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Clinical Record

# Papillary thyroid carcinoma with exuberant nodular fasciitis-like stroma: treatment outcome and prognosis

S Basu MBBS (Hons), DRM, DNB, N Nair MD, T Shet, MD*, A M Borges MD, FRCPath*

**Abstract**

Papillary thyroid carcinoma with nodular fasciitis-like stroma (PTC-NFS) is one of the extremely rare variants of papillary thyroid carcinoma. To date, the majority of reported cases have been published in the surgical pathology and cytopathology literature, addressing the diagnostic difficulties posed by the condition's extensive, reactive stromal proliferation. Because of the rarity of PTC-NFS among papillary thyroid carcinoma variants, it has been unexplored from a clinical viewpoint. A MEDLINE search on the clinical course, role of radioiodine, treatment outcome and long term follow up of this disease yielded no result.

We report the clinicoradiologic and histopathologic profile, together with post-treatment long term follow up, in a 35-year-old woman harbouring this rare entity. To the best of our knowledge, this is the first report of a five-year follow up of this rare variant of PTC following total thyroidectomy and radioiodine treatment. Our follow-up findings reiterate the disease's favourable clinical course when managed in the same manner as a classical, differentiated papillary carcinoma of the thyroid, akin to that predicted by the pathologists, and emphasize the importance of differentiating PTC-NFS as a separate entity from the papillary carcinoma variants with aggressive histology. Given the rarity of this condition, the experience gained from the present case is a useful addition to the current knowledge on disease prognostication and management.

A systematic review of the existing literature on PTC-NFS, including the case reported in the present paper, is also carried out, aiming to explore the patient characteristics and clinical behaviour pattern of this rare entity and to make appropriate recommendations on management strategy. The age of presentation ranges from 20 to 82 years, with a mean of 44.5 years. Female preponderance was observed, with a female to male ratio of 3 : 1. No racial predilection was observed. Tumour size varied from 2 to 9 cm along its greatest diameter (mean = 4.3 cm). Metastasis to lymph nodes at presentation occurred in 25 per cent of cases. Metastasis to surrounding structures (e.g. parathyroid and skeletal muscle) was observed in 12.5 per cent. There have been no reports of pulmonary or skeletal metastasis at presentation.

**Key words: Carcinoma; Papillary; Thyroid Neoplasms**

## Introduction

Papillary carcinoma of the thyroid gland with exuberant nodular fasciitis-like stroma (PTC-NFS) is a rare and relatively unexplored morphologic variant of conventional PTC. Ten reports have been published in the literature,[1–10] the majority of them highlighting this entity as an interesting pathological case vignette. No clinical data regarding the final outcome of PTC-NFS has been published. The terms 'papillary carcinoma of the thyroid with fibromatosis-like stroma' and 'papillary carcinoma forming myofibroblastic nodular tumours' have been used synonymously to describe the same entity. The condition is characterized by extensive reactive stromal proliferation, which may occupy up to 60–80 per cent of the tumour.[3] The stroma has a nodular fasciitis-like quality and comprises fascicles of spindle cells separated by varying amounts of mucoid matrix, collagen and extravasated red blood cells; this is regarded by some as a mesenchymal reaction to malignancy.[7]

## Case report

A 35-year-old Indian woman presented with a gradually increasing neck swelling of six months' duration without any associated symptoms. Clinical examination revealed a multinodular goitre involving both lobes, subsequently proven by neck ultrasonography. Multiple-site fine needle aspiration cytology (FNAC) suggested papillary carcinoma of the thyroid.

A near-total thyroidectomy was undertaken. On gross inspection, one lobe measured 6 × 4 × 2.5 cm and the other measured 3 cm along its greatest axis. The larger lobe showed a well circumscribed nodule, 3 cm in diameter. The cut surface of the nodule was greyish and fleshy. Another nodule, 1 cm in diameter, was present near the larger nodule. The other lobe showed a small, whitish nodule, 0.5 cm in diameter.

