Mediastinal Tumors

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Introduction

Primary mediastinal tumors are uncommon in the pediatric population. Mediastinal masses in children include a wide spectrum of pathology [1], from congenital lesions such as duplication cysts found incidentally, to lymphomas presenting with respiratory collapse. Sixty-five to 80 % of mediastinal lesions are malignant [2–5]; therefore they should be investigated without delay. About 40 % of mediastinal tumors occur in children younger than 2 years old.

Anatomy

One of the most fundamental surgical knowledge is the understanding of anatomy (Fig. 27.1). The best way to approach mediastinal lesions is to consider them by their location, which will also have implication on the optimal surgical approach. The mediastinum is divided into the anterior, middle and posterior compartments based on the lateral chest radiograph. The anterior mediastinum is located between the sternum and the pericardium. It contains the thymus, lymph nodes and fat; and is the most common site of pediatric mediastinal masses. The middle compartment is the busiest containing multiple vital structures including the heart, the trachea, the mainstem bronchi and their associated lymphatics, and the aortic arch and great vessels. This visceral compartment starts from the pericardium and ends posteriorly with the trachea. The posterior compartment extends from behind the trachea to the vertebral bodies and the paravertebral sulcus. The posterior compartment is home to the descending thoracic aorta, autonomic ganglia and nerves, esophagus, thoracic duct, lymph nodes, and fat. A clear understanding of the type of tissues present in each compartment is the key to the logical consideration of the differential diagnosis. Table 27.1 illustrates the different types of tumors common to each of the compartments.

The age of the patient at presentation is also important in the differential diagnosis. Infants and young children are more likely to present with neuroblastomas, lymphangiomas, teratomas, and congenital anomalies such as bronchopulmonary foregut malformations. Lymphomas and benign neurogenic tumors are more common in teenagers. Table 27.2 outlines the relationship between age and differential diagnosis of mediastinal masses.

Anterior mediastinal tumors account for 44 % of all mediastinal lesions [2], and 80 % of these are malignant. The major anterior mediastinal tumors can be characterized by the four "terrible" T's, in the order of frequency: *T*-Cell lymphomas, *T*eratomas and germ cell tumors, *T*hymus, and intrathoracic *T*hyroid. Although a physiologically enlarged thymus is common in children, thymoma and thoracic thyroid are extremely rare in the pediatric population. Cervical lymphatic malformations, commonly known as cystic lymphangiomas or hygromas, can also extend into the superior mediastinum, and rare cases of primary mediastinal lymphangiomas have been reported.

Twenty percent of mediastinal tumors are found in the middle compartment. These are primarily lymphocytic in origin and include Hodgkin's disease and non-Hodgkin's lymphomas. The rare cardiac and pericardial tumors are also found in this compartment.

Posterior mediastinal masses account for 36 % of all mediastinal tumors and two thirds of these are malignant [6]. These tumors usually arise from neurogenic structures located in the paravertebral sulcus; they include neuroblastomas, ganglioneuromas and neurofibromas, and are more commonly seen in infants and toddlers. Other sarcomas or primitive neuroectodermal tumors and, rarely, teratomas can

