Surgical Approaches to the Mediastinum

3

Introduction

Contrary to the belief of many, the mediastinum actually can be defined by specific boundaries and landmarks. Basically, the mediastinum encompasses the region from the thoracic inlet to the diaphragm as the superior and inferior boundaries, the pleural reflections laterally, the sternum anteriorly and the spine posteriorly. Interestingly, a number of different anatomical classifications have been put forth to describe the various compartments of the mediastinum, but, from a surgical standpoint, it perhaps is easiest and most straightforward to use the terms superior, middle, anterior, and posterior (Fig. 3.1). When we think in terms of surgical pathology, essentially all entities can be fitted into one of these compartments. There have been a number of attempts to further define mediastinal compartments such as that of the Japanese Association for Research on the Thymus (JART) [1]. Their classification is based on axial computed tomographic (CT) images and, as noted above, proposes four compartments: superior, anterior (prevascular zone), middle (peritracheoesophageal zone), and posterior (paravertebral zone). A retrospective look at data collected from 445 pathologically proven lesions allowed them to validate their proposed classification. Thymic epithelial neoplasms, lymphomas, and a majority of germ cell tumors were classified within the anterior mediastinum. The majority of substernal goiters were located in the superior compartment, while the majority of masses found in the middle mediastinum were cysts specifically of bronchopulmonary foregut origin or pericardial. Neurogenic lesions comprised the majority of lesions found in the paravertebral (posterior) zone.

A mediastinal mass may be discovered when a patient presents with symptoms suggestive of pulmonary pathology – such as chest pain or cough – but many are found serendipitously when a CT scan is done for some other reason. A large anterior mediastinal mass often may be suggested by the finding of an additional soft tissue mass seen on plain chest radiograph especially on the lateral projection. The so-called silhouette sign, where there is a loss of a normal border of an intrathoracic structure, may be noted. Once an abnormality is noted or suspected on a chest radiograph, the definitive study is a CT scan that provides cross-sectional imaging that defines the location of the lesion as well as the size and additional characteristics that may be present. Magnetic resonance imaging (MRI) has not been found to add any additional information if the lesion is solid. However, MRI clearly is superior to CT in delineating a cystic from a solid lesion and should be obtained if there is suspicion that a lesion may be cystic [2]. The location of a mediastinal mass as defined by the CT scan aids greatly in the differential diagnosis of a particular lesion. As a rule, more than half of all mediastinal masses locate to the anterior mediastinum, and the majority of these are thymic in origin, whether epithelial or the more common lymphoma. One fourth of lesions are found in the middle mediastinum and another fourth in the posterior compartment. The superior mediastinum or peri-tracheobronchial location is where lymph node metastasis from pulmonary pathology is found and may be approached for definitive histologic characterization either by mediastinoscopy or, more commonly in the current era, by endoscopic bronchial ultrasound localization (EBUS) and needle aspiration. As noted above substernal goiters also localize to the superior mediastinum [3].

Surgical Approaches to the Anterior Mediastinum

The typical computed tomographic (CT) appearance of a lesion found in the anterior mediastinum is seen in Fig. 3.2. The approach chosen depends to a great extent on the appearance of the lesion and the suspected diagnosis. A large, invasive lesion should be distinguished from a well encapsulated lesion since this distinction determines whether completely resecting the lesion or simply proceeding to obtain a tissue sample for definitive diagnosis is the more prudent approach. Lesions occurring in the anterior mediastinum include, but are not limited to, lymphoma, thymoma, and other primary lesions of thymic origin including thymic carcinoma, germ cell tumors and teratoma, substernal goiter, parathyroid adenoma,

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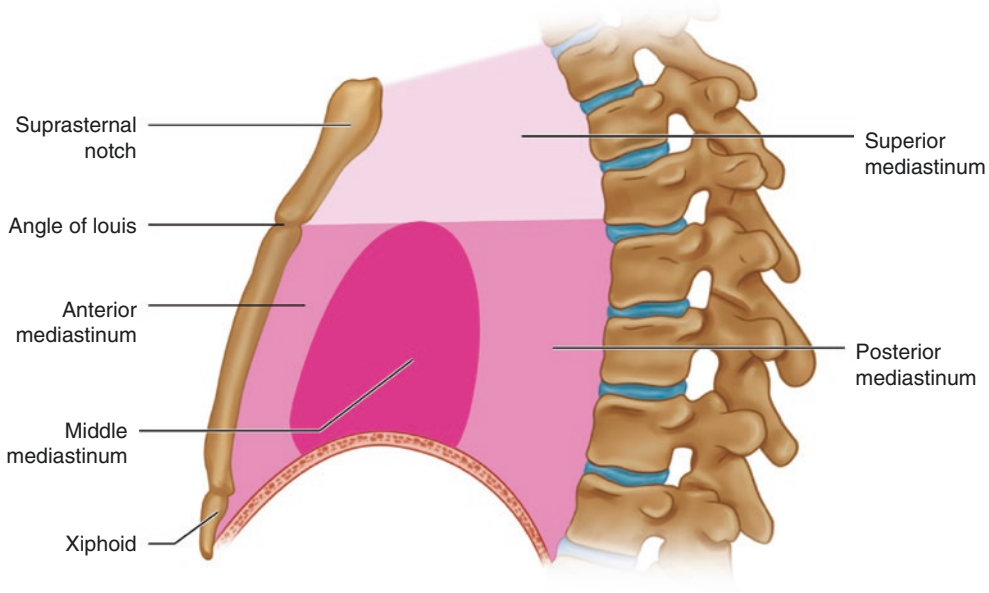

