Approaches and Surgical Techniques for Anterior Mediastinal Pathology

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Key Points

- Masses located in the anterior mediastinum vary in histology, malignant potential, treatment and prognosis
- Treatment is guided by cross-sectional imaging and serological markers
- Many masses require core-needle or surgical biopsy
- Surgical approach to resectable lesions depends on their type.

Introduction

The mediastinum is bordered laterally by the pleural cavities, inferiorly by the diaphragm, and superiorly by the thoracic inlet. It is arbitrarily divided into anterior, middle and posterior compartments to help categorise mediastinal diseases according to their location. However, no anatomical planes separate those compartments, and pathological masses may occupy more than one compartment. The anterior mediastinum is bordered anteriorly by the sternum and posteriorly by the anterior surfaces of the pericardium and great vessels. It contains the thymus, lymph nodes, fatty tissue, and, occasionally, ectopic thyroid or parathyroid tissue. All those organs and tissues may give rise to pathological mediastinal lesions, both malignant and benign.

Although anterior mediastinal masses are relatively uncommon, more than half of all mediastinal lesions in adults are located in this mediastinal compartment. The relative frequency of various mediastinal pathologies (shown in Table 1) varies between studies and is dependent on patients' age and sex. However, in the adult population, the most common anterior mediastinal lesions are thymic malignancies followed by lymphomas and substernal goiters.

The majority of anterior mediastinal masses is of primary mediastinal origin, although malignant metastases to local lymph nodes may also occur. Mediastinal lesions are usually asymptomatic and are often discovered incidentally when a chest radiograph or computed tomography (CT) scan is obtained for an unrelated reason. Any symptoms that occur result from the compression or invasion of mediastinal structures adjacent to the tumour. Coughing, chest pain, dyspnea, dysphagia, hoarseness or superior vena cava syndrome (SVCS) may be present. Some lesions may be also associated with generalized symptoms, like thymoma-associated myasthenia gravis (MG), lymphoma-associated B symptoms (chills, fever and weight loss) or gynecomastia accompanying some germ cell tumours (GCTs) with markedly elevated

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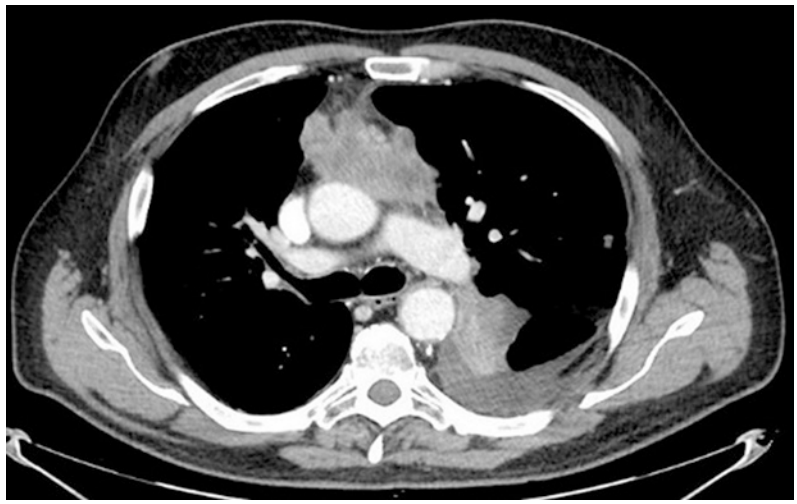

Fig. 1 Stage IV thymic carcinoma in an 60-year old patient. Contrast-enhanced CT showing heterogenous mass in the anterior mediastinum with left pleural effusion and left pleural metastasis

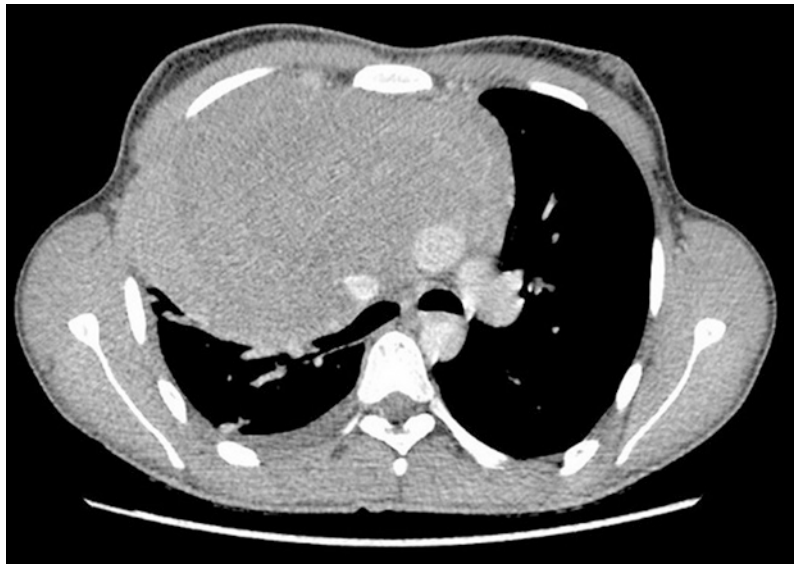

Fig. 2 Hodgkin disease in an 21-year old patient. Contrast-enhanced CT showing homogenous mass in the anterior mediastinum protruding into right hemithorax and compressing right lung

beta-human chorionic gonadotropin (β-hCG) levels. Malignant lesions are more likely to be symptomatic than benign ones. The short time elapsing from the onset of symptoms may be suggestive of highly aggressive tumours such as lymphoblastic lymphomas or non-seminomatous GCTs (NSGCTs).

