CASE REPORT

Papillary carcinoma thyroid with fibromatosis/fasciitis-like stroma: Report of a rare case with review of literature

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Abstract

Papillary Thyroid Carcinoma with Fibromatosis/Fasciitis-Like Stroma (PTC-FMS) represents a rare variant of Papillary Thyroid Carcinoma (PTC). Recently, these tumours are further divided into two variants: PTC with nodular fasciitis-like stroma and PTC with fibromatosis-like stroma. Within the framework of the WHO classification, these tumours are discussed under the umbrella term of PTC with fibromatosis/fasciitis-like/desmoid type stroma. As the epithelial component can be missed on FNAC/ needle biopsy, there exists a risk of misdiagnosing this tumour as mesenchymal lesions. This case report presents a novel case of PTC-FMS along with a concise review of relevant literature.

Keywords: Papillary thyroid carcinoma, fibromatosis-like stroma, beta catenin

Introduction

Papillary Thyroid Carcinoma (PTC) with fibromatosis/fasciitis-like stroma is a rare variant with predominantly fibroblastic stroma and scattered islands of PTC. First described by Ostrowski *et al*. [1] in 1989 as PTC with Fibromatosis-Like Stroma (PTC-FMS) and by Chan *et al*. [2] as PTC with Nodular Fasciitis-Like Stroma (PTC-NFS), there are about 30 global cases. Its rarity poses a risk of misinterpretation, particularly in small biopsies, where Fine-Needle Aspiration Cytology (FNAC) may yield inadequate results due to the predominance of spindle cells and fibrous stroma.

Differential diagnoses include desmoid fibromatosis, nodular fasciitis, fibrous thyroiditis, solitary fibrous tumour, and carcinosarcoma [3]. Accurate diagnosis relies on recognizing mutations in the CTNNB1 gene, USP6 rearrangements, and BRAFV600E, while detecting the epithelial component amid extensive fibrous stroma [4].

Case Report

A 46-year-old female with progressive neck swelling for 2 months, revealed a 2 × 2 cm firm, mobile, non-tender swelling in the thyroid. Right level II lymph node was enlarged and hard. Biochemical and haematology tests were normal. FNAC was initially inadequate, but a repeat was suggestive of PTC (Bethesda category VI). The patient underwent total thyroidectomy, and the specimen was submitted for histopathological evaluation. Histopathology revealed a well-circumscribed nodule with grey-white fibrous areas measuring 1.5 × 1.5 cm in the larger lobe, surrounded by thyroid parenchyma (Figure 1a). Histology revealed tumour islands (40% of the mass) dispersed in abundant fibromyxoid stroma (60% of the mass). Tumour islands showed arborizing papillae with delicate fibrovascular cores and varying-sized follicles lined by low columnar cells showing an isonucleosis, nuclear crowding,

overlapping Orphan Annie eye nuclei, showing prominent nucleoli, nuclear grooving and intranuclear inclusions, a moderate amount of eosinophilic cytoplasm (Figure 1b). Fibromyxoid stroma showed elongated slender fibroblasts, stellate myofibroblasts, collagen strands, focal lymphoplasmacytic infiltrate and congested blood vessels without mitosis or pleomorphism.

Immunohistochemistry showed Beta-catenin membrane positivity in epithelial cells and nuclear staining in stromal components (Figure 1c). Smooth Muscle Actin (SMA) showed cytoplasmic positivity in the stromal cells (Figure 1d). The tumour was diagnosed as PTC-fibromatosis/ fasciitis-like stroma (pTNM, AJCC stage T1a, N0, M0).

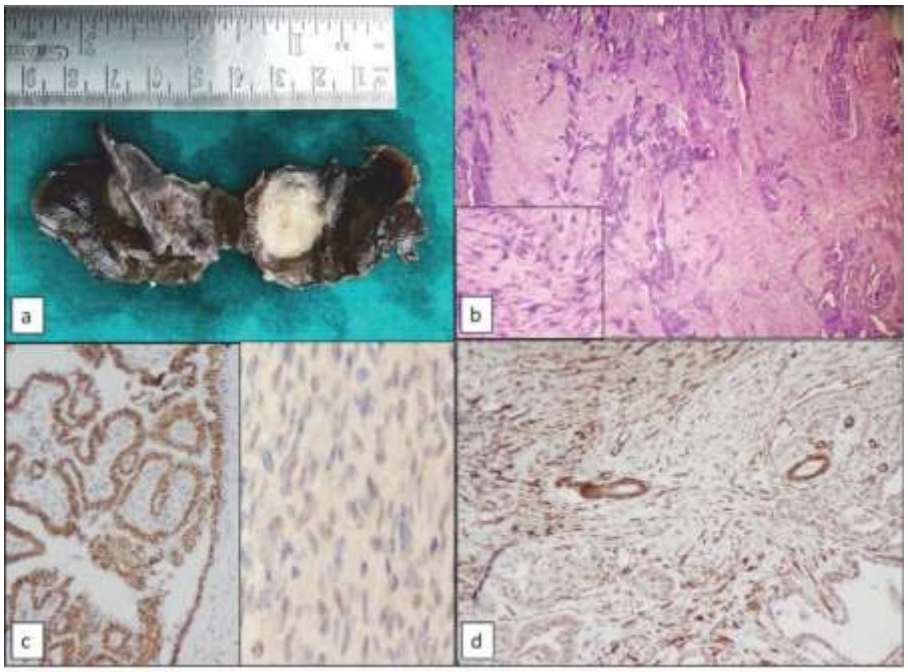

Figure 1a: Total thyroidectomy displaying a well-circumscribed, firm, grey-white nodule;
Figure 1b: Abundant fibromyxoid stroma with scattered tumor islands, H&E, 200x. Inset: Haphazardly arranged plump spindle cells, H&E, 400×;
Figure 1c: β-catenin highlights membrane staining in the epithelial component (left), occasional stromal cells exhibiting nuclear positivity (Right), β-catenin, 400×;
Figure 1d: SMA shows cytoplasmic staining in the spindle stromal cells, SMA, 400×.

