

# ENDOCRINE SYSTEM

## MUSEUM CATALOGUE

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# ENDOCRINE SYSTEM

## INTRODUCTION

Endocrine glands contain cells that secrete their product into adjacent blood vessels via which it is transported to its site of action, as opposed to exocrine glands, the cells of which secrete their product into a duct. The secretions of endocrine glands are generally called hormones (although certain substances also called hormones may be secreted by cells not conventionally regarded as being endocrine e.g. sex hormones from testis and ovary). The endocrine system includes the adrenals, parathyroids, thyroid, pancreatic islets of Langerhans, pituitary and the pineal gland.

The pituitary gland measures approximately 1cm in diameter and has two parts, anterior and posterior, which have different functions. It sits within the sella turcica and is close to the optic chiasm and cavernous sinuses, through which several cranial nerves and the internal carotid artery run.

The thyroid comprises 2 lateral lobes, each approximately 4cm in greatest dimension, connected anteriorly in the midline via an isthmus. It lies around the anterior and lateral aspects of the larynx and upper trachea. Its cut surface is deep yellow/brown/red due to its content of iodine containing colloid. Epithelial cells of the thyroid are simple cuboidal in type and are arranged around central follicles in which colloid is stored.

There are generally 4 parathyroid glands, each approximately 5mm in maximum dimension. Normally they are found on the posterior thyroid surface, but their location can vary. They appear yellow/brown and because of their small size and colour (similar to adipose tissue) can be difficult to identify surgically.

The adrenal glands lie on the upper poles of the kidneys. They are pyramidal in shape and approximately 4-6cm in greatest dimension. The cortex is yellow/brown in colour due to the lipid content of the steroid producing cells and the medulla, which has a different embryological origin and function, is darker in colour.

Mention will also be made here of the diffuse neuroendocrine system (DNES). The cells belonging to this system are dispersed individually in a wide variety of tissues including the epithelium of the GIT, bladder, lung and skin. The cells in the skin are known as Merkel cells, in the lung as Kulchitsky (K) cells, enteroendocrine cells in the GIT (G cells producing gastrin in the stomach are an example) and in the thyroid as parafollicular or C cells. These cells are thought to originate from the embryonic neural crest and have some features of neurones. They produce hormones, some of which act locally (paracrine). Such cells give rise to neuroendocrine tumours: the low grade ones mostly being known as carcinoid tumours, the high grade ones often being known only as small cell carcinoma (or undifferentiated small cell carcinoma) e.g. in the lung.

Strictly speaking, the thymus is not an endocrine organ, though specimens of thymic pathology are included in this section.

Any comments on this catalogue are welcome. Please contact a member of the department.

## HOW TO USE THIS CATALOGUE

This catalogue can be used as a tool to develop your knowledge, as well as provide an opportunity for revision.

It is divided into:

- Introduction and approach to specimens (pages 134-137).
- Index (pages 138-139). Examples of specific diagnoses can be found via the index.
- Core and classic disease processes (pages 140-154). This gives examples and discussion of core and/or classic diseases of the endocrine system. These are the conditions that students should focus on being able to identify initially. However, it depends to some extent on what you have covered in

lectures and practical classes or resource sessions as to what you should know. Some of the specimens and discussion are directed more towards clinical medical students.

- Main catalogue (pages 155-166). This section covers the specimens in numerical order. Questions and/or comments accompany some of the specimens to help you expand your knowledge. In order to fit more specimens in the museum, not all of the pots are in numerical order on the shelves, and large specimens are often found on the bottom shelves.

You might find it useful to work quietly with a few friends and to have a few textbooks handy (e.g. pathology, medical, anatomy). You will also find that you can learn some anatomy and clinicopathological correlation from the specimens and information given.

You do not have to examine every single specimen in the museum. However, just as in clinical practice, you will not become proficient in diagnosing something if you have only seen one case. Exposure to a variety of cases (specific diagnoses can be found via the index) to experience the variability in morphology will help your learning greatly. In general red and blue dots indicate basic and straightforward cases, whereas yellow dots indicate a more complex case. This is not a hard and fast rule, and you will find yellow dot specimens turning up in resource sessions/practical classes and even exams, if they represent classic pathology.

