



## THE PATHOLOGY OF MEDIASTINAL MASSES

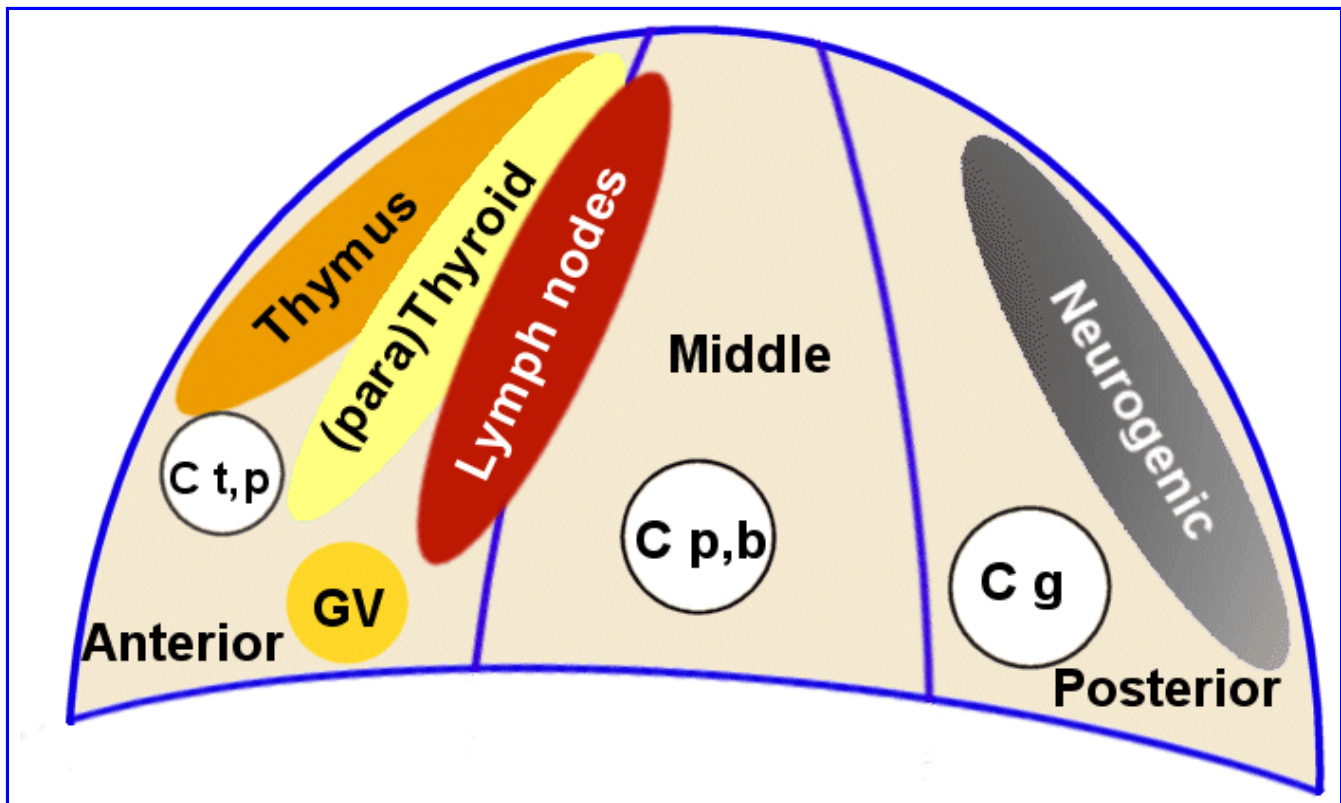
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### 1. INTRODUCTION

A wide range of process, neoplastic and non-neoplastic, can produce mediastinal masses. The relatively limited accessibility of the mediastinum to tissue biopsy can make arriving at a specific pathologic diagnosis relatively challenging. However, these lesions arise in fairly characteristic anatomic locations within the mediastinum, which is subdivided into the anterior, middle and posterior compartments as illustrated graphically in the image map below. A more realistic depiction is available at the [Virtual Hospital Chest Radiology](#) web site. We will go over the more common of these entities in class. Click on lesions of interest in the diagram below. Netscape 2.0 + or Internet Explorer 2.0 + is required for the map to work.

### Anatomic Distribution of Mediastinal Masses



C t,p: cysts, thymic and parathyroid; C p,b: cysts, pericardial and bronchogenic; C g: cysts, gastroenteric; GV: germ cell and vascular tumors

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## **2. THYMIC MASSES**

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**Thymoma** is the most common cause of a thymic mass and is the most common primary anterior mediastinal neoplasm.

