Cytopathologic and Molecular Diagnostic Clues to Poorly Differentiated Thyroid Carcinoma: A 10-year Single Institution Experience

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ABSTRACT

Background: Poorly differentiated thyroid carcinoma (PDTC) is a rare thyroid neoplasm with clinical behavior between differentiated thyroid carcinoma and anaplastic thyroid carcinoma. PDTC often displays insular architecture, necrosis and increased mitotic activity on histopathologic evaluation. However, there are few studies describing cytological features of this rare tumor, which are important for a preoperative diagnosis. In this retrospective study, we review our experience in the fine needle aspiration (FNA) diagnosis of PDTC.

Design: Cases of PDTC were collected from our archives, a tertiary referral hospital, between the years 2002-2012. Of 21 cases surgically diagnosed as PDTC, 16 patients had preoperative FNA evaluation and were included in this study. Four cases had BRAF mutation analysis in addition to cytological evaluation. These cases were retrospectively reviewed by two cyto-pathologists.

Results: Eleven patients were men and five were women. The mean age was 56 years, ranging from 22 to 70 years. The original cytological diagnoses (16 patients) were as follows: 1 "benign" (FNA performed on one calcified nodule contralateral to eventual malignancy), 7 follicular neoplasm, 2 positive for malignancy-NOS, 4 papillary thyroid carcinoma (PTC) and 2 PDTC. Nine cytological specimens were available for review, the cytological features of which were listed in Table 1. Four cases were tested for BRAF mutation; all were negative.

Conclusions: Our results illustrate that PDTC can be difficult to diagnose on cytological specimens. However, in FNA samples with high cellularity, absence of colloid, a trabecular architectural pattern and numerous single cells that exhibit pleomorphism with abundant cytoplasm, a diagnosis of PDTC should be considered. Necrosis and mitotic figures are very helpful, but unfortunately, are very rare in cytological specimens. BRAF mutation testing does not assist with the diagnosis.

BACKGROUND

Poorly differentiated thyroid carcinoma (PDTC) is a distinct type of thyroid neoplasia described in 1984 by Carcangiu et al. The biological features and morphological appearance fall between differentiated thyroid carcinomas and anaplastic thyroid carcinoma. PDTC is characterized by locally aggressive behavior and often displays insular architecture (formation of nests of tumor cells). Necrosis and increased mitotic activity has been reported on histopathologic evaluation. However, there are only few studies describing cytological features of this rare tumor, which are important for a preoperative diagnosis. Some cases were misdiagnosed cytologically as papillary or follicular carcinoma. In this retrospective study, we reviewed our experience in the FNA diagnosis of PDTC.

METHODS

Cases of PDTC were collected from our archives, a tertiary referral hospital, between the years 2002-2012. Of 22 cases surgically diagnosed as PDTC, 17 patients had preoperative FNA evaluation and were included in this study. Nine cytological specimens were available for review. Four cases had BRAF mutation analysis in addition to cytological evaluation. These cases were retrospectively reviewed by two cytopathologists.

RESULTS

Table 1. Clinicopathologic features of PDTC.

Average age (± SD)	56.4 ± 13.9
Gender	11M; 5F
Cytologic diagnosis (n=16)	
Benign (goiter) *	1 (6.3%)
Follicular neoplasm	7 (43.7%)
Poorly differentiated malignancy	2 (12.5%)
Papillary thyroid carcinoma	4 (25.0%)
Poorly differentiated carcinoma	2 (12.5%)
BRAF mutation analysis	0/4

* The FNA was done on a nodule adjacent to the tumor

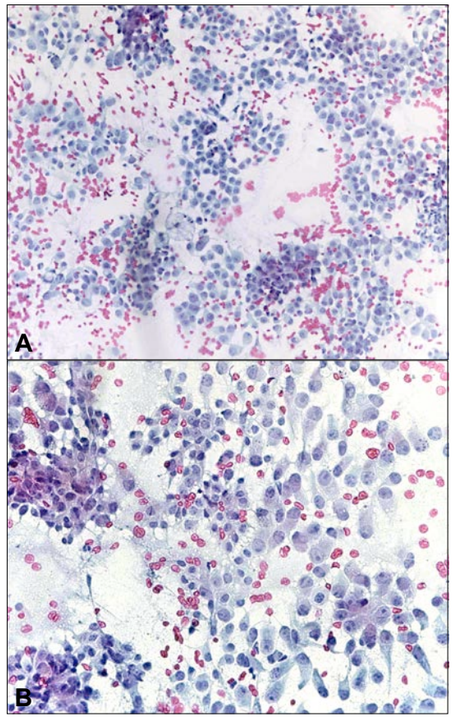

Figure 1. Cytological features of poorly differentiated thyroid carcinoma on fine needle aspiration biopsy. (**A**) FNA specimen from a 45 year old male patient with PDTC. The smear shows cohesive sheets and single scattered cells (x100). (**B**) Higher power view of the smear from the same patient as A, tumor cells show plasmacytoid changes with eccentrically located round to oval vesicular nuclei and small prominent nucleoli (x400).