On microscopy, the initial impression at the referring centre was papillary carcinoma of the thyroid, of a diffuse sclerosing variant. On review at the pathology department

From the Radiation Medicine Centre and the *Department of Pathology, Tata Memorial Hospital, Bombay, India.
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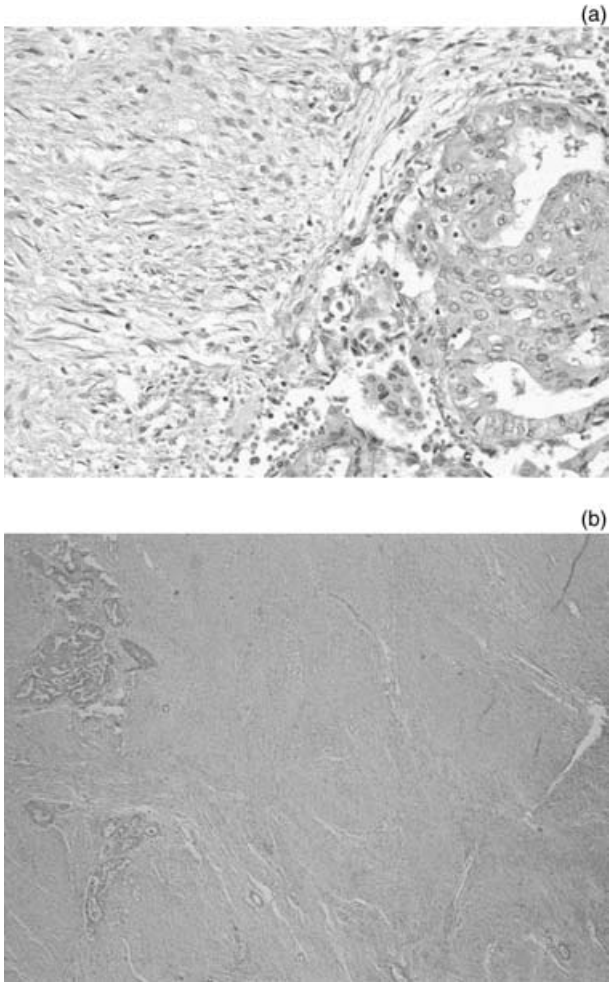


FIG. 1

(a) A higher-power view reveals the typical nuclear features of papillary carcinoma and the bland spindle stroma with plump myofibroblasts (H&E; × 200). (b) Low-power view of the fasciitis-like stroma with areas of papillary carcinoma (H&E; × 100).

of our institute, the tumour appeared to involve both lobes of the thyroid. In one lobe, the tumour was polypoid and intracystic, the polypoid area being almost entirely replaced by a bland, myofibroblastic proliferation with erythrocyte extravasation (Figure 1). A higher power view of the epithelial nests demonstrated the typical nuclear features of papillary carcinoma. The stroma showed plump myofibroblasts, in keeping with the myofibroblastic nature of the proliferation. The final diagnosis was differentiated papillary carcinoma of the thyroid, with nodular fascitis-like stroma.