As some of these specimens are very old (some up to 80 years), some of the investigations and treatments mentioned may be out of date.

In general

- read the clinical information given
- look at the entire specimen, not just the front
- identify and orientate the organ or tissue where possible.
- from your knowledge of pathology (which will come with time) look for relevant features to help you make the diagnosis. Of course to appreciate the abnormal you first need to have an appreciation of normal anatomy to be able to recognise and orientate the organ/tissue and the abnormalities
- make a diagnosis or differential diagnosis using any clinical information given to you – it is often relevant – sometimes the diagnosis is only made with a knowledge of the clinical features. Even when you know the diagnosis, attempt to identify relevant features in the specimen and understand why this is the diagnosis.
- attempt to correlate the pathological features with the clinical features (clinico-pathological correlation) i.e. explain how the pathological features have caused the patients symptoms and signs (when relevant)
- try to answer any questions presented yourself before reading the answers.

You may prefer to look at the specimen 'blind', without reading the clinical information given first.

In relation to pathology pot specimens in examinations, you may be asked

- for a diagnosis
- for a description
- about the pathogenesis of the disease
- about the predisposing factors and/or causes of the disease
- about the potential complications of the disease and how they arise
- to explain a patient's clinical symptoms and signs or investigation results in light of the pathological abnormalities present
- to describe the expected histological abnormalities in the abnormal areas or other searching questions that we can concoct.

## BASIC APPROACH TO INTERPRETATION AND DESCRIPTION OF OF ENDOCRINE PATHOLOGY SPECIMENS

Pathology is all about understanding disease – how it arises, its patterns, complications and how it causes symptoms and signs. That understanding of disease is aided by a having a visual appreciation of the morphological changes in tissues.

Powers of observation and description are not just of use in pathology. These are important when examining patients also. As soon as a patient walks into a room you should be observing them (are they fat, thin, pale, yellow, short of breath etc). Specific site, size, colour, texture, appropriate terminology etc are also important for describing lumps and skin lesions on a patient, and knowledge of pathological features is important in radiological diagnosis, so the observational and descriptive skills which you learn in pathology have a broader application.

Students are expected to be able to give a brief succinct description of relevant macroscopic features of a specimen using appropriate terminology, as well as to arrive at a diagnosis or differential diagnosis. Even if not asked for a description, identification of relevant features is helpful in the diagnostic process. Your descriptive skills will improve with practice.

In any aspect of medicine, one needs to approach things in a systematic manner, otherwise important points may be omitted.

- Read the clinical history, it will often provide relevant information
- Look at the front of the pot first (i.e. the one with the number and the dot), but always make sure to look at the back and sides as well.
- Identify and orientate the specimen. Identification of the organ/tissue should be possible for most specimens (though not all, as some only comprise a tumour with no surrounding normal tissue). This is a handy skill, as you are not necessarily told in an exam. Also orientate the specimen, making sure you know which side is which where appropriate. You should also have an appreciation of the normal size of organs.
- Identification of and description of the abnormality.
  - Decide and state whether the organ is of normal size, too large (hyperplastic, infiltrated by tumour, other?) or too small (? atrophic).
  - Assess where the abnormality is and decide whether it is focal, diffuse (involving an entire organ, region or tissue) or multifocal. You should describe the site of the lesion/s using appropriate anatomical terms, not for example, "at the top of the pot".  
The lesion itself should then be described.  
Focal lesion  
The description of a discrete or focal macroscopic lesion can incorporate a number of features.  
Size: Give an approximate measurement  
Shape  
Colour: What colour is it? Is it normal or pale or an unusual colour?  
Consistency: This is of course difficult when the specimen is in a pot and you are unable to touch it. But even just by looking you can get some idea: Does it look solid or firm? Does it look friable (as if it is falling to pieces) or are there bits missing or greyish areas (altered blood) to suggest necrosis? Firm pale tissue may be tumour or fibrosis.  
Margins: Are they well defined/demarcated (suggesting a benign process), or irregular or diffuse (suggesting a malignant process)?  
Diffuse  
Colour and consistency will also be relevant for a diffuse process, however, the other features may not.
- Identification of the major pathological process. In some cases it may be helpful to identify the general pathological process that the abnormality represents e.g. inflammatory, disorders of growth (e.g. atrophy, hyperplasia) or neoplastic (benign or malignant, primary or metastatic). This will be especially