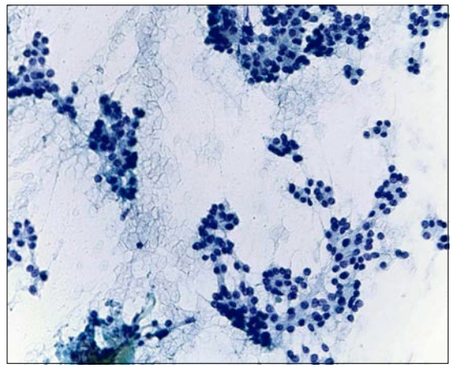

Figure 2. FNA smear from a 47 year old female patient with PDTC (diagnoses as SF follicular lesion on FNA), shows cohesive clusters of cells with round to oval nuclei and small nucleoli (x100).

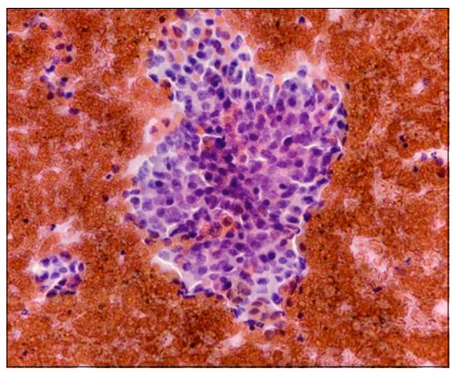

Figure 3. FNA smear from a 61 year old male patient with PDTC, shows clusters of tumor cells with endothelial wrapping (x400).

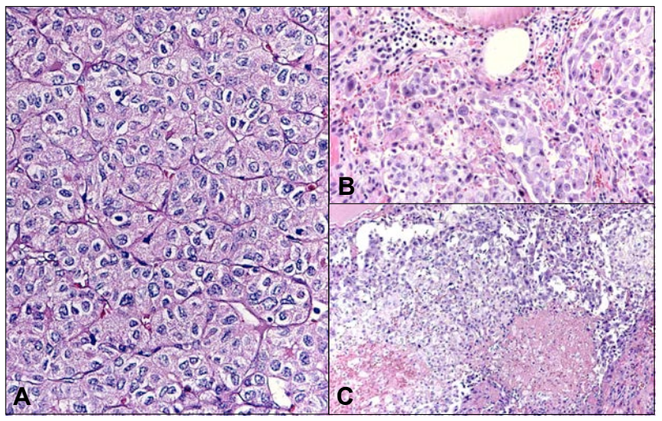

Figure 4. Morphological features of PDTC on surgical resection specimens (H&E). A, Tumor cells show typical insular growth pattern (same patient as Figure 3, x400). B&C, Nests of tumor cells show marked pleomorphism, increased mitotic figures and necrosis, B: x200, C: x100).

Table 2. Cytomorphology of Poorly Differentiated Thyroid Carcinoma

Cytomorphological Features	Cases (n)	%
High Cellularity	9	100
Absence of colloid	7	77.8
Trabecular architecture	6	66.7
Numerous single cells	6	66.7
Abundant cytoplasm	6	66.7
Pleomorphism	4	44.4
Papillary pattern	3	33.3
Microfollicular pattern	3	33.3
Plasmacytoid cells	3	33.3
Vacuoles	1	11.1
Endothelial Wrapping	1	11.1
Necrosis	0	0
Mitotic Figures	0	0

CONCLUSIONS

Our results illustrate that PDTC can be difficult to diagnose on cytologic specimens. However, in FNA samples with high cellularity, absence of colloid, a trabecular architectural pattern and numerous single cells that exhibit pleomorphism with abundant cytoplasm, a diagnosis of PDTC should be considered. Necrosis and mitotic figures are very helpful, but unfortunately, are very rare in cytologic specimens. BRAF mutation testing does not assist with the diagnosis.

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