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Current role and value of fine-needle aspiration in nodular goitre

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Thyroid nodules are common and, depending on the detection technique used, can affect 50% or greater of the population. The primary diagnostic test to assess the nature of these nodules is fine-needle aspiration cytology. Most thyroid nodules are benign and often are multiple. However, the morphology of these nodules may mimic neoplasms showing features such as papillary growth, micro-follicles and even oncocytic metaplasia. Lesions with these features may be considered indeterminate for neoplasm or malignancy, and often require surgical excision to define their nature. The role of cytopathology in this area is to screen those definitely benign nodules, thus preventing surgery and reassuring both the patient and the clinician. In this review, we demonstrate many of the morphological manifestations of nodular goiter and stress the necessity of careful preparatory techniques. Although the past several years have witnessed the development of molecular testing to refine diagnostic cytology in the thyroid, it is still the role of the cytopathologist to identify those "indeterminant" nodules which should be tested. Thus, the cytopathologist contributes both an essential diagnostic and an important cost saving role which hopefully will continue in the future.

Introduction

Thyroid nodules are common and vary in incidence in different parts of the world. In endemic goiter regions the frequency of thyroid nodules may be as high as 25%, whereas in non-iodine-deficient

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areas 4–7% of the population has palpable thyroid nodules. However, with the increasing use of ultrasound as screening tool, thyroid nodules can be encountered in up to 60% of the population [1–3].

The term Goiter (L, *gutter*, throat) is a clinical term, variably defined, and is often used to describe nodular or diffuse enlargement of the thyroid to twice the normal size or larger. Usually in clinical practice and in the pathology literature 'goiter' denotes a benign and hyperplastic process [4]. The variants of goiter, non-toxic and toxic, are defined on the basis of the functional activity of the gland [4,5]. Patients with non-toxic goiter are usually euthyroid but can also be hypothyroid, whereas toxic goiter represents hyper-functioning gland due to toxic multinodular gland [6,7].

'Non-toxic Goiter' occurs as a result of various factors, which affect the thyroid either by intrinsic or extrinsic mechanisms. In most cases there is increased production of thyroid stimulating hormone in response to low thyroid hormone synthesis leading to compensatory hyperplasia. The decreased hormone production can be due to various known and unknown causes [5].

Dietary iodine deficiency is the leading environmental trigger of 'non-toxic endemic goiter' in individuals with a genetic predisposition [8]. It is commonly seen in regions of South America, Africa, Asia and Europe [9]. 'Sporadic goiter' occurs in areas, where iodine is sufficient [5]. Several theories have been proposed regarding the pathogenesis of sporadic goiter. Some authors have suggested that diffuse and nodular goiter occur as the result of different mechanisms [7,10–16]. Others have postulated that both diffuse and nodular goiter can occur due to subtle derangements in thyroid hormonogenesis and thyroid stimulating hormone over-production [17]. Other causes of goiter include medications with antithyroid activity and goitrogenic effects; and thyroid-stimulating agents of non-pituitary origin [12,18–21].

The histopathologic features of both endemic and sporadic goiter are the same; these include hyperplasia, colloid accumulation and involution [22–24]. In the hyperplastic stage the gland is diffusely enlarged and shows crowding of thyroid follicles, scant colloid and minimal inter-follicular mesenchymal tissue. The follicles are lined by tall columnar epithelium; in some instances the epithelial hyperplasia may give rise to papillary pattern changes. Cellular atypia is usually infrequent, however, when present, especially in papillary areas, can be mistaken for papillary carcinoma. The hyperplasia may not persist in some follicles and is followed by a process denoted 'involution'. This is characterized by re-accumulation of colloid in the follicles and the epithelium becomes low cuboidal and flattened. Colloid accumulation can be excessive and may lead to expansion of the follicle leading to formation of macro-follicles lined by flattened/atrophic epithelium (Fig. 1). At this stage the thyroid grossly appears to be soft and has a glistening cut surface due to excess colloid. This stage of non-toxic goiter is also termed 'colloid goiter' [24,25].

'Nodular goiter' is a result of multiple events of hyperplasia and involution and the nodule formation involves the entire gland. However, this process is asymmetric and the nodules vary in size and

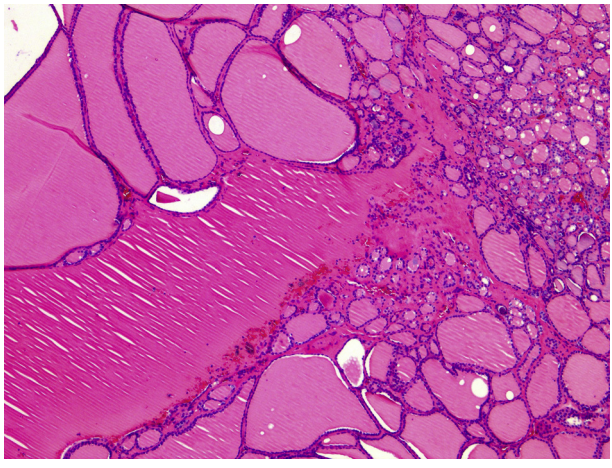

Fig. 1. A histopathologic section from a case of nodular goiter demonstrating an admixture of small (micro) and large (macro) follicles distended with watery colloid and lined by attenuated follicular epithelium (hematoxylin and eosin stain, 40×).