

incidence of lymph node metastases, it has become evident that at least a subset of the encapsulated follicular variant display biological features that are more comparable to minimally invasive follicular carcinomas (see later) than conventional papillary carcinomas.

The **tall-cell variant** has tall columnar cells with intensely eosinophilic cytoplasm lining the papillary structures. These tumors tend to occur in older individuals and have higher frequencies of vascular invasion, extrathyroidal extension, and cervical and distant metastases than conventional papillary thyroid carcinoma. Tall-cell variant papillary carcinomas harbor *BRAF* mutations in most (55% to 100%) cases, and often have *RET/PTC* translocations as well. The occurrence of these two aberrations together may synergistically enhance MAPK signaling, contributing to the aggressive behavior of this variant.

An unusual **diffuse sclerosing variant** of papillary carcinoma occurs in younger individuals, including children. The tumor has a prominent papillary growth pattern intermixed with solid areas containing nests of squamous metaplasia. As the name suggests, there is extensive, diffuse fibrosis throughout the thyroid gland, often associated with a prominent lymphocytic infiltrate, simulating Hashimoto thyroiditis. Lymph node metastases are present in almost all cases. The diffuse sclerosing variant carcinomas lack *BRAF* mutations, but *RET/PTC* translocations are found in approximately half the cases.

Finally, the **papillary microcarcinoma** is defined as an otherwise conventional papillary carcinoma less than 1 cm in size. These lesions most commonly come to attention as an incidental finding in patients undergoing surgery, and may be precursors of typical papillary carcinomas.

Clinical Course. Most conventional papillary carcinomas present as asymptomatic thyroid nodules, but the first manifestation may be a mass in a cervical lymph node. Interestingly, the presence of isolated cervical nodal metastases does not have a significant influence on prognosis, which is generally good. Most carcinomas are single nodules that move freely with the thyroid gland during swallowing and are not distinguishable on examination from benign nodules. Hoarseness, dysphagia, cough, or dyspnea suggests advanced disease. In a minority of patients, hematogenous metastases are present at the time of diagnosis, most commonly in the lung.

A variety of diagnostic tests have been used to help separate benign from malignant thyroid nodules, including radionuclide scanning and fine-needle aspiration. Papillary carcinomas are *cold* masses on scintiscans. Improvements in cytologic analysis have made fine-needle aspiration cytology a reliable test for distinguishing between benign and malignant nodules. The nuclear features are often demonstrated nicely in aspirated specimens.

Papillary thyroid cancers have an excellent prognosis, with a 10-year survival rate in excess of 95%. Between 5% and 20% of patients have local or regional recurrences, and 10% to 15% have distant metastases. The prognosis of someone with papillary thyroid cancers is dependent on several factors including age (in general, being less favorable among patients older than 40 years), the presence of extrathyroidal extension, and presence of distant metastases (stage).

Follicular Carcinoma

Follicular carcinomas account for 5% to 15% of primary thyroid cancers, but are more frequent in areas with dietary iodine deficiency, where they constitute 25% to 40% of thyroid cancers. They are more common in women (3:1) and present more often in older patients than do papillary carcinomas; the peak incidence is between 40 and 60 years of age.

MORPHOLOGY

Follicular carcinomas are single nodules that may be well circumscribed or widely infiltrative (Fig. 24-20A). Sharply demarcated lesions may be exceedingly difficult to distinguish from follicular adenomas by gross examination. Larger lesions may penetrate the capsule and infiltrate well beyond the thyroid capsule into the adjacent neck. They are gray to tan to pink on cut section and may be somewhat translucent due to the presence of large, colloid-filled follicles. Degenerative changes, such as central fibrosis and foci of calcification, are sometimes present.

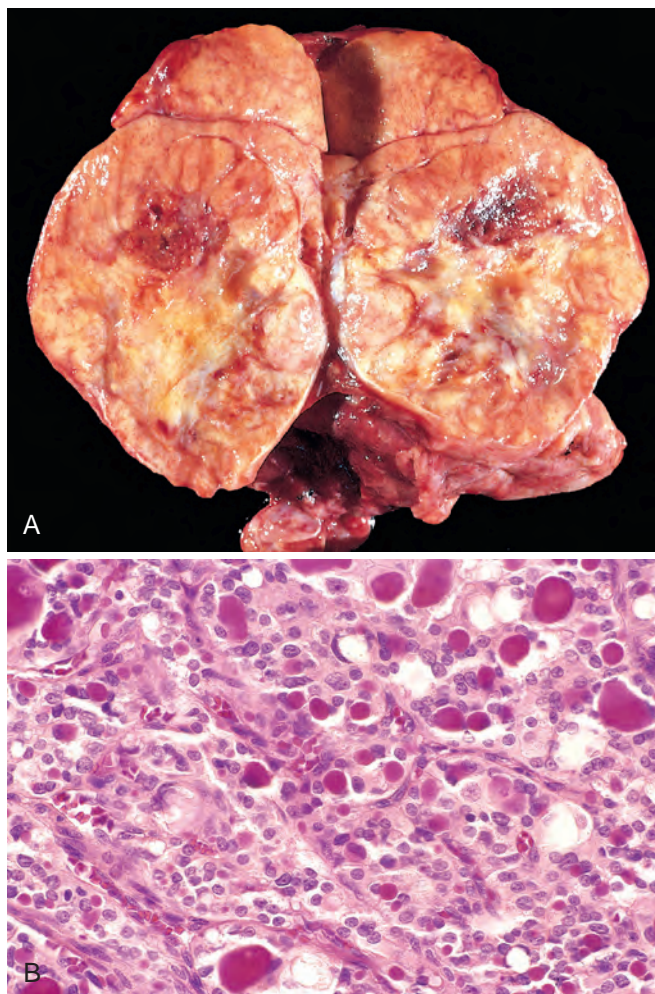


Figure 24-20 Follicular carcinoma. **A**, Cut surface of a follicular carcinoma with substantial replacement of the lobe of the thyroid. The tumor has a light-tan appearance and contains small foci of hemorrhage. **B**, A few of the glandular lumens contain recognizable colloid.