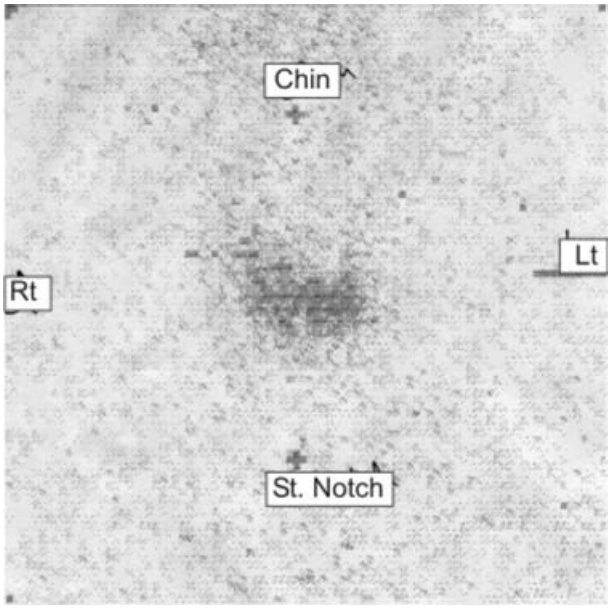


FIG. 2

3.7 MBq $^{131}$I neck scan showing residual tissue in the thyroid bed. Rt = right; Lt = left; St notch = suprasternal notch.

A diagnostic $^{131}$I uptake and scan was performed five weeks after surgery, with 3.7 MBq (100 microcurie) administered orally. The scan (Figure 2) revealed residual tissue in the thyroid bed, with a 24 hour neck uptake of 0.95 per cent of the dose. In view of the age, sex, histopathology and limited disease extent, the patient was treated with 1110 MBq (30 mCi) $^{131}$I and was subsequently prescribed thyroxine supplementation. A whole-body survey with 142.08 MBq of $^{131}$I, repeated six months after residual ablation, did not reveal any abnormal focal uptake anywhere in the body, and neck uptake at 24 hours had declined to 0.04 per cent. The profile scan of the whole body, using a shadow shield whole-body counter, obtained 72 hours after oral administration of 142.08 MBq of $^{131}$I, revealed no abnormal peak anywhere in the body (see Figure 3). The level of serum thyroglobulin was 0 ng/ml (in our institute, values are considered normal when below 20 ng/ml in patients not receiving thyroxine supplementation and below 10 ng/ml in patients receiving thyroxine supplementation). The patient was clinically disease free, with a normal chest roentgenogram. Thyroxine substitution was restarted and the patient advised to return for follow up after one year. The serum thyroglobulin levels (on thyroxine suppression) measured at the patient's subsequent four follow-up visits were within normal limits, and five years after the initial procedure she was disease free.

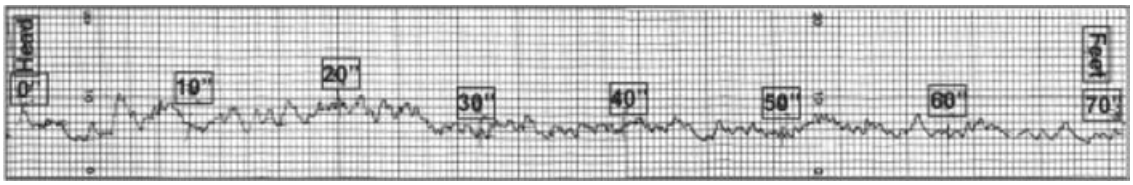


FIG. 3

Whole-body profile scan (using a shadow shield whole-body counter) at 72 hrs after oral administration of 142.08 MBq of $^{131}$I, revealing no abnormal peak anywhere in the body.

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## Discussion

Papillary thyroid carcinoma with nodular fasciitis-like stroma is an unusual and relatively unexplored morphologic variant of PTC. Since its first report,[6] published in 1991 by Chan *et al.*, PTC-NFS has been reported nine times,[1–5,7–10] mostly in pathology journals. Combining the 16 cases in these previous 10 reports and the present case, the patient age range varied from 20 to 82 years, with a mean of 44.5 years (Tables I and II). Female preponderance was observed, with a female to male ratio of 3 : 1. No racial predilection was observed. The tumour size along its greatest diameter varied from 2 to 9 cm (mean = 4.3 cm). Metastasis to lymph nodes at presentation occurred in four cases (25 per cent). Metastasis to surrounding structures was observed in two cases (to the parathyroid in one case and the surrounding muscles in the other). There was no report of skeletal or pulmonary metastasis. The surgery offered in the majority of cases was total thyroidectomy. Lymphadenectomy was performed in four cases with lymph node involvement.

