Medullary thyroid carcinoma (MTC) is an uncommon neuroendocrine neoplasm arising from calcitonin-producing C-cells. Most cases arise sporadically, but about 20 percent may be associated with familial syndromes such as multiple endocrine neoplasia (MEN) 2A (Sipple syndrome) or 2B (mucosal neuroma syndrome), familial medullary thyroid carcinoma syndrome, von Hippel-Lindau disease, or neurofibromatosis. Patients are surgically managed with a total thyroidectomy, and up to 50 percent will have metastatic disease found in regional lymph nodes.

The aspirates of MTC are generally hypercellular and contain malignant cells either singly or in loosely cohesive groups. The cells may be uniform or markedly pleomorphic, ranging from round to polygonal to spindled. The nuclei are frequently eccentrically placed, the chromatin often exhibits the stippled pattern characteristic of a neuroendocrine tumor, and there are inconspicuous nucleoli. The amount of cytoplasm varies from indiscernible to abundant, and azurophilic granules can sometimes be seen in modified-Giemsa-stained preparations. Intracellular inclusions and fluffy, finely granular or dense acellular material consistent with amyloid are frequently seen.

Immunocytochemistry will show immunoreactivity to calcitonin, CEA, neuroendocrine markers, and TTF-1. Elevated serum calcitonin levels help to confirm the diagnosis. The morphologic differential diagnosis includes entities such as a Hurthle cell neoplasm, papillary thyroid carcinoma, undifferentiated/anaplastic carcinoma, lymphoma, and metastatic disease.

(Kiri SR. Color Atlas of Differential Diagnosis in Fine-needle and Aspiration Cytology, 2nd ed. Images courtesy of Jennifer Brainard, MD, and Charles Sturgis, MD. Text by Kristen Natale, DO.)

**Cell block prep, calcitonin stain**

**Thyroidectomy specimen, H&E**

Left: 40x magnification. Dycohesive plasmacytoid cells with granular cytoplasmic staining.

Right: 60x magnification. Spindled cells arranged in fascicles with intranuclear inclusions.