnosed pathologically as a papillary carcinoma of the thyroid. After surgery, the patient was treated with radioactive iodine. Despite the fact that the metastases accumulated iodine, the masses in the lungs and mediastium continued to grow. The patient died of extensive lung metastases 5 years after surgery. No autopsy was performed.

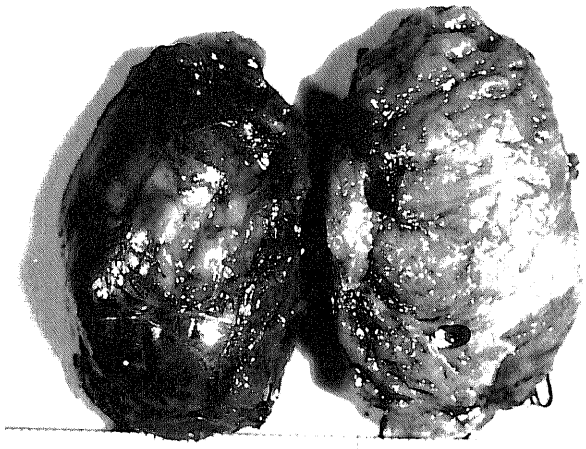

Fig. 1. The tumor is encapsulated and completely replaces the left thyroid lobe. The cut surface is bulgy and shows a brown-tan appearance.

PATHOLOGIC FINDINGS

The left thyroid lobe was completely replaced by a well-demarcated and nearly encapsulated tumor, weighing 76g and measuring 5.5x4x3.5 cm, with a solid bulging cut surface (Fig.1). The capsule that surrounded the tumor was relatively thin, and capsular

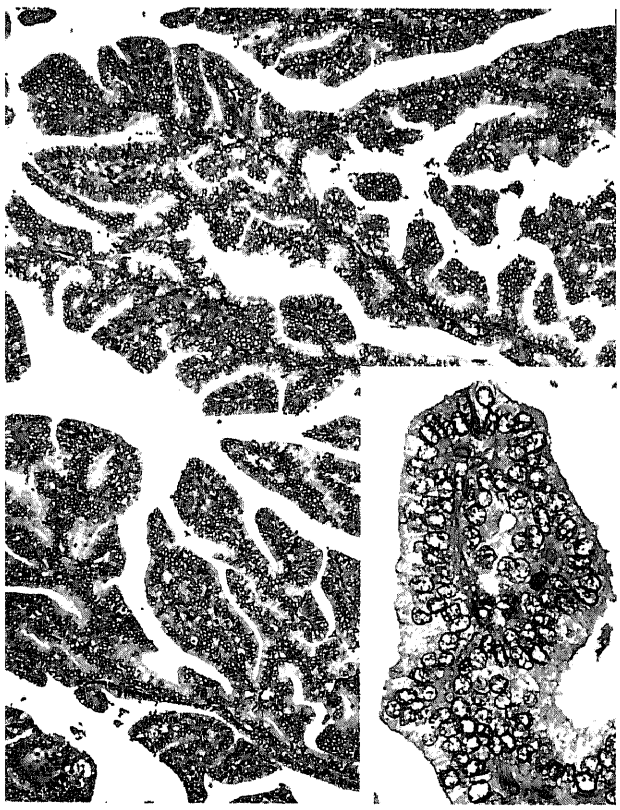

Fig. 2. Low-power appearance of the tumor. The tumor shows an extensive papillary growth pattern (HE). Well developed papillae are complex and branching. Inset: The papillae are lined by a layer of tall follicular cells, showing round to oval nuclei with stippled chromatin (HE).

