Graves Disease (Diffuse Hyperplasia)

3

Graves disease, an autoimmune disorder, is the most common cause of hyperthyroidism. Graves disease is associated with antibodies against the thyrotropin receptor that stimulate the receptor and promote synthesis and secretion of thyroglobulin and follicular cell proliferation. Patients present with goiter and symptoms of hyperthyroidism, including anxiety, tachycardia, palpitations, tremor, heat sensitivity, and weight loss, and may develop ophthalmopathy and dermopathy. Patients may be treated symptomatically with β-blockers and with antithyroid medications (propothiouracil and methimazole), radioactive iodine, and surgery. Complications of untreated Graves disease are thyroid storm, muscle catabolism with myopathy, and bone catabolism with osteoporosis, among others. Graves disease occurs in 1 in 2,000 people in the United States. A study from Olmstead County, Minnesota, reports an incidence of 30 cases per 100,000 person years [1]. Graves disease is more common in women than in men. There is a marked increase risk of Graves disease in the postpartum period. In men, Graves disease occurs at an older age and frequently is more severe and associated with greater ophthalmopathy. Graves disease occasionally occurs in children and has a high concordance in identical twins. Smoking is associated with an increased risk of Graves disease and Graves ophthalmopathy [2]. Patients have elevated serum thyroxine and low thyroid-stimulating hormone levels. There is an association with HLA-B8 and DR3, and patients may have a familial predisposition to autoimmune disease, including thyroid disease. Thyroid carcinomas occasionally occur in thyroids involved by Graves disease [3]. In a retrospective review of 61 thyroid carcinomas with concurrent Graves disease, 58 papillary carcinomas, 1 follicular carcinoma, 1 Hurthle cell carcinoma, and 1 medullary carcinoma were identified [4]. Most (80 %) of the tumors were 1 cm or smaller [4]. Incidental thyroid carcinomas are less prevalent in Graves disease than in multinodular goiter [5].

L.A. Erickson, *Atlas of Endocrine Pathology*, Atlas of Anatomic Pathology,
DOI 10.1007/978-1-4939-0443-3_3, © Springer Science+Business Media New York 2014

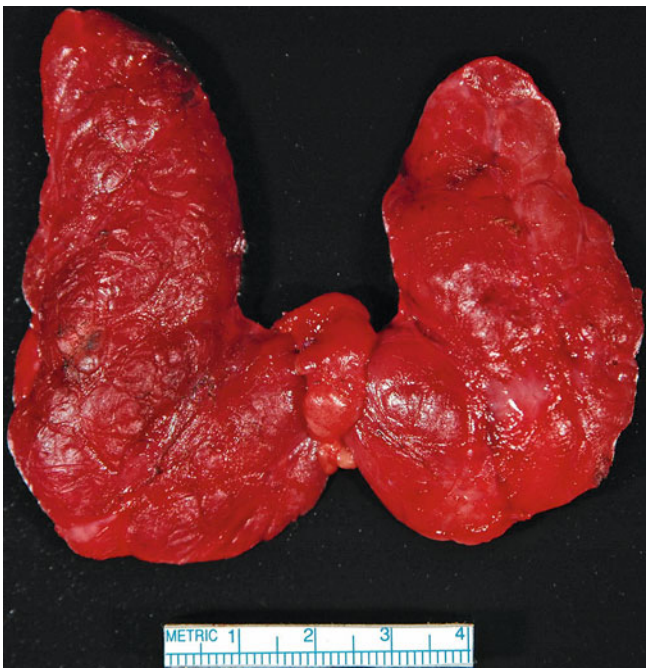

Fig. 3.1 Graves disease (diffuse hyperplasia). This diffusely enlarged thyroid is affected by Graves disease. Thyroids in Graves disease weigh 50–150 g. Toxic nodular goiters also may be associated with hyperthyroidism but have a multinodular appearance and focal histologic involvement, unlike the diffuse hyperplasia and diffuse involvement of the thyroid histologically in Graves disease. Hyper functioning thyroid tumors may be associated with hyperthyroidism, but they are single nodules rather than the diffusely enlarged thyroid of Graves disease