While reports in the surgical pathology literature[1,2,5–8] have stressed the need to distinguish PTC-NFS from the more aggressive PTC variants (e.g. anaplastic carcinoma and sarcoma), the major concern of reports published in the cytology literature has been the challenge of FNAC diagnosis, owing to the nodular fasciitis-like stroma forming the tumour bulk.[3,4] The pathogenesis of this stroma is still an open question. Some authors have proposed this exuberant stromal proliferation to be reactive in origin,[4,6] while others have speculated that autonomous proliferation of stromal cells may be the main mechanism of PTC-NFS pathogenesis.[1] The bulk of the tumour (60–80 per cent) is composed of nodular fasciitis-like stroma, which makes aspiration of the neoplastic epithelial component difficult, increasing the risk of false negative FNAC. On the other hand, FNAC of the nodular fasciitis-like stroma may lead to the erroneous diagnosis of sarcoma or, rarely, anaplastic carcinoma, if seen in association with PTC. In the case reported by Yang *et al.*,[4] the discovery of spindle cells with nuclear atypia and pleomorphism against a myxoid background led to an initial, erroneous FNAC diagnosis of myxoid sarcoma. Even in the histologic sections of the previous reports, the initial diagnostic considerations included PTC with anaplastic transformation and carcinosarcoma. In the case described by Us-Krasovec and Golouh,[3] the initial FNAC diagnosis was sclerosing variant of PTC. The PTC-NFS variant is distinguished from the occult sclerosing variant by the latter's stroma, which is very collagenous and lacks the plump myofibroblasts and cellular quality of the former. In the diffuse sclerosing variant, there is moderate to severe fibrous replacement of the thyroid tissue.[11] Abundant psammoma bodies, lymphocytic infiltrates and the diffuse nature of the fibrosis are characteristic findings in the diffuse sclerosing variant.[11]

Chan *et al.*[6] observed that, even in the thyroidectomy specimen, the neoplastic nature of the lesion may be obscured by the stromal component when large areas within the tumour mass are completely devoid of the carcinomatous component. They also reiterated that the PTC-NFS variant must be distinguished from the more aggressive papillary carcinoma variants with anaplastic transformation and from the so-called carcinosarcomas. These aspects were also highlighted by the subsequent authors and have been the major reasons why this entity has featured in the pathology literature. In the report by Toti *et al.*,[2] one case exhibited areas of transformation into poorly differentiated carcinoma of the thyroid. What prompted this stromal transformation was a matter of conjecture. Transforming Growth Factor beta (TGF-beta), the fundamental cytokine which mediates scarring and activation of myofibroblasts, was expressed in high amounts in both these authors' cases, as assessed by immunohistochemistry. This, according to these authors, was the central factor responsible for inducing the exuberant stromal proliferation.

TABLE I

PTC-NFS PATIENT* CHARACTERISTICS

| Parameter | *n* |
|---|---|
| *Sex* | |
| Male | 4 |
| Female | 12 |
| *Age* | |
| Range (years) | 20–82 |
| Mean (years) | 44.5 |
| Lymph node metastasis at presentation | 4 (25%) |
| Total | 16 |

*$n = 16$, from previous reports plus the present case. PTC-NFS = papillary thyroid carcinoma with nodular fasciitis-like stroma

Recognition of PTC-NFS is important, both to avoid diagnostic misinterpretations and to enable appropriate management. The implications of the current case are as follows.

(1) It represents the first endeavour to address this entity from a clinical perspective. A comprehensive review of the available clinical data (collated from the previous cases reported in the histopathology and cytology literature) has also been made.

(2) This case is the first long term (five years) follow-up report of this rare variant following surgery and radioiodine treatment. In a small percentage of reported cases, there has been only short term follow up available, for a maximum of two years.

