Imaging of Non-thymic Anterior Mediastinal Tumors

14

Roy A. Raad

Abstract

The mediastinum contains a variety of vital structures and organs, including the thymus, lymph nodes, adipose tissues, vascular structures, nerves, and esophagus, all of which can give rise to various masses and other nonneoplastic abnormalities. Imaging is the integral part of the workup for mediastinal tumors, specifically chest computed tomography (CT) and in equivocal cases magnetic resonance imaging (MRI), leading in many cases to a confident presumptive diagnosis, even without necessitating biopsy, surgery, or other confirmatory testing.

In this chapter, we focus on discussing the clinical manifestations, diagnosis, and treatment of non-thymic tumors, specifically germ cell tumors, lymphoma, and mesenchymal tumors. Although this is discussed in prior chapters, we start by discussing a generalized structured imaging approach that radiologists can use when evaluating anterior mediastinal tumors in general, aided by useful clinical and laboratory information when made available. Thymic benign and malignant tumors are discussed in detail in other chapters.

Keywords

Anterior mediastinum · Chest CT · Chest MR FDG PET/CT · Lymphoma · Seminoma Teratoma · Nonseminomatous germ cell tumor · Mesenchymal tumor

Abbreviations

AFP	Alpha-fetoprotein
CBC	Complete blood count
CT	Computed tomography
ESR	Erythrocyte sedimentation rate
FDG	Fluorodeoxyglucose
GCT	Germ cell tumor
HL	Hodgkin's lymphoma
HU	Hounsfield units
LBCL	Large B-cell lymphoma
LDH	Lactate dehydrogenase
MRI	Magnetic resonance imaging
PET/CT	Positron-emission tomography/computed tomography
SVC	Superior vena cava
β-hCG	Beta-human chorionic gonadotropin

R. A. Raad
Department of Radiology, New York University School of Medicine, New York, NY, USA

Department of Radiology, St. George Hospital University Medical Center, Beirut, Lebanon
e-mail: roy.raad@med.nyu.edu

M. Anzidei, M. Anile (eds.), *Diagnostic Imaging for Thoracic Surgery*,
https://doi.org/10.1007/978-3-319-89893-3_14

14.1 Introduction

Variable statistics exist in the medical literature regarding the true incidence of anterior mediastinal masses, due to a number of reasons, such as variations in the clinical and radiological classification schemes, as well as variation in the nomenclature of particular tumors. For instance, the traditional classification schemes used in radiologic practice are based on the lateral chest radiograph, as devised by Felson [1], which divides the mediastinum into anterior, middle, and posterior compartments. More recently in 2014, the International Thymic Malignancy Interest Group (ITMIG) introduced and adopted a new classification scheme of the mediastinal compartments based on cross-sectional imaging, after modifying an original model developed by the Japanese Association for Research on the Thymus (JART), reclassifying the mediastinum into prevascular, visceral, and paravertebral compartments [2]. According to the updated classification system, the prevascular compartment (previously known as the anterior mediastinum) is bordered by the thoracic inlet superiorly, the diaphragm inferiorly, the sternum anteriorly, the parietal mediastinal pleura laterally, and the anterior aspect of the pericardium posteriorly [3]. Its major contents include the thymus, fat, lymph nodes, and left innominate vein.

Despite these challenges, the most widely reported incidence for anterior mediastinal masses includes thymic malignancies in 35% of cases, lymphoma in 25% of cases, thyroid and other endocrine tumors in 15% of cases, malignant germ cell tumors in 10% of cases, and benign thymic lesions in 5% of cases (Table 14.1).

Table 14.1 Anterior mediastinal masses

Mass	Incidence (%)
Thymic malignancies	35
Lymphoma	25
Thyroid/other endocrine tumors	15
Malignant germ cell tumors	10
Benign thymic lesions	10
Mesenchymal tumors	5

14.2 General Approach to Mediastinal Masses

14.2.1 Clinical Approach

When evaluating mediastinal masses on any imaging modality, the first and foremost piece of information that the radiologist must make use of is all the clinical and laboratory details pertaining to the patient. Although this may be challenging in the private practice setting, it has become easily accessible nowadays at most academic centers with the increasing abundance of full access to electronic medical records that are readily available for the radiologist at the time of interpretation. In addition, a discussion between the radiologist and the clinician regarding the case in question should be encouraged whenever possible.

Basic demographic information such as patient age and gender may prove to be helpful in narrowing down the differential diagnoses. For instance, in both men and women older than 40 years of age, thyroid goiter and thymic malignancies account for more than two-thirds of anterior mediastinal masses, whereas lymphoma is the most common anterior mediastinal tumor in women between the ages of 10 and 39 [4]. Other relevant clinical information that should be evaluated includes the presence, severity, and duration of symptoms pertaining to the mediastinal structures, such as dyspnea, dysphagia, chest pain, hoarseness, or changes in voice, hemoptysis, palpable abnormalities, as well as "B symptoms" of lymphoma (fever, night sweats, weight loss). Relevant laboratory studies that should be assessed include lactate dehydrogenase (LDH), alpha-fetoprotein (AFP), and beta-human chorionic gonadotropin (β-hCG) levels. For example, in a young patient presenting with an anterior mediastinal mass, the presumptive diagnosis of lymphoma can be made with increased confidence if associated with "B" symptoms and elevated LDH levels. As another example, in a male aged 10–39 years presenting with an anterior mediastinal mass, the presumptive diagnosis of a malignant germ cell tumor can be suggested, in the presence of rapidly progressive symptoms

and elevated β-hCG and AFP levels. Attention should also be directed to the presence and details of preexisting medical conditions, such as myasthenia gravis, which is most commonly associated with thymomas, along with other less common conditions such as pure red cell aplasia and hypogammaglobulinemia [5].

14.2.2 Radiologic Approach

Close attention to details of the imaging appearance of mediastinal masses is of paramount importance, given that imaging is the most vital component in the workup of mediastinal masses, suggesting a certain diagnosis or guiding further investigations and confirmatory testing. Moreover, some mediastinal masses demonstrate a highly characteristic imaging appearance that leads to a presumptive diagnosis with high certainty without the need for biopsy or other confirmatory testing (Table 14.2). Other mediastinal masses demonstrate imaging findings that are suggestive of a certain diagnosis in a particular clinical context.

In all patients with mediastinal masses, the radiologist should describe the exact location, margins (well circumscribed vs. poorly circumscribed), shape (oval, round, or saccular), internal contents (fat, fluid, soft tissue or calcification), and organ of origin (if any) of the mass in question. For instance, an intrinsically high-attenuation anterior mediastinal mass, which enhances avidly following the administration of iodinated intravenous contrast and is continuous with the thyroid gland on a chest CT, can be reliably diagnosed as a thyroid goiter. On the other hand, a heterogeneous mass containing fat, soft tissue, and calcification can be diagnosed as a benign teratoma with a very high level of confidence. The presence of ancillary findings should also be assessed, such as lung metastases (which would suggest an aggressive tumor such as a malignant germ cell tumor), pleural and pericardial implants (suggestive of metastatic thymic tumor), or additional discrete intrathoracic lymph nodes (which would heighten the confidence level for the diagnosis of lymphoma).

Chest CT is the mainstay of imaging modality for evaluation of mediastinal masses, for evaluation of the above-described imaging characteristics, among others. The role of chest radiography is limited, usually limited to the incidental detection of the mere presence of a mediastinal mass, obtained as a routine imaging study or for evaluation of any symptoms. Chest MRI is usually indicated for evaluation of equivocal CT findings, mainly for better delineation of internal contents of the mass (cystic vs. enhancing soft-tissue components). 18-F-fluorodeoxyglucose (FDG) positron-emission tomography/computed tomography (PET/CT) is not usually indicated for evaluation of mediastinal masses, except in the setting of suspected or known lymphoma, for purposes of staging or guiding potential sites of biopsy.

Table 14.2 Anterior mediastinal masses with characteristic imaging findings

Mass	Imaging findings
Thyroid goiter	Hyperattenuating/enhancing mass connected to thyroid
Teratoma	Heterogeneous mass containing calcifications, fat, fluid, and soft-tissue components
Thymic cyst/cystic thymoma	Well-circumscribed fluid-attenuation mass near thymic bed
Pericardial cyst	Well-circumscribed fluid-attenuation mass at cardiophrenic angle
Invasive thymoma	Homogeneous or heterogeneous mass with subpleural or pericardial implants
Lipoma	Homogeneous fat-attenuation mass

14.3 Germ Cell Tumors

By definition, germ cell tumors (GCTs) are said to be "extragonadal" in patients with no primary malignancy identified in the testes or ovaries. The location of extragonadal germ cell tumors varies with age; however they usually arise in midline structures in all age groups. The anterior mediastinum is the most common location in adults, followed by the retroperitoneum, pineal, and suprasellar regions, whereas the anterior

mediastinum is very rare in the pediatric population, in which sacrococcygeal and intracranial germ cell tumors are more common. In general, extragonadal (including mediastinal) germ cell tumors are classified as seminomas (also termed as dysgerminomas in females and germinomas in children), nonseminomatous GCTs (nondysgerminomas in females and nongerminomas in children), and mature or immature teratomas. The main distinction between seminomas and nonseminomatous GCTs is significant because of important differences in terms of prognosis and treatment. Subtypes of nonseminomatous GCTs include yolk cell tumors, choriocarcinomas, and embryonal carcinomas. Germ cell tumors (including both benign teratomas and malignant germ cell tumors) comprise around 20% of anterior mediastinal masses [4, 6].

