Papillary Thyroid Carcinoma With Nodular Fasciitis-like Stroma
Pitfalls in Fine-Needle Aspiration Cytology

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- Papillary thyroid carcinoma with nodular fasciitis-like stroma is one of the rare variants of papillary thyroid carcinoma. The problems posed by the exuberant nodular fasciitis-like stroma, which obscures the neoplastic nature of the tumor, are recognized in surgical pathology but have received little attention in the cytopathology literature. We report a rare case of papillary thyroid carcinoma in which nodular fasciitis-like stroma posed difficulty on fine-needle aspiration cytology. The differential diagnosis of fibroproliferative processes in thyroid fine-needle aspirations is also discussed.

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Papillary thyroid carcinoma (PTC) is the most frequent malignant neoplasm of the thyroid gland. A few recent reports of PTC have illustrated extensive proliferation of the stroma, resembling granulation tissue or fibromatosis; these variants have been described as having fibromatosis-like stroma or nodular fasciitis-like stroma.1–5 The extensive proliferation of fibroblasts can occasionally obscure the neoplastic cells of PTC, causing difficulties in histologic diagnosis.5 The problems posed by such cases have received little attention in the cytopathology literature. We recently encountered a case of PTC carcinoma in which extensive nodular fasciitis-like stroma resulted in an erroneous fine-needle aspiration (FNA) diagnosis. This report draws attention to the major diagnostic problems caused by nodular fasciitis-like stroma in papillary carcinoma of the thyroid when using FNA cytology.

CASE REPORT

An 82-year-old man presented with a 1-week history of a rapidly growing mass in his right neck. The patient also complained of dysphagia and hoarseness for several days. Physical examination revealed an 8-cm, firm, oval mass extending from the lower to middle portion of the neck. The bulkiness of the mass and its fixation to the underlying soft tissue made it difficult to determine the relationship of the mass to the thyroid. Computed tomographic scan findings were equivocal and could not definitely establish the origin of the mass from the thyroid gland. Fine-needle aspiration was performed and was reported as “malignant neoplasm with cytologic features suggestive of a myxoid sarcoma.” An open biopsy was also performed, and 2 weeks later the patient underwent subtotal thyroidectomy.

METHODS

All cytologic and histologic material from the case was reviewed. Cytologic material was obtained by the cytopathologist using a 23-gauge needle attached to a 20-cc plastic syringe. Smears were either air-dried and stained with Diff-Quik or fixed immediately in 95% ethanol and stained with the Papanicolaou method. Surgical slides were stained with hematoxylin-eosin. Immunohistochemical studies were performed on paraffin sections with the avidin-biotin-peroxidase complex technique. The antibodies included vimentin (1:10, Dako Corporation, Carpinteria, Calif), thyroglobulin (1:1000, Dako), pancytokeratin (1:50, Novo- castra, Vector Laboratories, Burlingame, Calif), muscle-specific actin (1:100, Dako), desmin (1:600, Dako), and S100 protein (1:500, Dako). Positive and negative control results were appropriate.

RESULTS

Cytologic Findings

Fine-needle aspiration yielded predominantly a monomorphic population of bland spindle cells admixed with myxoid material in the background (Figure 1). Occasional spindle cells with hyperchromatic pleomorphic nuclei with conspicuous nucleoli were identified arranged singly and in clusters (Figure 2). No mitotic activity was identified. No thyroid follicular cells or colloid was detected. The FNA interpretation was that of a malignant neoplasm most consistent with myxoid sarcoma. An open biopsy was recommended for confirmation.

Gross Findings

The open biopsy, as well as the thyroidectomy specimen, revealed an irregular, tan, fleshy, poorly circumscribed tumor involving the right lobe of the thyroid gland. The aggregate dimension of the excised tumor mass was 7.0 × 7.0 × 6.0 cm.

Histologic Findings

The tumor was composed of epithelial and stromal components. The stromal component accounted for 80% of the tumor mass and was composed of irregular fascicles of spindle cells lying in a vascularized fibromyxoid matrix (Figures 3 and 4). The spindle cells had oval to elongated nuclei with fine chromatin and small distinct nucleoli. Occasional stromal cells with enlarged nuclei were also identified. Rare mitotic figures were present. Areas of pure...
stroma totally devoid of epithelial component, measuring 15 to 20 mm in diameter, were noted. Overall, the histologic features of the stromal component were reminiscent of nodular fasciitis-like areas. Rare degenerating skeletal muscle fibers entrapped in the periphery of the stromal component were also identified. Hemorrhagic and necrotic areas were noted in the vicinity of the needle tract of the prior FNA. The epithelial component was composed of glandular structures and papillae of cuboidal to columnar tumor cells. Intranuclear inclusions and overlapping, pale to ground glass, and grooved nuclei were identified (Figure 5). The histologic features of the epithelial component were typical for PTC.

Immunohistochemistry

The spindle cells were positive for vimentin and muscle-specific actin and negative for cytokeratin and thyroglobulin. Occasional spindle cells also stained with desmin. Cytokeratin and thyroglobulin staining was demonstrated in the epithelial component of the tumor.

