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Thyroid Papillary Carcinoma with Exuberant Nodular Fasciitis-like Stroma
- A Case Report -

Kyung Hwa Lee · Jae Hun Chung Jung Han Yoon[1] · Kyung Whan Min[2] Chan Choi · Ji Shin Lee

Departments of Pathology and [1]Surgery, Chonnam National University Medical School and Research Institute of Medical Science, Gwangju, Korea; [2]Department of Pathology, Deaconess Hospital, Oklahoma, USA

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Corresponding Author
Ji Shin Lee, M.D.
Department of Pathology, Chonnam National University Hwasun Hospital, 160 Ilsim-ri, Hwasun-eup, Hwasun-gun, Jeonnam 519-809, Korea
Tel: 061-379-7072
Fax: 061-379-7099
E-mail: jshinlee@hanmail.net

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Thyroid papillary carcinoma (TPC) with exuberant nodular fasciitis-like stroma is one of the rare variants of TPC. To date, only 19 cases have been reported in the English medical literature. We report here on the the first Korean case of TPC that contained a prominent nodular fasciitis-like stroma. A 40-year-old female presented with a hard painless right neck mass that had been present for two months. Total thyroidectomy disclosed a solitary nodule in the mid portion of the right lobe that measured 25 × 20 mm. The tumor was well delineated, but it was not encapsulated. Microscopically, the tumor was a typical papillary carcinoma except that large areas of the tumor were occupied by a stroma composed of irregular fascicular spindle cells. The stromal component accounted for 60% of the tumor mass. The spindle cells exhibited neither atypism nor mitosis, and the tumor's extensive stromal cell proliferation resembled the appearance of nodular fasciitis of the soft tissues. Immunohistochemically, the spindle cells were positive for vimentin and α-smooth muscle actin, but they were negative for thyroglobulin, thyroid transcription factor-1, S-100 protein, CD34 and desmin, and this represents myofibroblastic features.

Key Words : Thyroid neoplasms; Carcinoma, Papillary, Fasciitis

Papillary carcinoma is the most frequent malignant neoplasm of the thyroid gland.[1] Thyroid papillary carcinoma (TPC) is known to have several morphological variants. TPC with an exuberant nodular fasciitis-like stroma was first described by Chan *et al*.[2] in 1991. The term TPC with fibromatosis-like stroma or TPC forming a myofibroblastic tumor has been also used.[3-7] This rare variant of TPC is characterized by a prominent spindle cell proliferation with small foci of papillary carcinoma. To our knowledge, only 19 cases have been reported in the English literature.[2-14] The spindle cells in these tumors show features of myofibroblasts according to the immunohistochemistry and electron microscopy. We report here on the first Korean case of TPC that contained a prominent nodular fasciitis-like stroma. Immunohistochemical studies showed that the proliferative spindle cells in our case are identical to myofibroblasts.

CASE REPORT

A 40-year-old woman presented with an approximate two-month history of a non-tender, hard mass in the right neck. She had no past or family history of thyroid disease. Physical examination revealed a firm nodular mass, 3 cm in diameter, in the right neck. There were no palpable cervical lymph nodes. The routine laboratory examinations, including the thyroid function tests, were entirely within the normal ranges. Computed tomography revealed a well-demarcated nodule in the right lobe of the thyroid.

Fine needle aspiration of the thyroid nodule revealed malignant cells that were consistent with a papillary carcinoma. Total thyroidectomy was then performed. Grossly, the tumor that measured 2.5 cm at the maximum diameter was present in the right lobe. The cut surface of the mass was whitish yellow and

relatively well-demarcated. It showed a firm, solid and fibrous appearance in the whitish area (Fig. 1). Microscopically, the tumor consisted of both stromal and epithelial components (Fig. 2A).

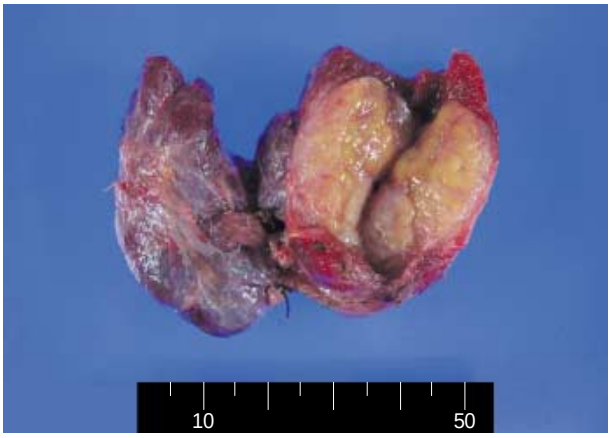

Fig. 1. The solitary tumor in the right lobe measures 25×20 mm. The cut surface of the nodule is yellowish to white.

