

Goitre and thyroid cancer

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Abstract

Goitre is the generic term for thyroid enlargement and encompasses relatively common benign disease as well as thyroid malignancy, which is uncommon. Unfortunately, the clinical presentations of benign and malignant thyroid disease are similar. The aim of clinical assessment and investigations is to identify the small number of cancers among the frequent non-malignant thyroid enlargements. Investigations include thyroid function tests and fine needle aspiration cytology. Benign thyroid disease requires treatment only in the presence of dysfunction or local compressive symptoms. The treatment of thyroid cancer is multidisciplinary and includes surgery, radioiodine therapy and life-long suppression of thyroid-stimulating hormone. The diagnosis and management of thyroid cancer are being centralized around a multidisciplinary team structure in order to improve outcomes in the UK. Recent developments in the management of thyroid cancer include the use of molecular biomarkers to identify malignancy in thyroid nodules and targeted therapy for advanced disease.

Keywords Follicular thyroid cancer; goitre; medullary thyroid cancer; MEN2; MRCP; papillary thyroid cancer; thyroid cancer; thyroid nodule

Introduction

The term 'goitre' describes any enlargement of the thyroid gland. It can be caused by a solitary nodule (Figure 1), multiple nodules (Figure 2) or a smooth enlargement of some or all of the gland. Goitres can be classified on the basis of epidemiology, aetiology, anatomical and morphological features or functional status (Table 1), or a combination of these (Table 2).

Endemic goitre is the most common form of thyroid enlargement worldwide. Goitre is defined as 'endemic' when the prevalence within a community or geographical area is >5% in children <12 years of age. If these conditions are not met, goitre is said to be 'sporadic'. Palpable thyroid nodules and/or goitre are found in up to 7% of the population in iodine-replete areas. Subclinical, ultrasound-detected thyroid nodules, either solitary or 'dominant' within a nodular goitre, are found in 45% of women and 32% of men at age 55 years.¹

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Key points

- Goitre, meaning enlargement of the thyroid gland, can be caused by single or multiple nodules
- Goitre has many causes: smooth enlargement of the thyroid gland is usually 'endemic' goitre or the result of iodine excess or drugs
- Benign thyroid nodules are common but require investigation to exclude thyroid cancer, which is uncommon
- The risk factors for thyroid cancer are radiation and family history, as well as thyroid nodules in male patients and at the extremes of age
- The mainstay of diagnosis of thyroid nodules is ultrasonography with or without fine needle aspiration
- Thyroid cancer is classified according to the cell type of origin
- The natural history of thyroid cancer is diverse, with prognosis ranging from excellent in well-differentiated papillary cancer in the young, to poor in elderly men, or very poor in anaplastic cancer
- Treatment of thyroid cancer is surgery with or without adjuvant therapy with radioiodine or chemotherapy, and suppression of thyroid-stimulating hormone with thyroxine
- Primary lymphoma of the thyroid gland is rare and is treated with chemoradiotherapy

Thyroid cancer represents 1% of all newly diagnosed cancers and is the most common endocrine malignancy. The number of new diagnoses in the UK in 2014 was 7 per 100,000 female individuals and 4 per 100,000 males; this has risen steadily, with an increase of 70% in the last decade alone, in part related to detection bias. The prevalence of malignancy in thyroid nodules presenting to a clinician is 5–6%; the challenge therefore lies in distinguishing uncommon malignancy from common benign nodules.

Aetiopathogenesis of goitre

The most common causes of goitre are:

- iodine deficiency – the prevalence of endemic goitre should decrease with iodine supplementation programmes
- iodine excess – iodine-excess goitre is seen in areas of Japan where seaweed and fish are heavily consumed
- goitrogenic drugs and foods – this can be caused by chronic lithium therapy or the consumption of vegetables (e.g. the Brassica family) that metabolize to the goitrogen thiocyanate
- heavy smoking – this can be associated with an increased prevalence of multinodular goitre.



Figure 1 A solitary nodule later found to be malignant on thyroid cytology.



Figure 2 A large multinodular goitre causing local compression.

Goitre classifications

Criterion	Groups
Epidemiology	Endemic Sporadic Familial
Aetiology	Iodine deficiency Graves' disease Hashimoto's thyroiditis (in the enlargement phase) Neoplasia Goitrogenous nutrients and drugs (thiocyanates, lithium) Dyshormonogenesis
Morphology	Diffuse Multinodular
Anatomy	Cervical Retrosternal
Functional status	Euthyroid Toxic

Table 1

The pathogenesis of benign goitres in iodine-replete areas remains incompletely understood. However, a small persistent increase in serum thyroid-stimulating hormone (TSH) coupled with even marginal iodine deficiency is thought to lead to thyrocyte proliferation and thyroid gland enlargement, particularly if this occurs during youth. The nodules that subsequently form are differentially sensitive to TSH stimulation, culminating in nodule autonomy.

Risk factors for thyroid malignancy are:

- epidemiology:
 - the rate of malignancy in thyroid nodules in male patients is twice that in female patients, twice as high at <30 or >60 years of age in comparison to age 30–60 years, and twice as high for children as adults
 - larger nodules may be associated with a higher risk of malignancy and reduced diagnostic accuracy on fine needle aspiration, even when this is ultrasound-guided
- family history:
 - medullary thyroid cancer (MTC) in the context of multiple endocrine neoplasia type 2 (MEN2) syndrome
 - familial papillary and follicular thyroid cancer²
- exposure to radiation:
 - evidence from survivors of the atomic bombs dropped on Japan in 1945 and the Chernobyl incident in 1986 confirm the carcinogenic effect of radiation, which appears to be most damaging if exposure occurs <14 years of age and coupled with iodine insufficiency
 - the fetuses of pregnant women exposed to radiation in Chernobyl were also at an increased risk of thyroid malignancy in later life.

Clinical presentation

History

Most goitres are asymptomatic and found incidentally by the patient, the general practitioner or radiological examination. Nodules occur at all ages and in both sexes but are increasingly common with advancing age. Those presenting in men or at the extremes of age should be treated with greater suspicion.

A short history of rapid enlargement in elderly individuals is suggestive of malignancy, whereas bleeding into a nodule or cystic enlargement can be responsible in young patients. A slow history of enlargement does not exclude malignancy. Dysphonia in the presence of a goitre suggests thyroid malignancy invading the recurrent laryngeal nerve and causing vocal cord paralysis. The presence of local compressive symptoms (dysphagia, dyspnoea) is not associated with malignancy but should be ascertained as these can be an independent indication for surgical intervention. If the local compressive symptoms are disproportionate to the size of the goitre, especially if the presentation includes pain, thyroiditis should be considered. Symptoms of hyperthyroidism, such as weight loss, tremor, anxiety or insomnia, are suggestive of toxicity, the management of which is discussed below (see 'Radionuclide imaging').

Specific risk factors for malignancy – a family history and history of radiation exposure – should be enquired about. If MTC is suspected, a focused history regarding MEN2 syndrome (i.e. pheochromocytoma, hyperparathyroidism) should be taken.

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