Diagnostic work-up. The most common initial imaging method used for investigating a suspected mediastinal mass is a chest radiograph. Posteroanterior and lateral chest radiographs can provide information regarding the location, size, composition and density of the lesion. Large lesions may present as soft-tissue masses with

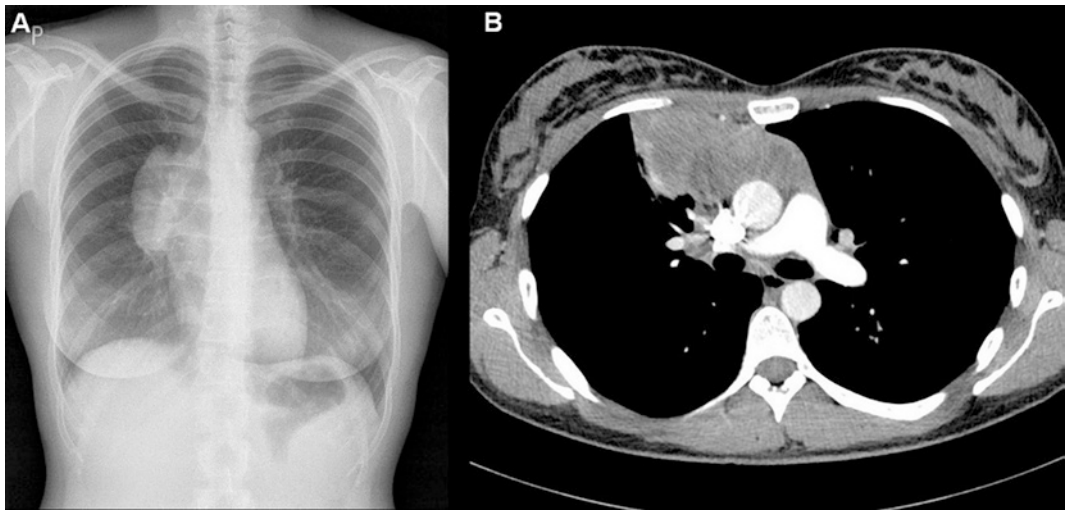

Fig. 3 Primary mediastinal B-cell lymphoma in an 31-year old patient. **a** Plain radiograph showing widening of the mediastinum. **b** Contrast-enhanced CT showing nonifiltrating, homogenous mass in the anterior mediastinum

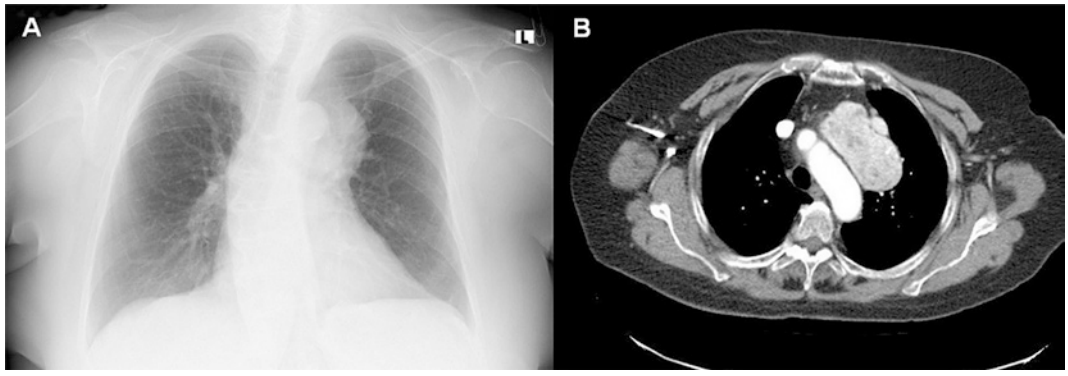

Fig. 4 Substernal goiter in an 72-year old patient. **a** Plain radiograph showing widening of the mediastinum and tracheal deviation. **b** Contrast-enhanced CT showing heterogenous, enhancing mass adjacant to aortic arch

a lack of normal mediastinal contours. Tracheal deviation or pleural effusion may also be present. However, small mediastinal lesions may present subtle radiological signs or may not be visible on chest radiographs at all. In every case, further diagnostic evaluation of the mediastinal mass with cross-sectional imaging like CT or magnetic resonance (MRI) is mandatory. Cross-sectional imaging is a key examination tool used to characterize the lesion, formulate a presumptive diagnosis and guide further treatment. Contrast-enhanced multidetector CT is the imaging modality of choice. It allows for a detailed morphological description of the lesion and assessment of the lesion's size, location and relation to the surrounding structures. An intravenous contrast study allows the involvement of great mediastinal blood vessels by the mass to be assessed. Although MRI does not require iodine contrast administration, it is inferior to CT in imaging most anterior mediastinal pathologies due to poorer spatial resolution. However, MRI is the most useful imaging modality for distinguishing cystic from solid lesions, as in the case of cystic lesions with dense contents that appear on CT images as solid masses. Also, when the CT image is inconclusive, thymic hyperplasia may be differentiated from thymic