(3) This case also reinforces the fact that, in limited PTC-NFS disease, residual tissue ablation with the standard 30 mCi radioiodine may be sufficient to achieve disease control. In previous reports, there has been no debate regarding the dose of post-operative $^{131}$I treatment. It is likely that because the previous cases featured as interesting pathological case vignettes, this issue was not addressed, even in cases with short term follow up. Our patient had limited disease at presentation, without any evidence of extrathyroidal extension or lymph node metastasis, and her management was hence similar to that for PTC. She showed no evidence of disease five years post-operatively. However, we maintain that a higher dose of $^{131}$I should be considered in the presence of locoregional or distant spread or adverse prognostic factors.

(4) Awareness of PTC-NFS by both the pathologists and the treating physicians is essential from both the diagnostic and management viewpoints as this variant, unlike the aggressive variants of PTC, usually implies a good prognosis.

- **Papillary thyroid carcinoma with nodular fasciitis-like stroma is an unusual and relatively unexplored morphologic variant**
- **In this case report treatment was with near-total thyroidectomy followed by radio-iodine**
- **The pathological features of this neoplasm are discussed. The authors point out that the stroma of the tumour can make diagnosis by aspiration cytology difficult**

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TABLE II

DETAILS OF THE CLINICAL PROFILE OF THE PATIENTS WITH PTC-NFS PATIENT CLINICAL PROFILES*

| Author | Year | Journal type | *n* | Age/sex, race | Presention (duration) | Tumour size† at surgery (cm) | Surgery | $^{131}$I treatment/ dose | Outcome |
|---|---|---|---|---|---|---|---|---|---|
| Chan *et al.*[6] | 1991 | Histopathol | 3 | 20/F, Chinese | Rt neck swelling (2 months) | 2 | Total thyroidectomy | NM | Well at 1 yr |
| | | | | 35/F, Chinese | Rt neck swelling (3 months) | 4 | Near-total thyroidectomy | NM | NM |
| | | | | 20/F, White | Left thyroid lobe 'cold' nodule on I scan | 3 | Lt lobectomy & ishmectomy | NM | NM |
| Michal *et al.*[7] | 1992 | Histopathol | 2 | 49/F, Caucasian | Goitre with lymphadenopathy & infiltration to 1 parathyroid | 5 | Thyroidectomy (extent NM) + metastases excision | NM | Well at 1 yr |
| | | | | 33/F, Caucasian | Goitre | 3 | Thyroidectomy (extent NM) | NM | Well at 2 yr |
| Mizukami *et al.*[10] | 1992 | Histopathol | 1 | 67/F, NM | Rt thyroid lobe cold nodule | 2 | Subtotal thyroidectomy | NM | Well at 1 yr |
| Mizukami *et al.*[8] | 1995 | Histopathol | 1 | 43/F, NM | Expansive growth from Lt thyroid lobe | 5 | Total thyroidectomy | NM | Well at 1 yr |
| Terayama *et al.*[5] | 1997 | Histopathol | 1 | 57/F, NM | Goitre | 4 | Thyroidectomy | NM | NM |
| Acosta *et al.*[9] | 1998 | Surg oncol | 1 | 41/F, NM | Large anterior cervical mass | 9 | Total thyroidectomy | 150 mCi | Well at 6 months |
| Toti *et al.*[2] | 1999 | Histopathol | 2 | 73/M, White | Long-standing multinodular goitre, 2 lymph nodes developed in Lt neck | 4 | Total thyroidectomy & lymphadenectomy | NM | NM |
| | | | | 24/F, White | Rt thyroid lobe nodule with lymphadenopathy | 2 | Total thyroidectomy & lymphadenectomy | NM | NM |
| Yang *et al.*[4] | 1999 | Cytol | 1 | 82/M, NM | Rapidly growing neck mass (8 cm at presentation), dysphagia, hoarseness | 7 | Total thyroidectomy | NM | Well at 1 yr |
| Us-Krasovec & Golouh[3] | 1999 | Cytol | 1 | 42/F, NM | Tender Lt-sided goitre (1 month) | 2 | Total thyroidectomy | NM | NM |
| Naganuma *et al.*[1] | 2002 | Histopathol | 2 | 52/M, NM | Lt lobe firm goitre | 6 | Lt hemithyroidectomy + MND | NM | NM |
| | | | | 40/M, NM | Rt-sided goitre + lymphadenopathy | 5 | Total thyroidectomy + MND | NM | NM |
| Basu *et al.* (present study) | 2006 | Otolaryngol | 1 | 35/F, Indian | Multinodular goitre | 6 | Total thyroidectomy | 30 mCi | Well at 5 years |