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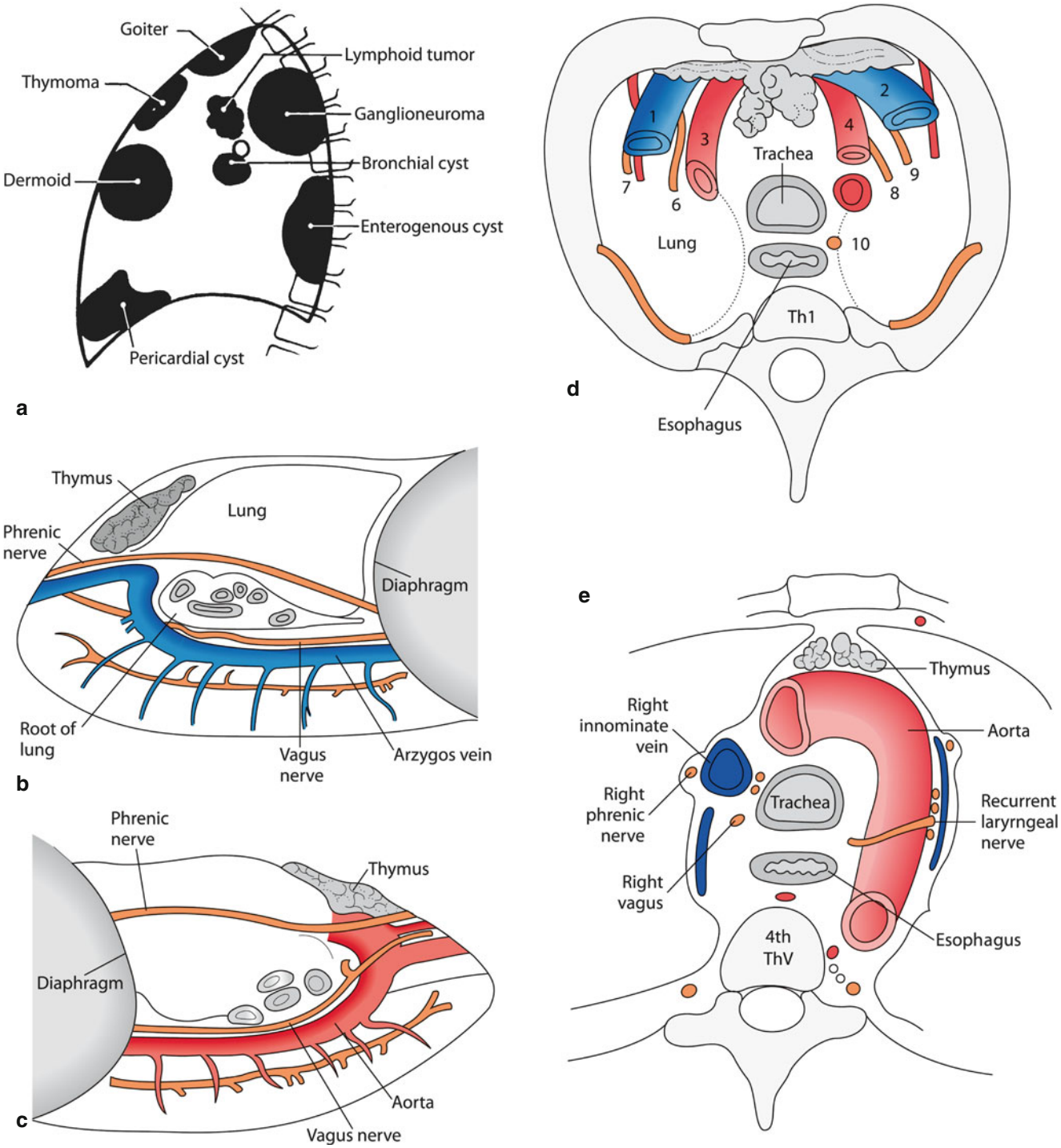

Fig. 27.1 (**a**) Diagram of the mediastinum. (**b**) Right hemi-thorax. (**c**) Left hemi-thorax. (**d**) Structures at the thoracic inlet. *1*+ *2*: Left and right innominate vein; *3*: innominate artery; *4*: left common carotid; *5*: left subclavian artery; *6*: right vagus nerve; *7*: right phrenic nerve; *8*: left vagus nerve; *9*: left phrenic nerve; *10*: recurrent laryngeal nerve; *11*: 1st thoracic nerve. (**e**) Structures at level of 4th thoracic vertebra

also be found in this compartment. Foregut duplications, bronchogenic cysts, pericardial cysts, and extralobar sequestration can be found in both the middle and posterior mediastinum. These are not neoplasms, but they should be considered in the differential diagnosis.

Clinical Presentation and Diagnosis

Clinical Presentation

Mediastinal tumors may be discovered incidentally or present in a wide range of symptomatology, resulting from direct

Table 27.1 Distribution of mediastinal tumors by compartment

Anterior mediastinum	Middle mediastinum	Posterior mediastinum
Lymphomas	Lymphoma	Neuroblastoma
Hodgkin's lymphoma	Lymphangioma	Ganglioneuroma
Non-Hodgkin's lymphoma	Hemangioma	Ganglioneuroblstoma
Germ cell tumors	Pericardial cysts	Schwannoma
Teratomas	Bronchogenic cysts	Neurofibroma
Malignant germ cell tumors	Gorham's Disease	Paraganglionma
Thymus		Primitive neuroectodermal tumor
Thymoma		Esophageal duplications
Thymolipoma		
Vascular malformation		
Lymphangiomas		
Hemangiomas		

Table 27.2 Diagnosis by age (Grosfeld et al.)

Newborns/Infants	Children	Teenagers
Thymus	Thymus	Lymphoma
Lymphangioma	Lymphangioma	Hodgkin's disease
Neuroblastoma	Ganglioneuroma	Teratoma
Teratoma	Inflammatory adenopathy	Ganglioneuroma
Duplication cyst	Neuroblastoma	Germ-cell tumor
Bronchogenic cysts	Teratoma	Schwannoma
Lipoma	Hodgkin's disease	Neurofibroma
Meningocele	Lymphoma	Peripheral neuroectodermal tumor
	Peripheral neuroectodermal tumor	Rhabdomyosarcoma
	Rhabdomyosarcoma	

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compression, tumor invasion, functional tumor secretion, or paraneoplastic syndrome. Incidental masses found during routine chest radiograph should be investigated without delay, as the incidence of malignancy is high. Mediastinal tumors can present with cadiorespiratory symptoms from direct mass effect. Compression of the trachea or mainstem bronchi can lead to cough, stridor, and dyspnea. Involvement of the superior vena cava (SVC) may lead to the SVC syndrome. Orthopnea and impending respiratory arrest may result from the combination of airway compression, venous obstruction and cardiac dysfunction. Vigilant anesthetic planning is crucial in the management of these patients as discussed in section "Anesthetic consideration for patients with mediastinal tumors".