Table 1 Anterior mediastinal lesions

Thymic malignancies (thymomas, thymic carcinoma, neurogenic tumours)
Lymphomas (Hodgkin lymphomas, primary mediastinal B-cell lymphomas, lymphoblastic lymphomas)
Substernal goiters
Germ cell tumours (teratomas, seminomas, non-seminomatous germ cell tumours)
Benign thymic lesions (thymic cysts, hyperplasia, thymolipomas)
Metastatic lymph nodes
Parathyroid adenomas
Mesenchymal tumours (lipomas, liposarcomas)

malignancies with chemical shift MRI techniques. A positron emission tomography (PET) scan has little role in the diagnostic work-up of anterior mediastinal lesions. This imaging modality is used to rule out distant metastases if disseminated disease is suspected. It is also used to stage and evaluate the response to treatment of lymphomas.

Serum marker assays play a significant role in the diagnostic work–up of anterior mediastinal masses. Assessment of the serum levels of β-hCG and α-fetoprotein (AFP) is highly useful in the differential diagnosis of GCTs. 70% of patients with NSGCTs have elevated AFP, and 30% have significantly elevated β-hCG. These tumour markers should be obtained in every young male patient with an anterior mediastinal mass, as elevated AFP levels are diagnostic for NSGCTs and the patient can proceed to upfront chemotherapy without the need for tissue confirmation. Serum *lactate dehydrogenase* (LDH) may be elevated in patients with some rapidly growing lymphomas and GCTs. The presence of the antiacetylcholine receptor antibody in a patient with symptoms of MG and an anterior mediastinal tumour virtually confirms the diagnosis of thymoma. Rare neuroendocrine tumours of the thymus may secrete corticotropin-releasing hormone. Substernal goiters may be associated with thyrotoxicosis and mediastinal ectopic parathyroid adenomas are occasional causes of hyperparathyroidism.

When a presumptive diagnosis of an anterior mediastinal tumour can be reliably made on the basis of radiological features and serum markers and the tumour seems to be resectable, the patient may proceed to upfront surgery and tissue biopsy is unnecessary. This is true for lesions like early-stage thymomas, substernal goiters, thymolipomas, teratomas or thymic cysts. Tissue diagnosis is required when the lesion cannot be diagnosed by other means, when upfront curative surgery cannot be undertaken due to local invasion, or when the lesion is to be treated non-surgically. Available techniques for the biopsy of anterior mediastinal lesions include non-surgical transthoracic biopsies (fine-needle aspiration—FNA—and core-needle biopsy) or surgical biopsies by mediastinotomy, video-assisted thoracic surgery (VATS) or mediastinoscopy. Non-surgical biopsies are less invasive and are performed with local anaesthesia. FNA is the least invasive and simplest biopsy method which allows benign and malignant conditions to be distinguished and carcinoma to be diagnosed. However, it has poor accuracy for diagnosing thymic malignancies and diagnosing and subtyping lymphomas, meaning its role in the work-up of anterior mediastinal masses is limited.

Definitive diagnosis of most mediastinal lesions requires core biopsy or open surgical biopsy. A CT-guided percutaneous core-needle biopsy provides a larger volume of tissue sample than FNA with preserved microarchitecture and allows all mediastinal masses to be diagnosed. However, although a less invasive method, its diagnostic accuracy is still inferior to surgical biopsy. The results of core-needle biopsies are often not conclusive and cause unnecessary delay in diagnosis and treatment of rapidly growing mediastinal masses. Surgical

biopsy is the gold standard for the biopsy of anterior mediastinal lesions because the large tissue specimens necessary for diagnosis can be selectively obtained. Surgical biopsy, however, requires general anaesthesia and is a more invasive procedure. The most commonly employed biopsy technique is anterior mediastinotomy (Chamberlain procedure), where a 3–4 cm incision is made over the second or third costal cartilage and the anterior mediastinum is entered through the bed of excised cartilage lateral to the internal mammary vessels. The Chamberlain procedure may also be used for the biopsy of aortopulmonary window lymph nodes (LN), usually during the staging of non-small cell lung cancer (NSCLC). Another approach is VATS, which provides good exposure of the anterior mediastinum and allows for precise dissection of the anterior mediastinum. However, it requires general anaesthesia, single lung ventilation and postprocedural chest drainage. Cervical mediastinoscopy may also be employed for tissue biopsies, although visualisation of the anterior mediastinum is difficult with this technique. This approach is suitable for lesions extending to the visceral mediastinal compartment or those associated with paratrachael or subcarinal lymphadenopathy. Mediastinoscopy is associated with less postoperative pain than both mediastinotomy and VATS. When mediastinal pathology is accompanied by peripheral lymphadenopathy, as is the case for some lymphomas, it is far more convenient to biopsy the easily accessible LN than the mediastinal mass.