Table 1: Summary of PTC-FMS described in literature

Age	20-82 years, Mean: 44.5years
Sex	F:M-3:1
Clinical presentation	Gradually increasing thyroid nodule, 1week - 7 months duration
Thyroid function test	Normal
Ultrasonography	Hypoechoic with scant vascularity
FNAC	AUS*/FLUS**/Suspicious for PTC/PTC/Myxoid sarcoma/ Inadequate / Nodular hyperplasia
Treatment	Lobectomy to total thyroidectomy with lymph node dissection
Metastasis	Lymph nodes (25%), Surrounding tissue (12.5%)
Size	2 - 10 cm, Mean: 4.3 cm
Gross	Well-circumscribed, firm, grey-white with trabeculated areas. Invasive margins (2 cases).
Microscopy	Biphasic, 40% to 95% stromal component with scattered epithelial islands. Lymphocytes, extravasated RBC, squamous and oncocytic metaplasia, leaf like projections with myxoid stroma (phyllodes-like), cystic change.
Immunohistochemistry expression	Epithelial cells: CK, TTF-1, Thyroglobulin, PAX8, CK7, CAM5.2, E-cadherin, Galectin 3, HBME1. Stromal cells: Vimentin, SMA, Desmin, β-catenin, Smad4, MMP3
DNA sequencing	Epithelial component: BRAFV600E. Mesenchymal component: CTNNB1
Follow-up	No recurrence

**Atypia of undetermined significance, **Follicular lesion of undetermined significance.*

Discussion

PTC are unique tumours with morphological variants including follicular, diffuse sclerosing, tall cell, and columnar cell, among others [5-6]. The rarest and inadequately described variant is PTC-FMS. It manifests as a dual tumour with prominent stromal proliferation, resembling fibroblastic/ myofibroblastic proliferative lesions of the soft tissue with scattered islands of PTC. The literature documents 32 reported cases of PTC-FMS summarized in Table 1 [2-4, 7].

The pathogenesis of stromal proliferation is elusive, some authors suggesting a myofibroblastic nature based on immunohistochemical and ultrastructural studies [8]. Earlier, the term PTC-NFS

was used synonymously with PTC-FMS. WHO Classification of Endocrine and Neuroendocrine Tumours 2022 describes them under PTC with fibromatosis/fasciitis-like/desmoid-like stroma [9].

Morphologically, they appear cytologically bland, so differentiation needs immunohistochemistry and molecular tests to identify CTNNB1(beta-catenin) mutations in Desmoids Fibromatosis (FM), USP6 rearrangements in Nodular Fasciitis (NF) and BRAFV600E mutations in PTC. Even though these entities are discussed in WHO, literature review suggests different clinical outcomes. PTC-FMS is potentially aggressive with a risk of recurrent disease [10], whereas PTC-NFS is indolent and self-limiting. NF and FM in soft tissue can be differentiated morphologically by subtle features such as increased mitotic figures, lymphocytes, and RBCs, which are present in NF.Na *et al*. [7] described a case with nuclear and cytoplasmic accumulation of β-catenin, cytoplasmic TGF-β, and nuclear Smad-2 and smad-4 in stromal cells, indicating a molecular profile consistent with FM. The epithelial cells showed similar positivity.

Rebecchini *et al*. [4] described 2 cases with heterozygous mutation in exon 3 of CTNNB1 in the mesenchymal component, contrary to the heterozygous BRAFV600E mutation in the epithelial component on DNA sequencing. In both cases, the epithelial component showed cytoplasmic and membrane staining for β-catenin. This suggests both components are neoplastic with distinct molecular alterations, refuting theories like reactive change to carcinoma cells, metaplastic spindle cell transformation of follicular derived lesion. They proposed that the presence of CTNNB1 mutation in the mesenchymal component confirms a neoplastic change in the WNT/β-catenin pathway comparable to that occurring in fibromatosis and never seen in NF and thus PTC with Desmoid-type Fibromatosis (PTC-DTF) is a better term to describe these tumours.

Surgical excision with clear margins is the effective treatment, as the predominant spindle cell component lacks thyroglobulin and is unlikely to respond to radio-iodine therapy. The diagnosis of PTC-FMS can be challenging on FNAC and histopathology. Aspiration of only mesenchymal components could be misinterpreted as sarcoma [10]. The present case was inconclusive on the first aspiration. A review of the slides showed haemorrhage with clusters of spindle cells. In situations where the epithelial component is not sampled, chances of misdiagnosing this tumour as benign (fibrous thyroiditis/ solitary fibrous tumour) exists. Carcinosarcoma can be excluded by the absence of pleomorphism and the non-epithelial nature of the spindle cell component using IHC.

Conclusion

PTC-FMS is a rare PTC variant with two subtypes: PTC-NFS and PTC-FMS/PTC-DTF, the latter being more aggressive. Follow-up showed no tumour recurrences and minimal lymph node metastasis. FNAC may be inadequate due to the spindle cell predominance, and tru-cut biopsy risks misdiagnosis. Unlike other thyroid cancers, radio-iodine therapy is usually ineffective for PTC-FMS.

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