useful if you don't immediately know what the diagnosis is, at least you will be able to 'ball park' it. To do this it may be helpful to go through the surgical/pathological sieve.

- Identification of related lesions. By now you should have some idea of what you think the diagnosis, or at least the differential diagnosis, is. You should now think about what you know of this condition and look for, and describe, other relevant features that may confirm or refute this diagnosis. It may be useful to include relevant negatives.
- Other pathologies. Have a look at the rest of the specimen to see if there are any other abnormalities. If they are present, describe them.
- Diagnosis. State your diagnosis or differential diagnosis. Be as precise and specific as possible. Use any relevant clinical information given to help you. Sometimes a precise diagnosis is not possible but a presumptive diagnosis based on the macroscopic and/or clinical findings is. If you can't decide on one diagnosis, give a list of reasonable differential diagnoses, in order of decreasing likelihood, give a more general diagnosis (e.g. malignant tumour), or at least attempt to identify the pathological process.

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# CORE AND CLASSIC DISEASE PROCESSES



## ADRENAL: CONGENITAL ADRENAL HYPERPLASIA

### CASE 10185

#### Clinical information

A one month old "male" infant was admitted because of failure to thrive. Examination showed loss of weight, apparently normal male genitalia but impalpable testes. The child died of a skin infection aged 2 months.

#### Describe the specimen

The specimen comprises both kidneys and adrenal glands and the bladder, uterus, vagina, Fallopian tubes, ovaries and 'prostate'. The adrenals are significantly enlarged for a child of this age.

#### What is the diagnosis?

Congenital adrenal hyperplasia

#### What is this condition, how does it arise and what effects does it have on embryological development?

There is a spectrum of congenital adrenal hyperplasias that are transmitted as autosomal recessive conditions. Each is characterised by a deficiency of one or another of the enzymes involved in the synthesis of adrenocortical hormones, particularly cortisol, from cholesterol. Steroidogenesis is then channelled into other pathways leading to increased production of androgens. The deficiency of cortisol results in increased production of ACTH from the anterior pituitary with secondary adrenal cortical hyperplasia, also amplifying the increased production of androgens that in a female embryo produce virilization. Certain enzyme defects may also impair aldosterone production leading to salt wasting.

## ADRENAL: ADRENOCORTICAL TUMOURS

### CASE 16075/91

#### Clinical information

The patient was a woman aged 56 with Conn's syndrome.

#### Describe the specimen

The specimen is of an adrenal gland containing a spherical well-demarcated 2.5cm diameter yellow nodule.

#### What is the diagnosis?

Adrenocortical adenoma

#### What is Conn's syndrome, what causes it and what effect does it have on the patient?

Conn's syndrome refers to primary hyperaldosteronism caused by an aldosterone secreting adrenocortical adenoma. The main clinical manifestations of hyperaldosteronism are hypertension and hypokalemia. The hypokalemia can lead to muscular weakness and tetany. Hypertension of course can have a variety of complications.

### CASE 4610

#### Clinical information

This 17 year old female was admitted in 1946 with a classical picture of virilism. She had been growing excessive hair on her limbs for 3 years and had had acne for 1 year. Her voice was deep and she had lost weight during the previous 6 months. Menstruation had not begun. When examined she had a BP of 100/125, male distribution of hair, undeveloped breasts and enlargement of the clitoris. Laryngoscopy demonstrated a larger than normal larynx. A peri-renal insufflation was performed and a left suprarenal tumour diagnosed. No secondary deposits were found on chest x-ray. Adrenalectomy was performed. Following the operation the patient's BP dropped considerably to 130/80.