The stromal component occupied approximately 60% of the tumor mass. The stromal component was made of irregular fascicular spindle cells (Fig. 2B). The spindle cells had elongated, bland nuclei with fine chromatin and a small distinct nucleolus; mitotic figures were almost absent. Intermixed with the spindle cells were scattered inflammatory cells. The overall appearance of the stroma areas resembled that of nodular fasciitis of the soft tissues. The epithelial component consisted of glandular structures and papillae of cuboidal cells (Fig. 2A). These cells had pale to ground-glass nuclei, and occasional intranuclear inclusions were also seen. These microscopic features of the epithelial component were identical to the conventional TPC. Some islands of papillary carcinoma cells were completely surrounded by stromal spindle cells. Immunohistochemically, the spindle cells in the stromal component were positive for vimentin (DAKO, Glostrup, Denmark, dilution 1:100), and α-smooth muscle actin (SMA) (DAKO, dilution 1:100), but the spindle cells were

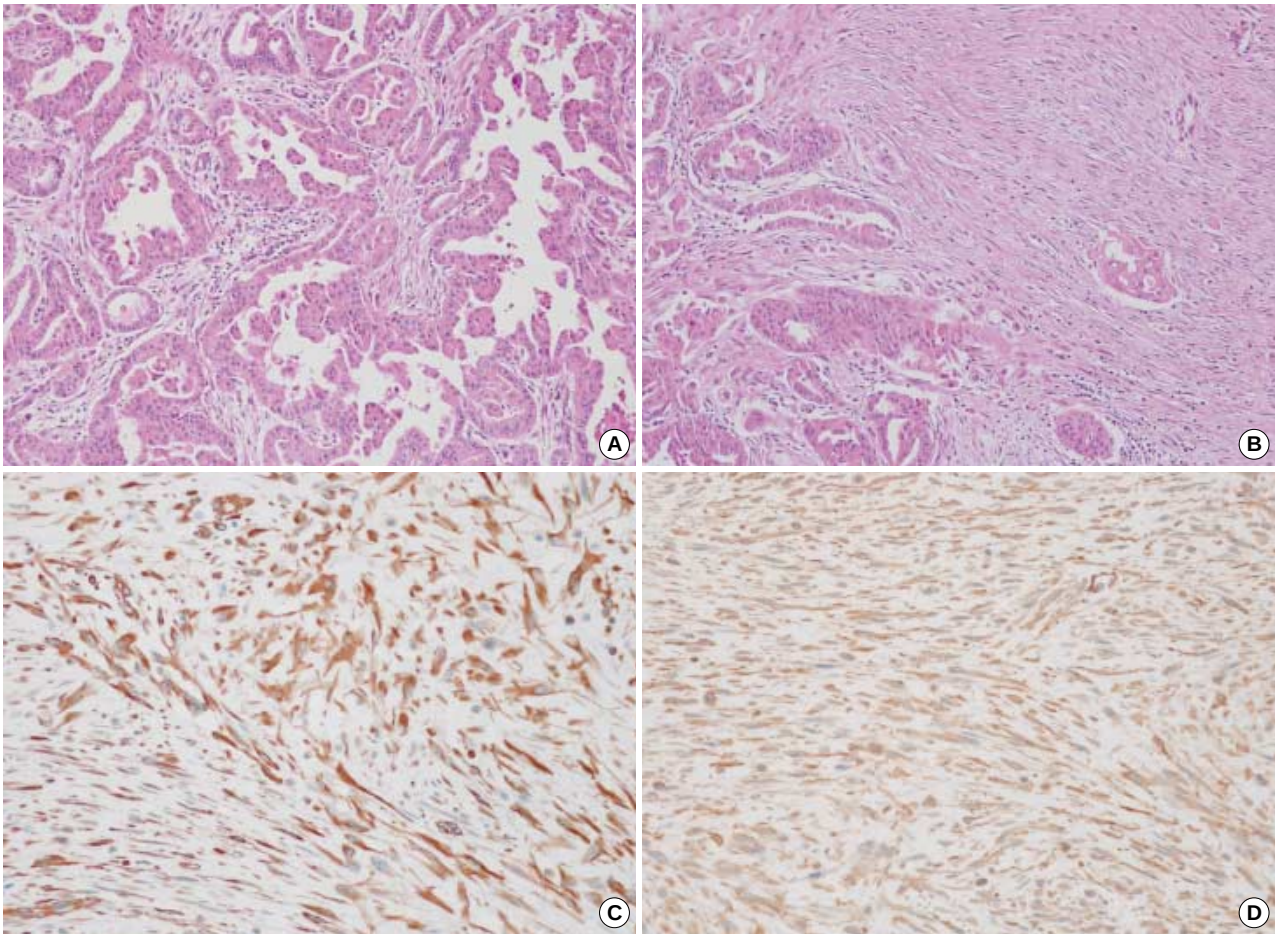

Fig. 2. Microscopic and immunohistochemical findings. The epithelial components show typical papillary carcinoma features (A). Prominent proliferation of stromal cells is accompanied by small foci of papillary carcinoma (B). The spindle cells are positive for vimentin (C) and α-smooth muscle actin (D).