14.3.1 Mature Teratomas

Clinical manifestations—By definition, mature teratomas of the mediastinum contain well-differentiated histologic components derived from at least two out of the three germinal cell layers (ectoderm, mesoderm, and endoderm). They are considered benign (as opposed to mature teratomas of the testes) and slow growing, and hence tend to be diagnosed incidentally while patients are still asymptomatic. When present, symptoms are typically secondary to compression and obstruction of adjacent mediastinal structures, and include chest pain, cough, postobstructive pneumonia [7], and in rare cases expectoration of hair (trichoptysis) [8].

Diagnosis—Most mature mediastinal teratomas are initially detected on chest radiography, whether obtained as a routine study or for evaluation of symptoms. Calcifications within the mass are present in 26% of cases, and in rare cases there is visualization of a tooth or well-formed bone within the mass (Fig. 14.1), which is further suggestive of the diagnosis. Chest CT, and in equivocal cases chest MRI, is very useful for accurate localization of the mass, determining its spatial relation to the adjacent thoracic structures, and for definitive delineation of internal components. Most mediastinal teratomas are composed of fat (typically between −40 and −120 Hounsfield units (HU) on chest CT), fluid (between 0 and 20 HU), soft tissue (greater than 20 HU), and/or calcifications (Fig. 14.1). The presence of a fat-fluid level is highly specific for teratomas; however this finding is much less common[9].

Treatment—Surgical resection is the main treatment modality for mature teratomas, and is curative in almost all cases [10]. Surgical approach is usually through a median sternotomy or posterolateral thoracotomy depending on the mass location, although thoracoscopic resection may be performed in a few select cases, especially in smaller masses [11]. In cases where radical resection cannot be performed without compromising neighboring vital mediastinal structures, subtotal resection may be performed for relieving compressive symptoms, followed by observation—the use of postoperative chemotherapy or radiation therapy in this setting has not demonstrated clear benefit, especially that these tumors are relatively insensitive to both chemotherapy and radiation therapy [7, 11].

14.3.2 Immature Teratomas

Along the same continuum of mature teratomas, immature teratomas contain mature elements of all three germinal layers, mixed with immature tissue. Imaging appearance is identical to that of mature teratomas in most cases, although there may be foci of hemorrhage or necrosis within the mass in some cases. Standardized treatment of these tumors is controversial, due to the lack of randomized controlled trials, partly due to rarity

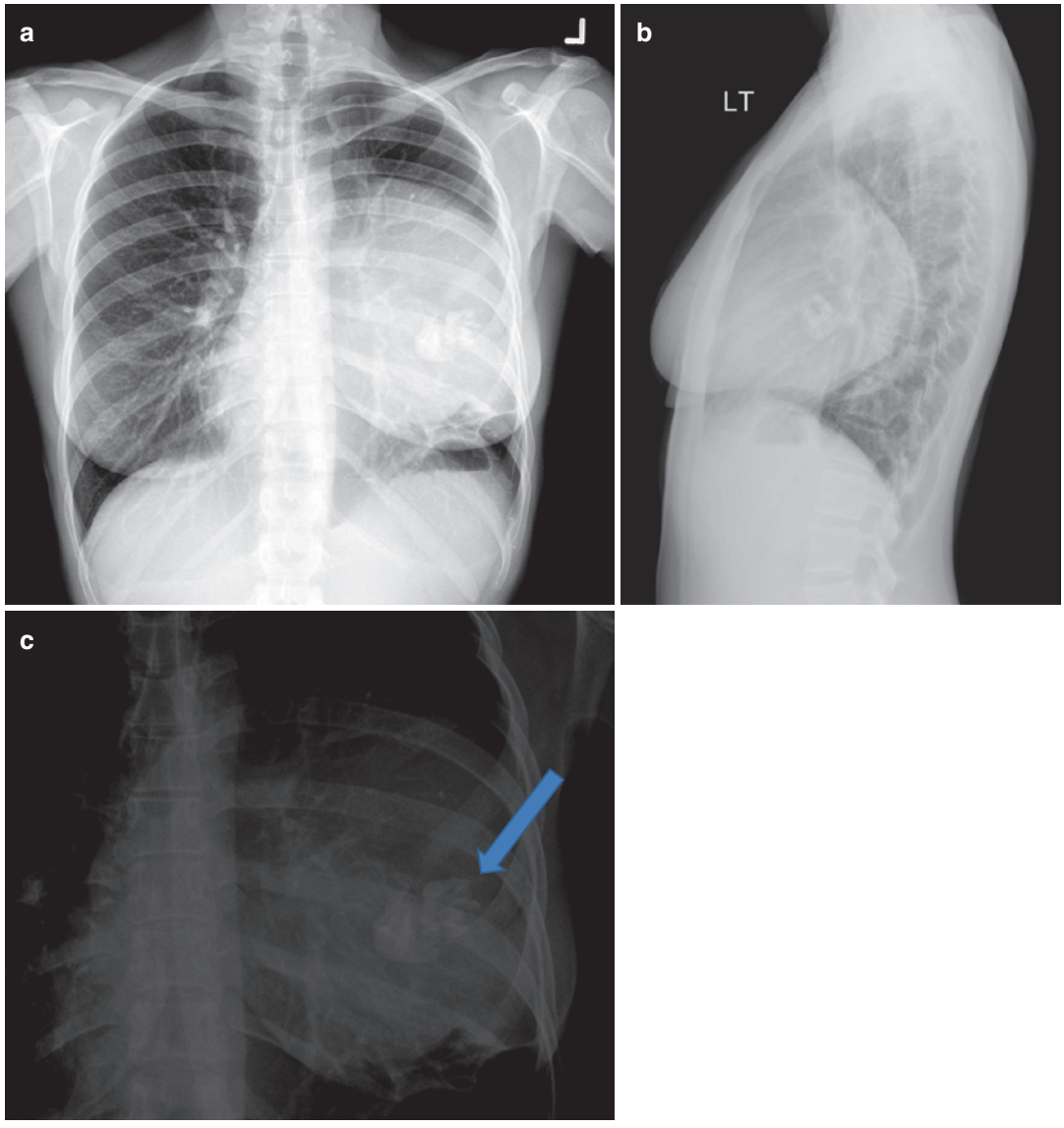

Fig. 14.1 *24-year-old female presenting with chest pain and hemoptysis.* PA (**a**) and lateral (**b**) chest radiographs demonstrate a large anterior mediastinal mass containing calcifications. (**c**) Magnified view of the PA chest radiograph identifies a "toothlike" appearance of the calcification (blue arrow). Axial (**d**) and coronal (**e**) chest CT demonstrates fat and soft-tissue attenuation within the large anterior mediastinal mass and confirms the presence of a tooth within it. Note the secondary mass effect and narrowing of the left pulmonary artery and left mainstem bronchus. Subsequent surgical resection confirmed the diagnosis of benign mature cystic teratoma

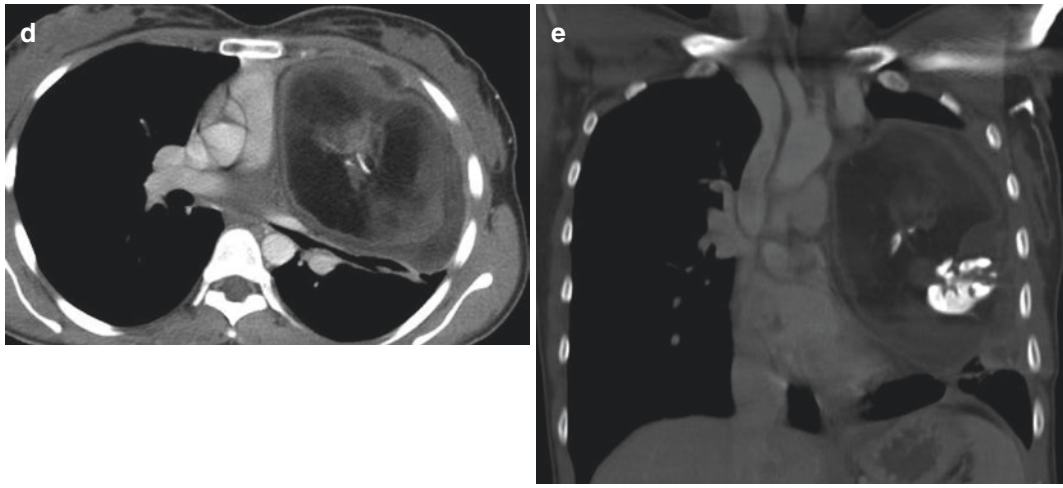

Fig. 14.1 (continued)

of this condition. The most common approach is however preoperative chemotherapy followed by radical resection. Although adults with primary immature mediastinal teratomas usually have a poor prognosis, long-term survival has been reported in patients treated with preoperative chemotherapy and aggressive surgical resection [12]. Malignant transformation of immature teratomas is also possible [13]. On the other hand, immature mediastinal teratomas in children behave as benign tumors, in a similar manner to mature teratomas.