#### Describe the specimen

The specimen is of an encapsulated oval tumour measuring 9cm in maximum dimension. Sectioning reveals a soft pale yellow tumour with areas of necrosis. No residual normal adrenal tissue is seen.

#### What is the diagnosis?

Adrenocortical carcinoma (confirmed histologically)

#### Which layer of the adrenal cortex normally produces sex steroids?

The zona reticularis

#### Comment

Adrenocortical tumours often have a yellow/brown cut surface due to the lipid content of the steroid producing cells. Many tumours are non-functioning and are asymptomatic. It is not possible to distinguish functioning from non-functioning tumours on the basis of morphological features of the lesion itself, though functioning ones tend to be associated with atrophy of the cortex. Adrenocortical carcinomas, which may be well circumscribed, are sometimes not readily distinguished from adenomas, however, most carcinomas are larger (>5cm diameter or 50g), contain more than rare mitoses and often areas of necrosis. The presence of metastases with a similar microscopic morphology will also differentiate the two.

How may an adrenocortical adenoma present clinically?

Many adenomas are non-functioning and are asymptomatic. Others produce excessive amounts of one or another of the hormones normally produced by the adrenal cortex:

- cortisol, causing Cushing's syndrome
- aldosterone, causing Conn's syndrome
- androgens, causing virilization

What other pathologies can cause Cushing's syndrome?

- production of cortisol by an adrenocortical carcinoma
- primary adrenal hyperplasia
- administration of exogenous glucocorticoids
- overproduction of ACTH from a pituitary adenoma causing adrenal cortical hyperplasia (termed Cushing's disease)
- non-pituitary neoplasms producing ACTH (e.g. small cell carcinoma of the lung, some carcinoid tumours) causing adrenal cortical hyperplasia

What is Addison's disease and how does it arise?

Addison's disease refers to the effects of primary chronic adrenocortical insufficiency that results from destruction of the gland by such problems as metastases, amyloidosis, TB, sarcoidosis and autoimmune disease. The clinical characteristics of Addison's disease include weakness, weight loss, gastrointestinal symptoms, electrolyte disturbances and hypotension (from lack of aldosterone), hyperpigmentation (related to stimulation of melanocytes in the skin by the action of a pituitary hormone which is increased in this disease)

## ADRENAL: PHAEOCHROMOCYTOMA

### CASE 10822/82

#### Clinical information

The patient was a woman aged 24. She had paroxysmal hypertension and elevated urinary catecholamine levels.

#### Describe the specimen

The specimen comprises a well-circumscribed brown coloured oval tumour measuring 55mm in maximum dimension. There is a central area of scarring. No recognisable rim of adrenal cortical tissue is apparent.

#### What is the diagnosis?

Phaeochromocytoma (not readily diagnosed from the specimen alone).

#### Are these tumours benign or malignant?

Most are benign but a proportion are malignant. Benign and malignant tumours cannot reliably be distinguished morphologically, the distinction being made on the presence or absence of metastases, which are commonly in bones.

#### Where do these tumours arise?

Most of these tumours (90%) arise in the adrenal medulla from chromaffin cells. Others arise in sites within the autonomic nervous system where there are similar neuroendocrine cells e.g. the carotid body and sympathetic chain. These adrenal and extra-adrenal cells are known as the paraganglion system. The tumours outside the adrenal are termed extra-adrenal paragangliomas.

#### How may a phaeochromocytoma present clinically?

Patients not uncommonly present with hypertension, which can be episodic and accelerated/malignant in type due to the catecholamines produced by the tumour cells. There are often associated palpitations, headache, sweating and tremor.

#### What is a neuroblastoma?

Neuroblastoma is another tumour of the adrenal medulla, but as with phaeochromocytoma, occasional tumours arise elsewhere along the sympathetic chain. Neuroblastomas usually arise in young children and are one of the most common solid tumours of childhood. They are malignant, the cells showing features of primitive neurones (i.e. neuroblasts).

