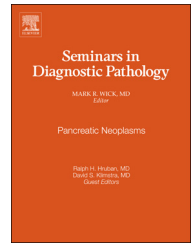


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Undifferentiated (anaplastic) thyroid carcinoma: Practical immunohistochemistry and cytologic look-alikes

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ABSTRACT

Aspirate smears of undifferentiated (anaplastic) thyroid carcinoma (ATC) are, in most instances, readily recognized as malignant. Nonetheless, pitfalls exist with this neoplasm in part due to the absence of epithelial markers, overlapping features with other malignancies that may metastasize to or arise within the thyroid, and potential confusion with non-neoplastic conditions that simulate malignancy. We highlight the salient morphologic features of ATC and its variants, useful discriminatory ancillary immunostains to recognize it, and ATC mimickers that have the potential to confuse the cytopathologist.

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Introduction

Undifferentiated (anaplastic) thyroid carcinoma (ATC) comprises 2–5% of all thyroid carcinomas.¹ The classic clinical scenario is an older woman ($x = 70$ yr) presenting with a rapidly growing (a matter of weeks) neck mass. Associated symptoms may include dysphagia, hoarseness, a feeling of “choking,” and dyspnea. ATC can develop in iodine-rich and -deficient regions, in patients with a long-standing “goiter,” and in those with a prior history of differentiated thyroid carcinoma or no prior thyroid disease at all.² ATC is extremely aggressive with extrathyroidal extension and metastases to regional lymph nodes and often at distant sites at the time of presentation. Mortality exceeds 95%, and the mean survival is less than 6 months.³

Most fine-needle aspiration (FNA) biopsy examples of ATC share certain morphologic features.^{4–8} Smears are moderately markedly cellular, but an occasional sparsely cellular example is encountered whenever ATC contains considerable

fibrosis or necrosis. ATC smears commonly contain cells exhibiting a variety of shapes including epithelioid/polygonal, spindle, plasmacytoid, rhabdoid (rare), binucleate, and multinucleated forms dispersed in variably sized syncytial clusters and as single cells. A single cell type may predominate, or several shapes may simultaneously exist on the same slide (s). Most cells are large, but a wide range of cell sizes is common. Cell nuclei are typically enlarged and variable in shape with elongated, fusiform, rounded, or pleomorphic contours. Nuclei have coarse chromatin, misshapen (often enlarged) nucleoli, and occasional intranuclear cytoplasmic inclusions (Fig. 1A). Cytoplasm varies from minimal to abundant; cytoplasmic vacuoles and squamoid features including focal keratinization are possible. Both typical and atypical mitotic figures may be seen. Smears often contain background necrotic debris, but colloid is minimal if present at all. A rather common feature of ATC smears is the presence of a florid neutrophilic background^{6,8} (Fig. 1B). This acute inflammatory infiltrate can occasionally be so overwhelming