Surgical treatment. There is no established standard surgical technique for the resection of anterior mediastinal tumours. For early stage thymomas, a standard thymectomy using a minimally invasive approach (transcervical, VATS, subxiphoid or robotic) is usually conducted. Minimally invasive techniques may also be used for thymic cysts or other small, non-invading mediastinal lesions. For larger or invading tumours, the standard approach is median sternotomy, which provides excellent exposure of the anterior mediastinum. Some tumours that extend into the hemithorax are best approached by a lateral thoracotomy or hemiclamshell incision, especially when the pulmonary hilum is invaded. Large masses that involve both hilums are best approached through a clamshell incision. When the mass is located near the thoracic inlet, an upper sternotomy or neck collar incision may be the most convenient approach.

The goal of surgery is complete resection of the lesion, including metastatic foci. Whenever possible, tumour-free surgical margins should be obtained. If the tumour is invasive, en-bloc removal of all affected structures should be conducted. However, care must be taken to preserve non-involved vital structures, like phrenic and recurrent nerves or great veins. In the case of lung infiltration, wedge resection of involved lung parenchyma is usually sufficient. In more advanced cases, anatomical resections, including pneumonectomy, may be performed if complete resection will be accomplished and the patient has adequate pulmonary reserve. The resection of the invaded or adhering pericardium is always conducted, sometimes with a patch reconstruction. The superior caval vein (SVC) or an innominate vein should be resected only if this is required in order to achieve complete resection. If only one innominate vein is affected, it can be resected without reconstruction. Focal involvement of SVC requires its partial resection with simple suturing or a patch reconstruction using autologous pericardium. For more advanced involvement of SVC or both innominate veins, complete resection and vessel reconstruction using vascular prosthesis (PTFE, bovine pericardial conduit or saphenous vein conduit) is necessary. If a single phrenic nerve is invaded by a malignancy and curative resection can be otherwise performed, it should be resected, if a patient's pulmonary reserve is sufficient. However, both phrenic nerves should never be resected. Instead, the tumour is skeletonized off the nerves. A decision to resect the phrenic nerve in severely myasthenic patients must be carefully judged, as loss of a hemidiaphragm function may be detrimental. Parietal pleural or pericardial implants should be widely resected. Diaphragmatic pleural implants are best removed by full-thickness excision of the involved diaphragm. Some patients may require

extrapleural pneumonectomy for complete clearance of pleural metastases. Some tumours, like malignant thymic tumours, require also regional lymphadenectomy.

In the sections below, a more detailed description of the most common anterior mediastinal masses is presented.

Thymic Malignancies

Thymic epithelial malignancies are the most frequent anterior mediastinal tumours. Thymomas are by far the most prevalent subtype, while thymic carcinomas and neuroendocrine tumours are less frequent. Thymic tumours have no gender predilection, and may occur in any age with peak incidence in the fourth to sixth decade of life. More than half of patients with thymomas are asymptomatic, and one-third present with autoimmune disorders, mainly MG, but also pure red cell aplasia or hypogammaglobulinemia. Patients with larger thymomas or with thymic carcinomas may present with compression symptoms. On a CT scan, a thymoma usually forms a solid, spherical or ovoid, homogenous or slightly heterogenous mass in the anterior mediastinum. Pleural or pericardial effusions may be present, but lymphadenopathy is typically absent. When the mass is infiltrating, large, heterogenous and with lymphadenopathy or distant metastases, a thymic carcinoma or thymic carcinoid should be suspected (Fig. 1).

The resectability of the tumour is the main factor influencing treatment. If the diagnosis of a thymic tumour is highly probable on the basis of cross-sectional imaging and radical surgical resection is achievable, the patient proceeds to curative surgery without the need for a biopsy. Biopsy should be performed in the case of unequivocal CT results suggesting a lymphoma, or in the case of unresectable tumours, before induction chemotherapy or definitive chemoradiation. Tissue may be sampled using percutaneous core-needle biopsy or incisional surgical biopsy through mediastinotomy or VATS. FNA is not recommended. Further information concerning the treatment of thymic malignancies is presented in chapter "Approaches and surgical techniques in the thymus pathology".

Lymphomas

Lymphomas are a diverse group of neoplastic diseases originating from lymphocytes or their progenitors. The most widely used classification system is the World Health Organization (WHO) classification. Primary mediastinal lymphomas originating from lymphoid tissue of the thymus or mediastinal LNs constitute around 25% of anterior mediastinal masses. The mediastinum is also often a metastatic site for a disseminated lymphoma originating elsewhere. Most primary lymphomas are located in the anterior mediastinum, but involvement of the middle mediastinal compartment may occasionally occur. The most common primary mediastinal lymphoma, representing more than half of all cases, is Hodgkin lymphoma (HL). Mediastinal non-Hodgkin lymphomas (NHL) have a more aggressive clinical course than HL and are represented in the adult population mostly by primary mediastinal large B-cell lymphomas (PMLBL).