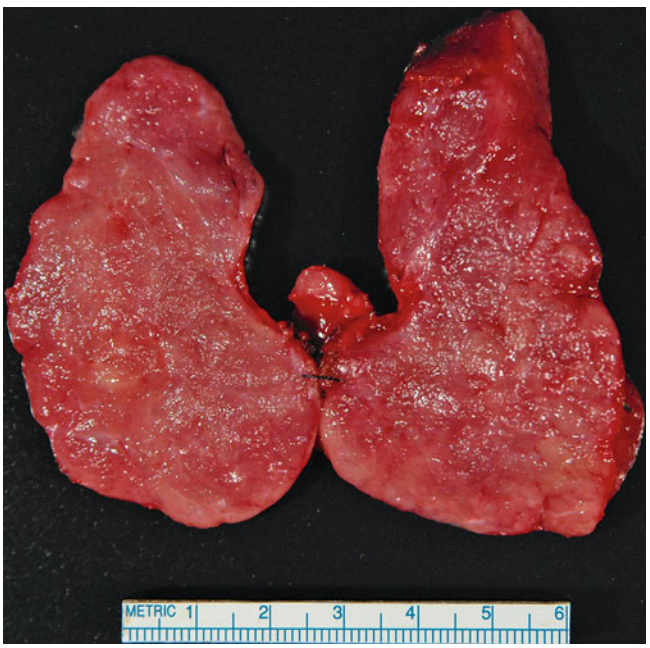

Fig. 3.2 Graves disease (diffuse hyperplasia). Shown is a cut section from a thyroid affected by Graves disease. The thyroid shows diffuse enlargement and has a red cut surface. Untreated Graves may be a very deep red, whereas glands treated preoperatively are lighter in color with less vascularity. Note the diffusely homogenous appearance of the parenchyma in this cut section, which differs from the multinodular appearance of multinodular goiter. The cut surface of Hashimoto thyroiditis is lobulated and may appear yellow-tan as a result of prominent lymphoid infiltrate

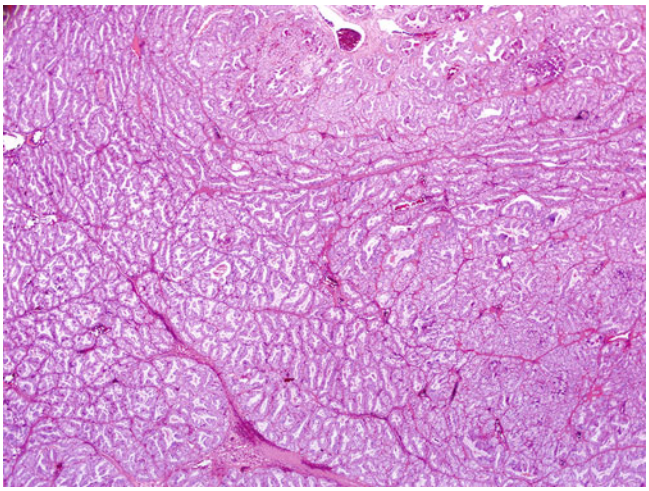

Fig. 3.3 Graves disease (diffuse hyperplasia). This low-power photomicrograph shows the diffuse hyperplasia characteristic of Graves disease. Papillae with fibrovascular cores are prominent and diffusely involve the thyroid gland

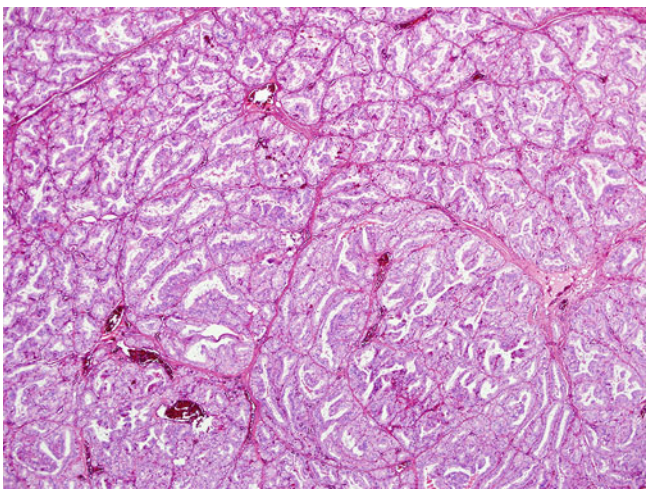

Fig. 3.4 Graves disease (diffuse hyperplasia). The thyroid parenchyma is diffusely involved by hyperplasia in Graves disease. Fibrosis generally is absent or only focal, unlike Hashimoto thyroiditis, which may have prominent fibrosis. Although focal chronic inflammation may be seen in Graves disease in the stroma, it is quite limited, unlike the prominent chronic inflammatory infiltrate in Hashimoto thyroditis, which has lymphoid follicles with germinal centers. Also, Hurthle cells/oncocytic metaplasia are more prominent in Hashimoto thyroiditis than Graves disease

