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Assessment of nodular goitre

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Nodular goitres are enlargements of the thyroid gland. In the absence of thyroid dysfunction, autoimmune thyroid disease, thyroiditis and thyroid malignancy, they constitute an entity described as non-toxic nodular goitre, which occurs both endemically and sporadically. In the early phase of goitrogenesis, goitres are diffuse and, with time, such goitres tend to become nodular. Concomitantly, thyroid function often becomes autonomous, and therefore the patients gradually develop hyperthyroidism. Some non-toxic goitre patients have no symptoms at all, or just complaints of cosmetic disfigurement. In the diagnostic evaluation protocol, neck palpation and several imaging methods are available: ultrasonography (US), the new developed US elastography, scintigraphy, computed tomography (CT) scan and magnetic resonance imaging (MRI). Fine-needle aspiration biopsy (FNAB) provides the most direct and specific information about a thyroid nodule. Recently, a combination of cytology and molecular testing has shown significant improvement in the diagnostic accuracy and allowed for better prediction of malignancy in thyroid nodular disease.

Nodular goitres (NGs) are clinically recognisable enlargements of the thyroid gland. In the absence of thyroid dysfunction, autoimmune thyroid disease, thyroiditis and thyroid malignancy, they constitute an entity described as non-toxic NG.[1] NG occurs both endemically, mainly related to iodine deficiency when goitre prevalence in children 6–12 years of age within a population is more than 5%, and sporadically, when this number is 5% or less. In the early phase of goitrogenesis, goitres are diffuse and, with time, diffuse goitres tend not only to grow but also to become nodular. In general, NG can be

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divided into solitary nodular and multinodular thyroid disease.[1] Concomitantly, thyroid function often becomes autonomous, that is, thyroid hormone secretion becomes independent of thyreotropin secretion, and therefore the patients gradually develop subclinical hyperthyroidism and eventually overt hyperthyroidism.[1] Thus, the natural history of NG is characterised clinically by thyroid growth, nodule formation and the development of functional autonomy. The clinical forms include toxic multinodular goitre (TMNG) and toxic thyroid adenoma (TA).

Epidemiology of NG

Epidemiological studies of nodular goitre are hampered by problems such as selection criteria (e.g., age and sex), influence of environmental factors (e.g., iodine and drug intake and smoking and drinking habits), evaluation of size and morphology (i.e., palpation, sonography and scintigraphy) and determination of thyroid function.[2] The clinical grading of thyroid size is subjective and imprecise. More recently, ultrasonography (US) has been used in epidemiologic studies to assess thyroid size.[3] A pattern of increased thyroid volume and nodularity in areas with iodine deficiency is the rule.[2–5] A recent cross-sectional study using modern technologies on the spectrum of thyroid disorders occurring in a community with mild-to-moderate iodine deficiency in the south of Italy[5], clearly showed that the prevalence of goitre and thyroid nodularity increased with age. The prevalence of goitre increased from 16% in children to 60% in adults. NG was negligible in the 15- to 25-year age class, but increased up to 29% in the 56- to 65-year age class.[5]

In the Whickham survey of a representative sample of the adult population from a geographic area with adequate iodine supply of the United Kingdom, 15.5% of the participants had a palpable goitre (8.6% had a small goitre), with a female-to-male ratio of 4.5:1.[6] There was a weak association between goitre and thyroid autoantibodies and no correspondence with urinary iodine excretion. In Framingham, Massachusetts, where iodine intake was also sufficient, 1% of persons between 30 and 59 years of age had multinodular goitre by palpation.[7] In Connecticut, 2% of the adults were reported to have nodular glands.[8] In Denmark, palpable goitre was demonstrated in 9.8% of a mildly iodine-deficient population and 14.6% of a moderately iodine-deficient population.[4] This frequency increased to 15.0% and 22.6%, respectively, when goitre was defined by sonographic determination of thyroid volume.[4] There are a vast number of such studies underscoring the inaccuracy of and also the large observer variation in the determination of goitre and thyroid size by clinical examination.[9] In the Whickham survey[6], solitary thyroid nodules were estimated to be present in 5.3% of women and 0.8% of men (ratio, 6.6:1). No details were provided about nodule size, function or their association with goitre. In Framingham, this frequency was 4.6% in all (6.4% in women and 1.6% in men).[7] However, these numbers are markedly changed if sonography is used. Then, the prevalence of thyroid nodules, even if defined as more than 10 mm in diameter, is usually 20–30% in unselected populations[10] and even higher in older age groups and in areas with insufficient iodine intake.[11]

Natural history of NG and epidemiology of functional autonomy

The natural history of NG is characterised clinically by thyroid growth, nodule formation and the development of functional autonomy. Non-autoimmune hyperthyroidism is usually encountered in subjects with long-standing nodular goitre and is a major cause of morbidity in iodine-deficient areas.[5,12] The clinical forms include TMNG and TA. Thyrotoxicosis is usually preceded by a long phase of subclinical hyperthyroidsm (abnormally low serum thyroid-stimulating hormone (TSH), with normal circulating thyroid hormones) due to the secretion of thyroid hormones independent from TSH regulation (thyroid autonomy).

Toxic or autonomous multinodular goitre has a multifaceted clinical presentation, spanning from a single hyperfunctioning nodule within a goitre where several non-functioning nodules also coexist with NG where multiple hyperfunctining areas, not confined to distinct nodules, are barely distinguishable from non-functioning nodules. TMNG is the most common cause of thyrotoxicosis in iodine-deficient areas. The critical role of iodine deficiency in the development of iodine-induced hyperthyroidism is demonstrated by the decreased incidence of this disease that occurred in several countries[13] after institution and implementation of iodine prophylaxis. The incidence of different types