Case #1

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Case -1

• Clinical history:
  – 45-year-old female
  – Solitary nodule in left lobe of thyroid
  – Partially cystic
  – 1.3 cm

• Procedure:
  – Ultrasound-guided fine needle aspiration biopsy
• Cytological features:
  – Single cells and clusters of cells
  – Vacuolated cytoplasm
  – Round to oval nuclei
  – No nuclear grooves; no nuclear pseudoinclusions
• Immediate Impression:
  – Predominantly macrophages
• Final Interpretation:
  – Papillary carcinoma
• Final Diagnosis:
• Thyroid, total thyroidectomy:
  – Papillary carcinoma
  – Extrathyroidal extension, focal
  – Metastatic carcinoma in 1/20 lymph nodes
• Cystic change in thyroid nodules
  – Not uncommon\textsuperscript{1}
  – Incidence: $\sim$32\%\textsuperscript{2}
  – Malignancy in cystic lesions: 9.1\% to 13\%\textsuperscript{3,4}
  – Cystic PTCs: false negative diagnoses\textsuperscript{3,5}
    • Scant epithelial cellularity
    • Degenerative changes\textsuperscript{6}
    • Admixed with macrophages, hemosiderin, cellular debris

\textsuperscript{1}Faquin WC, Cibas ES, Renshaw AA. \textsuperscript{2}Lin JD, Hsuen C, et al.\textsuperscript{3}Layfield L. \textsuperscript{4}Hsu C, Boey J. \textsuperscript{5}Castro-Gomez L et al. \textsuperscript{6}Kini SR et al.
Kini SR

- Nodular goiter with cystic change
  - Exclusively or predominantly histiocytic cell population with variable numbers of follicular cells.
  - Normal size follicular cells.

- Cystic papillary carcinoma
  - Exclusively or predominantly histiocytic cell population, mixed with variable numbers of malignant follicular cells.
  - Malignant cells variably enlarged.

Renshaw AA

• 7 (6%) PTCs with neoplastic cells resembling histiocytes

• Atypical cytological features
  – Size: Large--cell and nucleus
  – Nucleus: Nucleoli; no grooves or inclusions
  – Cytoplasm: Vacuolated
  – Calcifications: Present (6/7)

• CK+
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# Atypical Histiocytoid Cells versus Benign Histiocytes

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Cyst-lining cells

- Cohesive flat epithelial sheets
- Spindle-shaped nuclei
- Distinct borders
- Intercellular windows
- No intranuclear inclusions or grooves

Faquin WC et. al.
Histiocytic aggregates in nodular goiter mimicking PTC\textsuperscript{1}

- Histiocytes can form large tissue fragments and monolayer sheets.
- Cytoplasm
  - Foamy
- Nuclear atypia
  - Enlarged nuclei
  - Elongated nuclei
  - Nuclear clearing
  - Nuclear grooves
  - Nuclear membrane thickening

\textsuperscript{1}Nassar et al.
Conclusions

• Papillary thyroid carcinoma (PTC) with atypical histiocytoid cells
  – Rare pattern
  – Cells intermediate between those of PTC and histiocytes.
  – Atypical histiocytoid cells may represent the only diagnostic cells.
  – Immunostains (CK, TTF-1, CD68) are helpful.
  – Not restricted to cystic lesions.

1Renshaw AA. 2Harsh M et al.
References

Papillary Thyroid Carcinoma with Atypical Histiocytoid Cells

Papillary thyroid carcinoma (PTC) is the most common malignant thyroid neoplasm [1,2]. Unlike follicular neoplasms, the diagnostic specificity and accuracy of PTC by fine needle aspiration is high—approximately 94%[3]. Most PTCs have a “classical” pattern. Typically smears show neoplastic cells arranged as two-dimensional sheets and papillary clusters. The nuclei are often enlarged and elongated and display fine chromatin, intranuclear pseudoinclusions, and grooves. Nucleoli are inconspicuous or pinpoint.

Also, there is literature describing diagnostic cytological hallmarks of other variants of PTC, such as follicular, oncocytic, and tall cell, which are diagnosed on histology and listed in the WHO classification [4-7]. Kini, in 1996, briefly illustrated PTC with cells having features resembling those of histiocytes [8]. Although this is not a recognized entity by the WHO, identification of the neoplastic nature of the atypical histiocytoid cells, which can predominate in cytological specimens, can be challenging [9].

The characteristics of PTC with atypical histiocytoid cells have been elaborated on by Renshaw and Harshan et al (Table 1) [9,10]. Cytological preparations from these specimens typically show pleomorphic, enlarged cells with high nuclear-to-cytoplasmic ratios usually forming clusters with occasional single cells. The cells have cytoplasm with large vacuoles. The nuclei are also enlarged, tend to be mostly round to oval and have prominent, conspicuous nucleoli. In some cases, intranuclear pseudoinclusions and grooves are also present. The background is devoid of colloid and has ‘normal’ histiocytes, including hemosiderin-laden macrophages. Cells typical of classical PTC may also be found.

Given that cystic change can be identified in approximately one third of thyroid nodules [11] [12], the atypical vacuolated cells may be interpreted as benign histiocytes and part of a cystic nodule, especially in cases that lack intranuclear pseudoinclusions, grooves, and fragments/sheets of epithelial cells. Several features can help distinguish ‘normal’ histiocytes from atypical histiocytes of PTC (Table 2). Most commonly, histiocytes, in
contrast to atypical histiocytoid cells, occur singly, have low nuclear-to-cytoplasmic ratios, smooth nuclear borders, no nucleoli, finely vacuolated cytoplasm and hemosiderin.

The differential diagnosis for the vacuolated cells also includes primary thyroid carcinoma with clear cell change and metastases. Renal cell carcinoma represents approximately half the metastases to the thyroid [13]. Features that favor primary thyroid carcinoma with clear cell change include presence of papillary and follicular growth patterns [14]. Also, the cell clusters of PTCs with atypical histiocytoid cells are not associated with vessels, a feature that may be expected in renal cell carcinoma. A limited panel of immunostains (cytokeratin, TTF-1 and/or CD68) on additional material, if available, is also helpful in making the distinction between epithelial cells of thyroid origin and histiocytic cells.

Interestingly, in the surgical resections of PTCs with the atypical histiocytoid cells, the cystic areas are often focal [9] [10]. Also, on histology both classical PTC and areas with atypical histiocytoid cells are identified, with the latter representing a minor component. The histiocytoid cells tend to line the cyst walls, form aggregates in the cyst spaces, or associate with calcifications. Classical PTC, meanwhile, is present more distant from the cystic spaces.

The presence of atypical histiocytoid cells along the cystic component suggests that perhaps the cystic microenvironment plays a role in the altered morphological appearance. Another theory suggests that the changes may be related to the presence of calcifications [10]. Additional cases need to be examined to assess the cause of this change and interpret its significance, if any.
Table 1: Papillary thyroid carcinoma versus papillary thyroid carcinoma with atypical histiocytoid cells

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Harshan et al. PTC: papillary thyroid carcinoma;

Table 2: Atypical histiocytoid cells of papillary carcinoma versus benign histiocytes*

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* Most common features.
Key words:

Thyroid, papillary carcinoma, histiocytes, histiocytoid

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