Virchows Arch (1997) 431:291–295

CASE REPORT

Kiyomi Terayama · Syuji Toda · Nobuhisa Yonemitsu
Norimasa Koike · Hajime Sugihara

Papillary carcinoma of the thyroid with exuberant nodular fasciitis-like stroma

Received: 29 August 1996 / 26 May 1997

Abstract We describe a rare case of papillary carcinoma with extensive proliferation of stromal cells. The stromal cells were immunocytochemically positive for vimentin, α-smooth muscle actin and desmin, but negative for cytokeratin, epithelial membrane antigen, S-100, thyroglobulin and CD34. These results and the ultrastructure of the stromal cells, which exhibited the characteristics of both fibroblasts and smooth muscle cells, indicated an origin from myofibroblasts. We conclude that myofibroblastic proliferation may contribute to the stromal response in the slow growth of the papillary carcinoma.

Key words Papillary carcinoma · Stromal variant · Myofibroblasts

Introduction

Papillary carcinoma, the most common malignant tumour of the thyroid, is known to have several morphological variants. Stromal features include sclerosing fibrosis, hyalinization and calcification. Some reports of papillary carcinoma describe extensive proliferation of the stroma resembling myofibroblastoma or inflammatory pseudotumour, and this variant has been described as having fibromatosis-like stroma or nodular fasciitis-like stroma [2, 6, 7]. Immunohistochemical and ultrastructural studies have shown that the proliferative stromal cells in these lesions should be regarded as myofibroblasts. We report a case of papillary carcinoma with tumour-like myofibroblastic stroma and speculate about the pathogenesis of this stromal reaction.

K. Terayama (✉)[1] · S. Toda · N. Yonemitsu · H. Sugihara
Department of Pathology, Saga Medical School, Saga, Japan

N. Koike
Koike Hospital, Kase, Nakabaru, Saga, Japan

[1] *Mailing address:*
Department of Pathology, Kawasaki Medical School,
577 Matsushima, Kurashiki-City, Okayama, 701-01 Japan
Tel.: (+81) 86-462-1111 (Ext. 2441), Fax: (+81) 86-462-1199

Clinical history

A 57-year-old Japanese woman discovered a lump in her neck in August 1994 and consulted hospital physicians in October. Sonographic examination revealed two well-demarcated nodules in the left lobe of the thyroid and one well-demarcated nodule in the right lobe. Thyroid function tests were normal. Cytological study revealed malignant cells suggesting papillary carcinoma in these nodules. There were no palpable cervical lymph nodes. A subtotal thyroidectomy and lymphadenectomy of the left parabronchial region were performed in early December. The patient has been well for the 22 months since surgery.

Materials and methods

The resected tissue of the thyroid was fixed in 10% formalin solution, routinely processed and embedded in paraffin. Deparaffinized sections were stained with haematoxylin-eosin and periodic acid–Schiff, Azan–Mallory and silver impregnation stain. These sections were also immunohistochemically stained with antibodies to desmin (monoclonal, Bio-Science, USA), α-smooth muscle actin (SMA; monoclonal, Nichilei, Tokyo), vimentin (monoclonal, Dako, Tokyo), S-100 (polyclonal, Nichilei), CD34 (monoclonal, Nichilei), cytokeratin (monoclonal, Nichilei), epithelial membrane antigen (EMA; monoclonal, Dako) and thyroglobulin (monoclonal, Dako). The indirect method with an avidin-biotin peroxidase conjugate was used for these procedures, and negative control experiments were done. The material was salvaged from the paraffin block and processed using standard methods. Thin sections were also examined by electron microscopy EM 100-S.