It is a neoplasm of the thymic epithelium which is usually associated with a large number of non-neoplastic lymphocytes. It may present with mass effects or odd systemic manifestations such as myasthenia gravis or anemia due to red blood cell aplasia. Thymomas are usually solid but can be partially or even mainly cystic. Thymic cysts can also occur uncommonly in the absence of a thymoma and are thought to be developmental in origin. You probably should also be aware that there are a number of rare thymic tumours (such as thymic carcinoids, thymic carcinomas, thymic lymphomas ...) but you don't really need to know the details of these. Thymus glands can also undergo hyperplasia which may or may not produce a measurable enlargement and which can be due to lymphoid follicle formation only or to an increase in the entire gland structure.

Something internists like to ask junior housestaff about on rounds:

30-45% of patients with a thymoma get myasthenia gravis (MG), but:

- only 10% of pts with MG have a thymoma
- 65% of pts with MG have thymic hyperplasia (the kind with lymphoid follicle formation)
- 25% of pts with MG have normal thymuses (or is that thymi?)

Thymomas can be subtyped based on histologic appearance but staging is the most important determinant of management and prognosis. Most cases can be cured by excision and can be considered benign. Locally invasive tumors may also need radiation. Some cases spread to pleura and pericardium but distant metastases are rare.

Images:

1. [Normal thymus, low power](#): In adults the thymus involutes and consists of islands of mainly lymphoid tissue scattered through fat
2. [Normal Thymus, medium power](#): admixed lymphocytes and whorls of squamous epithelium (Hassal's corpuscles)
3. [Thymoma, resected gross specimen](#): solid and/or cystic, appears circumscribed but may infiltrate microscopically, note the scale which is in centimeters - this mass was about 15 cm in diameter!
4. [Thymoma, microscopic, low power](#): dense fibrous bands interspersed through cellular areas
5. [Thymoma, microscopic, high power](#): numerous benign lymphocytes surround the larger neoplastic epithelial cells which are not usually "malignant" looking. Hassal's corpuscles are rare or absent.
6. [Thymoma, microscopic, keratin immunostain](#): this stain uses an antibody to label the epithelial cells with a brown colour and can be useful in distinguishing thymoma from lymphoma.
7. [Thymic hyperplasia, microscopic](#): the gland weight is normal to slightly increased but the most important feature is the presence of secondary lymphoid follicles with germinal centres
8. [Thymic hyperplasia, high power](#): just a close up view showing a germinal centre and adjacent Hassal's corpuscle

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## **3. THYROID & PARATHYROID MASSES**

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Thyroid tissue masses in the anterior mediastinum can arise either from ectopic thyroid tissue or via extension

of a cervical thyroid lesion into the mediastinum. Goitres, adenomas and carcinomas can all arise in ectopic thyroid although this is fairly rare. More common is a cervical thyroid goitre which extends substernally. Distinguishing between these scenarios is important prior to surgical resection as the blood supply differs. Ectopic parathyroid tissue is not uncommonly found adjacent to the thymus gland and the mediastinum is the most common location for ectopic parathyroid adenomas.

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#### **4. MEDIASTINAL LYMPHADENOPATHY**

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Lymphadenopathy is probably the most common cause of mediastinal masses overall. The most likely causes will vary depending on the patient (age, medical history etc) and the clinical setting, but in general the differential will include:

- metastatic carcinoma, especially [lung cancer](#)
- lymphoma
- infectious/inflammatory conditions, especially granulomatous process such as tuberculosis, histoplasmosis (or other fungal infections depending on the geographic location) and [sarcoidosis](#)

We will discuss **mediastinal lymphoma** a bit in class as it is not covered elsewhere in the respiratory lectures. Most types of lymphoma can involve the mediastinum but the commonest to present as a mediastinal mass are:

1. Nodular sclerosis Hodgkin's disease: classically in young women
2. Lymphoblastic lymphoma: occurs in children, can grow very rapidly
3. Diffuse large cell: can occur at any age

As for other mediastinal lesions the pathologic diagnosis can be challenging because of the difficulty in obtaining good biopsies. Furthermore, a number of other tumors (eg thymoma, neuroblastoma, seminoma, metastatic small cell carcinoma) can mimic lymphoma under the microscope, particularly in small or crushed biopsies. The distinction is important as apart from metastatic carcinoma these lesions have a reasonable chance of cure and therapy is quite different in each case.