Fig. 3.1 Diagram showing the classical description of the compartments of the mediastinum

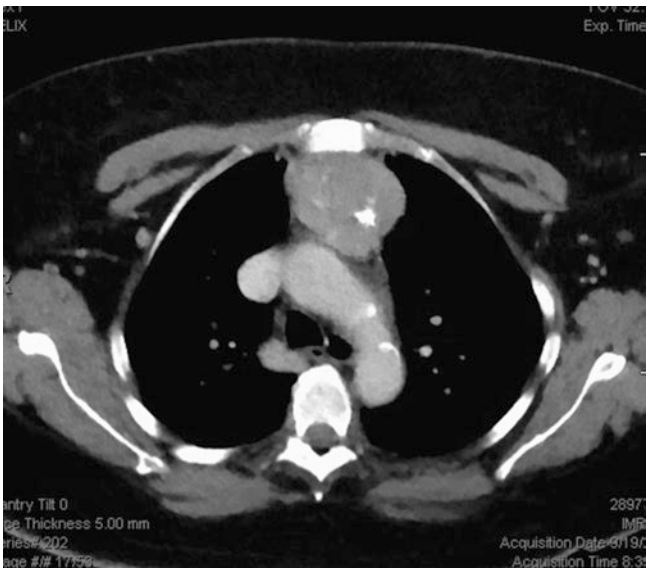

Fig. 3.2 CT scan of a thymoma. Note the location in the anterior mediastinum in close proximity to the aorta and superior vena cava

thymic cysts, and pericardial cysts. A large invasive lesion where lymphoma is suspected requires an approach that allows for a tissue sample to be obtained (Fig. 3.3). A core needle biopsy may yield sufficient tissue for complete phenotyping and genotyping of a lymphoma, but if more tissue is needed, a more invasive procedure is required. Lesions located in the anterior mediastinum are not accessible via mediastinoscopy as the reach of the mediastinoscope is limited to the superior mediastinum. The mediastinoscope is passed along the anterior aspect of the trachea posterior to the innominate artery and the aorta, allowing for sampling of lymph nodes in the paratracheal region as well as the subcarinal space.

The anterior mediastinum may be accessed via several approaches, with the one chosen based most commonly on the location of the lesion but using the least invasive approach. The most direct approach involves an anterior mediastinotomy either through the second intercostal space or excision of the second costal cartilage on the involved side (Fig. 3.4). With excision of the cartilage, it is possible and preferable to remain extrapleural in approaching the lesion, thus avoiding having to place a chest tube. Once the lesion is visualized, sufficient material is easily obtained to allow for a definitive pathologic diagnosis.

Alternatively, a video-assisted thoracoscopic approach (VATS) may be utilized to obtain tissue. This requires single lung ventilation to allow for the placement of a thoracoscope into the appropriate pleural space. Despite being characterized as "minimally invasive," this approach actually is the more invasive approach compared to the anterior mediastinotomy that allows one to remain extrapleural. It is recommended that a frozen section be performed on the specimen obtained to assure that diagnostic material is present. It is clearly preferable not to have to subject the patient to a repeat procedure if only on permanent section it is determined that inadequate material was obtained.

Thymoma

Tumors of the thymus gland account for approximately 50% of the epithelial lesions occurring in the anterior mediasti-

num [3]. The presentation of these lesions varies from the incidental discovery of a mass on a CT scan of the chest done for some other reason to symptoms caused by a variety of paraneoplastic syndromes, the most common one being myasthenia gravis. Other associated syndromes include pure red cell aplasia and Eaton-Lambert syndrome. Imaging studies demonstrate a spectrum of appearances as they can vary from a well encapsulated discrete lesion with no obvious evidence of invasion to a large clearly invasive mass (Fig. 3.5a, b). There have been a number of staging systems proposed for characterizing thymomas, but the one most commonly utilized is that of Masaoka [4]:

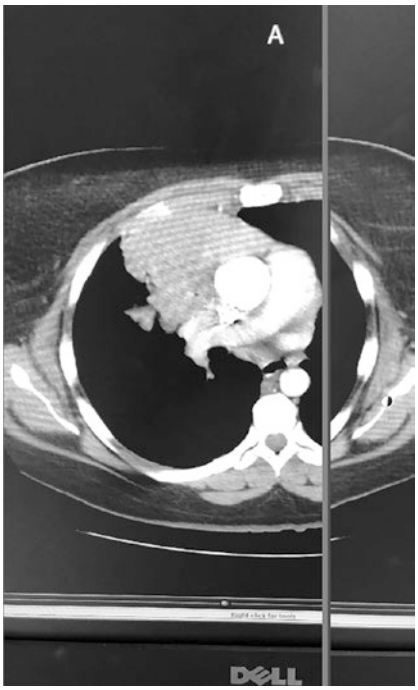

Fig. 3.3 A large, invasive anterior mediastinal mass characteristic of lymphoma. The appearance warrants a biopsy for histologic confirmation as well as obtaining tissue for further molecular and genetic characterization

Stage I: Macroscopically and microscopically completely encapsulated
Stage IIA: Microscopic transcapsular invasion
Stage IIB: Macrosopic invasion into surrounding fatty tissue or grossly adherent to but not through mediastinal pleura or pericardium
Stage III: Macroscopic invasion into neighboring organs, such as the pericardium, lung, great vessels)
Stage IVA: Pleural or pericardial dissemination
Stage IVB: Lymphogenous or hematogenous metastasis