#### Comment

The tumour in the specimen is brown because it has been fixed in a chromate solution. This oxidises the catecholamines present in the granules within the cytoplasm of tumour cells -> brown staining.

## PITUITARY: ADENOMA

### CASE 21729

#### Clinical information

A woman aged 72 had had a pituitary adenoma partially removed 8 years previously. Five years later she developed a carcinoma of the descending colon for which a left hemicolectomy was performed. Abdominal symptoms returned 6 months before her final admission. At that time a persistent left upper temporal visual field defect was noted. She died from recurrent abdominal carcinomatosis.

#### Describe the specimen

The specimen is through the sphenoid bone and contains the pituitary fossa and associated structures. A pale mass measuring 1.5cm across protrudes upwards through the sella turcica. (The optic chiasm has been removed.)

#### What is the diagnosis?

Pituitary adenoma

#### How may a pituitary adenoma present clinically?

- From excess production of one or another of the anterior pituitary hormones
  - Prolactin: causing galactorrhoea and amenorrhoea
  - ACTH: causing hypercortisolism and Cushing's disease
  - Growth hormone: causing gigantism in children or acromegaly in adults
  - TSH (rare): causing hyperthyroidism
- A non-functional tumour may compress the remainder of the gland causing hypopituitarism
- By causing visual field defects (classically bitemporal hemianopia) from compression of the optic chiasm
- From the effects of raised intracranial pressure with large lesions

#### Comment

Note the position of the internal carotid arteries, optic nerves and right 3<sup>rd</sup> cranial nerve, left 4<sup>th</sup> cranial nerve and both 6<sup>th</sup> cranial nerves in the specimen.

## PARATHYROID: ADENOMA

### CASE 24397

#### Clinical information

This 63-year old man was admitted in a disorientated state, with a history of mental deterioration, anorexia, renal calculi and epigastric pain. His serum calcium was elevated. He died following a cardiac arrest 10 days after admission.

#### Describe the specimen

The specimen comprises the larynx, upper trachea and thyroid. The thyroid is mildly and diffusely enlarged. Protruding downwards from the left side of the thyroid is an oval encapsulated pale mass 3cm in maximum dimension. It contains small areas of cystic degeneration.

#### What is the diagnosis?

Parathyroid adenoma

#### What is the likely cause of the patient's mental deterioration, anorexia, renal calculi and epigastric pain?

Hypercalcemia.

#### What are the causes of hypercalcaemia?

- Primary hyperparathyroidism (parathyroid adenoma > hyperplasia > carcinoma)
- Tertiary hyperparathyroidism
- Widespread bone destruction from osteolytic tumours (metastases and multiple myeloma)
- Bone breakdown due to long term immobility
- Paraneoplastic: due to production of parathyroid hormone related protein by various malignancies
- Excessive action (e.g. sarcoidosis) or intake of vitamin D
- Excessive calcium intake
- Certain drugs

#### Comment

Without the clinical history, this diagnosis is not readily made from the macroscopic features alone, although its location is in keeping with a parathyroid lesion. Macroscopically, an enlarged tumour replaced lymph node is another thing to consider. Histology reportedly showed an adenoma composed mainly of chief cells.

## THYROID: DEVELOPMENTAL ABNORMALITIES

### CASES 19091 and 7285

#### CASE 19091: Lingual thyroid

##### Clinical information

The patient was a woman aged 51 who died from carcinoma of the caecum with numerous liver metastases. The abnormality was an incidental finding at post-mortem.

##### Describe the specimen

The specimen comprises the tongue, larynx and upper trachea. At the base of the tongue in the region of the foramen caecum is a round nodule 2.5cm in diameter. There does not appear to be any thyroid tissue in the normal location on the reverse of the specimen, although this is difficult to appreciate without sectioning the tissue.

##### What is the diagnosis?

Lingual thyroid (This diagnosis was confirmed histologically)

#### CASE 7285: Thyroglossal duct cyst

##### Clinical information

The patient was a man aged 61 who died of lobar pneumonia.