All mediastinal lymphomas are treated non-surgically. Even when a diagnosis of lymphoma is highly probable on the basis of clinical and radiological features, tissue sampling for histopathological diagnosis and subtyping is mandatory to guide management. Most primary mediastinal lymphomas require tissue samples of adequate size obtained from surgical biopsy. Diagnosis and subtyping of a lymphoma is the most common indication for a mediastinal surgical biopsy. An excisional biopsy of easily accessible metastatic peripheral LN is sufficient for diagnosis and subtyping a primary mediastinal lymphoma and makes mediastinal biopsy unnecessary, thus it is important to assess the status of extrathoracic LNs in every patient with a mediastinal mass. When mediastinal biopsy has to be carried out, the usual approach is anterior mediastinotomy or VATS. Lymphomas extending into the visceral mediastinum or that involve subcarinal or paratracheal LNs may be biopsied through cervical mediastinoscopy. Staging is

done clinically according to the Ann Arbor classification using PET/CT.

Hodgkin lymphoma is a monoclonal B-cell lymphoid neoplasm characterized by the presence of Reed-Sternberg cells. The main HL subtype involving the mediastinum is nodular sclerosis classical HL. It occurs mostly in patients in their twenties and thirties, with slight female predominance. Mediastinal HL usually arises from mediastinal LNs, but may also originate from the thymus. HL spreads to contiguous LN groups, with frequent involvement of hilar, lower cervical and supraclavicular LNs. Typical clinical presentation is a nontender cervical lymphadenopathy. In one-third of patients, general B symptoms are present. Compression symptoms are rare. Other less common symptoms include pain of enlarged LNs after alcohol ingestion, Pel-Epstein fever (intermittent intervals of fever every few weeks) or generalized pruritus. On CT examination, HL presents as mildly-enhancing, homogenous, lobulated soft tissue mass or a group of enlarged LNs in the anterior mediastinum, often with neck or axillary lymphadenopathy. The mass often encircles the great vessels without infiltrating them, a feature that distinguishes HL from other mediastinal tumours. Lung metastases are typically absent (Fig. 2).

Tissue sampling is necessary before initiating treatment. Diagnosis is based on the identification of Reed-Sternberg cells or its variants in the inflammatory environment. As Reed-Sternberg cells are relatively rare in the background lymphoid reaction and mediastinal lymphomas are often fibrotic, large tissue samples have to be obtained during surgical biopsy. The mainstay of HL treatment is chemotherapy, with the optional addition of radiotherapy or stem cell replacement.

Primary mediastinal large B-cell lymphoma is an aggressive lymphoma originating from thymic B cells. It is seen mainly in young adults in their twenties and thirties, with slight female predominance. It is a rapidly growing tumour, usually presenting with compression symptoms like chest pain, dyspnea or coughing, developing over weeks to months. SVCS and pleural or pericardial effusions are common. B symptoms may also occur. Serum LDH is often elevated.

On a CT scan, PMLBL is a homogenous soft tissue mass localized in the thymic area, with frequent lung infiltration. It may contain heterogenous areas of necrosis or haemorrhage (Fig. 3). Although mediastinal, supraclavicular or cervical LNs may be involved, distant lymphadenopathy is uncommon. Dissemination to distant extranodal sites occurs in advanced cases. Diagnosis requires sizeable tissue samples obtained from surgical biopsy due to prominent tissue sclerosis. The mainstay of treatment is chemotherapy and immunotherapy, with the addition of radiotherapy and autologous bone marrow BM transplantation in selected cases.

Lymphoblastic lymphoma is a very aggressive lymphoma usually originating from T cells, although B-cell origin is also possible. Morphologically, a lymphoblastic lymphoma is indistinguishable from acute lymphoblastic leukemia and leukemia is arbitrary defined as a disease with prominent bone marrow involvement. Lymphoblastic lymphomas affect mostly males in the second decade of life, but may occur at any age in both sexes. Usually, the disease is not confined to the chest and also involves extrathoracic lymph nodes, bone marrow or blood. A typical patient presents with enlargement of peripheral lymph nodes, B symptoms and acute compression symptoms due to the rapidly growing mediastinal mass. Symptoms develop acutely over the course of days to weeks. Life-threatening presentations like tracheal compression with stridor, SVCS or cardiac tamponade may occur. Pleural or pericardial effusions are often present and serum LDH level is markedly elevated. On a CT scan, lymphoblastic lymphoma presents as a bulky, heterogenous mediastinal mass that typically involves the thymus with frequent mediastinal lymphadenopathy. As lymphoblastic lymphomas have unique cytologic features, they can be diagnosed using samples obtained by FNA of peripheral LNs, bone marrow biopsies or thoracentesis, making mediastinal biopsies usually unnecessary for diagnosis. Treatment is based on chemotherapy,

with the optional addition of radiotherapy or bone marrow transplantation.