14.3.3 Mediastinal Seminomas

Clinical manifestation—Mediastinal seminomas account for one-third of mediastinal malignant GCTs, predominantly occurring in men between 20 and 40 years old [14, 15]. Despite the fact that testicular seminomas are unlikely to spread to the mediastinum in the absence of retroperitoneal adenopathy [16], it is advised that all men with suspected mediastinal seminoma should undergo a testicular ultrasound for exclusion of a testicular mass. Furthermore, mediastinal dysgerminomas, the female counterpart to seminomas, are rare in women with histologically normal ovaries. Most patients (75%) are asymptomatic at the time of presentation; however presenting symptoms may include chest pain, dyspnea, cough, weight loss, and superior vena cava (SVC) syndrome [17].

Diagnosis—Serum AFP levels must be normal since seminomas do not produce AFP, and serum β-hCG levels may be elevated up to 1000 international units (IU)/L [17]; abnormal AFP levels or elevation of β-hCG levels >1000 IU/L indicates the presence of coexisting nonseminomatous components. On chest radiograph, mediastinal seminomas manifest as bulky anterior mediastinal masses with usually well-defined borders [18], and radiographically detectable calcification may be seen in a minority of cases [19]. Cross-sectional imaging appearance on chest CT or MRI is not highly specific, although mediastinal seminomas typically present as a well-circumscribed anterior mediastinal mass, demonstrating homogeneous density and low-level homogeneous enhancement following intravenous contrast administration [20]. Foci of central necrosis and hemorrhage within the tumor may be present (Fig. 14.2). Most patients present with metastatic disease at the initial presentation, most commonly to intrathoracic lymph nodes, and less commonly to lungs, liver, and/or bones [17].

Treatment and Prognosis—In general, seminomas are extremely sensitive to both cisplatin-based chemotherapy and radiation therapy. Treatment recommendations are mainly established via small

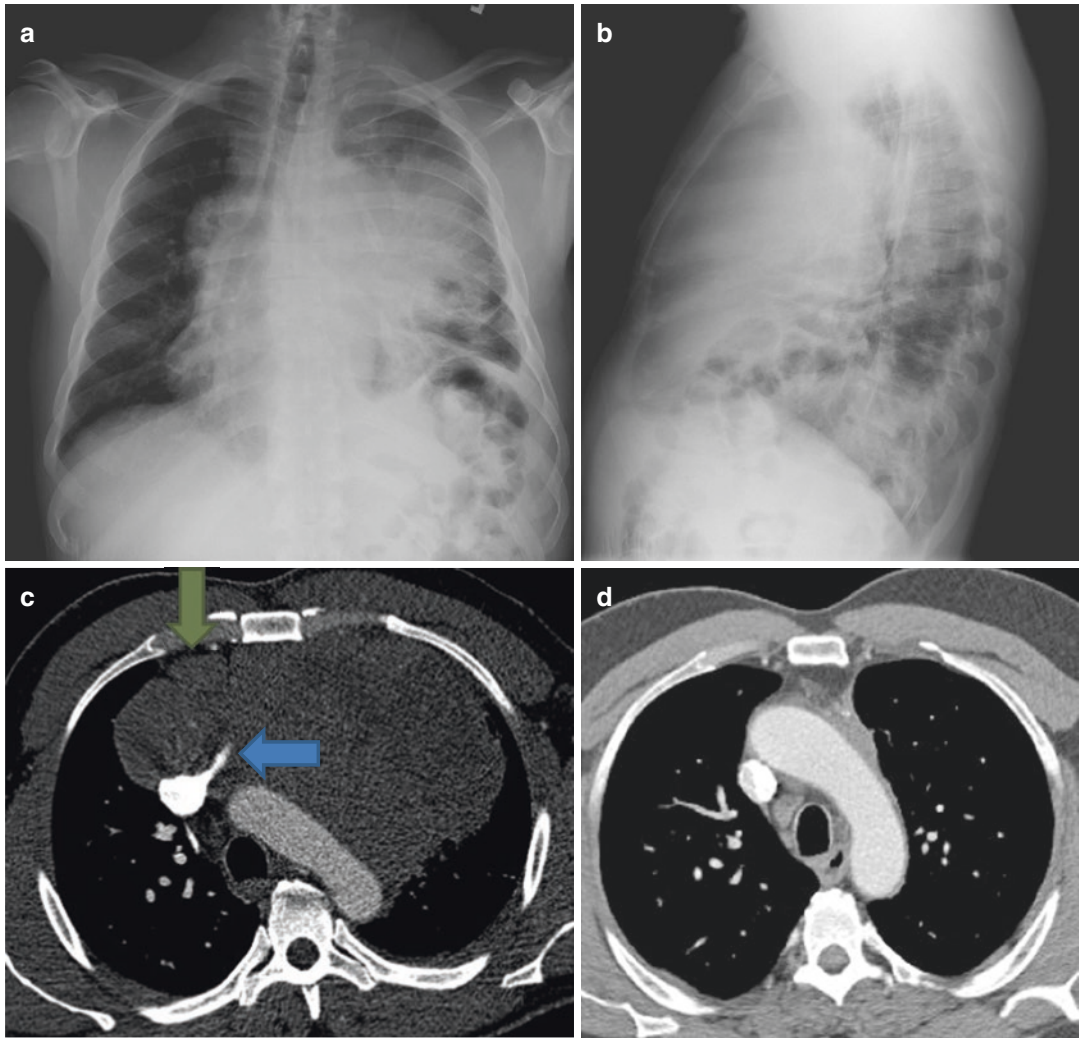

Fig. 14.2 *44-year-old male presenting with tachycardia and shortness of breath.* PA (**a**) and lateral (**b**) chest radiographs demonstrate a large anterior mediastinal mass on both sides of midline. (**c**) Axial images of a contrast-enhanced chest CT at the time of presentation demonstrate a large slightly heterogeneous anterior mediastinal mass, containing areas of necrosis anteriorly. Note the significant mass effect and narrowing of the adjacent structures such as the left innominate vein (blue arrow). Additional small discrete mediastinal lymph nodes were also identified (green arrow). No imaging evidence of lung or other distant metastases at the time of diagnosis. CT-guided biopsy of the mass revealed seminoma. (**d**) Follow-up chest CT 2 years later following chemotherapy demonstrates near-complete resolution of the mass

case series and retrospective reviews rather than randomized clinical trials. Most clinical institutions favor chemotherapy over radiation therapy, due to reduced concerns for toxicity and reduced risk of cardiovascular complications and secondary radiation-induced malignancies, especially since most patients are young adults (20–40 years old). In patients where radiation therapy is used as an alternative strategy for patients with localized disease in the mediastinum (who are not appropriate chemotherapy candidates for instance), careful treatment planning is essential to avoid toxicities, and the radiation fields should include the mediastinum and bilateral supraclavicular regions. In general, surgery plays no role in the initial management of these tumors, due to the typical initial

presentation of bulky and/or metastatic disease [17]. Around 90% of patients treated with chemotherapy have an excellent prognosis with a long-term disease-free survival [17]. Patients treated with radiation therapy are also cured; however the recurrence rate is high, and the 5-year disease-free survival rate is only up to 67% [21].

14.3.4 Mediastinal Nonseminomatous Germ Cell Tumors

Clinical manifestations—Among the mediastinal nonseminomatous GCTs, yolk sac tumor is the most common subtype, whereas choriocarcinoma and embryonal carcinoma are less frequently encountered in the mediastinum. They occur more commonly in men than women, usually between the ages of 20 and 40 years. Most patients present with symptoms at the time of diagnosis, including fever, chills, weight loss, and SVC syndrome. In addition, patients with mediastinal nonseminomatous GCTs have a high incidence of developing various hematologic disorders, such as acute megakaryoblastic and myelogenous leukemia, myelodysplasia, and malignant histiocytosis, with the incidence reaching 6% in one series [22]. The exact reason of this increased incidence is not known; however it may be related to the presence of hematopoietic precursor cells arising within the components of the GCT [23].