##### Describe the specimen

The specimen consists of the right half of the tongue, larynx and upper trachea. There is a bilocular cyst measuring 3x2cm lying in the midline anterior to the thyroid cartilage. At its upper posterior pole there is a blunt projection of the cyst behind the hyoid bone. The cyst contents comprise inspissated cream-coloured material.

##### What is the diagnosis?

Thyroglossal duct cyst

##### How do these lesions develop?

During embryological development, thyroid tissue begins to form at the base of the tongue (foramen caecum) and it descends into the neck in the midline as the embryo grows. Sometimes the thyroid does not descend, or descends incompletely, leaving thyroid tissue anywhere along the normal line of descent. This heterotopic thyroid tissue can be completely functional.

As the thyroid tissue descends into the neck it is connected to the base of the tongue by the thyroglossal duct that normally degenerates. However, remnants of the duct can remain at birth giving rise to benign epithelial lined cysts anywhere in the normal line of descent. Sometimes they don't become clinically evident until adulthood. Communications may arise between a cyst or persistent portions of thyroglossal duct and overlying skin forming a sinus.

## THYROID: MULTINODULAR GOITRE

### CASE 8570

#### Clinical information

No clinical information is available for this surgical specimen except that the patient was male.

#### Describe the specimen

The specimen consists of a very large thyroid gland with a nodular cut surface that shows variably sized nodules containing follicles full of colloid and bounded by pale fibrous septa. Several colloid cysts are present and towards the lower left-hand side there is a solid paler more cellular mass 3.5x3cm surrounded by a capsule formed from compression of the surrounding tissue.

#### What is the diagnosis?

Multinodular goitre

#### What is the pathogenesis of this abnormality?

Multinodular goitres probably develop from an initially diffusely hyperplastic gland but then due to variable hyperplasia and degeneration within the gland, it becomes multinodular with fibrosis, variably sized follicles, calcification and cyst formation. In regions of 'endemic goitre', the hyperplasia is due to iodine deficiency causing low hormone levels and elevation of TSH. The cause of the hyperplasia in sporadic cases is unknown, but probably results from subtle derangements of normal hormone production, possibly from genetic abnormalities in hormone synthesis and/or dietary factors inhibiting the formation of hormone.

#### Are patients with this condition normally euthyroid, hyperthyroid or hypothyroid?

Patients with sporadic multinodular goitre are usually euthyroid. Sometimes there is hyperfunction of a dominant nodule resulting in hyperthyroidism from 'toxic nodular goitre'.

#### How does this disease present?

Usually as a lump in the neck. Some can become very large and cause compression of the trachea. Uncommonly it will present with hyperthyroidism.

#### Comment

The nature of the pale mass is unknown. It could be a more cellular hyperplastic area of the goitre or a tumour. Only histological assessment would answer the question. One cannot determine whether multinodular goitres are 'toxic' from the morphological features.



## THYROID: CYST

### CASE 23495

#### Clinical information

This 80-year old woman was admitted with left hemiplegia and died of septicaemia. The pathology was an incidental finding at post-mortem.

#### Describe the specimen

The specimen consists of larynx, upper trachea and thyroid. The right lobe of the thyroid is almost completely replaced by a thin-walled unilocular cyst.

#### What is the diagnosis?

Thyroid cyst

#### How do these arise?

Thyroid cysts arise from enlargement of a thyroid follicle, often in the setting of a multinodular gland (which is not necessarily enlarged).

#### What is the definition of a cyst?

A cyst is an enclosed epithelial lined sac filled with fluid or semi-solid (e.g. keratin) material.

## THYROID: GRAVES DISEASE

### CASE 23615

#### Clinical information

This 58-year old man presented 2 years previously with a myocardial infarction. He later developed congestive cardiac failure that responded to digoxin and diuretics. He also complained of claudication in the legs. He later had loss of muscle power (distribution not specified) and felt hot. Borderline thyrotoxicosis was diagnosed. He died after a severe bout of chest pain.

#### Describe the specimen

The specimen is of larynx and thyroid gland. The thyroid shows diffuse enlargement of both lobes. Cut section shows a homogeneous red/brown appearance.

