Thyroid lump or swelling

A lump or swelling in the thyroid gland can be a source of considerable anxiety for patients. There are numerous causes but, broadly speaking, a thyroid swelling is either a ***solitary nodule, a multinodular goitre or a diffuse goitre*** . Nodular thyroid disease is more common in women and occurs in approximately 30% of the adult female population. The majority of thyroid nodules are impalpable but may be identified when imaging of the neck is performed for another reason, such as during Doppler ultrasonography of the carotid arteries or computed tomographic pulmonary angiography. Increasingly, thyroid nodules are identified during staging of patients with cancer with computed tomography (CT), magnetic resonance imaging (MRI) or positron emission tomography (PET) scans.

Palpable thyroid nodules occur in 4–8% of adult women and 1–2% of adult men, and classically present when the individual (or a friend or relative) notices a lump in the neck. Multinodular goitre and solitary nodules sometimes present with acute painful enlargement due to haemorrhage into a nodule. Patients with thyroid nodules often worry that they have cancer but the reality is that only 5–10% of thyroid nodules are malignant.

A nodule presenting in *childhood or adolescence*, particularly if there is a past history of head and neck irradiation, or one presenting in an *elderly* patient should heighten suspicion of a primary thyroid malignancy . The presence of cervical lymphadenopathy also increases the likelihood of malignancy.

Rarely, a **secondary deposit** from a renal, breast or lung carcinoma presents as a painful, rapidly growing, solitary thyroid nodule. Thyroid nodules identified on PET scanning have an approximately 33% chance of being malignant.

18.13 Causes of thyroid enlargement

Diffuse goitre

- Simple goitre
- Hashimoto's thyroiditis[1]
- Graves' disease
- Drugs: iodine, amiodarone, lithium
- Iodine deficiency (endemic goitre)[1]
- Suppurative thyroiditis[2]
- Transient thyroiditis[2]
- Dyshormonogenesis[1]
- Infiltrative: amyloidosis, sarcoidosis etc.
- Riedel's thyroiditis[2]

Multinodular goitre

Solitary nodule

- Colloid cyst
- Hyperplastic nodule
- Follicular adenoma
- Papillary carcinoma
- Follicular carcinoma
- Medullary cell carcinoma
- Anaplastic carcinoma
- Lymphoma
- Metastasis

[1]Goitre likely to shrink with levothyroxine therapy. [2]Usually tender.

Clinical assessment and investigations

Swellings in the anterior part of the neck most commonly originate in the thyroid and this can be confirmed by demonstrating that the swelling moves on swallowing . It is often possible to distinguish clinically between the three main causes of thyroid swelling. There is a broad differential diagnosis of anterior neck swellings, which includes ***lymphadenopathy, branchial cysts, dermoid cysts and thyroglossal duct cysts*** (the latter are classically located in the midline and move on protrusion of the tongue).

An ultrasound scan should be performed urgently, if there is any doubt as to the aetiology of an anterior neck swelling. Serum T3, T4 and TSH should be measured in all patients with a goitre or solitary thyroid nodule. The finding of biochemical thyrotoxicosis or hypothyroidism (both of which may be subclinical) should lead to investigations, as already described in previous lectures.

Thyroid scintigraphy

Thyroid scintigraphy with 99m technetium should be performed in an individual with a low serum TSH and a nodular thyroid to confirm the presence of an autonomously functioning ('hot') nodule .In such circumstances, further evaluation is not necessary. 'Cold' nodules on scintigraphy have a much higher likelihood of malignancy, but the majority are benign and so scintigraphy is not routinely used in the evaluation of thyroid nodules when TSH is normal.

Toxic adenoma

A solitary toxic nodule is the cause of less than 5% of all cases of thyrotoxicosis. The nodule is a follicular adenoma, which autonomously secretes excess thyroid hormones and inhibits endogenous TSH secretion, with subsequent atrophy of the rest of the thyroid gland. The adenoma is usually greater than 3 cm in diameter.

Most patients are **female** and over 40 years of age. Although many nodules are palpable, the diagnosis can be made with certainty only by thyroid scintigraphy . The thyrotoxicosis is usually mild and in almost 50% of patients the plasma T3 alone is elevated (T3 thyrotoxicosis). 131I (400–800 MBq (10–20 mCi)) is highly effective and is an ideal treatment since the atrophic cells surrounding the nodule do not take up iodine and so receive little or no radiation. For this reason, permanent hypothyroidism is unusual. Hemithyroidectomy is an alternative management option.

Thyroid neoplasia

Patients with thyroid tumours usually present with a **solitary nodule** . Most are benign and a few of these, called 'toxic adenomas', secrete excess thyroid hormones. Primary thyroid malignancy is rare, accounting for less than 1% of all carcinomas, and has an incidence of 25 per million per annum. It can be classified according to the cell type of origin. With the exception of medullary carcinoma, thyroid cancer is more common in females.

18.16 Malignant thyroid tumours

Type of tumour	Frequency (%)	Age at presentation (years)	10-year survival (%)
Follicular cells			
Differentiated carcinoma:			
Papillary	75–85	20–40	98
Follicular	10–20	40–60	94
Anaplastic	<5	>60	9
Parafollicular C cells			
Medullary carcinoma	5–8	>40*	78
Lymphocytes			
Lymphoma	<5	>60	45

*Patients with medullary carcinoma as part of multiple endocrine neoplasia (MEN) types 2 and 3 (p. 688) may present in childhood.