Pathological findings

Macroscopically, the resected right lobe was seen to contain a relatively well-demarcated tumour consisting of an apparently encapsulated mass. The main tumour in the right lobe measured 4×2×2 cm. The cut surface of the nodule was yellowish white and exhibited expansive growth. Histologically, the mass consisted of two distinct components. The peripheral epithelial component of the mass consisted of atypical cells with pleomorphic and grooved nuclei; this component was diagnosed as a papillary carcinoma. The central tumour-like portion of

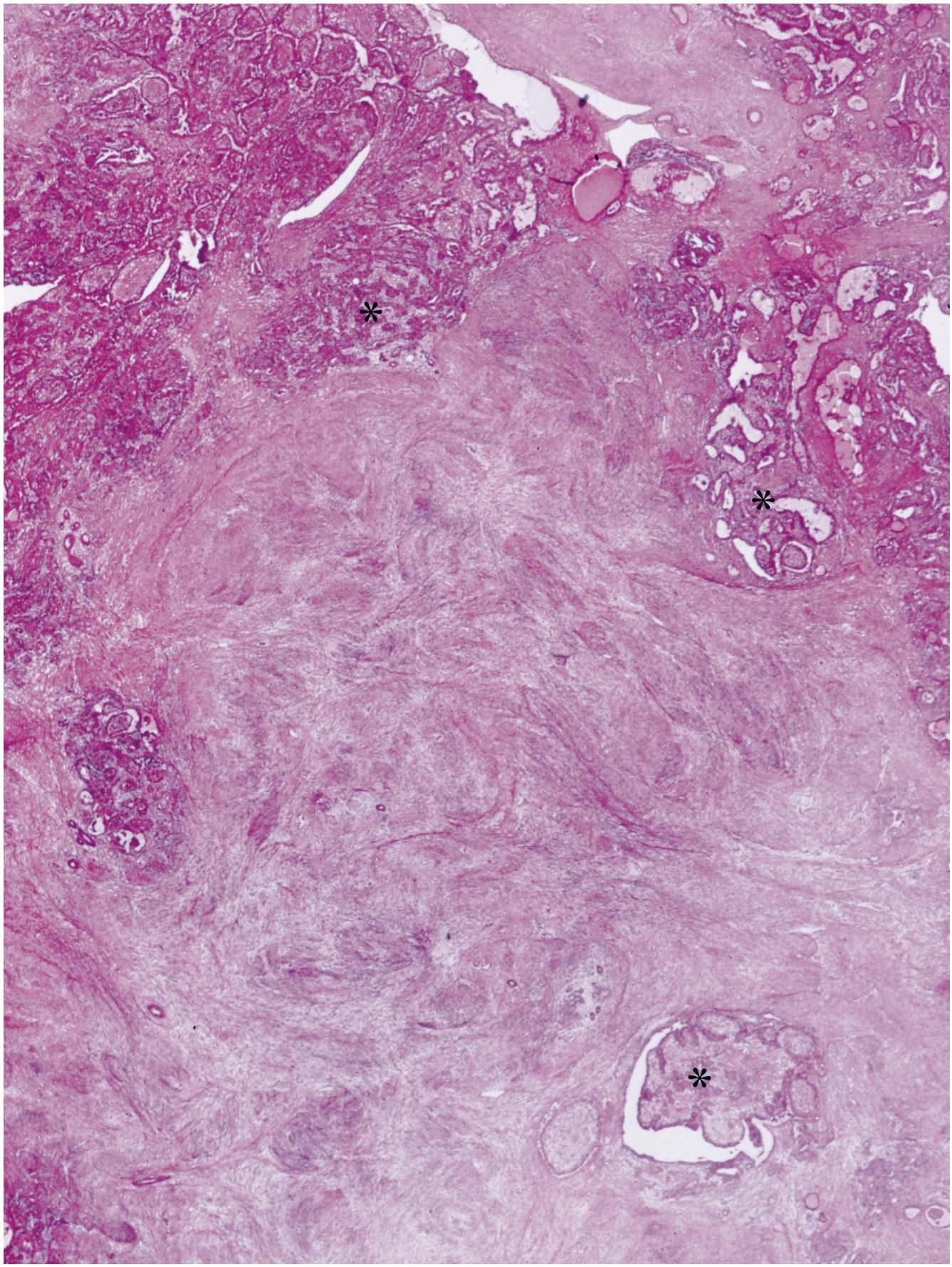
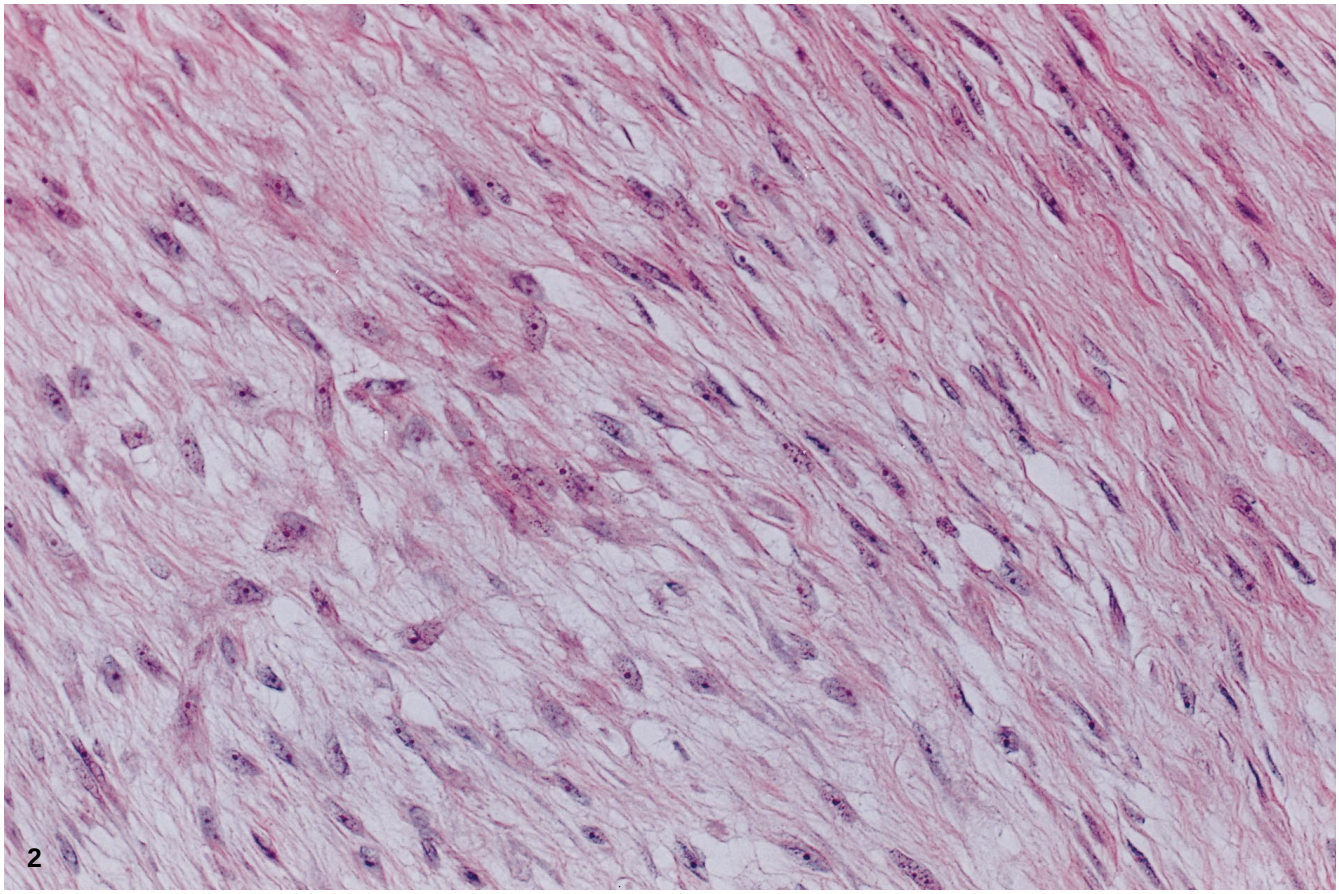