#### What is the diagnosis?

While not diagnostic from the specimen, the features are in keeping with Grave's disease. The differential diagnosis from the macroscopic appearance is diffuse goitre. The latter is not normally associated with hyperthyroidism, however.

#### What is the pathogenesis of this disease?

Graves disease is an autoimmune disease of the thyroid. A variety of autoantibodies form, including IgG antibodies with affinity to different parts of the TSH receptor -> activation of the receptor and hyperplasia of the gland. As with other autoimmune diseases, there is a genetic link with certain HLA types. Patients also often have other autoimmune diseases and there is an association with Hashimoto's disease. Immune mechanisms are also involved in the pathogenesis of the ophthalmopathy that often occurs in this disease, in which lymphoid infiltrates, mucopolysaccharide deposition and fibrosis occur in the orbit and extraocular eye muscles.

#### What histological changes are seen in the gland in this disease?

The gland is hypercellular with diminished colloid, often also with lymphoid infiltrates and germinal centre formation. The hyperplastic epithelium lining the follicles is thrown into folds and the cells become columnar rather than cuboidal.

#### What are the potential causes of hyperthyroidism?

- Grave's disease
- hyperfunctioning ('toxic') multinodular gland/goitre
- hyperfunctioning ('toxic') adenoma
- granulomatous thyroiditis
- occasional cases of Hashimoto's disease
- hyperfunctioning thyroid carcinomas
- some ovarian teratomas (containing thyroid tissue)
- excessive iodine or thyroxine treatment
- certain drugs
- neonatal associated with maternal Graves disease
- choriocarcinoma and hydatidiform moles
- TSH secreting pituitary adenomas

## THYROID: HASHIMOTO'S DISEASE

### CASE 3131

#### Clinical information

No clinical information is available.

#### Describe the specimen

The specimen consists of an enlarged nodular thyroid gland. The cut surface is pale and firm.

#### What is the diagnosis?

While the clinical history is unknown, the features are in keeping with Hashimoto's Disease.

(Histology reportedly showed very few small thyroid follicles remaining, the gland being infiltrated by masses of lymphocytes and plasma cells, interspersed with fibrous tissue.)

#### What is the pathogenesis of this disease?

Hashimoto's disease is an autoimmune disease of the thyroid. A variety of autoantibodies form including anti-peroxidase, anti-thyroglobulin, anti-TSH receptor and others. As with other autoimmune diseases, there is a genetic link with certain HLA types. Patients also often have other autoimmune diseases and there is an association with Grave's disease. The antithyroid immune response results in destruction of functioning follicular cells. Multiple immunologic mechanisms, cell and antibody mediated, contribute to destruction of the gland. Most patients become hypothyroid, but a proportion may have a hyperthyroid stage. The gland may or may not be enlarged and enlargement may be focal.

#### What histological changes are seen in the thyroid in this disease?

Histologically there are few follicles, these being replaced by many lymphocytes, plasma cells and germinal centres (where B lymphocytes are differentiating into plasma cells) with variable fibrosis. Residual epithelium becomes oncocytic in type (Hurthle cells). These cells have abundant eosinophilic granular cytoplasm.

#### Why does the thyroid appear pale in this disease?

The thyroid becomes pale as the normal follicles filled with colloid (which give the gland its normal brown/yellow colour) are destroyed and replaced by lymphoid tissue, giving the gland the appearance of lymph node.

#### What are the potential causes of hypothyroidism?

- Hashimoto's thyroiditis and the related lymphocytic thyroiditis
- genetic and developmental causes
- iodine deficiency
- certain drugs
- surgical removal
- radiation injury
- pituitary lesions impairing TSH production
- hypothalamic lesions impairing TRH production

## THYROID: ENCAPSULATED THYROID NODULE

### CASE 22566

#### Clinical information

The patient was a woman aged 81 who had a history of 'toxic goitre' 3 years before death. Iodine 131 controlled the toxic symptoms.