This staging system has been clinically validated, and there is a direct correlation with prognosis. The World Health Organization (WHO) developed a histological classification system in 1999, with revisions in 2004 and later 2015 [5]. This system also correlates with prognosis both independently and when used alongside the Masaoka classification. Moran and colleagues looked at 250 cases of thymoma with an emphasis on the WHO histologic subtyping and found that more than 50% of tumors after subtyping fell into mixed categories, effectively diminishing the clinical impact of histologic subtyping over staging [6]. The authors propose a staging system that is statistically significant for both overall

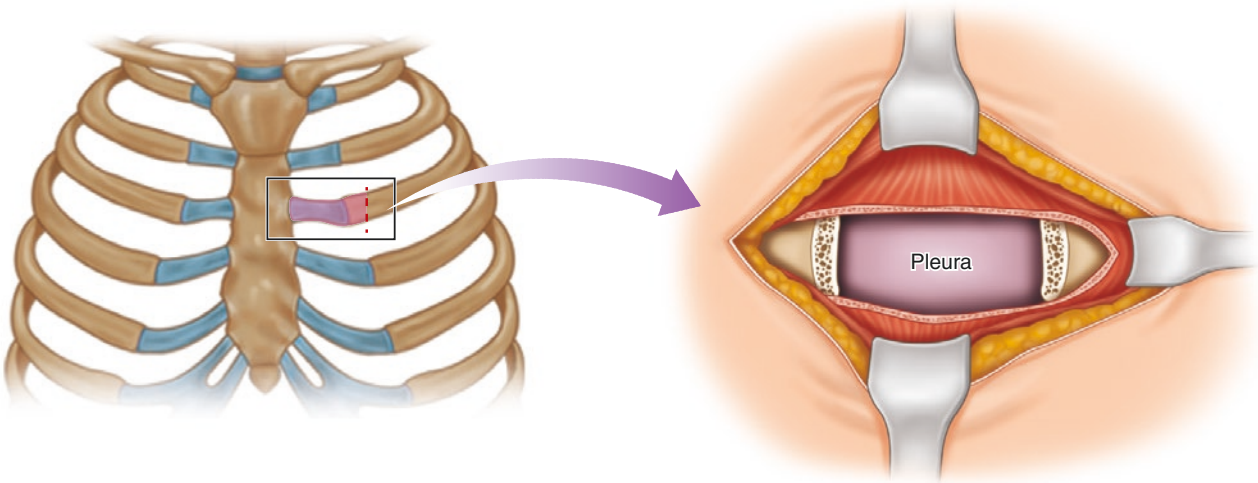

Fig. 3.4 Diagram showing the approach for a mediastinotomy with excision of the second costal cartilage to gain access and remain extrapleural

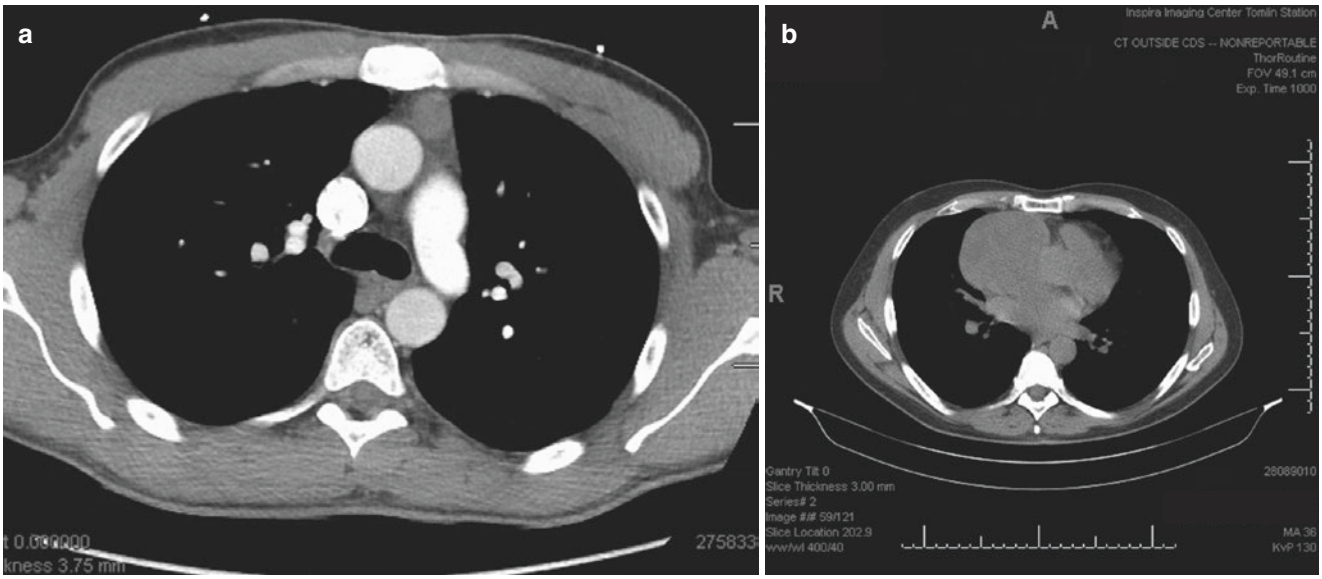

Fig. 3.5 (**a**) A small, well encapsulated thymoma that should be easily excised via a minimally invasive approach. (**b**) An invasive thymoma that warrants a multidisciplinary approach including resection

and recurrence-free survival and offers better stratification and improved histological definitions for proper staging [7].