Fig. 1 The largest nodule in the right lobe. The nodule consists of two different areas, a central area of stromal proliferation and a peripheral area of papillary carcinoma (*asterisk*). H&E, ×3.5



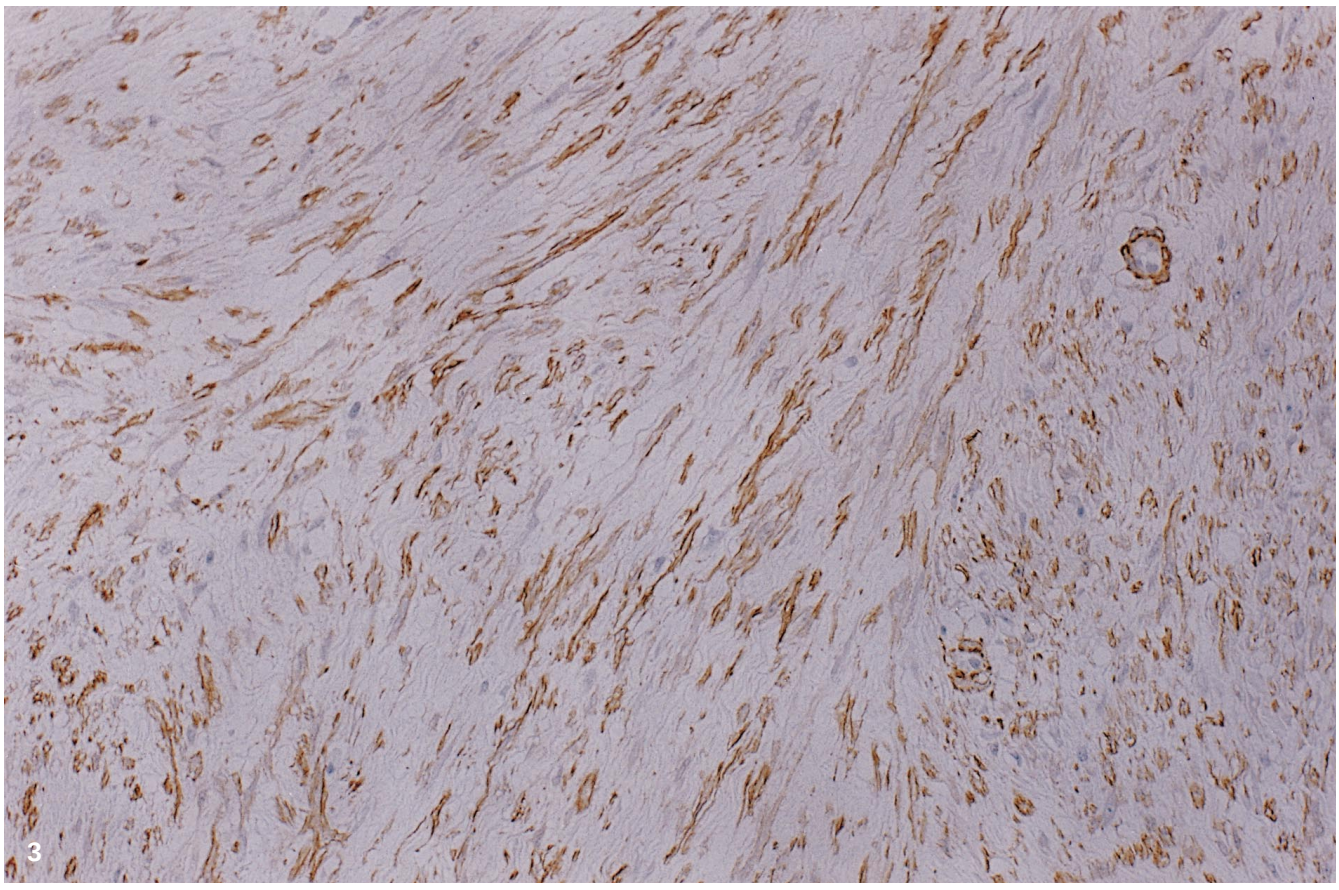


Fig. 2 Fascicular spindle cells show blunt ended nuclei with distinct nucleoli. They exhibit loose myxoid stroma (*lower left*) and possess wavy collagen bands (*upper right*). H&E, ×300

Fig. 3 Immunoreactivity of α-smooth muscle actin in the stromal cells. Spindle cells demonstrate intracytoplasmic positivity. H&E, ×300