Diagnosis—Serum AFP levels are elevated in most patients, whereas β-hCG levels are elevated in a minority of patients. In those with combined elevation of serum AFP and β-hCG levels, the diagnosis of a nonseminomatous GCT can be made even without tissue diagnosis at some institutions. Moreover, serum AFP and β-hCG levels can be used for monitoring response to therapy and detecting tumor recurrence. On chest radiograph, nonseminomatous GCTs manifest as a bulky anterior mediastinal mass (Fig. 14.3a, b), commonly exerting mass effect on adjacent mediastinal structures. Contrast-enhanced chest CT typically demonstrates a large heterogeneous anterior mediastinal mass frequently containing extensive areas of central necrosis and hemorrhage (Fig. 14.3c), as well as enhancing lobular papillary-like peripheral projections in some cases [18, 20]. Chest CT should also be queried for ancillary findings, such as lung nodules, mediastinal and hilar lymphadenopathy, and pleural and pericardial effusions [24], which would raise concern for metastatic disease. Follow-up chest CT is useful in documenting favorable response to chemotherapy or disease progression (Fig. 14.3d, e).

Treatment and prognosis—Since most patients present with metastatic disease, the usual treatment approach consists of initial chemotherapy followed by surgical resection of any residual masses. Cisplatin, etoposide, and ifosfamide (VIP) regimen is preferred to the bleomycin, etoposide, and cisplatin (BEP) regimen at many institutions [25], especially that most patients end up undergoing thoracic surgery, which can provoke bleomycin-induced pneumonitis. Most patients have residual masses at the conclusion of chemotherapy, requiring surgical resection, even in the presence of rising tumor markers, since the alternative of salvage chemotherapy offers dismal results usually [17]. Surgery is usually aggressive and complex necessitating performance by an experienced thoracic surgeon with these tumors. Mediastinal nonseminomatous GCTs have a distinctly worse prognosis than seminomas or teratomas, with a 5-year overall survival rate of 40-45% [17], in patients treated with this combined modality approach.

14.4 Mediastinal Lymphoma

Lymphoma accounts for around 25% of anterior mediastinal masses. The two most common subtypes of primary mediastinal lymphomas are Hodgkin's lymphoma (13%) and large B-cell lymphoma (12%), both of which will be the focus of the discussion.

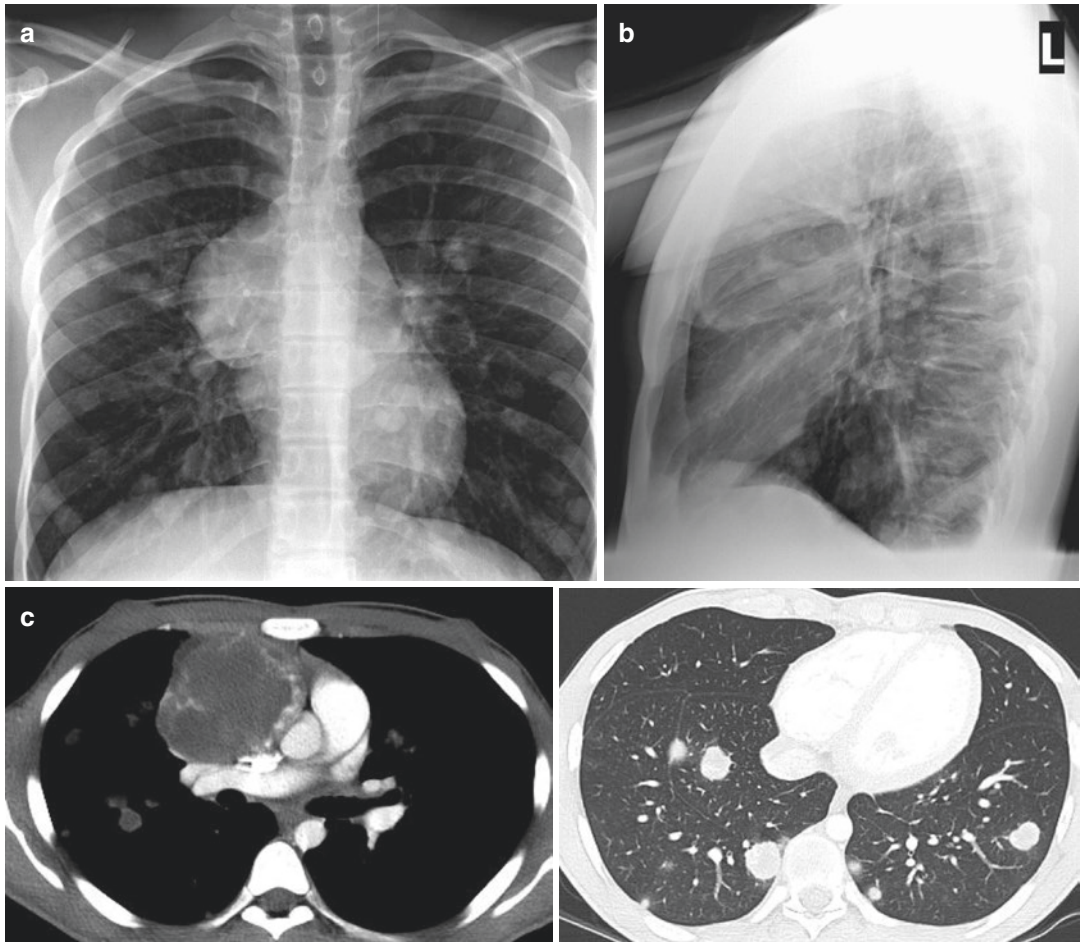

Fig. 14.3 *16-year-old with metastatic choriocarcinoma presenting with weight loss and night sweats, as well as markedly elevated AFP and b-hCG levels.* PA (**a**) and (**b**) lateral chest radiographs demonstrate a large anterior mediastinal mass and bilateral lung nodules. (**c**) Axial contrast-enhanced chest CT demonstrates a large heterogeneous anterior mediastinal containing large foci of central necrosis and peripheral enhancing papillary-like projections. Bilateral lung nodules were also seen, consistent with lung metastases. Patient was treated with chemotherapy, resulting in favorable response in the anterior mediastinal mass and marked response in the lung metastases on follow-up chest CT (**d**), coupled with normalization of AFP and b-hCG levels. This was followed by surgical resection of the residual anterior mediastinal mass (**e**)

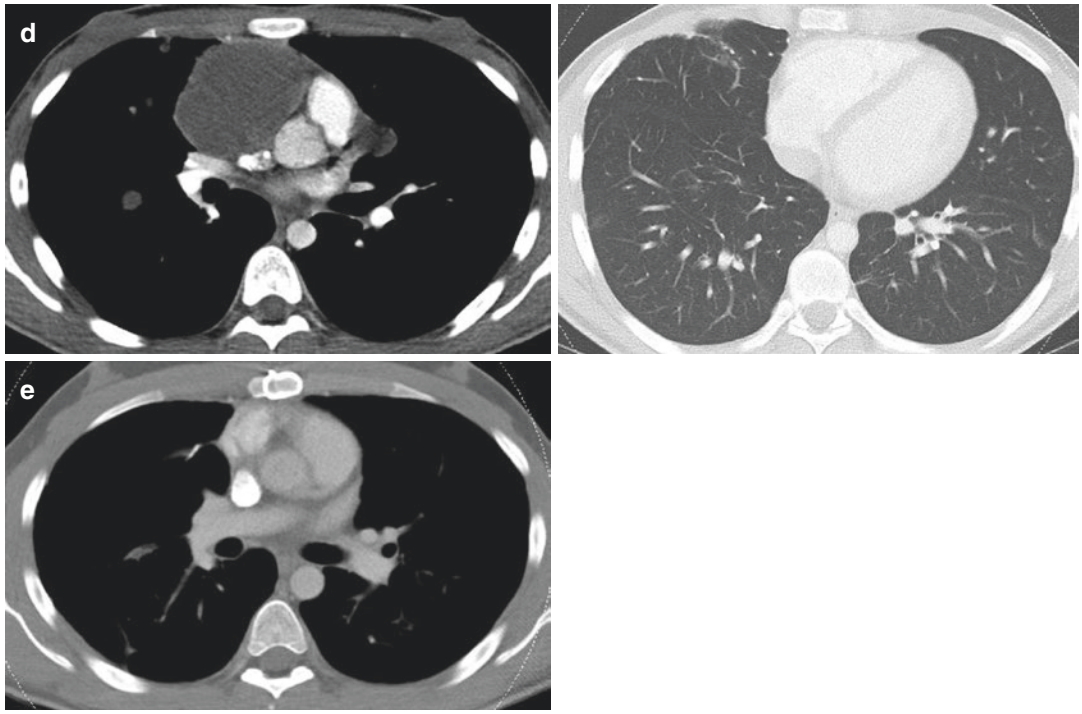

Fig. 14.3 (continued)

14.4.1 Mediastinal Hodgkin's Lymphoma

Clinical manifestations—Primary classic Hodgkin's lymphoma (HL) is relatively rare, with the nodular sclerosis subtype being the most common subtype in more than 95% of cases [26]. Typically affecting young women, 30–50% patients are asymptomatic at the time of presentation, with the condition diagnosed incidentally by imaging for other reasons. Around 30% of patients develop B-symptoms such as fever, night sweats, and weight loss, whereas 10-15% present with generalized pruritus [26]. Although symptoms related to extrinsic compression of the mediastinal structures may occur, it is unusual in the setting of classic HL, where the nodal mass tends to displace the adjacent structures without significant compromise even in patients with bulky disease.