Additionally, there has been a recent push to utilize the classic tumor-node-metastasis (TNM) classification with modifications provided by the International Thymic Malignancies Interest Group (ITMIG), among others, so it would be included in the 8th edition of the American Joint Committee on Cancer's *AJCC Cancer Staging Manual* [8]. This system has a number of similarities to the modified Masaoka classification especially as it relates to the T component in addition to including parts of the WHO classification.

Surgical resection remains the definitive treatment for thymoma with high overall and disease-free survival rates in patients with stage I and II disease [9, 10]. Detterbeck, in a review of the existing literature, notes 5-year survival rates ranging from 80% to 100% after resection of stage I thymoma, with an average rate of 91% [11]. An average 5-year survival of 80% was reported for stage II thymoma, with a higher variability in results among the series (range 42–100%). Average overall 10-year survival rates were 87% (range 75–100%) for stage I and 67% for stage II [12–15]. The average recurrence rate was 3% after resection of stage I tumor and 11% for stage II thymoma. Well-encapsulated stage I tumors have a complete resection rate of 100%, while complete resection of stage II lesions averages close to 90%, but depending on the report, these rates can vary widely. Despite the temptation to remove only the tumor itself, definitive treatment for thymomas should include a total thymectomy as there are at least anecdotal reports of the later appearance of myasthenia gravis when residual thymus is left behind [16, 17]. Wang reported significantly better survival at 5 years following complete thymectomy compared to tumor resection alone (92% vs 59%), although this difference did not hold up at 10 years [18]. Conversely, a more recent study showed no difference in survival between total thymectomy and tumor resection alone [19].

With more invasive lesions, specifically Masaoka stage III where there is tumor invasion of adjacent structures, definitive resection still is the treatment of choice with the recognition that a more radical procedure may be required [20–22]. Resection of the pericardium or a portion of lung presents no real additional challenge, but superior vena cava or innominate vein involvement produces some increased complexity. The innominate vein usually can be resected with impunity, but superior vena caval involvement requires reconstruction ideally with autogenous material preferably a spiral vein graft. Alternatively, prosthetic material can be used to reconstruct the superior vena cava [23]. Hemidiaphragm, if involved, also may be resected and reconstructed with a prosthetic patch usually polytetrafluoroethylene (PTFE). The key with these lesions is to accomplish a complete resection ideally with negative margins. Even in those cases where pleural involvement is present, it is reasonable to proceed with resection and pleurectomy in an attempt to remove all gross disease [24, 25]. In selected patients, pleuropneumonectomy also may be considered [24, 26]. Justification exists to proceed with these extended procedures recognizing if a complete resection is accomplished survival rates can approximate those achieved in stage I and II tumors [27]. In a study from the Massachusetts General Hospital, the overall survival for patients with stage III disease was 71% at 5 years and 54% at 10 years. For those patients where a complete

resection could be accomplished, the 5- and 10-year survival was 86% and 69%, respectively. Alternatively, for those who had an incomplete resection, 5-year survival was 28% and only 14% at 10 years. Radiation therapy did not significantly alter survival following incomplete resection [28, 29].

It is illustrative here to briefly discuss the surgical approaches to the anterior mediastinum that are common for any lesion in this location whether thymoma, germ cell tumor or other. The standard operation has been the median sternotomy with total thymectomy and resection of the tumor. As noted above, any invaded structures are taken en bloc, and reconstruction is carried out as required. There are situations, depending on the location of the tumor, when a posterolateral thoracotomy may be the approach of choice, but the sternotomy allows access to both pleural reflections as well as nicely exposes the brachiocephalic vessels. In recent years, VATS has been used to resect smaller less invasive lesions, and very recently robotic approaches have been championed. The increased degrees of freedom allowed by the robotic arms facilitate the dissection [30, 31]. For small, well encapsulated lesions, a transcervical approach also has been used to resect the entire gland and the tumor [32–34].

Germ Cell Tumors

Primary mediastinal germ cell tumors are extremely rare and occur mostly in males. They represent only about 10% of all anterior mediastinal masses. They may present as mature teratomas with no malignant feature or seminomatous or non-seminomatous tumors [35]. A specific staging classification has been proposed for these tumors [36]. Mature teratomas, which account for 60–70% of all mediastinal germ cell tumors, are fascinating lesions characterized by mature elements from all three germinal layers, ectoderm, endoderm, and mesoderm, and thus may contain fat, cartilage, bone, teeth, and glandular epithelia (Fig. 3.6) [37, 38]. Imaging studies demonstrate most commonly a multilocular, well circumscribed partially cystic mass containing fluid and fat density and often calcifications [39]. The serum markers, beta-HCG and alpha-fetoprotein, usually are not elevated. Complete excision usually via median sternotomy is the definitive treatment for these lesions, but they need to be closely examined to assure the absence of any malignant elements [38, 40].

Primary mediastinal seminomatous germ cell tumors (PMSGCT) are seen most commonly between the ages of 20 and 40 years and present as a lobulated, homogenous mass [36, 41, 42]. Serum beta-HCG and alpha-fetoprotein usually are normal or very mildly elevated. Histologic confirmation is required and usually can be obtained with fine needle aspiration or with a VATS procedure. First-line treatment usually is systemic chemotherapy with radiation therapy if chemotherapy results in less than an optimal result. Surgical resection occasionally is recommended if residual tumor exists following first-line therapy [43, 44].