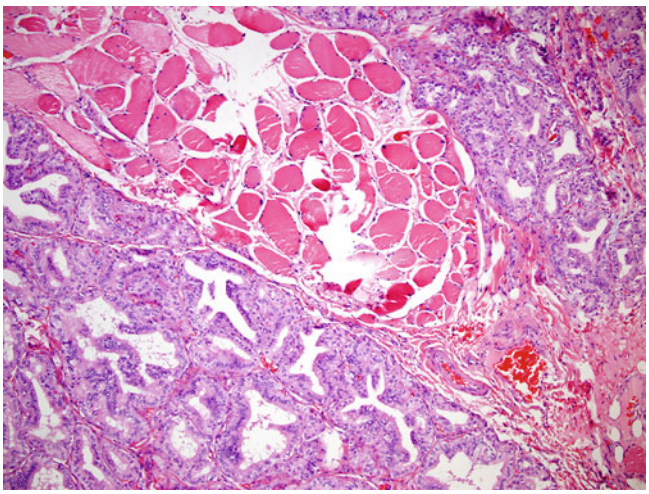

Fig. 3.5 Graves disease (diffuse hyperplasia). Diffuse hyperplasia of Graves disease enveloping skeletal muscle. The hyperplasia in Graves disease is extensive and appears similar throughout the thyroid

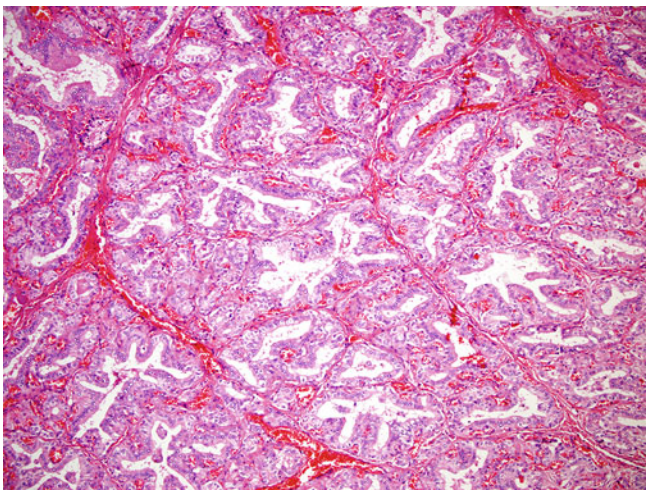

Fig. 3.6 Graves disease (diffuse hyperplasia). The cells in Graves disease are tall columnar cells with basally located round nuclei amphophilic to eosinophilic cytoplasm. Occasional oncocytic cells may be seen in Graves disease, particularly with preoperative treatment, but the oncocytic change is very focal compared with the extensive oncocytic change in Hashimoto thyroiditis

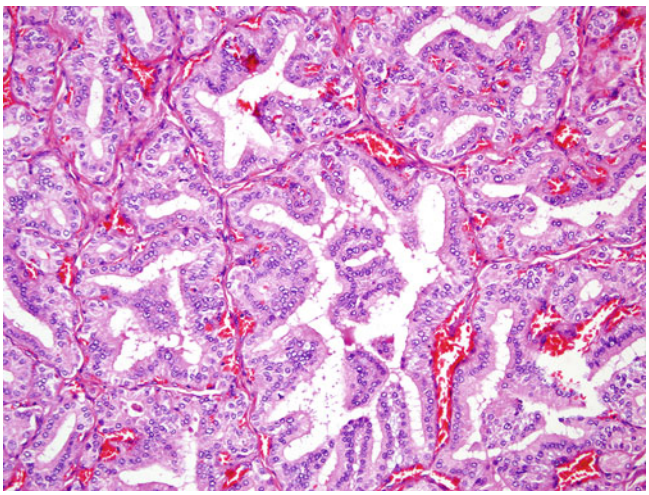

Fig. 3.7 Graves disease (diffuse hyperplasia). Papillae with fibrovascular cores in Graves disease may be mistaken for papillary thyroid carcinoma. The overall appearance of the thyroid diffusely involved by the hyperplasia is helpful in recognizing Graves disease. Cytologic features of papillary thyroid carcinoma with cytoplasmic clearing, large nuclei with irregular nuclear membranes, nuclear clearing, nuclear grooves, and intranuclear holes are helpful in differentiating papillary thyroid carcinoma from Graves disease. In difficult cases, p27 protein and HBME-1 may be used to separate these two lesions. p27 shows higher expression in Graves disease compared with papillary thyroid carcinoma [6]. HBME-1 usually is positive in papillary thyroid carcinoma and negative in papillary hyperplasia [7]