Other lymphomas presenting as mediastinal masses, like mediastinal gray-zone lymphomas, thymic extranodal marginal zone lymphomas of the mucosa-associated lymphoid tissue or anaplastic large cell lymphomas are rare and will not be covered in this chapter.

Endocrine Lesions

Substernal goiter is an extension of the thyroid below the plane of the upper thoracic inlet in a patient in supine position. A goiter grows slowly over many years, extending along the fascial planes usually into the anterior mediastinum, although extension into the medium or posterior mediastinum also occurs. A substernal goiter may be classified as primary, arising from ectopic mediastinal thyroid tissue and with no anatomical continuity with the cervical thyroid, or secondary, which is a mediastinal extension of a cervical goiter. Primary substernal goiters are rare (1–2% of all substernal goiters) and are vascularized by mediastinal vessels (tributaries from internal mammary artery, aorta or other thoracic vessels, depending on localization). Secondary substernal goiters retain thyroid vascularization from superior and inferior thyroid arteries. A substernal goiter is usually discovered in patients in their fifties or older, as goiters grow slowly and takes years to grow large enough to produce symptoms. In the vast majority of patients, iodine deficiency is the main etiologic factor. The spectrum of clinical presentation is broad and ranges from a complete lack of symptoms to acute respiratory failure. The most common clinical presentation is exertional or positional dyspnea resulting from compression of the trachea, occurring in 60% of patients. Other symptoms include coughing, dysphagia, stridor, dysphonia or, rarely, SVCS. When symptoms develop rapidly, they may indicate thyroid cancer, which can be found in up to 10% of patients with substernal goiters.

In all patients, goiters should be evaluated by ultrasonography (USG) and contrast-enhanced CT. All suspected nodules revealed on USG should undergo FNA biopsy, following the guidelines for the treatment of a normal-sized thyroid. On a CT scan, a substernal goiter is a heterogenous (with regions of low attenuation representing cystic changes), hyperdense mass, enhanced after contrast administration (Fig. 4). Continuity with the cervical thyroid is diagnostic for secondary substernal goiters. A biopsy is not necessary to make a diagnosis. In the case of a thyroid carcinoma, loss of distinct mediastinal fascial planes or cervical lymphadenopathy may be present.

The laboratory work-up of substernal goiters includes thyroid function tests, as the disease may be associated with thyrotoxicosis. Iodine-131 scintigraphy should be performed if thyroid-stimulating hormone (TSH) levels are below normal. All patients with substernal goiters causing symptoms should undergo a thyroidectomy. An asymptomatic retrosternal goiter is an indication for surgery only in relatively younger patients, who have a high risk of developing symptoms or malignancy over the years. The vast majority of substernal goiters can be resected through standard cervical collar incision. In rare cases, manubrial transection, sternotomy or thoracotomy is necessary, mainly in cases of ectopic goiters, goiters localized in the medium or posterior mediastinum or extremely large goiters. Complications after thyroidectomies for substernal goiters are more common than after regular thyroidectomies, with enhanced risk for recurrent laryngeal nerve injury, intraopertative bleeding and postoperative hypoparathyroidism. Large substernal goiters with tracheal compression are associated with a risk of transient postoperative tracheomalacia.

Mediastinal ectopic parathyroid adenomas are rare causes of hyperparathyroidism requiring surgical exploration of the mediastinum. The mediastinal localization of parathyroid tissue is a result of their abnormal migration during embryogenesis. These lesions are usually small and require careful preoperative work-up using scintigraphy (technetium-99 sestamibi single-photon emission computed tomography)

fused with CT or MRI, as an intraoperative search for an ectopic parathyroid adenoma is time-consuming and often ineffective. A mediastinal ectopic parathyroid located above the brachiocephalic vein can be approached using a cervical collar incision. Although the traditional approach for lesions located lower in the mediastinum was median sternotomy or lateral thoracotomy, nowadays, after precise preoperative localization with imaging techniques, they can be successfully excised using minimally invasive techniques like VATS, mediastinoscopy or robotic procedures.

Germ Cell Tumours

Mediastinal GCTs are a group of neoplasms arising from ectopic primordial germ cells that were displaced during midline migration in early embryogenesis. GCTs represent 10–15% of all anterior mediastinal tumours, with the mediastinum being the most common site of extragonadal GCTs. GCTs are divided into subtypes that have different malignant potential, prognosis and treatment. Two thirds of GCTs are benign teratomas, for which surgical resection alone is curative. Half of the remaining GCTs are malignant seminomas presenting with good prognosis after chemotherapy. The remaining NSGCTs are highly malignant and have the worst prognosis of all GCTs. In the case of those tumours, treatment is based on primary chemotherapy followed by surgical resection of any residual mass. Although mediastinal metastases of primary testicular GCTs are very rare (especially in the absence of retroperitoneal LNs metastases), in every patient with an anterior mediastinal mass, testicular GCTs must be excluded by physical examination or ultrasound.