#### Describe the specimen

The specimen consists of the posterior tongue, larynx, the upper trachea and thyroid gland. The right side of the thyroid is atrophic. Its cut surface shows one small colloid cyst. The left lobe contains an ovoid encapsulated nodule measuring 3cm in maximum diameter, with some cystic degeneration and one small area of recent haemorrhage.

#### What is the diagnosis?

The differential diagnosis of this encapsulated lesion in the thyroid includes

- dominant nodule in a multinodular gland (possible, although the remainder of the gland does not appear nodular, the iodine 131 treatment will have affected the architecture and caused atrophy)
- adenoma (possible, as the remainder of the gland, although atrophied, does not appear nodular)
- encapsulated carcinoma (unlikely as these do not usually cause hyperthyroidism and presumably this diagnosis would have been made 3 years prior)

#### What is the differential diagnosis of a clinically solitary thyroid nodule?

- cyst
- dominant nodule in a multinodular gland
- asymmetric enlargement of inflammatory or autoimmune processes
- adenoma
- carcinoma

#### Comment

Solitary thyroid nodules are more likely to be malignant

- at extremes of age
- in males
- if there is associated local lymphadenopathy
- if 'cold' rather than 'hot' on a radionuclide scan
- if solid rather than cystic

## THYROID: CARCINOMA OF THE THYROID

### CASE 23724

#### Clinical information

This 69-year old hypertensive woman had suffered a stroke six years previously giving her a right hemiparesis. Since that time she had complained of a recurring lump in the right side of her neck. Six weeks before admission she became progressively dyspnoeic, was unable to swallow fluids and noted increasing size of the lump. On examination on admission she was dyspnoeic and had a husky voice. Biopsy revealed an anaplastic carcinoma of the thyroid with a few foci of probable squamous differentiation. Tracheostomy was performed and radiotherapy was commenced. She deteriorated mentally and eventually became comatose and died.

#### Describe the specimen

The specimen shows a longitudinal section of the neck structures and tongue with an infiltrative, pale, firm, poorly demarcated mass measuring 9cm in maximum dimension on the right side. It is causing tracheal narrowing above a tracheostomy site. There is marked tracheal deviation to the left.

#### What is the diagnosis?

Carcinoma of the thyroid

#### What are the main types of thyroid malignancy, and what are their characteristics?

##### Papillary carcinoma

- commonest thyroid neoplasm (75-85%)
- many arise de novo but irradiation during the 1st two decades of life predisposes
- well differentiated tumour, infiltrative lesions, may be multifocal
- patients usually euthyroid
- metastasise via lymphatics and often present with cervical lymphadenopathy. Distant spread is rare. Very good prognosis, even with lymph node metastases
- histologic diagnosis relies on presence of characteristic nuclear features: enlarged nuclei, cytoplasmic intranuclear inclusions, cleared nuclear chromatin, nuclear grooves. Many cases contain psammoma bodies.

##### Follicular carcinoma

- uncommon
- mostly in middle-aged - older women
- minimally (encapsulated) and widely invasive variants
- metastasise via blood
- most have follicular architecture histologically
- less favourable prognosis

##### Anaplastic carcinoma

- rare
- in elderly persons
- three histologic variants
- aggressive tumours with very poor prognosis
- some arise in pre-existing papillary thyroid carcinoma

##### Medullary thyroid carcinoma

- neuroendocrine tumours of C cell origin
- some arise in patients with MEN syndromes
- variable prognosis

##### Lymphoma

- often arise in patients with Hashimoto's disease

- usually B cell non-Hodgkin's lymphomas

Explain the likely pathogenesis of the patient's husky voice.

The tumour has probably invaded the right recurrent laryngeal nerve that innervates most of the muscles of the larynx, affecting speech.

Comment

The patient had reportedly complained of a recurring lump in the right side of her neck for 6 years. Her anaplastic thyroid carcinoma had not been present for all this time as they are very aggressive lesions. It is possible that the lump was unrelated, or even that it was a papillary carcinoma of the thyroid, a more indolent lesion, in which anaplastic carcinomas can sometimes arise.