COMMENT

This case represents a rare morphologic variant of PTC previously described as PTC with nodular fasciitis-like stroma. For surgical pathologists, the importance of recognizing this variant of PTC is that when one encounters
a fibroproliferative lesion of the thyroid, a diligent search should also be made for PTC.5 This variant must also be distinguished from the vastly more aggressive PTCs with anaplastic transformation and the so-called carcinosarcomas.5 This article describes the potential pitfalls in interpreting FNAs of thyroid glands harboring this variant and also discusses the differential diagnosis of fibroproliferative processes in thyroid FNAs.

A population partially or solely comprising spindle cells may be encountered in FNAs of the thyroid gland.6 The diagnostic dilemma pertaining to spindle cells is on one hand related to atypical reactive myoﬁbroblasts with pleomorphic nuclei, prominent nucleoli, and mitotic ﬁgures, which can be seen in goiters and inﬂammatory thyroiditis. On the other hand, spindle cells with nuclear atypia may represent anaplastic carcinoma and medullary carcinoma or sarcoma. Although in most cases careful attention to chromatin pattern, pleomorphism, mitotic activity, and anaplasia can distinguish between benign and malignant spindle cells in thyroid aspirates,7 at times the distinction between benign reactive ﬁbroblasts and malignant spindle cells may be diﬃcult or impossible.

Extensive ﬁbrosis may be encountered in some forms of thyroiditis, such as ﬁbrous variant of Hashimoto’s thyroiditis, Riedel’s thyroiditis, and de Quervain’s thyroiditis. Aspirates of such lesions are usually paucicellular and may yield ﬁbroblasts with unusual cytologic features. Thoroug sampling of such lesions may help identify foci of Hürthle cells and lymphocytes in Hashimoto’s thyroiditis8 and multinucleated cells in de Quervain’s thyroiditis.9 Riedel’s thyroiditis is rarely seen in practice. Aspirate smears contain few cells composed of lymphocytes, scattered ﬁbroblasts, few follicular cells, and rare multinucleated cells. Although distinguishing between Riedel’s thyroiditis and the ﬁbrous variant of Hashimoto’s thyroiditis may be diﬃcult on the basis of cytologic evaluation alone, clinical features may be useful.6 A history of dyspnea and constrictive symptoms related to involvement of local structures by ﬁbrotic processes are common in Riedel’s thy-
roiditis, and antimicrosomal antibody titers are commonly elevated in patients with Hashimoto’s thyroiditis. Bland spindle cells compatible with ﬁbrous stroma occurring in association with tumor cells of PTC have also been described on aspirate smears.10

In our case, the spindle cells with nuclear atypia and pleomorphism and myxoid background were misinterpreted as malignant tumor cells, resulting in an erroneous diagnosis of myxoid sarcoma. The diagnostic hazard of cellular atypia and myxoid background in nodular fasciitis resulting in a false-positive diagnosis has been described previously.11 Diagnosis on histologic sections was also very challenging in our case. Initial diagnostic considerations based on the exuberant spindle cell component included PTC with anaplastic transformation and carcinosarcoma. However, the diagnosis of nodular fasciitis-like process was supported by the lack of atypical mitotic ﬁgures, the immunohistochemical proﬁle compatible with myoﬁbroblasts, and the clinical history of a rapidly growing mass. The stroma taken in isolation in our case resembled the nodular fasciitis-like stroma described in other case reports.1-5 A retrospective review of aspirate smears in conjunction with histologic slides revealed that the spindle cells on the aspirate smears represented a component of nodular fasciitis-like stroma. The identiﬁcation of nodular fasciitis-like stroma in the preoperative FNA excluded the possibility that the stromal changes in histologic sections were due to the FNA (iatrogenic).

Recognition of a variant of a tumor is important if the variant has a diﬀerent clinical outcome or if its identiﬁcation is critical in avoiding diagnostic misinterpretations. Although long-term follow-up is not available for the cases of PTC with nodular fasciitis-like stroma, short-term follow-up on reported cases does not appear to be any diﬀerent from that of classic PTC. Our patient was alive and well and had no evidence of disease 1 year following surgery. Chan et al13 emphasized that the importance of recognizing PTC with nodular fasciitis-like stroma is that the neoplastic nature of the lesion may be missed as a result
of attention to the stromal component forming the bulk of the tumor; there may be large areas within the tumor mass completely devoid of the carcinomatous component. In their series, a provisional diagnosis of fibroproliferative lesion was made at the time of intraoperative frozen section in 1 of 3 cases.

Our case illustrates that aspiration cytology in such cases may be even more diagnostically challenging. It is conceivable that if the bulk of this tumor is composed of nodular fasciitis-like stroma, the aspiration of the epithelial component of the tumor may be difficult or impossible. In our case, despite 3 passes we were not able to demonstrate any neoplastic epithelial component. Furthermore, nodular fasciitis-like stroma may be mistaken for a neoplastic process, such as a sarcoma. If seen in association with PTC, these findings may result in the erroneous diagnosis of anaplastic carcinoma (ie, transformation of PTC), especially in an elderly patient. Hence, an open biopsy may be required for definitive diagnosis.

In conclusion, PTC with exuberant nodular fasciitis-like stroma may be difficult to diagnose accurately using FNA, especially if the bulk of the tumor is composed of such stroma and the papillary carcinoma is so small that it may be missed during FNA. Awareness of the association of nodular fasciitis-like stroma with PTC may prevent diagnostic errors in FNAs of the thyroid gland. Excisional biopsy studies may be required for definitive diagnosis.

References