Teratoma is a benign GCT that consists of somatic tissue derived from two or three germ layers (ectoderm, endoderm or mesoderm). It may be either mature (composed exclusively of mature tissues) or immature, composed partially or totally from embryonic or foetal tissues and potentially malignant. Teratomas may contain virtually any histologic type of tissue and commonly contain skin and cutaneous appendages, bronchial and gastrointestinal mucosa, pancreatic and neural tissue, smooth muscle and fat. Less frequently, skeletal muscle, cartilage or bone may be present within the lesion. Teratomas typically arise in the anterior mediastinum and often protrude to one hemithorax, but may also be occasionally seen in the posterior mediastinum. Both sexes are affected with equal frequency, and the peak of incidence is between the second and forth decade of life.

Teratomas are usually asymptomatic, slow-growing tumours detected during imaging studies for an unrelated condition. They can grow large and cause compression symptoms (pain, dyspnea, coughing, dysphagia) or lung atelectasis. In rare cases, teratomas may rupture into adhering structures, causing pleural effusion, cardiac tamponade or lung abscesses. When a teratoma erodes into the tracheobronchial tree, the patient coughs up hair (trichoptysis) or sebum. Teratomas may also fistulize to the skin, presenting as sinus drainage. As they frequently contain pancreatic tissue, episodes of hypoglycemia due to hyperinsulinism may be present. Serum tumour markers are not elevated.

On a CT scan, teratomas are large (often exceeding 10 cm), heterogenous, multilocular cystic masses with a combination of coexisting densities of fat, soft tissue, fluid and areas of calcification. Sometimes, bone and tooth-like elements may be identified. Diagnosis is based on imaging studies and does not require biopsy before the initiation of surgical treatment.

As teratomas might complicate and may be potentially malignant, they should always be completely excised, even in asymptomatic patients. The usual approach is by sternotomy or thoracotomy. Occasionally, en-bloc removal of adjacent structures (mainly the lung) is required due to strong adhesions. Due to the large size, adhesions to neighbouring structures and serious consequences of intraoperative rupture of the lesion, VATS approach is limited to small and non-adhering tumours.

Mediastinal seminoma is a malignant neoplasm composed of cells resembling primordial germ cells. It occurs almost exclusively in

young men, with peak incidence in their thirties. Many patients remain asymptomatic at the time of diagnosis. When symptoms occur, they are results of compression, with chest pain and dyspnea being the most common complaints. Seminomas do not tend to invade local chest structures, but around 40% of patients have distant metastases at the time of diagnosis, with lungs being the most common metastatic site. Metastasis to regional LNs is uncommon.

On CT examination, pure seminomas manifest as large, lobular, homogenous soft-tissue masses located in the anterior mediastinum, indistinguishable from lymphomas. However, lung metastases, relatively often accompanying seminomas, are highly unusual in lymphomas. In pure seminomas, AFP is never elevated, and serum levels of β-hCG are normal or only slightly elevated. LDH serum levels are often elevated. When a mediastinal seminoma is combined with an NSGCT component, which can be diagnosed with serologic markers, it is classified as an NSGCT and managed accordingly. Any elevation of AFP indicates the presence of an NSGCT component, regardless of biopsy. Also, β-hCG above 100 ng/mL is unusual for a pure seminoma and suggests the presence of an NSGCT component as well.

A seminoma requires diagnosis from a tissue biopsy before initiation of treatment. CT-guided transthoracic core biopsy is sufficient in many cases and should be performed first. When biopsy results are inconclusive, the lesion should be biopsied surgically. The treatment of seminomas is based on chemotherapy, with radiotherapy applicable for recurrent or persistent mediastinal masses. Surgical excision plays no role in the treatment of mediastinal seminomas.

Mediastinal NSGCTs include embryonal carcinomas, yolk sac tumours or choriocarcinomas. An NCGCT may consist of an isolated single subtype or, often, be mixed with a different subtype of NGCT, or a teratoma, seminoma or even carcinoma or sarcoma. All those tumours are grouped together because they share a similar biology, clinical course and treatment. Any NSGCT may be additionally accompanied by hematologic malignancies or idiopathic thrombocytopenia. Patients are almost exclusively males, usually in their twenties to mid-thirties.

All NGCTs are rapidly growing tumours, presenting with compression symptoms like chest pain, dyspnea, coughing, SVCS or hoarseness, arising in a time period of days to weeks. Generalized symptoms like fever, chills or weight loss can be present. In patients with a choriocarcinoma component, high β-hCG-secretion manifesting as gynecomastia may be present.

At the time of diagnosis, most patients have distant metastases. On CT scans, NSGCTs are large, heterogeneous masses with central areas of necrosis and haemorrhage, infiltrating surrounding structures, often with lung or liver metastases. Cystic spaces indicate a teratoma component within the lesion. Determining serum tumour markers plays a pivotal role in the diagnostic work-up of NSGCT patients. In 90% of cases, serum AFP or β-hCG is significantly elevated, a finding that is pathognomonic for NSGCTs. LDH may also be elevated. A significant elevation of AFT (>500 ng/mL) or β-hCG (above 100 ng/mL) always indicates the presence of a nonseminomatous component of the tumour, and in these patients chemotherapy should be initiated without delaying to perform tumour biopsy. When serum markers are not elevated, or β-hCG is elevated only slightly, histologic confirmation with transthoracic biopsy is required to initiate treatment. Treatment, usually multimodal, begins with cisplatin-based chemotherapy.