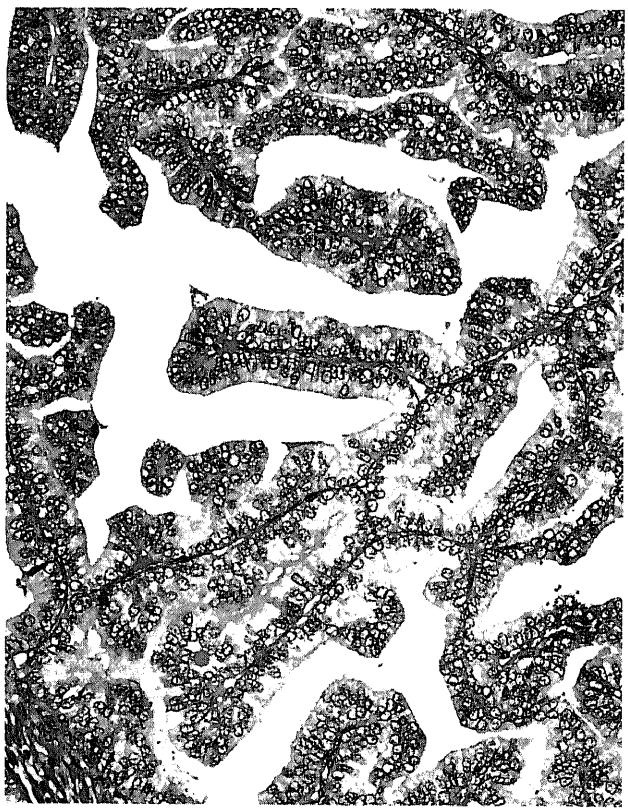

Fig. 3. The typical papillary growth pattern. The papillae contain a thin central fibrovascular core. The tall follicular cells have abundant light cytoplasm and basally located nuclei (HE).

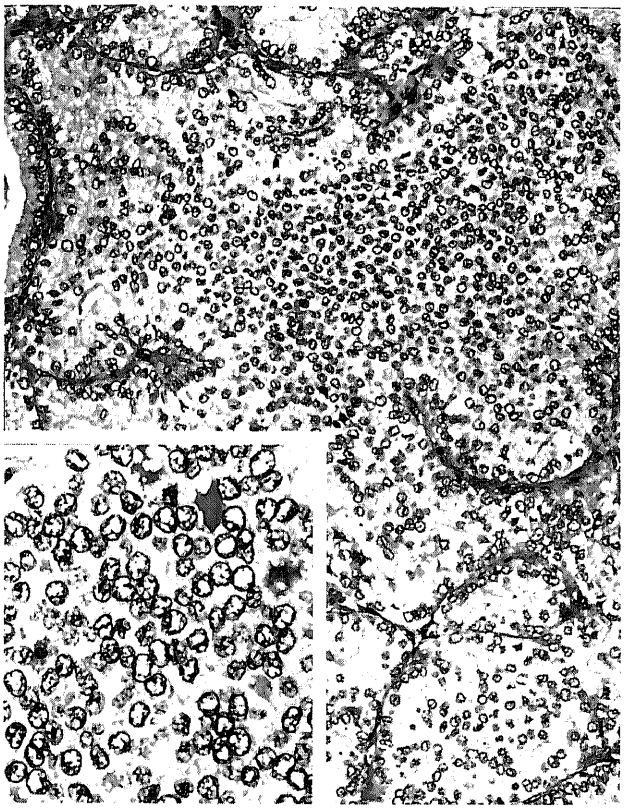

Fig. 4. In only a few small foci of the tumor, the poorly organized follicular structure associated with solid growth area is observed (HE). Inset: The tumor cells of the solid growth area have round to oval and moderately hyperchromatic nuclei (HE).