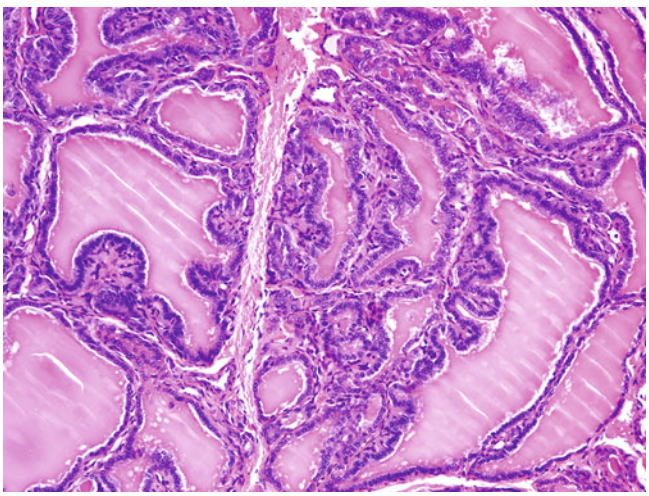

Fig. 3.8 Graves disease (diffuse hyperplasia). This thyroid involved by Graves disease shows some scalloping of colloid, and the cells are still fairly columnar, compatible with hyperthyroidism. However, the increased colloid and decreased vascularity are compatible with the thyroid having been treated preoperatively with iodine

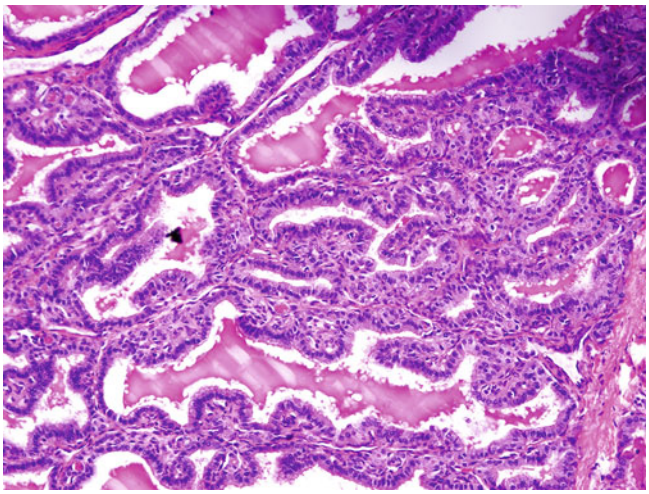

Fig. 3.9 Graves disease (diffuse hyperplasia). The follicular epithelium in this thyroid appears cuboidal, and colloid is increased, findings that indicate preoperative treatment of Graves disease. The decreased vascularity in this photograph compared with the previous images also indicates that this thyroid was treated preoperatively with radioactive iodine

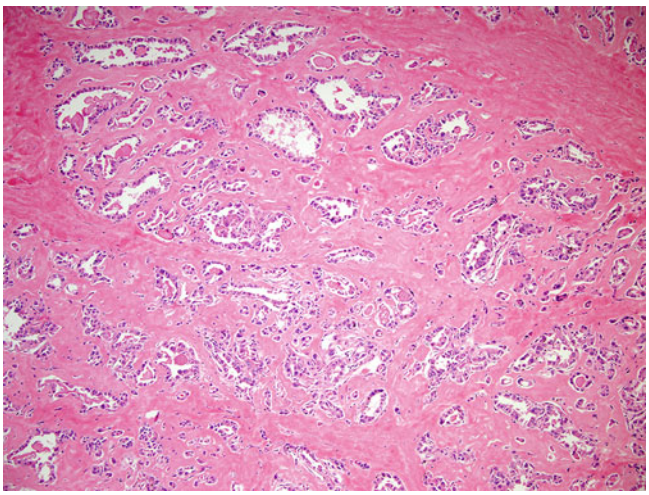

Fig. 3.10 Graves disease (diffuse hyperplasia). This thyroid involved by Graves disease is from a patient extensively treated with iodine before surgery. Patients treated preoperatively with iodine show involution of the epithelium with cuboidal rather than columnar cells, increased colloid, and decreased vascularity. In this thyroid, the involutional changes are marked

References

1. Furszyfer J, et al. Graves' disease in Olmsted County, Minnesota, 1935 through 1967. Mayo Clin Proc. 1970;45(9):636–44.
2. Balazs C, Stenszky V, Farid NR. Association between Graves' ophthalmopathy and smoking. Lancet. 1990;336(8717):754.
3. Brandle M, et al. Medullary thyroid carcinoma in Graves' disease. Clin Endocrinol. 1999;50(4):545–6.
4. Chao TC, Lin JD, Chen MF. Surgical treatment of thyroid cancers with concurrent Graves disease. Ann Surg Oncol. 2004;11(4):407–12.
5. Pascual Corrales E, et al. Incidental differentiated thyroid carcinoma is less prevalent in Graves' disease than in multinodular goiter. Endocrinol Nutr. 2012;59(3):169–73.
6. Erickson LA, et al. p27kip1 expression distinguishes papillary hyperplasia in Graves' disease from papillary thyroid carcinoma. Mod Pathol. 2000;13(9):1014–9.
7. Casey MB, Lohse CM, Lloyd RV. Distinction between papillary thyroid hyperplasia and papillary thyroid carcinoma by immunohistochemical staining for cytokeratin 19, galectin-3, and HBME-1. Endocr Pathol. 2003;14(1):55–60.