negative for cytokeratin (AE1/AE3) (DAKO, dilution 1:100), thyroglobulin ((DAKO, dilution 1:100), thyroid transcription factor-1 (TTF-1) (DAKO, dilution 1:100), S-100 protein (DAKO, dilution 1:100), CD34 (DAKO, dilution 1:100) and desmin (DAKO, dilution 1:100) (Fig. 2C, D). However, the epithelial cells were positive for cytokerain, thyroglobulin and TTF-1, and they were focally positive for vimentin.

Thus, the diagnosis of TPC with exuberant nodular fasciitis-like stroma was made. The seven-month follow-up period was uneventful.

DISCUSSION

Papillary carcinoma is the most common malignant tumor of the thyroid, and it's known to have several morphological variants.[14] The term TPC with exuberant nodular fasciitis-like stroma was first reported by Chan *et al*. to describe three cases of TPC that had prominent stromal components resembling nodular fasciitis.[2] This variant of TPC has been also reported under the name of TPC with fibromatosis-like stroma.[3-6] Naganuma *et al*.[7] have recently proposed the new name of "TPC forming myofibroblastic nodular tumors". The stromal components in these tumors resemble the appearance of nodular fasciitis or fibromatosis of the soft tissues, and this may occupy 60-70% of the tumor. Immunohistochemical and ultrastructural analyses have shown that the spindle cells exhibit the characteristic of myofibroblasts. To date, only 19 cases have been reported in the English medical literature.[2-14] These tumors usually occur in middle aged patients, and there is a female predilection. The clinical behavior of these patients is analogous to that of patients with conventional TPC. Local nodal metastases have been reported in only two cases and distant metastasis has never been reported. Our case fulfilled the histologic criteria of TPC with exuberant nodular fasciitis-like stroma. The tumor was characterized by a prominent spindle cell proliferation without any massive growth of papillary carcinoma. The stromal component accounted for 60% of the tumor. Immunohistochemically, the spindle cells were positive for vimentin and α-SMA, which is consistent with myofibroblastic differentiation. Our patient was alive and well and had no evidence of disease for eighteen months following surgery.

The pathogenesis of the spindle cell proliferation in this variant of TPC is still unknown and rather puzzling. Chan *et al*. have interpreted the stromal proliferation as a reaction to the carcinoma cells.[2] In our case, the stromal component was confined to the tumor. The spindle cells had neither atypism nor mitosis. These findings support that the stromal proliferation may be reactive in nature. Toti *et al*. have found that numerous carcinoma cells in the stromal area were immunoreactive for transforming growth factor β (TGF-β), suggesting that TGF-β may be related to the stromal change of the tumors.[11] However, Naganuma *et al*. failed to find immunoreactivity for TGF-β in both stromal cells and carcinoma cells.[7] Further studies are necessary to uncover the pathogenesis of the marked spindle cell proliferation in these tumors.

The differential diagnosis of our case includes a large variety of thyroidal spindle cell proliferations. TPC with an exuberant nodular fasciitis-like stroma can be distinguished from the extensive fibrosis observed in some forms of thyroiditis, such as the fibrous variant of Hashimoto's thyroiditis and Riedel's thyroiditis, by the presence of papillary carcinoma.[12] Conventional TPC is frequently accompanied by a fibrous stroma and scars that are formed as a host reaction; however, it seldom forms nodular tumors.[7] Benign mesenchymal tumors, including solitary fibrous tumor, may arise in the thyroid gland.[15] However, the demonstration of TPC after conducting a thorough sampling may lead to the correct diagnosis. It is especially important to differentiate between our case and TPC with anaplastic transformation (spindle cell anaplastic carcinoma), because anaplastic carcinoma of the spindle cell type is a fatal disease.[16] The diagnosis of TPC with exuberant nodular fasciitis-like stroma in our case was supported by the lack of atypism or mitoses and also the presence of spindle cells that exhibited immunohistochemical features consistent with myofibroblasts.

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