Images:

1. [Nodular sclerosis Hodgkin's disease, low power](#): the marked fibrosis is typical as the name suggests. It can sometimes be hard for the surgeon to get good biopsies because the nodes are so hard.
2. [Nodular sclerosis Hodgkin's disease, high power](#): the neoplastic Reed-Sternberg cells have a distinctive multi-lobed nucleus and prominent nucleoli while the background shows a mixture of benign inflammatory cells.
3. [Sarcoidosis involving mediastinal lymph nodes, low power](#): the nodes are replaced by non-necrotizing epithelioid granulomas and surrounding fibrous tissue.
4. [Sarcoidosis involving mediastinal lymph nodes, high power](#): epithelial granulomas - to exclude infectious causes such as TB and fungal infections.
5. [Histoplasmosis in mediastinal lymph nodes, high power](#): this is a silver stain of granulomas which could look like sarcoidosis on routine stains but which contain multiple black yeast forms of histoplasma

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## 5. GERM CELL AND VASCULAR TUMORS

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**Lymphangiomas** and **hemangiomas** are benign proliferations of lymphatic channels and blood vessels respectively which can occur anywhere in the mediastinum but are most common in the anterior compartment. Other benign mesenchymal tumours such as lipomas can also occur in the mediastinum but sarcomas are distinctly uncommon.

**Germ cell tumours** are believed to arise from primitive undifferentiated cells found normally in the ovaries and testicles, but which can get "lost" in various other sites of the body during embryogenesis, especially along the midline (retroperitoneum, mediastinum, skull base).

- most mediastinal germ cell tumours occur in young men
- they are classified histologically as seminoma (i.e. pure seminoma) and non-seminomatous germ cell tumours (NSGCT's) which include teratoma, choriocarcinoma, yolk sac tumour, embryonal carcinoma and all mixtures thereof (these mixed germ cell tumours are the most common form of NSGCT and they may include a component of seminoma as well)
- typically spread via lymphatics but can metastasize anywhere, especially choriocarcinoma
- young men with mediastinal masses should have testes checked (testicular germ cell tumours can metastasize to the mediastinum) and serum AFP (alpha fetoprotein - goes up with yolk sac tumour) and HCG (human chorionic gonadotropin - goes up with choriocarcinoma) measured

Microscopic Images: (the morphology is essentially the same as for testicular germ cell tumours and is included here for interest only)

[1. Terratoma:](#) this example shows an admixture squamous epithelium and cartilage. The tissue can look very benign but this is still considered a malignant tumour, although usually it is very indolent.

[2. Seminoma:](#) sheets of oval to polygonal cells in a fibrous stroma rich in lymphocytes

[3. Mixed tumour:](#) germ cell tumours often consist of a mixture of tumour types with in this case the large glands at the top being embryonal carcinoma while the fine mesh-like tissue below is yolk sac tumour.

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## 5. MEDIASTINAL NEUROGENIC TUMOURS

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**Neurogenic tumours** are the most common cause of a posterior mediastinal mass and they rarely arise elsewhere in mediastinum. Most are of these tumours are benign, with the malignant ones generally occurring in younger patients. They are classified as:

1. Tumours of sympathetic nervous system

- i) neuroblastoma - rare, malignant, occur in those under age 10 usually
- ii) ganglioneuroblastoma - more common, intermediate prognosis
- iii) ganglioneuroma - most common, benign, can occur in young adults

2. Tumours of peripheral nerve and nerve sheath

- i) schwannoma (neurilemoma) - benign, most common of all mediastinal neurogenic tumours
- ii) neurofibroma - benign, may be associated with Von Recklinghausen's disease
- iii) malignant nerve sheath tumours / schwannomas - very rare

Images:

1. [Neuroblastoma, high power:](#) a very undifferentiated tumour composed of small cells with a high nuclear:cytoplasmic ratio

2. [schwannoma, resected specimen, external surface](#): a lobulated, encapsulated mass
3. [schwannoma, resected specimen, gross photo](#): a very circumscribed tumor with a true capsule visible at the edges and a characteristic yellow and white cut surface
4. [schwannoma, low power](#): the capsule is visible and contains nerve branches from which this tumour arose
5. [schwannoma, high power](#): the tumour is made up of uniform spindled cells with no significant mitotic activity

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## **5. MEDIASTINAL CYSTS**

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Most mediastinal cysts are developmental in origin, are benign and are incidental findings on imaging. Some neoplasms such as thymomas and teratomas can be cystic and occasionally hematomas can appear cyst-like on imaging. The most common types by mediastinal compartment are:

- Anterior: thymic, cystic thymoma, parathyroid, lymphangioma, cystic teratoma
- Middle: pericardial, bronchogenic (the most common congenital mediastinal cyst)
- Posterior: gastroenteric

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