Undifferentiated thyroid carcinoma

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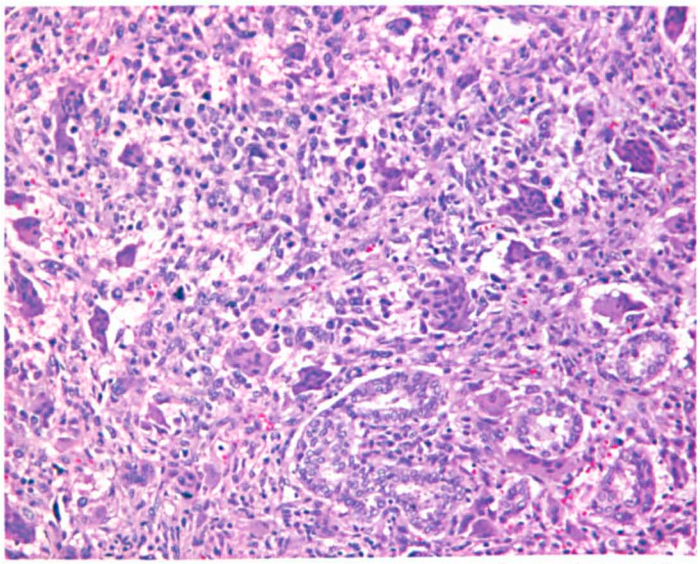

Figure 1. An undifferentiated carcinoma is present in association with a papillary carcinoma (lower right). Note the osteoclastic-type giant cells.

Undifferentiated carcinoma (also known as *anaplastic carcinoma)* of the thyroid gland is a highly aggressive malignant neoplasm composed of undifferentiated cells that exhibit immunohistochemical or ultrastructural epithelial differentiation. Nearly all patients report a long history of thyroid gland disease, often goiter or Hashimoto thyroiditis. In most cases, there is a transformation from a papillary (80%) or follicular carcinoma into undifferentiated carcinoma. Radiation exposure is reported in about 10% of patients.

While accounting for only 2% of all thyroid gland malignancies, undifferentiated carcinoma accounts for >60% of thyroid cancer mortality. The majority of patients are elderly, with a slight female predilection. Patients present with a rapidly enlarging, firm-hard neck mass, usually involving a single lobe (60%). In addition, many patients also report hoarseness, vocal fold paralysis, and pain. Soft-tissue or adjacent organ (esophagus, trachea) extension by the tumor is common.

In spite of multimodality therapy, the prognosis is still grave, with >95% of patients dead from disease in <9 months. There is a worse prognosis for patients aged >60 years, male, with >5-cm tumors or extensive local disease. By definition, all tumors are pT4 and separated into groups IVA, IVB, and IVC based on extent of local and metastatic disease. The tumors are fleshy to firm, usually replacing the thyroid gland parenchyma, with an infiltrative and irregular border. They nearly always show extrathyroid gland extension. The tumors are large, with a mean size of 6 cm.

Histologically, undifferentiated thyroid carcinomas show a variety of patterns, from sheet-like, storiform, fascicular, angiomatoid, and meningothelial to solid, exhibiting extensive lymph-vascular invasion. There is usually extensive coagulative-type necrosis, hem-

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part of the class I major histocompatibility complex antigen, is the major protein constituent of the amyloid fibrils. It fails to cross the dialysis membrane, resulting in the formation of amyloid fibrils.[2]

Amyloid involvement of the oral tissues is rather rare; when it does occur, the tongue is the most frequent location, and amyloidosis in this area usually manifests as rubbery or firm macroglossia.[3] Amyloidosis of the tongue results in white-yellow nodules >1 mm in diameter and firmer than the other parts of the tongue.[4] Petechiae, ecchymoses, and hemorrhagic blisters may also be present.[1,3] Zhou et al[5] reported 14 patients with oral amyloidosis, 12 of whom had macroglossia. Our patient did not show macroglossia, but hemorrhagic and ulcerated nodules were observed on the tongue and buccal mucosa.

In one study, 8 cases of DRA were found as tongue amyloid nodules among 103 long-term (>20 years) hemodialysis patients.[6] Our patient had been on hemodialysis for only 8 years. The definitive diagnosis is made by tissue biopsy.[7] Treatment of DRA has been limited to surgical removal of amyloid deposits. Clinical therapeutic strategies for DRA include dialysis, medical or surgical therapy, and renal transplantation to obtain normal serum levels of β2-microglobulin.[4,8]

New high-flux, biocompatible dialysis membranes are more permeable and are effective in treating amyloidosis.[4] More effective preventive therapy strategies will be helpful for patients with DRA. Benign epithelial and connective tissue neoformation—including fibrosarcoma, malignant fibrous histiocytoma, leiomyoma, papilloma, lipoma, lymphangioma, neuroma, hemangioma, and adenoma—must be considered in the differential diagnosis of oral masses.[3]

References

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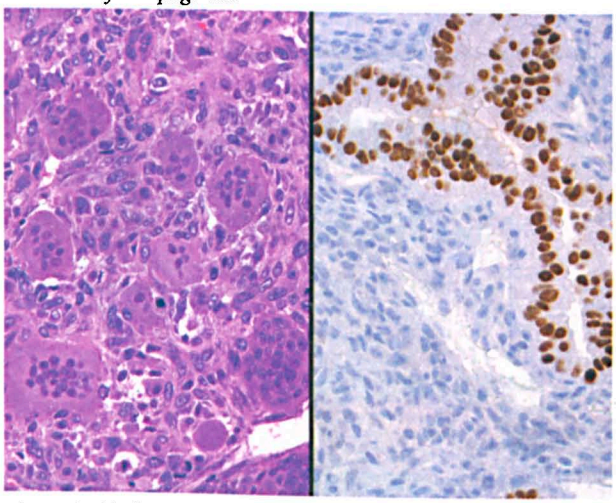

Figure 2. ***Left:*** *Numerous osteoclastic-type giant cells are present, with a pleomorphic population in the background, including mitoses.* ***Right:*** *The papillary carcinoma is strongly immunoreactive with TTF-1, while the undifferentiated carcinoma is negative.*

orrhage, and degeneration. Colloid is absent, but entrapped follicles can mimic colloid production.

The tumor cells are poorly differentiated, yielding a polygonal, pleomorphic, spindle, giant, epithelioid, or squamoid appearance. Tumor giant cells and osteoclastic giant cells are seen (figure 1). Mitoses are easily identified, are increased, and include atypical forms. Several histologic variants are recognized and include spindle cell, pleomorphic giant cell, squamoid, osteoclastic, rhabdoid, and angiomatoid variants, among others.

Because of the pleomorphic nature of the tumor, immunohistochemistry is frequently employed to confirm a diagnosis. Most tumors exhibit vimentin, keratin, CAM5.2, EMA, β-catenin, and p63 immunoreactivity, while usually negative with thyroglobulin and TTF-1 (figure 2); p53 and Ki-67 are usually strongly positive. The histologic differential diagnosis includes metastases to the thyroid gland (carcinoma, sarcoma, melanoma); primary sarcoma, lymphoma, and several primary thyroid gland malignancies (including medullary thyroid gland carcinoma); and Riedel thyroiditis.

Suggested reading

Chiacchio S, Lorenzoni A, Boni G, et al. Anaplastic thyroid cancer: Prevalence, diagnosis and treatment. Minerva Endocrinol 2008;33(4):341-57.

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