Diagnosis—Laboratory abnormalities in patients with classic HL include abnormal complete blood count (CBC) such as leukocytosis, leukopenia, or anemia. Erythrocyte sedimentation rate (ESR) and LDH are usually elevated and may correlate with the presence of bulky disease [26]; however neither is specific for the diagnosis of HL. Chest radiographs usually demonstrate a smoothly marginated or lobulated anterior mediastinal mass, or mediastinal widening [27]. On chest CT, patients may demonstrate a solitary bulky anterior mediastinal mass with lobulated contour, or multiple discrete lymph nodes that may be confluent (Fig. 14.4). Masses usually demonstrate mild-to-moderate enhancement following IV contrast administration, with occasionally cystic spaces and necrosis [28]. The most common region involved in the anterior mediastinum is the prevascular compartment [27]. In some patients, there may be additional mediastinal, hilar, axillary, supraclavicular, or internal mammary chain lymph nodes. Following the definitive diagnosis of HL by histologic sampling, most patients undergo FDG PET/CT for initial staging, which usually demonstrates intense FDG uptake within the anterior mediastinal mass

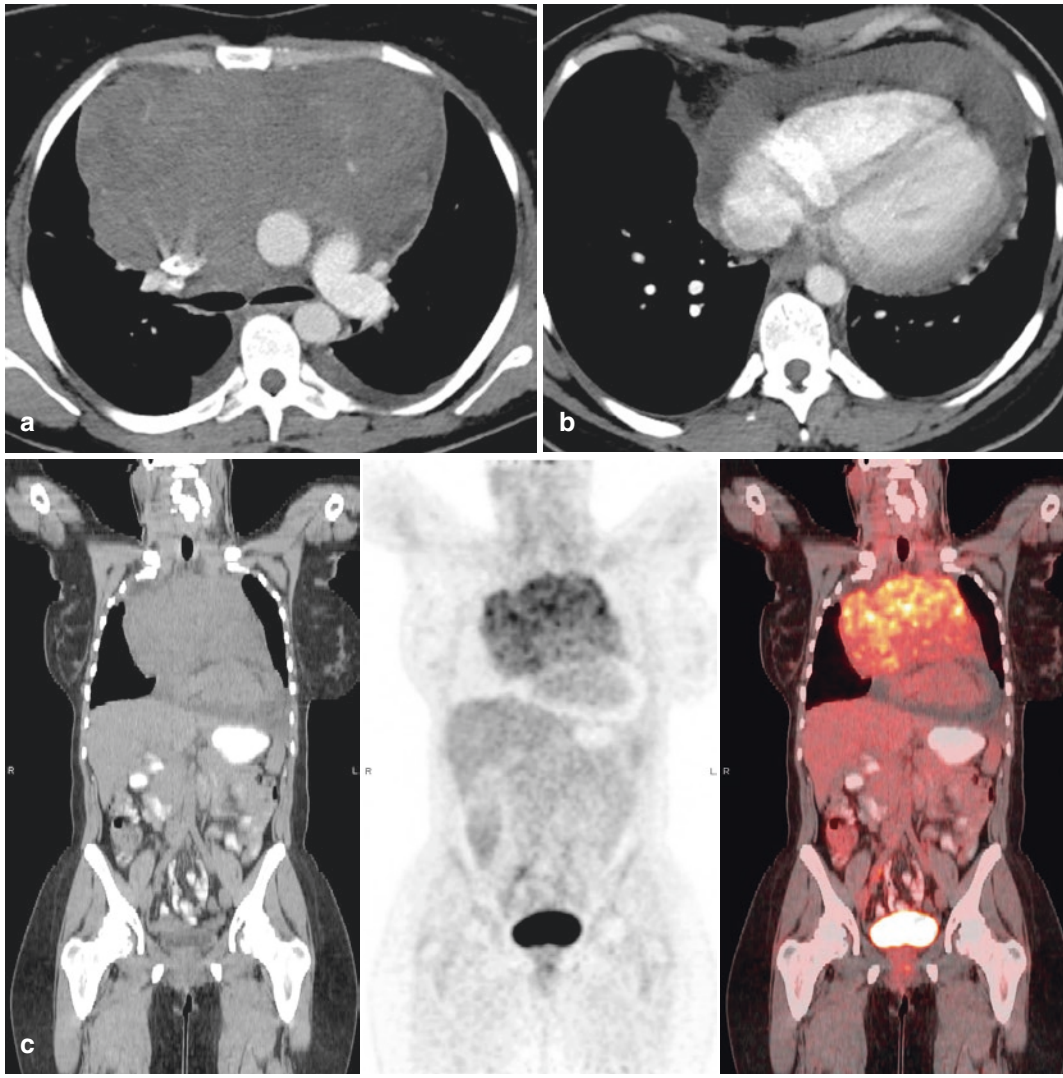

Fig. 14.4 *34-year-old female with classic Hodgkin's lymphoma.* Axial chest CT (**a**, **b**) demonstrating a bulky heterogeneous anterior mediastinal mass with lobulated contours. Note the presence of pleural and pericardial effusions. CT-guided biopsy of the mass confirmed Hodgkin's lymphoma. Initial staging of FDG-PET/CT (**c**) revealed intense uptake within the mass (SUV 11.1), with no additional hypermetabolic lymph nodes

(Fig. 14.4), with standardized uptake values (SUVs) greater than 10 correlating with higher grade of lymphoma [29]. FDG PET/CT also helps detect additional sites of lymphoma above or below the diaphragm with higher sensitivity compared to CT [30], and is also an excellent modality for monitoring treatment response [31], as well as detection of lymphoma relapse [32]. Bulky mediastinal disease is defined by the presence of a mass measuring >10 cm.

Treatment and prognosis—Patients with mediastinal HL are usually categorized as either stage I (single lymph node group or thymus involvement) or stage II (two or more lymph node groups on the same side of the diaphragm), according to the Costwolds modified Ann Arbor classification [33]. Poor prognostic or "unfavorable" factors include bulky mediastinal disease, presence of B-symptoms, and elevated ESR [26]. In general, patients without bulky disease are treated with

concurrent chemotherapy and radiation therapy of the involved site(s), with an excellent prognosis, including a 10-year survival rate of 95% for patients with stage I or II disease and no unfavorable factors [34]. On the other hand, patients with bulky mediastinal disease are also treated with concurrent chemotherapy and radiation therapy, with however more cycles of the chemotherapy regimen compared to the non-bulky disease patients. These patients, especially in the presence of unfavorable factors, tend to have a worse prognosis and a relapse rate of 15% [34].

14.4.2 Mediastinal Large B-Cell Lymphoma

Clinical manifestations—Primary mediastinal large B-cell lymphoma (LBCL) is a clinically aggressive subtype of lymphoma thought to arise from B cells of thymic origin, predominantly affecting females with a median age of 30–40 years old at the time diagnosis [35]. Most cases manifest as a locally invasive anterior mediastinal mass, with patients often presenting with signs of airway compromise or SVC syndrome. In one series, SVC syndrome was present in 57% of patients, whereas 80% of patients had some degree of mass effect on the SVC by the anterior mediastinal mass [36]. Prompt clinical recognition of SVC syndrome is of paramount importance since prompt management is critical, as will be discussed in the "treatment" section below. Shortness of breath is the most common symptom, with other more specific signs including facial swelling and redness, which may be exacerbated by lying down or bending forward. Other oncologic emergencies with which patients with mediastinal LBCL may present include tumor lysis syndrome and pericardial tamponade. Systemic B symptoms, pleural or pericardial effusions, may be present in up to 50% of the cases [37].

Diagnosis—The majority of mediastinal LBCL patients present with elevated serum LDH levels [37]. Chest radiograph demonstrates the presence of a large mediastinal mass; however this is no longer obtained frequently, as most patients present with worrisome signs and symptoms as described above, leading to acquisition of a chest CT directly. Findings on chest CT are not very specific, and include a large anterior mediastinal mass, with additional discrete intrathoracic lymph nodes, vascular encasement, pleural or pericardial effusion, and in a few cases invasion into the adjacent chest wall, lung parenchyma, or overlying skin [38]. In addition, signs of SVC syndrome can be easily recognized on CT, including encasement and/or narrowing of the SVC, venous collaterals in the chest wall anteriorly or posteriorly, or "hot quadrate" sign in the liver (Fig. 14.5c). Almost all patients with mediastinal LBCL demonstrate intense uptake on FDG PET/CT (Fig. 14.5a, b), rendering it an excellent modality for staging and for evaluation of residual viable lymphoma following completion of therapy.