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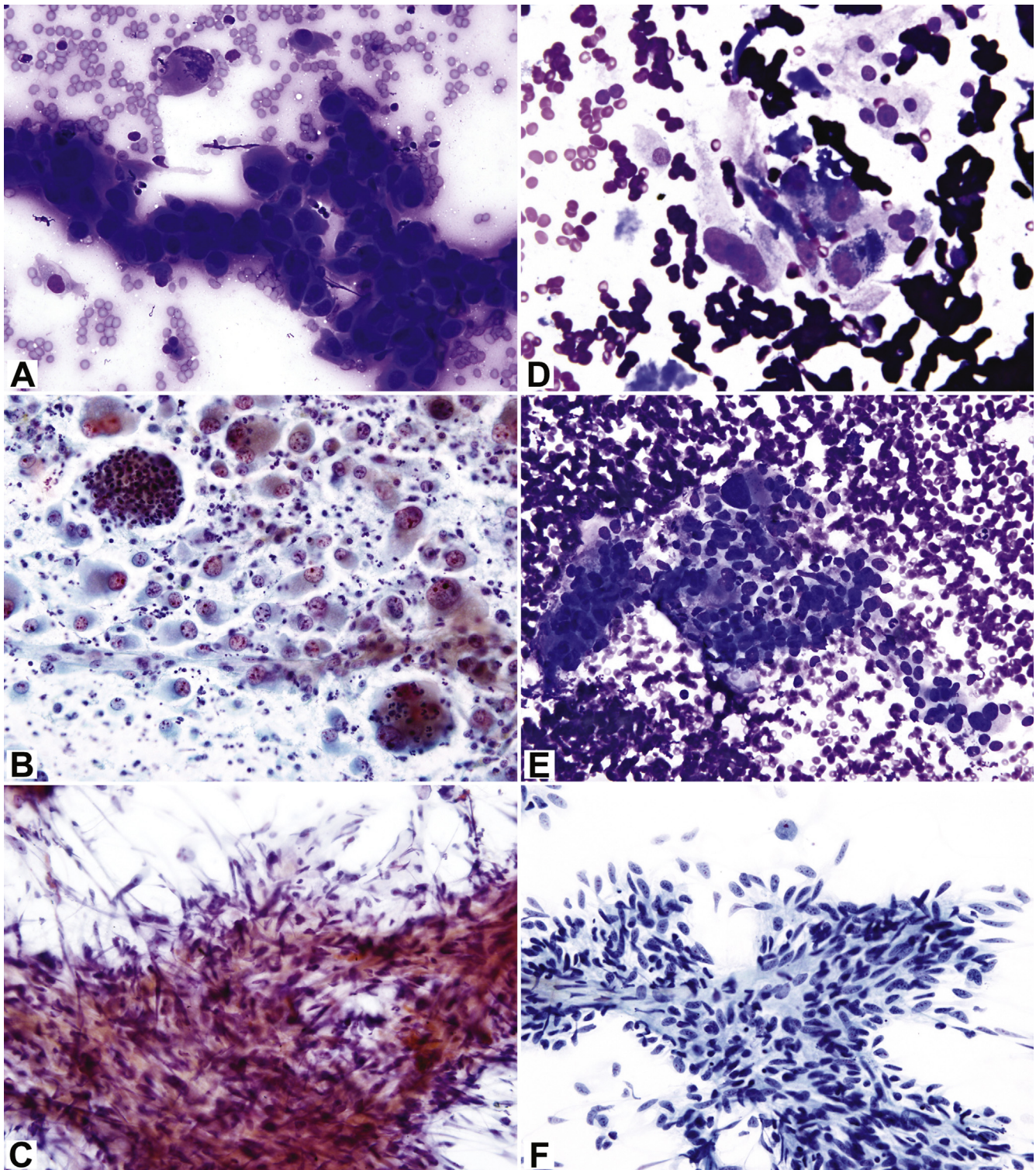


Fig. 1 – (A) ATC. Pleomorphic epithelioid cells in a cord-like arrangement exhibit marked size variation. Note the atypical mitotic figure near the top of the field, Romanowsky stain. **(B)** ATC. A dense neutrophilic infiltrate accompanies cells in a dissociated pattern. Eccentric nuclear placement and binucleation are reminiscent of malignant melanoma. Neutrophilic emperipolesis partially obscures some cell nuclei, Papanicolaou stain. **(C)** Sarcomatoid variant of ATC shows a 3-dimensional hypercellular syncytium of monotonous malignant spindled cells, Papanicolaou stain. **(D)** Benign thyroid. Markedly atypical, but reactive fibroblasts are a minor component of this benign thyroid aspirate. Microfragments of colloid are seen, Romanowsky stain. **(E)** Medullary thyroid carcinoma. A huge hyperchromatic polygonal cell appears “out of place” or “alien” in this population of otherwise isomorphic rounded cells, Romanowsky stain. **(F)** Angiosarcoma. This spindle cell sarcoma is almost a perfect mimic of the spindled ATC illustrated in **(C)**, Papanicolaou stain.

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