*Reports taken from the English Literature. †Along greatest diameter. Histopathol = histopathology; Cytol = cytology; Surg oncol = surgical oncology; NM = not mentioned; Rt = right; Lt = left; MND = Modified neck dissection

**References**


1 Naganuma H, Iwama N, Nakamura Y, Ohtani N, Ohtani H, Takaya K *et al*. Papillary carcinoma of the thyroid gland forming a myofibroblastic nodular tumor: report of two cases and review of the literature. *Pathol Int* 2002;**52**: 54–8
2 Toti P, Tanganelli P, Schurfeld K, Stumpo M, Barbagli L, Vatti R *et al*. Scarring in papillary carcinoma of the thyroid: report of two new cases with exuberant nodular fasciitis-like stroma. *Histopathology* 1999;**35**:418–22
3 Us-Krasovec M, Golouh R. Papillary thyroid carcinoma with exuberant nodular fasciitis-like stroma in a fine needle aspirate: a case report. *Acta Cytol* 1999;**43**:1101–4
4 Yang YJ, LiVolsi VA, Khurana KK. Papillary thyroid carcinoma with nodular fasciitis-like stroma. Pitfalls in fine-needle aspiration cytology. *Arch Pathol Lab Med* 1999;**123**:838–41
5 Terayama K, Toda S, Yonemitsu N, Koike N, Sugihara H. Papillary carcinoma of the thyroid with exuberant nodular fasciitis-like stroma. *Virchows Arch* 1997;**431**:291–5
6 Chan JK, Carcangiu ML, Rosai J. Papillary carcinoma of thyroid with exuberant nodular fasciitis-like stroma: Report of three cases. *Am J Clin Pathol* 1991;**95**:309–14
7 Michal M, Chlumska A, Fakan F. Papillary carcinoma of thyroid with exuberant nodular fasciitis-like stroma. *Histopathology* 1992;**21**:577–9
8 Mizukami Y, Kurumaya H, Kitagawa T, Minato H, Nonomura A, Michigishi T *et al*. Papillary carcinoma of the thyroid gland with fibromatosis-like stroma: a case report and review of the literature. *Mod Pathol* 1995;**8**:366–70
9 Acosta J, Rodriguez JM, Sola J, Alcaraz M, Illan F, Nieto A *et al*. Nodular fasciitis-type papillary thyroid carcinoma. Presentation of a new case. *Eur J Surg Oncol* 1998;**24**:80–1
10 Mizukami Y, Nonomura A, Matsubara F, Michigishi T, Ohmura K, Hashimoto T. Papillary carcinoma of the thyroid gland with fibromatosis-like stroma. *Histopathology* 1992;**20**:355–7
11 Caruso G, Tabarri B, Lucchi I, Tison V. Fine needle aspiration cytology in a case of diffuse sclerosing carcinoma of the thyroid. *Acta Cytol* 1990;**34**:352–4



Address for correspondence:
Dr Sandip Basu,
c/o Radiation Medicine Centre,
Tata Memorial Centre Annexe,
Jerbai Wadia Road, Parel,
Bombay 400 012, India.

E-mail: drsanb@yahoo.com



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