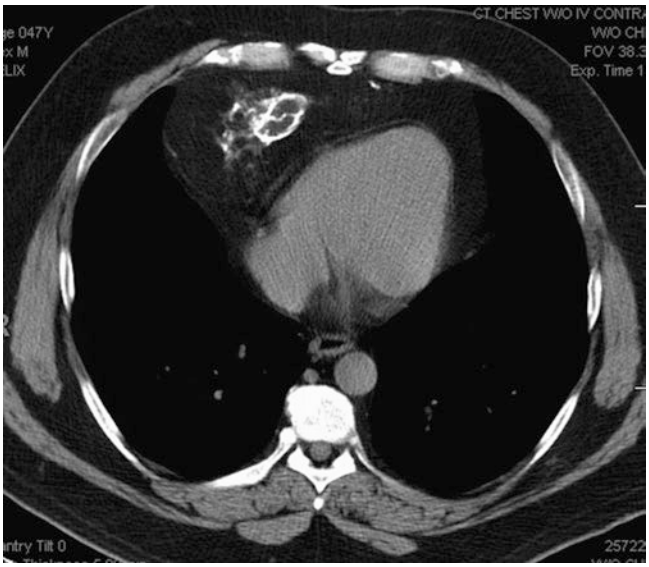

Fig. 3.6 Classic appearance of a mature teratoma. Note the significant calcification as well as the extensive fat density

Non-seminomatous primary mediastinal germ cell tumors may occur as choriocarcinoma or embryonal or yolk sac tumor. Not uncommonly, all three elements are found in one of these tumors [36]. They commonly present with chest pain or cough and usually when first seen already are large invasive masses. Serum markers are elevated in essentially all of these tumors with a few rare exceptions. If markers are elevated, a tissue diagnosis is not required as the patient is treated with platinum-based chemotherapy. These lesions have a poorer prognosis than those arising in either the testis or retroperitoneum, with an overall 5 y survival of approximately 50% compared with 80% for testis [45–49]. The role of surgical resection for these lesions remains somewhat controversial. Previously, the only indication for operation was residual tumor with negative serum markers. Now there are centers that recommend resection for residual tumor even with markers remaining elevated [50–52]. Median sternotomy is the most commonly employed approach to resect these lesions though VATS, and robotic-assisted techniques have their own adherents.

Parathyroid Adenomas

The inferior parathyroids originate from the third pharyngeal pouch and are those with the most variable location, since they may migrate with the thymus and parathyroid tissue can occur anywhere along this course. In a surgical series of 112 patients, inferior parathyroids were found in 60% of cases in a mediastinal location [53]. Less commonly are superior parathyroid glands found in aberrant locations as they arise

from the fourth pharyngeal pouch. Patients suspected of having primary hyperparathyroidism usually have a localization study done to image the adenoma. Often, a minimal incision can be performed to remove a single parathyroid adenoma that has been localized to the neck. The rapid parathormone assay that can be performed while the patient is in the operating room to assure removal of the offending adenoma has greatly aided the parathyroid surgeon [54]. If an aberrant inferior gland is localized in the mediastinum, several approaches may be employed (Fig. 3.7). Some surgeons have simply removed as much thymus as they can through their standard incision. Others have employed a median sternotomy or VATS approach to remove the aberrant gland [55–57]. We have utilized a transcervical approach employing a specially made retractor that lifts the manubrium to allow visual access as we remove the thymus gland that contains the adenoma [58] (Fig. 3.8).

Surgical Approaches to the Posterior Mediastinum

The posterior mediastinum is bounded anteriorly by the posterior pericardium and extends posterior to the chest wall and laterally includes the costovertebral sulci. There are a number of structures within this compartment including the descending thoracic aorta, the inferior vena cave, the azygous vein, the sympathetic chain, the thoracic duct, the esophagus, and the intercostal nerves and nerve roots arising from vertebral foramina. The majority of lesions occurring within the posterior mediastinum are benign, and this fact significantly informs our choice of surgical approach. Lesions are classified as cystic or solid with the cystic lesions being part of the

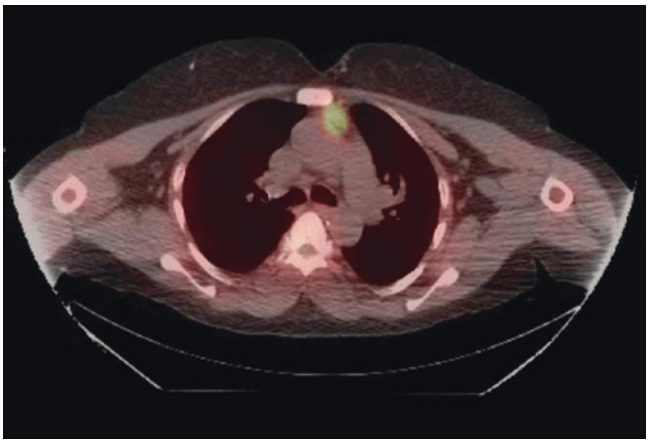

Fig. 3.7 Localization of a parathyroid adenoma in the anterior mediastinum in close proximity or within the thymus gland