Differentiated carcinoma

Papillary carcinoma

This is the most common of the malignant thyroid tumours and accounts for 90% of radiation-induced thyroid cancer. It may be multifocal and spread is initially to regional lymph nodes. Some patients present with cervical lymphadenopathy and no apparent thyroid enlargement; in such instances, the primary lesion may be less than 10 mm in diameter.

Follicular carcinoma

This is usually a single encapsulated lesion. Spread to cervical lymph nodes is rare. Metastases are blood-borne and are most often found in bone, lungs and brain.

Management

The management of thyroid cancers should be individualized and planned in multidisciplinary team meetings that include all specialists involved in the service; this should include thyroid surgeons, endocrinologists, oncologists, pathologists, radiologists and nurse specialists. Large tumours, those with adverse histological features and/or tumours with metastatic disease at

presentation are usually managed by total thyroidectomy followed by a large dose of ^{131}I ((approximately 30 or 100 mCi)) to ablate any remaining normal or malignant thyroid tissue. Thereafter, long-term treatment with levothyroxine in a dose sufficient to suppress TSH (usually 150–200 µg daily) is given, as there is evidence that growth of differentiated thyroid carcinomas is **TSH-dependent**. Smaller tumours with no adverse histological features may require only thyroid lobectomy.

Follow-up involves measurement of serum thyroglobulin, which should be undetectable in patients whose normal thyroid has been ablated and who are taking a suppressive dose of levothyroxine. Thyroglobulin antibodies may interfere with the assay and, depending on the method employed, may result in a falsely low or high result. Detectable thyroglobulin, in the absence of assay interference, is suggestive of tumour recurrence or metastases, particularly if the thyroglobulin titre is rising across serial measurements. Local recurrence or metastatic disease may be localised by ultrasound, CT, MRI and/or whole-body scanning with ^{131}I, and may be treated with further surgery and/or ^{131}I therapy.

Those with locally advanced or metastatic papillary and follicular carcinoma that is refractive to ^{131}I may be considered for therapy with **sorafenib** or **lenvatinib**. These drugs are multi-targeted **tyrosine kinase inhibitors** and have been shown in trials to prolong progression-free survival by between 5 and 14 months.

Prognosis

Most patients with papillary and follicular thyroid cancer will be cured with appropriate treatment. Adverse prognostic factors include older age at presentation, the presence of distant metastases, male sex and certain histological subtypes.

Anaplastic carcinoma and lymphoma

These two conditions are difficult to distinguish clinically but are distinct cytologically and histologically. Patients are usually over 60 years of age and

present with rapid thyroid enlargement over 2–3 months. The goitre is hard and there may be stridor due to tracheal compression and hoarseness due to recurrent laryngeal nerve palsy. There is no effective treatment for anaplastic carcinoma, although surgery and radiotherapy may be considered in some circumstances. In older patients, median survival is only 7 months.

The prognosis for lymphoma, which may arise from preexisting Hashimoto's thyroiditis, is better , with a median survival of 9 years. Some 98% of tumours are non-Hodgkin's lymphomas, usually the diffuse large B-cell subtype. Treatment is with combination chemotherapy and external beam radiotherapy .

Medullary carcinoma

This tumour arises from the parafollicular C cells of the thyroid. In addition to calcitonin, the tumour may secrete 5-hydroxytryptamine (5-HT, serotonin), various peptides of the tachykinin family, adrenocorticotrophic hormone (ACTH) and prostaglandins. As a consequence, carcinoid syndrome and Cushing's syndrome may occur.

Patients usually present in middle age with a firm thyroid mass. Cervical lymph node involvement is common but distant metastases are rare initially. Serum calcitonin levels are raised and are useful in monitoring response to treatment.

Treatment is by total thyroidectomy with removal of regional cervical lymph nodes. Since the C cells do not concentrate iodine and are not responsive to TSH, there is no role for 131I therapy or TSH suppression with levothyroxine. External beam radiotherapy may be considered in some patients at high risk of local recurrence. Vandetanib and cabozantinib are tyrosine kinase inhibitors licensed for patients with progressive advanced medullary cancer. The prognosis is less good than for papillary and follicular. Medullary carcinoma of the thyroid occurs sporadically in 70–90% cases; in 10–30% of cases, there is a genetic predisposition that is inherited

in an autosomal dominant fashion and is due to an activating mutation in the RET gene. This inherited tendency normally forms part of one of the MEN syndromes (MEN 2 (also known as MEN 2a) or MEN 3 (also known as MEN 2b), but, occasionally, susceptibility to medullary carcinoma is the only inherited trait (familial medullary thyroid cancer).

Riedel's thyroiditis

This is not a form of thyroid cancer but the presentation is similar and the differentiation can usually be made only by thyroid biopsy. It is an exceptionally rare condition of unknown aetiology, in which thereis extensive infiltration of the thyroid and surrounding structures with fibrous tissue. There may be associated mediastinal and retroperitoneal fibrosis. Presentation is with a slow-growing goitre that is irregular and stony-hard. There is usually tracheal and oesophageal compression necessitating partial thyroidectomy. Other recognised complications include recurrent laryngeal nerve palsy, hypoparathyroidism and eventually hypothyroidism.