2. THE PATHOLOGY OF THYROID CANCER

SYLVIA L. ASA

Professor, Department of Laboratory Medicine & Pathobiology, University of Toronto; Pathologist-in-Chief, University Health Network and Toronto Medical Laboratories; Freeman Centre for Endocrine Oncology, Mount Sinai & Princess Margaret Hospitals; Toronto, Ontario Canada

Thyroid nodules are extremely common in the general population; it has been estimated that about 20% of the population has a palpable thyroid nodule and approximately 70% has a nodule that can be detected by ultrasound (1). The prevalence of thyroid nodules is greater in women than in men, and multiple nodules are more common than solitary nodules.

The differential diagnosis of the thyroid nodule includes numerous entities, non-neoplastic and neoplastic, benign and malignant (2–5). The pathologist has an important role to play in their evaluation. The use of fine needle aspiration biopsy has significantly improved our ability to identify specific high-risk disorders and to facilitate their management in an expeditious and cost-effective manner. Patients who require surgery for further confirmation of the disease process rely upon the pathologist to correctly characterise their nodule and pathologists are actively involved in research to clarify the pathogenesis of thyroid disease.

While some of these entities are readily diagnosed based on specific features seen in a routine slide stained with conventional dyes, the morphologic evaluation of many of these lesions is fraught with controversy and diagnostic criteria are highly variable from Pathologist to Pathologist (6). Nevertheless, histology remains the gold standard against which we measure outcomes of cytology, intraoperative consultations, molecular and other studies, and it represents the basis on which we determine patient management and the efficacy of various therapies. Unfortunately, no current morphologic criteria provide adequate information to predict outcome for many follicular nodules of thyroid.

Advances in our understanding of the molecular basis of thyroid cancer will allow more accurate characterisation of specific subtypes of neoplasia and malignancy even on single cells obtained at fine needle aspiration biopsy. This should further enhance the usefulness of this technique and better guide the management of patients with a thyroid nodule.

THYROID FOLLICULAR HYPERPLASIA AND NEOPLASIA

Follicular nodules are the most commonly encountered problems in the surgical pathology of the thyroid. These lesions can be classified along the full spectrum of thyroid pathology from hyperplastic nodules to benign follicular adenomas and malignant follicular carcinomas.

Nodular goitre

Sporadic nodular goitre is characterised by numerous follicular nodules with heterogeneous architecture and cytology, features that have suggested a hyperplastic rather than neoplastic pathogenesis (7–10). The gland may be distorted by multiple bilateral nodules and can achieve weights of several hundred to a thousand grams, but this disorder is often identified as a dominant nodule in what clinically appears to be an otherwise normal gland. Histologically, the nodules are irregular; some are poorly circumscribed while others are surrounded by scarring and condensation of thyroid stroma, creating the appearance of complete encapsulation. They are composed of follicles of variable size and shape. Some follicles are large, with abundant colloid surrounded by flattened, cuboidal or columnar epithelial cells, often with cellular areas composed of small follicles lined by crowded epithelium with scant colloid in a small lumen, alone or pushing into large colloid-filled follicles as "Sanderson's polsters" (Figure 1). There may be focal necrosis, haemorrhage with haemosiderin deposition and cholesterol clefts, fibrosis, and granulation tissue; these degenerative changes are usually found in the centre of large nodules, creating stellate scars.

The morphologic classification of cellular follicular nodules in nodular glands can be extremely difficult. Hyperplasia may be extremely difficult to distinguish from neoplasia. Classical guidelines that allow distinction of a hyperplastic nodule from a follicular adenoma include the following: (i) multiple lesions suggest hyperplasia whereas a solitary lesion is likely to be neoplastic, (ii) a poorly encapsulated nodule is likely hyperplastic; a well developed capsule suggests a neoplastic growth, (iii) variable architecture reflects a polyclonal proliferation whereas uniform architecture suggests a monoclonal neoplastic growth, (iv) cytologic heterogeneity suggests hyperplasia; monotonous cytology is characteristic of neoplasia, (v) the presence of multiple lesions in hyperplasia means that areas similar to the lesion in question will be present in the adjacent gland; in contrast, neoplasms have a distinct morphology compared with the surrounding parenchyma, (vi) classically hyperplastic nodules are said not to compress the surrounding gland whereas neoplasms result in compression of the adjacent parenchyma. For the most part, large nodules in multinodular glands tend to be incompletely encapsulated and poorly demarcated from the internodular tissue. However, in some glands, large encapsulated lesions with relatively monotonous architecture