In addition to the direct mass effect, patients may have symptoms associated with systemic effects of the disease process. Patients with lymphoma may have fever, night sweats, and weight loss. Myasthenia gravis is seen in thymomas, and virilization may be present in germ cell tumors. Posterior mediastinal lesions can present with neurologic symptoms due to intra-spinal extension, or Horner's syndrome resulting from the involvement of the cervicothoracic sympathetic ganglia. Paraneoplastic syndromes such as opsoclonus-myoclonus or watery diarrhea induced by vasoactive intestinal peptide are rare modes of presentation for neurogenic tumors (Fig. 27.2).

Investigation

The definitive diagnosis of a mediastinal tumor should start with a thorough history and physical examination. Close attention to respiratory status and presence of lymphadenopathy is essential. The lateral chest radiograph helps to identify the location of the tumor and guides additional laboratory studies. Complete blood count with differential and comprehensive chemistry panel should be obtained. Urinary catecholamines should be sent in patients with a posterior mediastinal mass, and alpha-fetoprotein (AFP) and beta-human chorionic gonadotropin (β-HCG) should be sent if germ cell tumors are suspected.

CT scan of the chest should be the first diagnostic imaging study to provide more detailed characterization of the tumor and its relationship to the surrounding structures. In the present day technology, the examination can be performed in a matter of seconds and will require no or minimal sedation even in an anxious child [7]. Modern MR imaging is often equivalent to CT in the evaluation of mediastinal masses and avoids radiation. It is also the imaging modality of choice to assess spinal involvement in posterior mediastinal neurogenic tumors [7]. *M*-iodobenzylguanidine (MIBG) scan is a useful nuclear medicine modality in the preoperative staging assessment of suspected neuroblastomas.

Once the specific diagnosis is confirmed, treatment strategies of the mediastinal tumor can be tailored to the disease process. Lymphomas are treated with systemic chemotherapy and