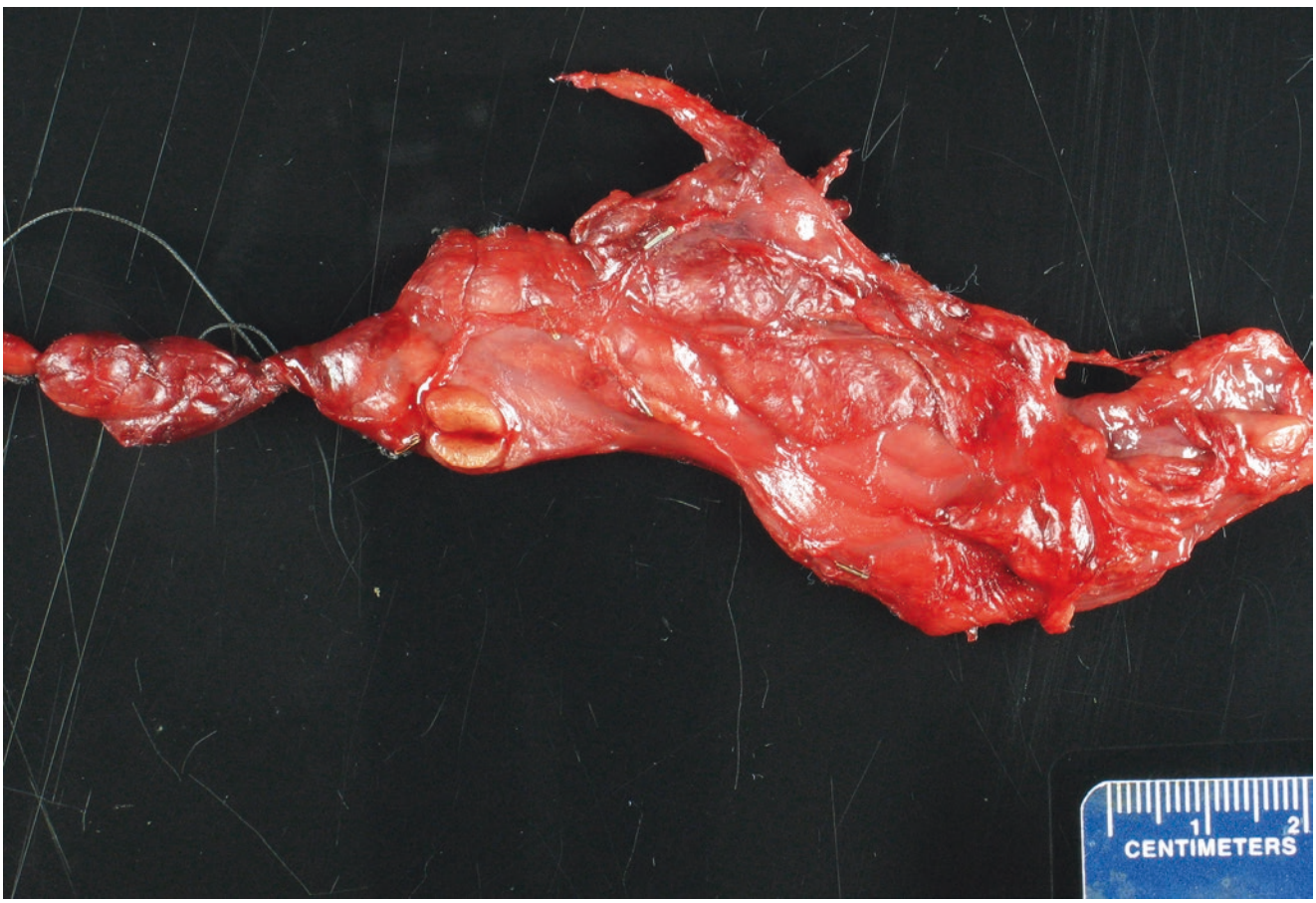

Fig. 3.8 Parathyroid adenoma within the resected thymus gland

spectrum of bronchopulmonary foregut abnormalities specifically either bronchogenic cysts or esophageal duplication cysts [59, 60]. These lesions rarely communicate with either the esophagus or bronchus, but ruling out either of those possibilities at times is critical. Solid lesions most commonly are either schwannomas, ganglioneuromas, or neurofibromas [61–63]. Occasionally, a pheochromocytoma or ganglioneuroma arises from random rests of mediastinal paraganglionic cells and may be hormonally active. A patient who presents with a posterior solid mediastinal mass and hypertension that is difficult to control should be screened with urinary catecholamine testing.

Cystic lesions if asymptomatic may be simply observed, though they can become symptomatic if they get infected. When infection occurs, it is extremely difficult to eradicate, and surgical excision is the treatment of choice (Fig. 3.9). Often, the patient is uncomfortable knowing there is a mass in their chest and wishes to have it excised. Bronchoscopy and esophagoscopy should be carried out to assure no communication prior to resection so as to plan the surgical approach. Most of these may be removed via a VATS approach and occasionally via mediastinoscopy [64, 65]. The entire cyst wall should be resected unless it is so adherent to an adjacent structure, in which case a portion of the cyst wall can remain [66]. Often, it is helpful to drain the lesion of what usually is thick mucoid material prior to dissecting out the wall, though I must admit it is very satisfying to be able to resect the entire cystic lesion intact as it makes for a very nice photograph. These lesions tend not to recur. Surprisingly, some of them may attain quite a large size prior to becoming symptomatic and may compress adjacent structures including the trachea or main stem bronchus.