A persistent mediastinal mass after chemotherapy is a common finding. Although on pathological examination, this mass may occasionally be a completely necrotic tumour, more often it is a residual NSGCT, a persistent teratoma or a carcinoma/sarcoma. As salvage chemotherapy is rarely efficient, the remaining tumour should be surgically excised whenever technically feasible. Surgical access depends on the exact location and extension of the mass. Usually sternotomy or lateral thoracotomy is utilized. For larger tumours with hilar involvement, a hemiclamshell or clamshell incision needs

to be used. The aim of the surgery is en-bloc radical resection of any residual mass from the invaded surrounding structures such as the lung, thymus, pericardium or, sometimes, great veins or phrenic nerve. In the case of disseminated disease, a pulmonary *metastasectomy* should also be performed.

Benign Thymic Lesions

Thymic hyperplasia. True thymic hyperplasia is a uniform symmetric enlargement of a normal-shaped, triangular thymus, with preservation of normal histologic architecture. It typically occurs after the resolution of a stressful event such as a burn or injury, but also after chemotherapy, radiotherapy or therapy with corticosteroids. Another form is lymphoid follicular thymic hyperplasia, associated with autoimmune diseases like MG, hyperthyroidism or systemic lupus erythematosus. The normal-shaped thymus is enlarged and the thymic cortex is replaced with multiple lymphoid follicles and germinal centres. Thymic enlargement may also not be uniform, but more nodular and similar to thymomas or other malignancies. Chemical shift MRI with in-phase and out-of-phase gradient-echo sequences helps in differential diagnosis in cases of equivocal CT. Alternatively, a follow-up CT scan may be obtained after three months to allow the size of the thymus to decrease. Unless associated with MG, thymic hyperplasia is not an indication for surgical treatment.

Thymic cysts may be congenital or acquired. Congenital thymic cysts are unilocular and commonly located in the neck or anterior mediastinum extrathymically along the developmental tract of the thymus. They are caused by persistence of the thymopharyngeal duct. Acquired, multilocular thymic cysts are the result of thymic degeneration seen in autoimmune diseases, after medical or surgical treatment of mediastinal lesions (e.g. radiotherapy for HL) or in primary thymic malignancies. Malignancy should always be ruled out, as thymomas, lymphomas and GCTs may have cystic components.

Thymic cysts are usually asymptomatic and discovered incidentally on routine chest radiographs. They can grow large and cause compression symptoms. On cross-sectional imaging they present as unilocular or multilocular thin-walled cystic lesions with clearly defined contours and low-attenuating contents. Occasionally, after an intracystic haemorrhage, they may present as lesions with soft tissue attenuation and can be confused with solid thymic tumours. MRI is conclusive in cases of equivocal CT images. Diagnosis is established on the basis of cross-sectional imaging. Resection should be performed for every symptomatic or growing cyst or when malignancy cannot be firmly ruled out by imaging. The traditional surgical approach is median sternotomy or thoracotomy, but nowadays most thymic cysts are resected using minimally invasive techniques (VATS, subxiphoid or transcervical approach). While a complete local excision is sufficient for simple unilocular cysts, a standard thymectomy is advocated for multilocular cysts.

Thymolipoma is a benign lesion originating from the thymus, composed of both thymic epithelial and adipose tissue, with fat accounting for more than half of the tumour mass. Although slow-growing, it can grow very large before symptoms occur. Most thymolipomas are found in young adults, often during diagnostic work-up for recurrent pulmonary infections. Although thymolipomas do not invade adjacent structures, they often present with compression symptoms, which are sometimes significant when the lesion is large. CT scans show a large anterior mediastinal mass of predominantly fat density with strands of soft tissue density, representing normal thymic tissue. It often extends to one hemithorax. Diagnosis is established by cross-sectional imaging alone and tissue biopsy is unnecessary. Thymolipomas should be resected even in asymptomatic patients to prevent further growth and development of symptoms.

Self-study

Which mediastinal mass is the most common indication to surgical biopsy:

A. Thymoma
B. Lymphoma (correct)
C. NSCGC
D. Substernal goiter.

Elevation of serum AFP level is diagnostic for:

A. Hodgkin disease
B. Seminoma
C. NSGCT (correct)
D. Thymic carcinoma.

Primary treatment of seminoma is:

A. Chemoterapy (correct)
B. Surgical excision
C. Radiotherapy
D. Immunotherapy.

Which mediastinal lesion should be always excised:

A. Substernal goiter
B. Teratoma (correct)
C. Thymic cyst
D. Thymic hyperplasia.

The most useful imaging modality of thymic cysts is:

A. Contrast-enhanced CT
B. PET/CT
C. EBUS (transbronchial ustrasonography)
D. MRI (correct).

Bibliography

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