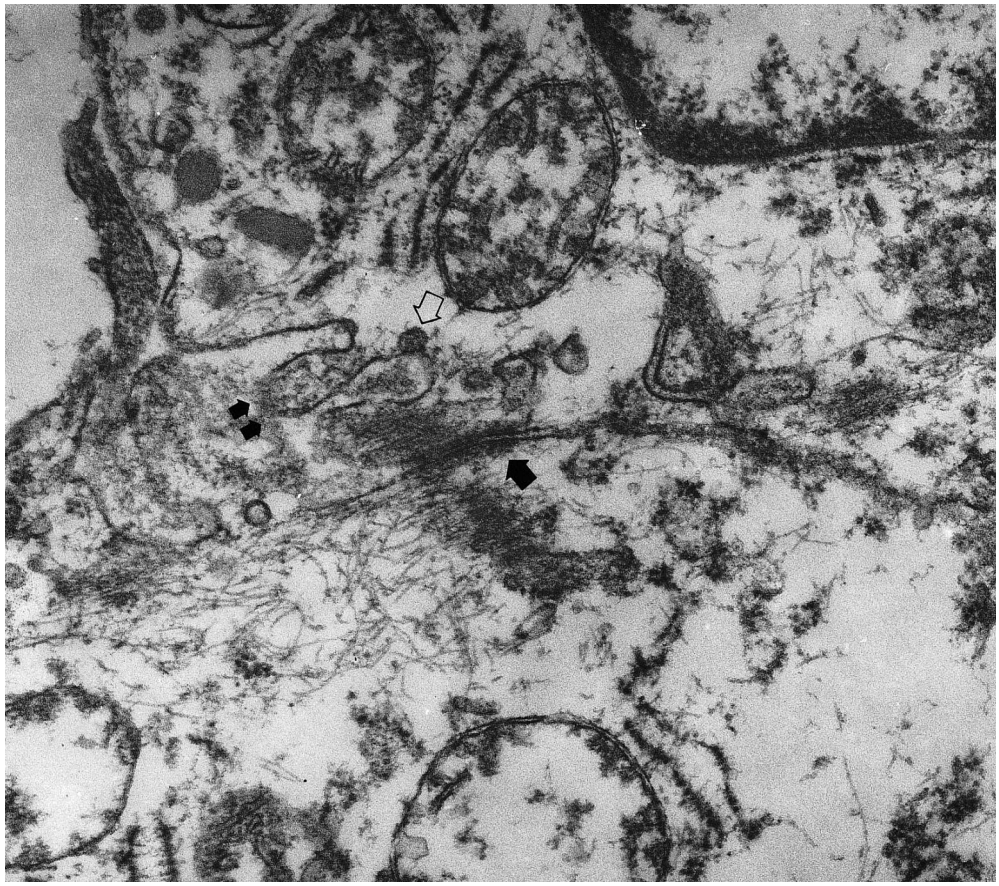


Fig. 4 Ultrastructural findings of the stromal cells. Spindle cells possess cytoplasmic bundles of microfilaments with dense bodies, rough endoplasmic reticulum and mitochondria. Gap junction (*closed arrow*) is present, followed by an intermediate junction (*double arrow*) between two myofibroblasts and pinocytotic invagination (*open arrow*). ×15,000

Table 1 Results of immunohistochemical examination of the stromal cells (*EMA* epithelial membrane antigen, *SMA* smooth muscle actin, – absent, + present, ++ abundant or commonly seen)

Desmin	+
Vimentin	++
SMA	++
Cytokeratin	–
EMA	–
Thyroglobulin	–
S-100	–
CD34	–

the mass constituted of a nonepithelial component of spindle cells, showing extensive proliferation into interlacing fascicles or in storiform patterns (Fig. 1). Some islands of papillary carcinoma cells were studded with spindle cells. These spindle cells exhibited distinct nucleoli without conspicuous nuclear atypia (Fig. 2). Two nodules in the left lobe were papillary carcinomas with sclerosing and calcified fibrous stroma (data not shown).

The results of immunohistochemistry for the spindle cell component are shown in Table 1. These spindle cells showed positive cytoplasmic staining for vimentin and SMA (Fig. 3). Reactivity to desmin was weakly positive. Cytokeratin, EMA, thyroglobulin, S-100 and CD34 were not detected on immunohistochemistry. Ultrastructural examination of the spindle cells revealed cytoplasmic bundles of microfilaments with dense bodies, rough endoplasmic reticulum and pinocytotic vesicles, all findings characteristic of myofibroblasts (Fig. 4).