Treatment and prognosis—The optimal treatment strategy for patients with primary mediastinal LBCL is controversial. For management purposes, patients are classified as having limited-stage disease (can be contained with one radiation field) or advanced-stage disease, which includes disease that cannot be contained with one radiation field, bulky disease (>10 cm) or associated pleural/pericardial effusion. For both stages, the usual regimen involves induction chemoimmunotherapy, such as rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP), with advanced-disease patients requiring more cycles than those with limited disease [39]. The decision of following this with radiation therapy of the involved field is more controversial and depends on many factors, such as patient and tumor characteristics, choice of the chemoimmunotherapy agents, and whether disease is confined to the chest [40]. Monitoring of treatment response is best achieved by FDG PET/CT, which should be obtained 6–8 weeks following completion of chemotherapy and 12 weeks following completion of radiation therapy [41], unless there is clinical suspicion of progression earlier, in order to avoid false-positive results related to the therapy itself. Recent studies report cure rates similar to patients with diffuse LBCL treated with aggressive therapy, with

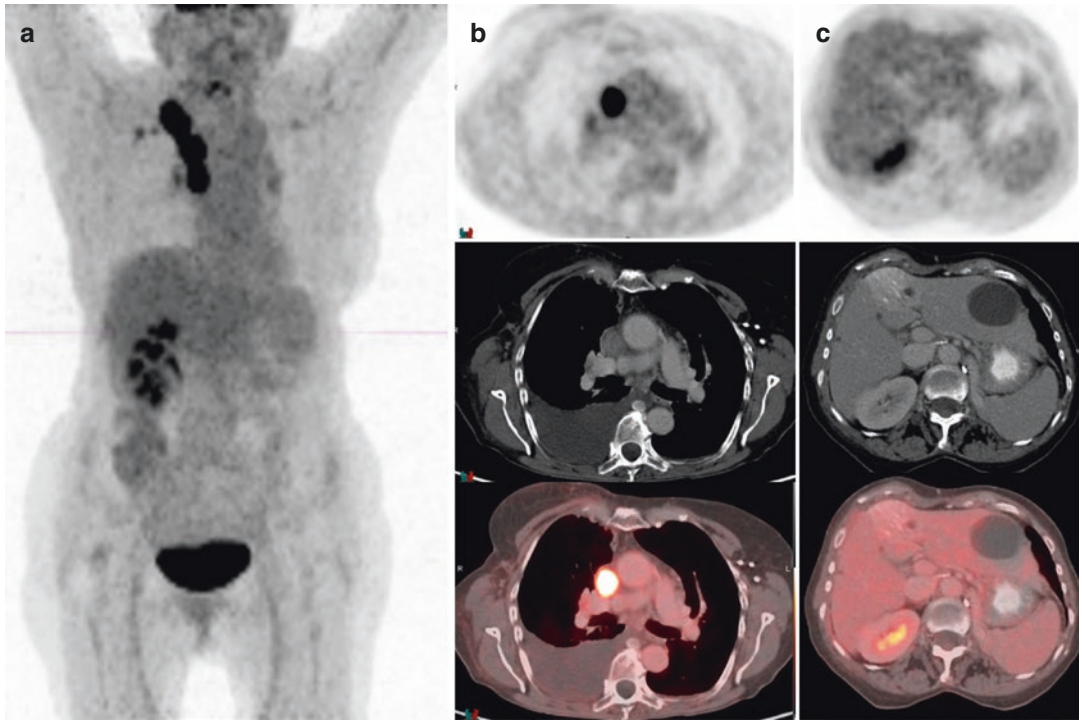

Fig. 14.5 *35-year-old female with newly diagnosed mediastinal LBCL.* (**a**) MIP and (**b**) axial PET, CT, and fusion images demonstrating a large anterior mediastinal mass completely invading the SVC. Note the presence of an additional hypermetabolic right hilar lymph node and a right pleural effusion. (**c**) Images through the liver demonstrating a "hot quadrate" sign. Findings consistent with SVC syndrome

overall survival rates up to 72% [35]. However, in patients with relapse or disease progression, salvage therapy is rarely curative.

14.5 Mediastinal Mesenchymal Tumors

Mesenchymal tumors of the mediastinum are rare, comprising around 5% of mediastinal tumors [42], with a higher prevalence and malignant potential in children. This group of neoplasms consists of tumors of various origins, such as those originating from muscle, adipose tissue, lymphatics, blood vessels, skeletal tissue, and fibrous tissue, including both benign and malignant tumors (Table 14.3). For the purposes of our discussion, we briefly discuss mediastinal lipoma, rhabdomyosarcoma, and chondrosarcoma as examples of mesenchymal tumors.

14.5.1 Mediastinal Lipoma

Lipomas are rare in the mediastinum, accounting for less than 2% of all mediastinal masses, predominantly located in the anterior mediastinum [43]. They tend to grow in areas of minimal or absent resistance such as the right paratracheal space. Almost all patients are asymptomatic at presentation, and most lipomas are detected incidentally on imaging studies obtained for other purposes. Chest radiograph may demonstrate the incidental anterior mediastinal mass or simply thickening of the right paratracheal stripe. On chest CT, mediastinal lipomas demonstrate the characteristic appearance of a well-circumscribed mass with homogenous fat attenuation (Fig. 14.6). Chest MRI is rarely needed for the diagnosis given the characteristic appearance on CT. Surgical resection may be performed for relief of compression on adjacent mediastinal structures, and is often curable. Inhomogeneous fat attenuation or

Table 14.3 Primary mesenchymal tumors of the mediastinum

Tissue of origin	Benign tumor	Malignant tumor
Muscle	Leiomyoma	Leiomyosarcoma
	Rhabdomyoma	Rhabdomyosarcoma
Fibroblastic	Fibromatosis	Fibrosarcoma
		Malignant fibrous histiocytoma (MFH)
Lymphatic	Lymphangioma	
Adipose	Lipoma	Liposarcoma
	Lipoblastoma	
Skeletal	Chondroma	Chondrosarcoma
		Osteosarcoma
Blood vessels	Hemangioma	Hemangioendothelioma
		Angiosarcoma

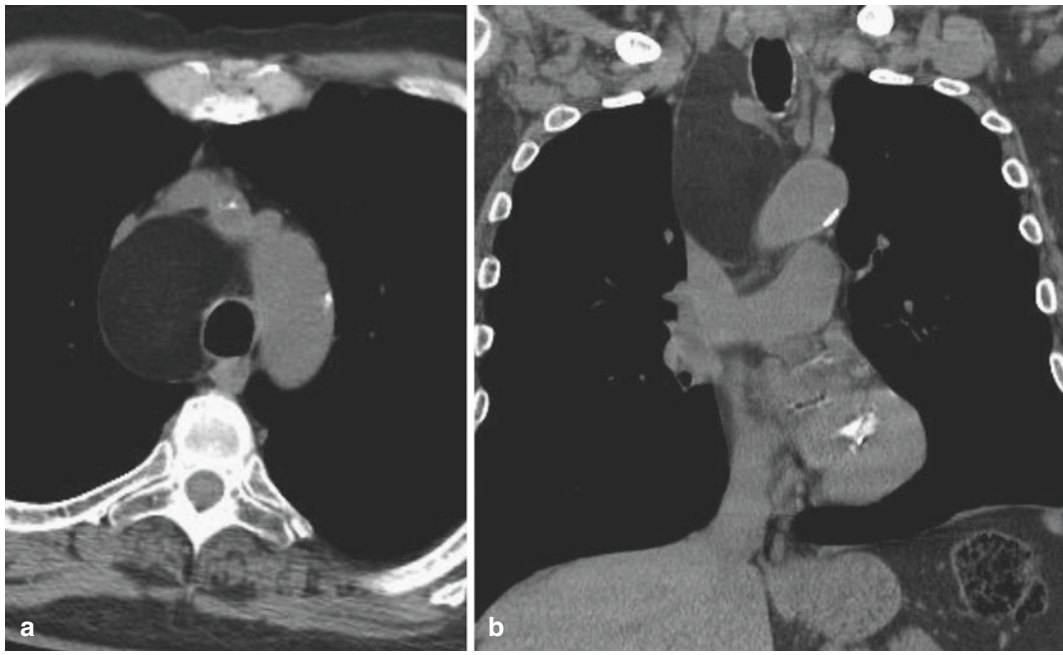

Fig. 14.6 *86-year-old male with an incidental anterior mediastinal mass.* Axial (**a**) and coronal (**b**) nonenhanced chest CT images demonstrating a well-circumscribed right paratracheal mass with homogeneous fat attenuation, consistent with a lipoma

presence of any soft tissue or nonfat density on chest CT or MRI should raise the suspicion for a liposarcoma, which is usually treated with resection followed by radiation therapy.