The approach to solid lesions in the posterior mediastinum is similar to that utilized for cystic lesions. As previously noted, the majority of lesions occurring in the posterior mediastinum are benign. Schwannoma, or neurilemoma, is the most common tumor seen and occurs as a benign, encapsulated lesion in which the cellular architecture is structurally identical to the syncytium of Schwann cells (Fig. 3.10a, b) [61, 67, 68]. While the perineurium forms the capsule of the mass, the neoplastic cells proliferate within the endoneurium. These lesions may originate from either peripheral or sympathetic nerves and occasionally from cranial nerves. Most commonly, they are found as incidental findings on a CT scan done for some other reason as they, for the most part, essentially are asymptomatic [68]. Often, they are found immediately adjacent to a vertebral body closely aligned with a neural foramen (Fig. 3.11). Especially for larger lesions, it is critically important to obtain, in addition to the CT scan, an MRI to look specifically at the neural foramen to assure there is no tumor in the foramen or, more importantly, in the spinal canal [69]. These so-called dumbbell tumors need to be recognized preoperatively since the surgical management differs from that of a tumor without intraspinal extension [70].

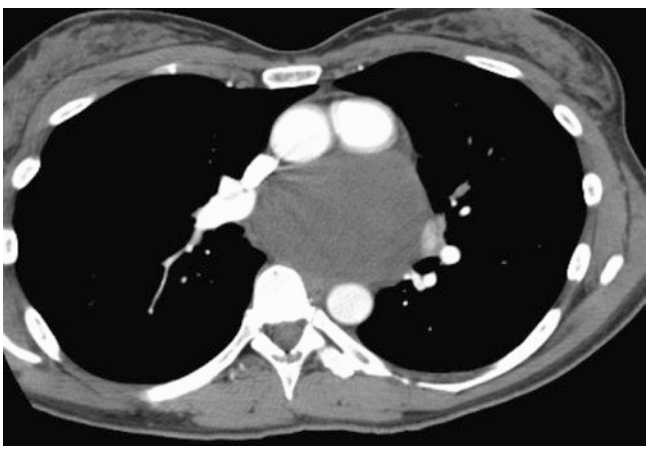

Fig. 3.9 A large bronchogenic cyst compressing major vasculature

A video-assisted thoracoscopic approach is the procedure of choice for these benign usually encapsulated lesions as long as there is no extension into the spinal canal [71]. Robotic-assisted approaches also are becoming increasingly utilized as the additional degrees of freedom afforded by the robotic arms facilitate dissection [72, 73]. Under one-lung ventilation, the videothoracoscope is inserted and the lesion visualized. Simply incising the overlying pleura allows for mobilization of the mass [74]. Depending upon from where the tumor has arisen, it may be necessary to put a clip on a nerve root as it exits the foramen. Securing the nerve root is critically important since the level of the extension of the dural sheath varies, and, if not secured, a spinal fluid leak may occur with significant consequences. The lesion usually just peels off the vertebral body or rib. For lesions with intraspinal extension, a combined approach usually with a neurosurgeon is indicated. Ideally, the intraspinal portion is accessed by the neurosurgeon through a posterior laminectomy approach and resected [70, 75, 76]. Then the patient is positioned for VATS, and the intrathoracic portion of the lesion is removed. If intraspinal extension is unrecognized and the tumor removed leaving part in the spinal canal, there is the likelihood of hemorrhage within the canal that could have dire neurological consequences if not dealt with expeditiously. The complete removal of benign posterior mediastinal schwannomas should result in cure with the risk of local recurrence very low.

As mentioned earlier, there are rare cases of malignant posterior mediastinal tumors, and, when suspected, it is best to approach these via open thoracotomy since they often are adherent to adjacent structures including the aorta [77, 78]. Malignant schwannomas account for approximately 1–2% of all neurogenic tumors occurring in the posterior mediastinum [61].

