10 Thyroid Pathology

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10.1 Normal Thyroid

The normal thyroid is a bilobed gland, connected by an isthmus. It is encased by a thin capsule that does not strip easily and contains sizable venous channels. The weight of normal thyroid in the United States ranges from 10 to 20 g. The follicle is the functional unit of the thyroid and averages about 20 µm in diameter [1,2,3,4]. A thyroid lobule consists of 20–40 follicles bound together by a thin sheath of connective tissue and supplied by a lobular artery [3,5]. The thyroid follicles are formed by a single layer of low cuboidal epithelium. The nucleus of the follicular cell is round to ovoid in shape; it is usually centrally placed with an inconspicuous nucleolus. The follicle is enveloped by a basal lamina and is surrounded by numerous capillaries and lymphatics [5,6]. The follicular lumen contains colloid, partly composed of thyroglobulin, which is evenly applied to the luminal cell borders. Calcium oxalate crystals are common in the colloid of adults.

Electron microscopy demonstrates that the normal flat to low cuboidal follicular cells interdigitate and overlap one another, and that they are intimately related to the capillaries that surround the follicle; microvilli on the apical surface are numerous near the cellular margins [6,7].

C cells are intrafollicular and are seen next to the follicular cells and within the basal lamina that surrounds each follicle of the normal gland. C cells are most numerous in the central portions of the middle and upper thirds of the thyroid lobes [3]. They are believed to originate from the C cells that arise from the neural crest and migrate with the ultimobranchial body into the thyroid. C cells are typically more numerous in thyroids of infants as compared to adult glands [8,9]. They are polygonal to spindle shaped, have “light” or low density, cytoplasm, and contain numerous membrane-bound cytoplasmic granules containing calcitonin. A small number of C cells (or cells similar to them) contain somatostatin and can increase in number in some patients [10–13].

C cell aggregates can be sizeable (hyperplastic) in some adults without any known endocrinologic
abnormality [14]. C cell hyperplasia is defined as consisting of more than 40 C cells/cm² and the presence of at least three low-power microscopic fields containing more than 50 C cells [15]. The small solid cell nests of ovoid to spindled epidermoid cells in thyroid are also considered to be of ultimobranchial origin [15]. Typically, the nests have about the same distribution in the thyroid lobes as the C cells [16,17]. The term “mixed follicles” [18] applies to follicles which are lined by follicular cells and epidermoid cells (and sometimes C cells) and contain both colloid and mucoid material. The ultimobranchial structures probably also give rise to a small proportion of normal thyroid follicles [18].

Oxyphil cells (oncocyttes, Askanazy cells, Hürthle cells) are altered/metaplastic follicular cells; they are enlarged, have granular eosinophilic cytoplasm, and have large, hyperchromatic, or bizarre nuclei [19]. The cytoplasm is filled with enlarged mitochondria. They are common in longstanding Graves’ disease, autoimmune thyroiditis, thyroids affected by radiation, follicular-derived neoplasms, and some adenomatous nodules [19–21].

Small aggregates of lymphoid cells in the thyroid stroma can be seen in normal thyroid gland [22]. Also present in the interstitial tissue are antigen-presenting dendritic cells; these are sparse in the normal gland but are increased in autoimmune thyroid disease [23,24].

10.2 Developmental Variations

The thyroglossal tract extends in the midline from the foramen cecum at the base of the tongue to the isthmus of the normal gland [25]. The tract consists of connective tissue, the thyroglossal duct, lymphoid tissue, and thyroid follicles; it is attached to and may extend through the center of the hyoid bone and is intimately related to the surrounding skeletal muscle. Thyroid tissue may persist at the base of the tongue in some patients may be the only thyroid present [25,26]. The thyroglossal duct is typically lined by ciliated pseudostratified epithelium. If the duct is traumatized or infected, the epithelium may undergo alteration to transitional or squamous type, or maybe totally be replaced by fibrous tissue. Foreign body reaction and chronic inflammation may be conspicuous. If fluid accumulates in part of the thyroglossal duct, a thyroglossal cyst may develop [3,27,28].

Any type of diffuse thyroid disease can involve lingual thyroid and the thyroid tissue along the thyroglossal tract [28–30]. In rare instances portions of thyroglossal duct are included within the thyroid gland proper and, rarely, can serve as the origin of an intrathyroidal cyst [25]. Parathyroid glands, thymic tissue, small collections of cartilage, and glands lined by ciliated cells may be seen in normal thyroids, presumably related to defective development of the branchial pouches [31–33].

Because of the intimate relationship that exists in the embryo between the immature thyroid tissue and the adjacent developing skeletal muscle, strips of striated muscle are occasionally included within the thyroid [34–36].

Thyroid tissue can be found in close proximity or within the perithyroidal skeletal muscle. Such collections of thyroid tissue are particularly prominent when the gland is hyperplastic or is affected by chronic lymphocytic thyroiditis; these should not be confused with carcinoma [34,37].

Groups of thyroid follicles in lateral cervical lymph nodes always represent metastatic carcinoma (papillary carcinoma) [34,37,38]. A few experienced pathologists state normal thyroid follicles rarely occur in cervical lymph nodes [39]. Hence normal thyroid tissue lying only within the capsule of a midline node may represent an embryologic remnant and not metastatic cancer [39,40].

10.3 Goiter

Goiter is a diffuse or nodular enlargement of the gland usually resulting from a benign process or a process of unknown origin [41–43]. When there is a deficiency of circulating thyroid hormone because of inborn errors of metabolism, iodine deficiency, or goitrogenic agents, and if the hypothalamic-pituitary axis is intact, production of thyroid-stimulating hormone (TSH; thyrotropin) is increased; consequently, cellular activity and increased glandular activity and glandular mass result in an attempt to achieve the euthyroid state [43–45].

Worldwide, the most common cause for a deficient output of thyroid hormone is an inadequate amount of iodine in the diet, leading to iodine-deficiency goiter (endemic goiter) [46,47]. Other causes of hyperplasia include inborn errors of thyroid metabolism (dyshormonogenetic goiter) [48,49], dietary goitrogens, and goitrogenic drugs and chemicals [50–53].

The pathologic changes of simple non-toxic goiter include one or more of the following: (1) hyperplasia, (2) colloid accumulation, and (3) nodularity [41,54,55]. Hyperplasia represents the response of the thyroid follicular cells to TSH, other growth factors, or to circulating stimulatory antibodies [34,55,56]. The hyperplasia may compensate for thyroid hormonal