14.5.2 Mediastinal Rhabdomyosarcoma

Rhabdomyosarcomas may present at any age, and however are much more common in children during the first decade of life [42]. Mediastinal location is rare, accounting for less than 2% of childhood rhabdomyosarcomas [43]. Rhabdomyosarcomas include pleomorphic, alveolar, and embryonal subtypes. Initial radiologic evaluation should include radiography followed by CT or MRI of the affected area. Chest CT may also be part of the metastatic workup, in addition to bone marrow aspiration and/or radionuclide bone scans. The role of FDG PET/CT for initial staging is not clear [44]. Most tumors are bulky and heterogeneous at the time of presentation

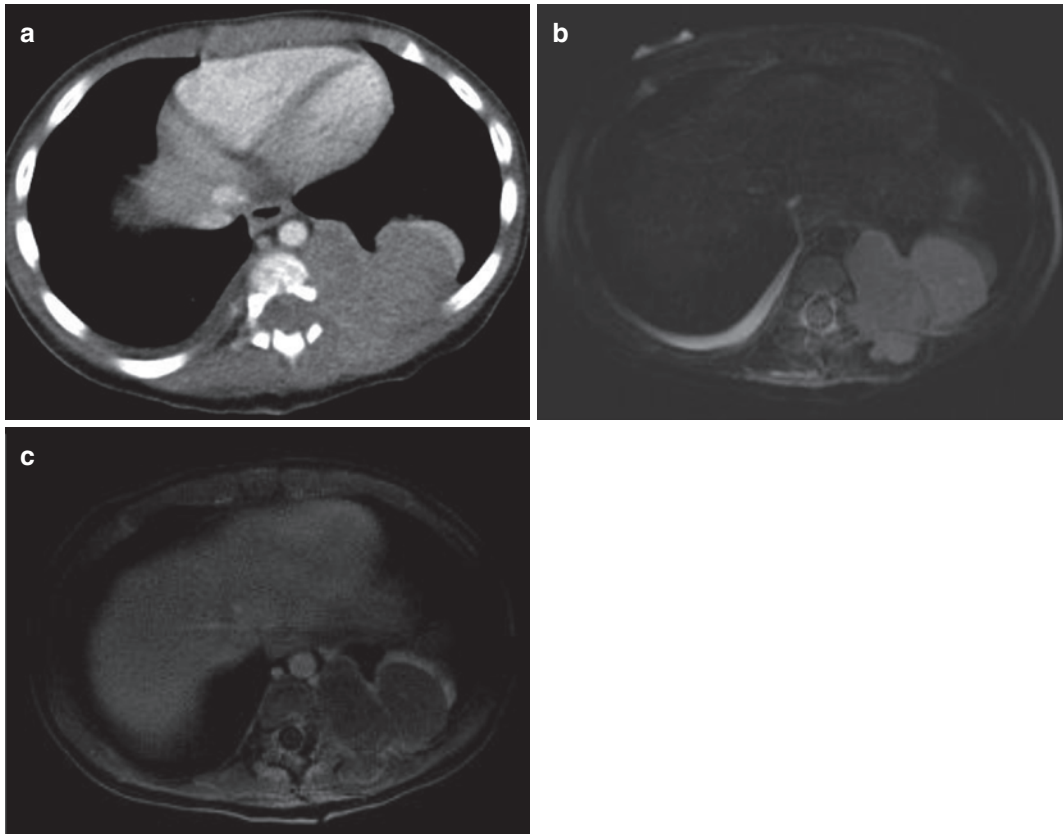

Fig. 14.7 6-year-old boy with posterior mediastinal rhabdomyosarcoma. Axial CT (**a**), T2 fat-saturation MR (**b**), and T1 post-contrast (**c**) images of the chest demonstrating a large infiltrative mildly enhancing mass in the posterior mediastinum extending into the adjacent neural foramina and into the posterior chest wall. Partial resection and biopsy revealed rhabdomyosarcoma

(Fig. 14.7). Treatment of rhabdomyosarcomas has evolved significantly over the past decades, with cure rates up to 70% using combined modality therapy [45]. These improved outcomes have been largely due to development of large international cooperative groups, such as the Soft Tissue Sarcoma Committee of the Children's Oncology Group (COG). Modern therapy for these tumors includes chemotherapy for local control and metastatic disease, followed by surgery if feasible, and radiation therapy for longer term control especially for sites of micrometastatic disease.

14.5.3 Mediastinal Chondrosarcoma

Chondrosarcomas are the third most common primary bone tumor after myeloma and osteosarcoma [46]. Extraosseous chondrosarcomas represent 2% of all soft-tissue sarcomas, most often arising from the chest wall [47]. The exact incidence of primary mediastinal chondrosarcoma is unknown due to scarce data in the literature, with a reported incidence of just 0.5 in 1 million [48]. Imaging appearance on chest CT is nonspecific, demonstrating a heterogeneous mass with cystic components and calcifications in some cases (Fig. 14.8). The few case reports in the literature describe masses arising from the sternum, cartilaginous portions of the ribs, and thyroid cartilage [47]. In general, chondrosarcomas are resistant to chemotherapy and radiation therapy, especially the low- to intermediate-grade tumors, which comprise around 90% of cases [49]. Therefore, surgery is the mainstay of treatment, with radiation therapy reportedly used in a few mediastinal chondrosarcomas, especially in high-grade tumors.

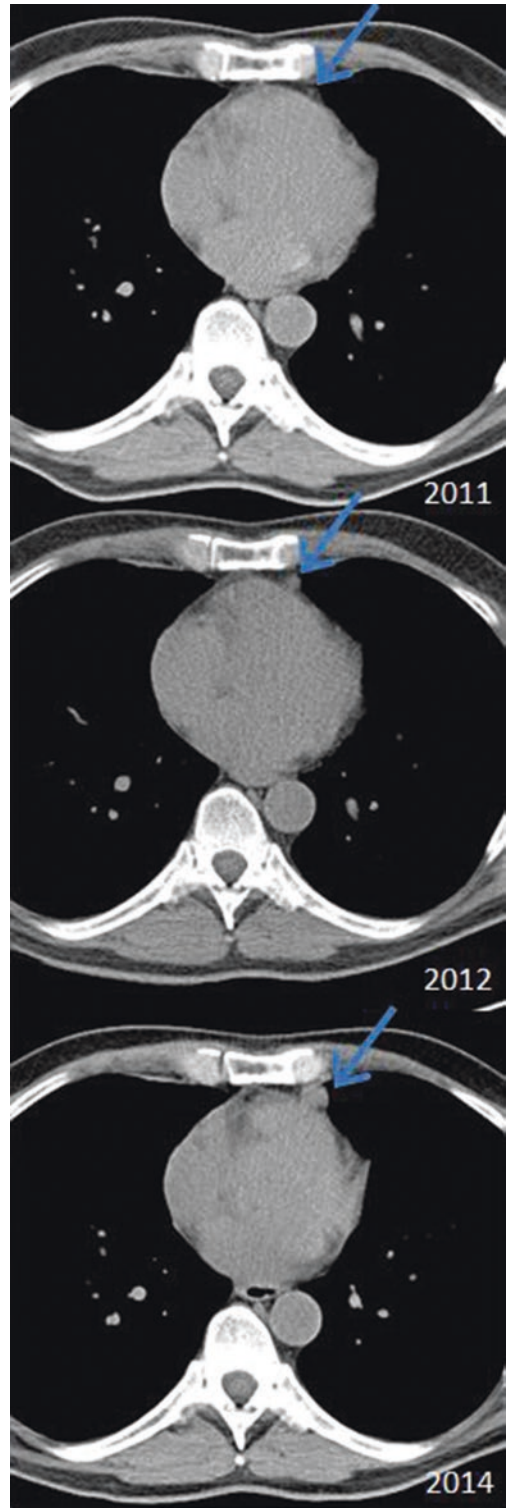

Fig. 14.8 67-year-old male with a history of anterior mediastinal chondrosarcoma treated with resection and radiation therapy. Axial CT images obtained over the course of 3 years demonstrating a small anterior mediastinal soft-tissue nodule progressively enlarging. Patient underwent subsequent resection, histopathology revealing recurrent chondrosarcoma