Discussion

Papillary carcinoma with fibromatosis-like stroma is classified as a special variant of thyroid carcinoma characterized by proliferative and bulky intratumoural stromal cells accompanied by a scanty inflammatory infiltrate [1]. Proliferating stromal cells have been identified as myofibroblasts by immunohistochemical and ultrastructural examinations [7]. In our case, focal myofibroblastic proliferation was located in the central part of the neoplasm and not in the peripheral invasive tumour front. A scanty inflammatory infiltrate was seen.

In immunohistochemical studies with vimentin, desmin and SMA, myofibroblasts are subdivided into four cytoskeletal phenotypes: one expressing vimentin only (V), one expressing vimentin, SMA, and desmin (VAD), one expressing vimentin and SMA (VA), and one expressing vimentin and desmin (VD) [3, 8]. Myofibroblasts in the tumour stroma usually represent the VA phenotype, which accords with the myofibroblasts in our case [8].

Stromal proliferation in any neoplasm reflects various responses including the peripheral stromal reaction to invasive neoplastic cells or an intratumour stromal reaction. The latter may be classified into three types: contracted scar formation, a diffuse desmoplastic reaction, and a nodular or tumour-like stromal proliferation. The last type is rare and was observed in this case.

Formerly, only fibroblasts were noted in stromal proliferation, but recent immunohistochemical and ultrastructural studies have demonstrated a mixed proliferation of myofibroblasts and fibroblasts [5]. Myofibroblasts are the progenitor cells of fibroblasts and are considered to be derived from those cells by expression of SMA. The timing of the switch from fibroblastic to myofibroblastic phenotype is related to stromal tissue contraction [4], and myofibroblasts appear in the reactive processes induced by the invasion of neoplastic cells as well as by inflammation. In breast carcinoma and pulmonary adenocarcinoma, proliferation of myofibroblasts has usually been observed in the peripheral invasive front of the tumour stroma. This is not so common in thyroid carcinoma [8], which suggests that pathogenesis of this stromal variant may result from pathologic tissue remodelling [7] and should be differentiated from diffuse desmoplastic proliferation accompanying neoplastic invasion. Negativity for CD34 in these stromal cells also indicated that the stromal tumour was not neoplastic. We prefer the term “tumour-like myofibroblastic stroma in papillary carcinoma of the thyroid” to the term “fibromatosis-like stroma”, because the former definitely designates reactive myofibroblastic proliferation in the stroma.

Acknowledgements We would like to thank H. Ideguchi, H. Muto, and S. Nakahara for the excellent technical assistance rendered.

References

1. Chan JK (1990) Papillary carcinoma of the thyroid: classical and variants. Histol Histopathol 5:241–257
2. Chan JK, Carcangiu ML, Rosai J (1991) Papillary carcinoma of thyroid with exuberant nodular fasciitis-like stroma. Am J Clin Pathol 95:309–314
3. Gabbiani G (1992) The biology of the myofibroblast. Kidney Int 41:530–532
4. Grinnell F (1994) Fibroblasts, myofibroblasts, and wound contraction. J Cell Biol 124:401–404
5. Hasegawa T, Hirose T, Kudo E, Abe J, Hizawa K (1990) Cytoskeletal characteristics of myofibroblasts in benign neoplastic and reactive fibroblastic lesions. Virchows Arch [A] 416:375–382
6. Mizukami Y, Nonomura A, Matsubara F, Michigishi T, Ohmura K, Hashimoto T (1991) Papillary carcinoma of the thyroid gland with fibromatosis-like stroma. Histopathology 20:355–357
7. Mizukami Y, Kurumaya H, Kitagawa T, Minato H, Nonomura A, Michigishi T, Noguchi M (1995) Papillary carcinoma of the thyroid gland with fibromatosis-like stroma: a case report and review of the literature. Mod Pathol 8:366–370
8. Sternberg SS (1992) Histology for pathologists: myofibroblast. Raven, New York, pp 109–144