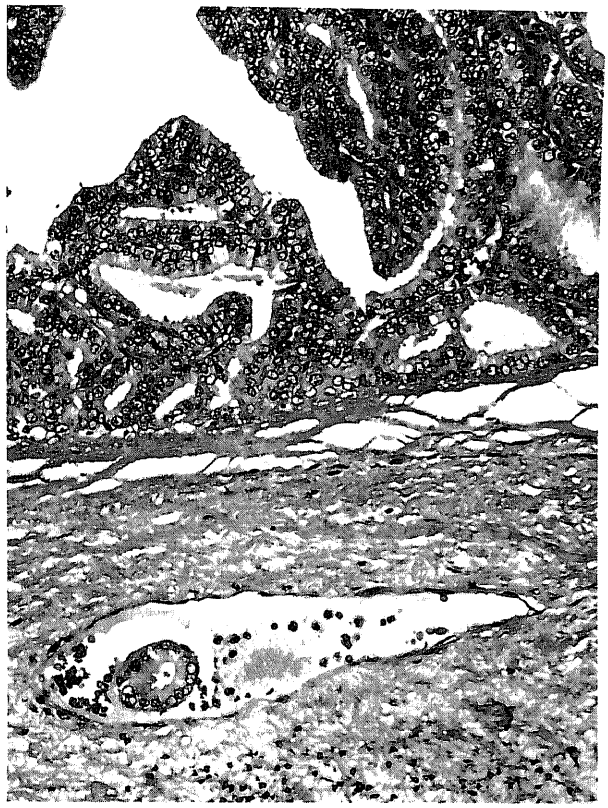

Fig. 5. The tumor cells, forming a small follicle, infiltrate into a small vessel within the tumor capsule (HE).

invasion of the tumor was not noted grossly. The right thyroid lobe was normal-looking and no nodular lesions were found. Both resected lymph nodes revealed metastases.

Microscopically, the tumor consisted of an extensive papillary proliferation of tall follicular epithelium (Fig.2). Most of the papillae had long and narrow fibrovascular cores resembling true papillae of papillary thyroid carcinoma (Figs.2and 3). The lining tall follicular epithelium showed varying degrees of cytoplasmic clearing with no cytoplasmic oxyphilia. The nuclei of these tall epithelium were located basally and they were exclusively round to oval and moderately hyperchromatic with stippled chromatin (Fig.2inset). No nuclei showing a clear and ground-glass appearance or nuclear grooving, resembling those of papillary carcinoma, were identified anywhere in the tumor. Colloid materials were generally scarce. In some small foci of the tumor, the tumor cells formed irregularly-shaped follicles or poorly organized follicles or solid nests (Fig.4). There were two or three mitotic figures per 10 high-power fields (x400). Sclerotic changes were minimal and psammoma bodies were not evident. The tumor grew expansively associated with a thin fibrous capsule, but in only a few foci did the tumor cells invade into the perithyroidal soft tissues beyond the capsule. The tumor cells invaded prominently into vessels within or outside the capsule (Fig.5)

The tumor cells showed a considerable PAS positivity that was not abolished by diastase treatment. Thyroglobulin immunostaining was present in the cytoplasm of the tumor cells (Fig.6a),whereas immunostainings for calcitonin, carcinoembryonic antigen and chromogranin A yielded negative results. Epithelial membrane antigen was positively stained throughout the tumor, but cytokeratin was focally positively stained. Immunostaining for proliferating