References

1. Felson B. Chest roentgenology. Philadelphia, PA: Saunders; 1973.
2. Carter BW, Tomiyama N, Bhora FY, et al. A modern definition of mediastinal compartments. J Thorac Oncol. 2014;9:S97–101.
3. Carter BW, Benveniste MF, Madan R, et al. ITMIG Classification of mediastinal compartments and multidisciplinary approach to mediastinal masses. Radiographics. 2017;37:413–36.
4. Carter BW, Marom EM, Detterbeck FC. Approaching the patient with an anterior mediastinal mass: a guide for clinicians. J Thorac Oncol. 2014;9:S102–9.
5. Osserman KE, Genkins G. Studies in myasthenia gravis: review of a twenty-year experience in over 1200 patients. Mt Sinai J Med. 1971;38:497–537.
6. Davis RD Jr, Oldham HN Jr, Sabiston DC Jr. Primary cysts and neoplasms of the mediastinum: recent changes in clinical presentation, methods of diagnosis, management, and results. Ann Thorac Surg. 1987;44:229–37.
7. Lewis BD, Hurt RD, Payne WS, et al. Benign teratomas of the mediastinum. J Thorac Cardiovasc Surg. 1983;86:727–31.
8. Adebonojo SA, Nicola ML. Teratoid tumors of the mediastinum. Am Surg. 1976;42:361–5.
9. Moeller KH, Rosado-de-Christenson ML, Templeton PA. Mediastinal mature teratoma: imaging features. AJR Am J Roentgenol. 1997;169:985–90.
10. Takeda S, Miyoshi S, Ohta M, et al. Primary germ cell tumors in the mediastinum: a 50-year experience at a single Japanese institution. Cancer. 2003;97:367–76.
11. Feo CF, Chironi G, Porcu A, et al. Videothoracoscopic removal of a mediastinal teratoma. Am Surg. 1997;63:459–61.
12. Arai K, Ohta S, Suzuki M, et al. Primary immature mediastinal teratoma in adulthood. Eur J Surg Oncol. 1997;23:64–7.
13. Donadio AC, Motzer RJ, Bajorin DF, et al. Chemotherapy for teratoma with malignant transformation. J Clin Oncol. 2003;21:4285–91.
14. Moran CA, Suster S, Przygodzki RM, et al. Primary germ cell tumors of the mediastinum: II. Mediastinal seminomas--a clinicopathologic and immunohistochemical study of 120 cases. Cancer. 1997;80:691–8.
15. Dulmet EM, Macchiarini P, Suc B, et al. Germ cell tumors of the mediastinum. a 30-year experience. Cancer. 1993;72:1894–901.
16. Bohle A, Studer UE, Sonntag RW, et al. Primary or secondary extragonadal germ cell tumors? J Urol. 1986;135:939–43.
17. Bokemeyer C, Nichols CR, Droz JP, et al. Extragonadal germ cell tumors of the mediastinum and retroperitoneum: results from an international analysis. J Clin Oncol. 2002;20:1864–73.
18. Strollo DC, Rosado-de-Christenson ML. Primary mediastinal malignant germ cell neoplasms: imaging features. Chest Surg Clin N Am. 2002;12:645–58.
19. Shin MS, Ho KJ. Computed tomography of primary mediastinal seminomas. J Comput Assist Tomogr. 1983;7:990–4.
20. Rosado-de-Christenson ML, Templeton PA, Moran CA. From the archives of the AFIP. Mediastinal germ cell tumors: radiologic and pathologic correlation. Radiographics. 1992;12:1013–30.
21. Hainsworth JD, Greco FA. Extragonadal germ cell tumors and unrecognized germ cell tumors. Semin Oncol. 1992;19:119–27.
22. Hartmann JT, Nichols CR, Droz JP, et al. Hematologic disorders associated with primary mediastinal nonseminomatous germ cell tumors. J Natl Cancer Inst. 2000;92:54–61.
23. Orazi A, Neiman RS, Ulbright TM, et al. Hematopoietic precursor cells within the yolk sac tumor component are the source of secondary hematopoietic malignancies in patients with mediastinal germ cell tumors. Cancer. 1993;71:3873–81.
24. Nichols CR. Mediastinal germ cell tumors. Clinical features and biologic correlates. Chest. 1991;99:472–9.
25. Fizazi K, Culine S, Droz JP, et al. Primary mediastinal nonseminomatous germ cell tumors: results of modern therapy including cisplatin-based chemotherapy. J Clin Oncol. 1998;16:725–32.
26. Pina-Oviedo S, Moran CA. Primary mediastinal classical Hodgkin lymphoma. Adv Anat Pathol. 2016;23:285–309.
27. Strollo DC. Rosado de Christenson ML, and Jett JR Primary mediastinal tumors. Part 1: Tumors of the anterior mediastinum. Chest. 1997;112:511–22.
28. Shahrzad M, Le TS, Silva M, et al. Anterior mediastinal masses. AJR Am J Roentgenol. 2014;203:W128–38.
29. Itti E, Meignan M, Berriolo-Riedinger A, et al. An international confirmatory study of the prognostic value of early PET/CT in diffuse large B-cell lymphoma: comparison between Deauville criteria and DeltaSUVmax. Eur J Nucl Med Mol Imaging. 2013;40:1312–20.
30. Schaefer NG, Hany TF, Taverna C, et al. Non-Hodgkin lymphoma and Hodgkin disease: coregistered FDG PET and CT at staging and restaging--do we need contrast-enhanced CT? Radiology. 2004;232:823–9.
31. Hutchings M, Barrington SF. PET/CT for therapy response assessment in lymphoma. J Nucl Med. 2009;50(Suppl 1):21S–30S.
32. Zinzani PL, Stefoni V, Tani M, et al. Role of [18F] fluorodeoxyglucose positron emission tomography scan in the follow-up of lymphoma. J Clin Oncol. 2009;27:1781–7.
33. Lister TA, Crowther D, Sutcliffe SB, et al. Report of a committee convened to discuss the evaluation and staging of patients with Hodgkin's disease: Cotswolds meeting. J Clin Oncol. 1989;7:1630–6.
34. Diehl V, Thomas RK, Re D, Part II. Hodgkin's lymphoma--diagnosis and treatment. Lancet Oncol. 2004;5:19–26.
35. Nguyen LN, Ha CS, Hess M, et al. The outcome of combined-modality treatments for stage I and II primary

large B-cell lymphoma of the mediastinum. Int J Radiat Oncol Biol Phys. 2000;47:1281–5.
36. Jacobson JO, Aisenberg AC, Lamarre L, et al. Mediastinal large cell lymphoma. An uncommon subset of adult lymphoma curable with combined modality therapy. Cancer. 1988;62:1893–8.
37. Savage KJ, Al-Rajhi N, Voss N, et al. Favorable outcome of primary mediastinal large B-cell lymphoma in a single institution: the British Columbia experience. Ann Oncol. 2006;17:123–30.
38. Tateishi U, Muller NL, Johkoh T, et al. Primary mediastinal lymphoma: characteristic features of the various histological subtypes on CT. J Comput Assist Tomogr. 2004;28:782–9.
39. Hamlin PA, Portlock CS, Straus DJ, et al. Primary mediastinal large B-cell lymphoma: optimal therapy and prognostic factor analysis in 141 consecutive patients treated at Memorial Sloan Kettering from 1980 to 1999. Br J Haematol. 2005;130:691–9.
40. Rieger M, Osterborg A, Pettengell R, et al. Primary mediastinal B-cell lymphoma treated with CHOP-like chemotherapy with or without rituximab: results of the Mabthera International Trial Group study. Ann Oncol. 2011;22:664–70.
41. Juweid ME, Stroobants S, Hoekstra OS, et al. Use of positron emission tomography for response assessment of lymphoma: consensus of the Imaging Subcommittee of International Harmonization Project in Lymphoma. J Clin Oncol. 2007;25:571–8.
42. Lee KH, Song KS, Kwon Y, et al. Mesenchymal tumours of the thorax: CT findings and pathological features. Clin Radiol. 2003;58:934–44.
43. Macchiarini P, Ostertag H. Uncommon primary mediastinal tumours. Lancet Oncol. 2004;5:107–18.
44. McCarville MB, Christie R, Daw NC, et al. PET/CT in the evaluation of childhood sarcomas. AJR Am J Roentgenol. 2005;184:1293–304.
45. Raney RB, Walterhouse DO, Meza JL, et al. Results of the Intergroup Rhabdomyosarcoma Study Group D9602 protocol, using vincristine and dactinomycin with or without cyclophosphamide and radiation therapy, for newly diagnosed patients with low-risk embryonal rhabdomyosarcoma: a report from the Soft Tissue Sarcoma Committee of the Children's Oncology Group. J Clin Oncol. 2011;29:1312–8.
46. Dorfman HD, Czerniak B. Bone cancers. Cancer. 1995;75:203–10.
47. Ostergaard ML, Petersen RH, Kalhauge A. A chondrosarcoma in the anterior mediastinum mimicking a thymoma. Acta Radiol Open. 2015;4:2058460115595659.
48. Widhe B, Bauer HC, Scandinavian Sarcoma G. Surgical treatment is decisive for outcome in chondrosarcoma of the chest wall: a population-based Scandinavian Sarcoma Group study of 106 patients. J Thorac Cardiovasc Surg. 2009;137:610–4.
49. Angelini A, Guerra G, Mavrogenis AF, et al. Clinical outcome of central conventional chondrosarcoma. J Surg Oncol. 2012;106:929–37.