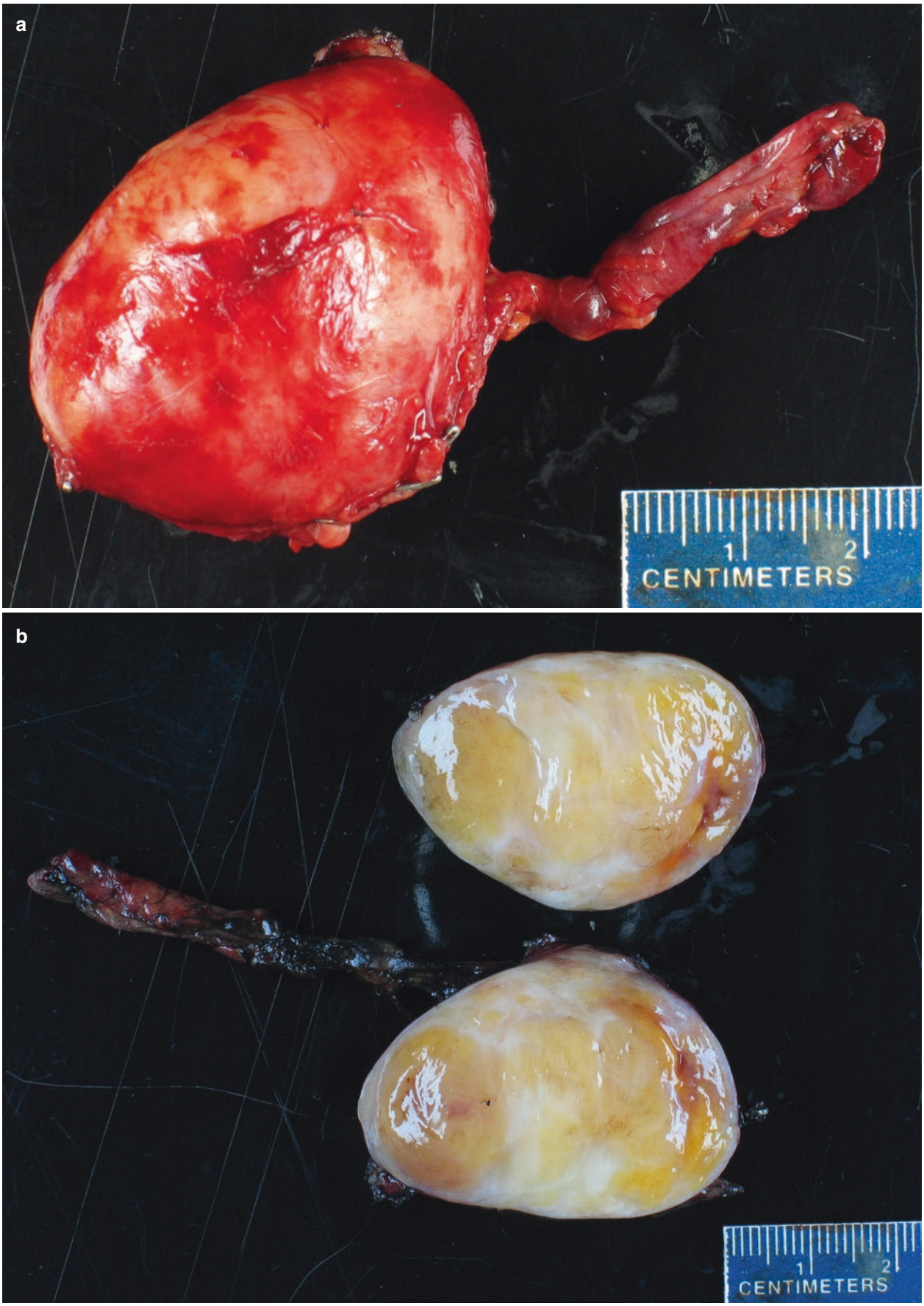

Fig. 3.10 (**a**) Benign schwannoma or neurilemmoma with the nerve root. (**b**) The appearance of the lesion bisected

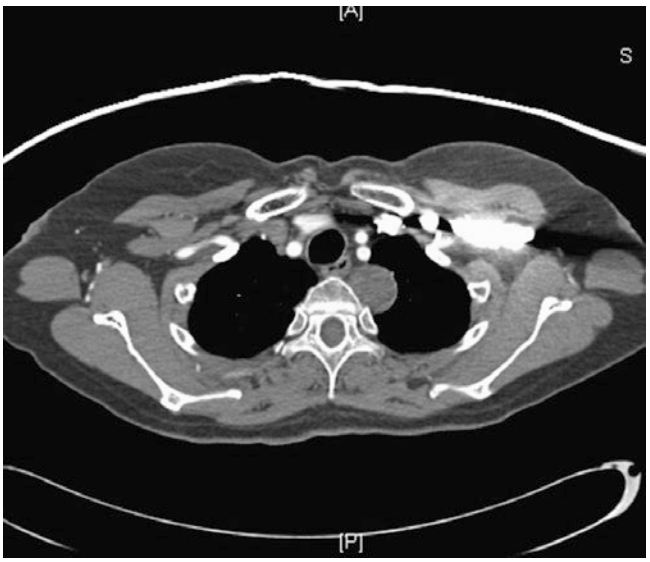

Fig. 3.11 CT scan of a paravertebral mass, classic for a benign schwannoma. This lesion is easily accessible with a VATS or robotic-assisted approach

Care must be taken to avoid the thoracic duct which lies on the vertebral bodies and, if injured, results in a chyle leak that can be devastating if left untreated. The intent is to achieve a complete resection of all gross disease. A suspected pheochromocytoma occurring in the posterior mediastinum requires pretreatment with the usual alpha blocker and potentially beta blockade as well. Ganglioneuroma, neuroblastoma, and ganglioneuroblastoma – tumors of sympathetic ganglion origin – occur almost exclusively in infants and young children, with the latter two lesions considered malignancies. Principles of resection remain the same for these lesions with the exception that the malignant lesions usually are treated with a chemotherapeutic regimen prior to any attempt at surgical resection.

Lesions of the mediastinum are among the more intriguing issues faced by thoracic surgeons. The decision as to whether to first obtain a tissue diagnosis as opposed to embarking on a complete resection can be challenging. It is safe to say no thoracic surgeon wants to complete a radical resection with a vascular reconstruction only to find out the offending lesion proved to be a lymphoma. Frozen section diagnosis can be unreliable for certain anterior mediastinal masses; thus, it often proves beneficial to wait for the permanent sections to be read. Some pathologists are perfectly comfortable with relying on the frozen section for a definitive diagnosis, thus allowing the surgeon to proceed with resection. Median sternotomy has been the mainstay approach to the mediastinum for many years, but with the advent of minimally invasive surgical techniques, that is rapidly changing. VATS and robotic-assisted approaches are applicable for many lesions, but larger, invasive lesions still require a sternotomy. The aim of any definitive operation for a mediastinal mass is a complete resection with negative resection margins, and thus the surgeon must be prepared to do whatever is necessary to accomplish that aim. That includes being prepared to take the innominate vein, resect a portion of the superior vena cava and reconstruct it, resect a portion of atrium or diaphragm, or remove a portion or an entire lung. The CT scan with coronal and sagittal reconstructions is helpful in planning the operative approach along with the judicious use of MRI scans, especially if there is a concern of vascular or nerve invasion. Great care must be taken in assessing posterior mediastinal lesions that lie in the costovertebral angle in proximity to neural foramina to assure lack of invasion into the spinal canal.

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