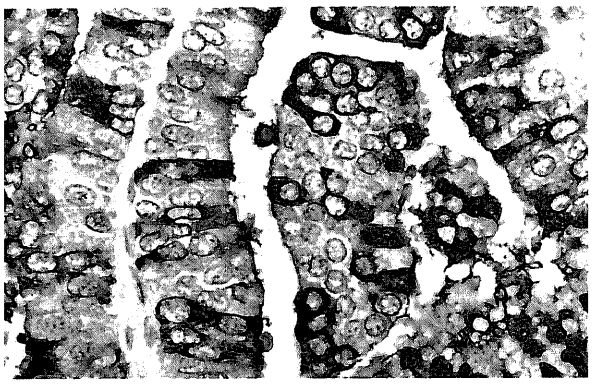

Fig. 6a

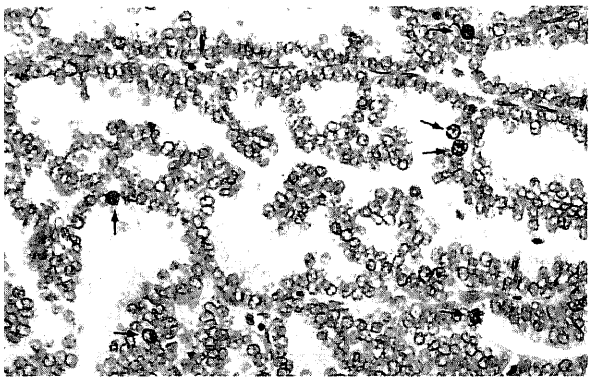

Fig. 6b

g. 6.(a) TG immunostaining. Many TG-positive cells are distributed in the tumor.
(b) PCNA immunostaining. PCNA-positive nuclei (arrows) are frequently observed throughout the tumor.

ll nuclear antigen (PCNA) showed a high frequency positive nuclei (mean 4-7/ HPF) (Fig.6b)

The lymph node metastases showed essentially the me histologic appearance to that of the primary ith a slight increase of areas of follicular growth ttern. The right thyroid lobe showed only a focal filtration of lymphocytes.

DISCUSSION

The present thyroid tumor showed a prominent pillary growth pattern with a formation of true pallae as seen in papillary thyroid carcinoma ; they d a long and narrow fibrovascular stalk beneath the ithelium. The tall follicular cells lining the papillae d generally basally located nuclei, and these structral and cellular features resembled the tall cell varit of papillary thyroid carcinom a [3,4]. The nuclear atures of these follicular cells were, however, entirely different from those of papillary carcinoma, and were similar instead to those of follicular thyroid carcinoma. In addition to the nuclear characteristics of the tumor cells, the presence of foci showing a follicular growth pattern or poorly organized follicular structure supported the interpretation that this thyroid tumor belongs to follicular carcinoma of the thyroid.

A focal papillary growth pattern might be found in some types of thyroid carcinoma other than papillary carcinoma, such as poorly differentiated "insular" thyroid carcinom[5,6] and oxyphilic cell (Hurthle cell) thyroid carcinoma[7,8]. In such cases, despite an intermixture of more or less papillary growth areas in the tumors, the tumor cells tend to show nuclear features of follicular carcinoma rather than of papillary carcinoma[5-8]. Columnar cell carcinoma of the thyroid is characterized by a prominent papillary growth pattern of tall columnar cells with marked nuclear stratification, but the nuclei of the columnar cell carcinomas resemble those of follicular carcinoma[9-12]. The current tumor did not show a insular growth pattern, cytoplasmic oxyphilia or nuclear stratification. Thus, the histologic and cytologic features of the present thyroid tumor were different from those of any of previously reported cases.

The potentially aggressive biologic behavior of this tumor was suggested histologically by the high mitotic activity[13] and prominent vascular invasion by the tumor cells. The high frequency of PCNA-positive nuclei also suggested the highly proliferative nature of the tumor[13].

The present case showed metastases concomitantly to the regional lymph nodes and to the lungs. Papillary carcinomas usually metastasize to regional lymph nodes, whereas follicular carcinomas metastasize to distant sites[14-16]. Such a characteristic biologic behavior found in the present case suggested that the current tumor shares the clinical properties both of follicular and papillary carcinoma. The aforementioned poorly differentiated "insular" carcinoma and columnar cell carcinoma also have been shown to share such dual clinical properties[5,6,9-12]. At present, such thyroid carcinomas have been recommended to be grouped into the clinicopathological entity, "poorly differentiated carcinoma of the thyroid", because it is generally difficult to decide morphologically whether

they belong to the follicular or papillary group, and because they are usually associated with a poor prognosis[16]. The present case certainly belongs morphologically to the follicular group, but clinically it might be grouped into the category of "poorly differentiated carcinoma of the thyroid", because the clinical behavior was more aggressive compared with that of usual follicular carcinomas.

Studies of additional cases are awaited to reach more definite conclusions concerning the tumor morphology and clinical behavior of this rare thyroid carcinoma.

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高度の乳頭状増殖パターンを示した甲状線沪胞癌
－沪胞癌の乳頭亜型か？－

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