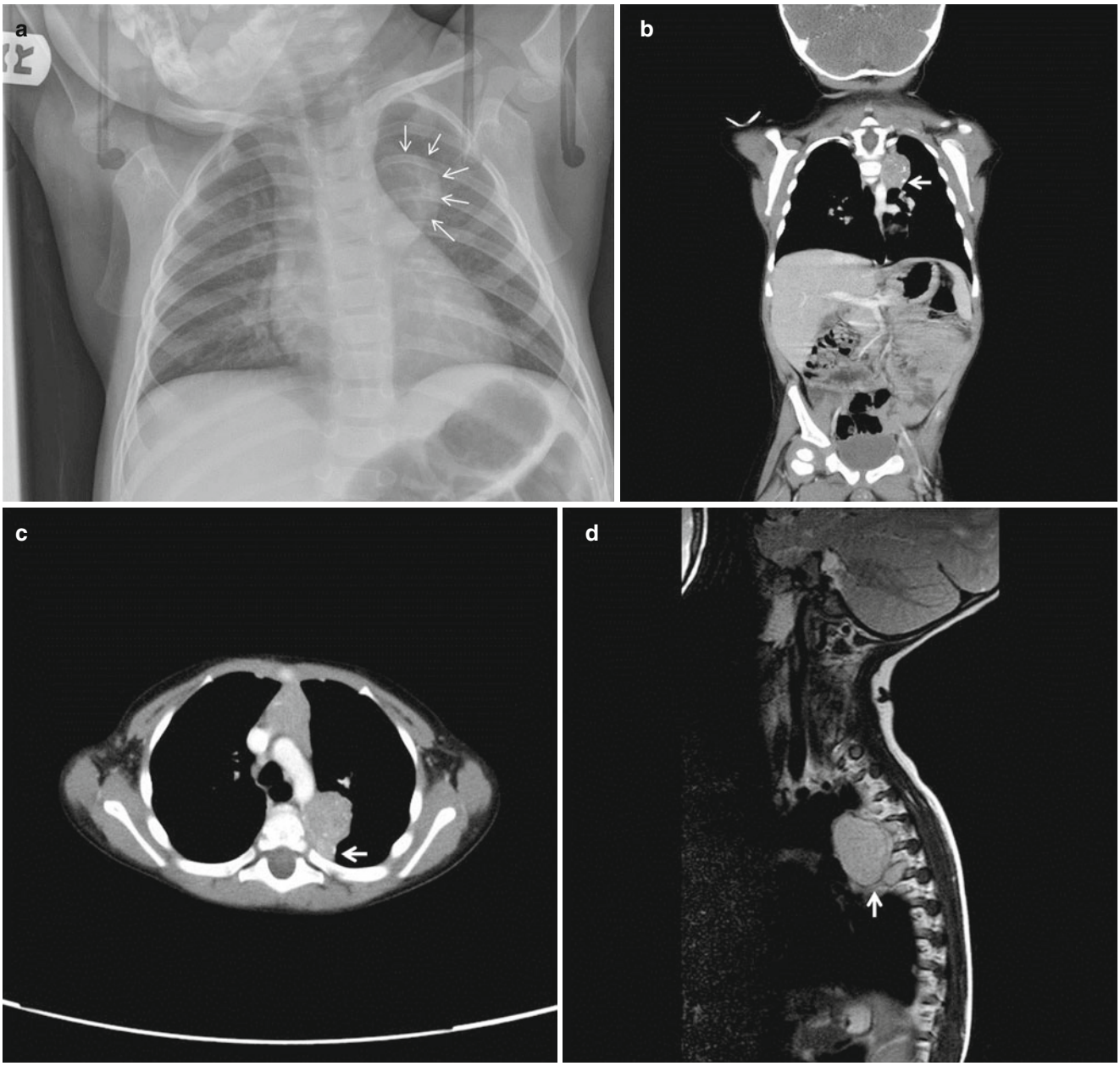

Fig. 27.2 (**a**) A 17 month old boy presented with opsoclonus myoclonus. A brain MRI was negative and a chest radiograph obtained for suspected pneumonia showed a left paravertebral lesion (*arrows*), CT (**b**, **c**) and MRI (**d**) showed a lesion sitting adjacent to but not extending into the spinal canal (*arrow*). The tumor was resected thoracoscopically with concomitant excision of adjacent lymphadenopathy. The final pathology showed neuroblastoma with unfavorable histology and two lymph nodes with metastatic neuroblastoma (INSS stage 2B). He was treated with observation only and received treatment with steroids and IVIG for his opsoclonus/myoclonus, which were slow to resolve despite negative imaging for residual disease 2 years post resection

radiation, and malignant germ cell tumors will benefit from neoadjuvant chemotherapy. Otherwise, surgical resection is the definitive treatment for most mediastinal pathologies.

Anterior Mediastinal Tumors

Children with anterior mediastinal tumors can pose significant challenges in diagnosis and management. An algorithmic approach with multidisciplinary involvement provides the optimal care for these fragile patients [8]. The pediatric surgeon is often called upon to coordinate care between pediatric oncologist, critical care/intensivist, anesthesiologist, and interventional radiologist; and to decide the best approach to obtain adequate tissue for diagnosis in concert with the pathologist. Once a child presents with a symptomatic anterior mediastinal mass, a careful search of extra-mediastinal involvement is essential. The least invasive and lowest risk

procedure should be utilized first [9]. Peripheral blood smear and flow cytometry may be diagnostic of leukemia. Elevated serum AFP will point to yolk-sac germ cell tumors. A mass containing mixed solid/cystic elements and fat on CT scan or MRI will lead to the diagnosis of teratoma. Chest radiograph may reveal pleural effusion, in which case fluid obtained by pleurocentesis can be sent for flow cytometry and cytology. Careful physical examination may reveal cervical lymphadenopathy that can be biopsied under local anesthesia with conscious sedation.

Lymphomas

Malignant lymphoma is the most common mediastinal tumor in children, accounting for approximately 60 % of all pediatric mediastinal lesions. These arise from the thymus and/or the mediastinal lymph nodes. Two-thirds are non-Hodgkin's lymphomas and one-third are Hodgkin's disease [10, 11]. T-cell lymphoblastic lymphomas are the most common histologic subtype of non-Hodgkin's lymphomas, followed by large cell lymphomas [11, 12].

Children with non-Hodgkin's lymphoma frequently present with symptoms related to local compression such as tachypnea, cough, stridor, and occasionally superior vena cava syndrome (Fig. 27.3). Up to 55 % of children with mediastinal Hodgkin's lymphoma have radiographic evidence of tracheal compression (Fig. 27.4) [13]. Pleural effusion and cervical lymphadenopathy are frequently present and should be the first choice for obtaining cells or tissue for diagnosis [14]. These tumors have an excellent response to chemotherapy and radiotherapy despite the fact that disseminated disease is often present [1]. Peripherally-inserted central venous access should be obtained during diagnostic procedures performed under local anesthesia when contraindications to general anesthesia are present. The surgeon's role is to obtain adequate tissue for diagnostic studies with minimal morbidity. Diagnosis and differentiation of histologic subtypes based on immunohistochemistry, cytogenetics and flow cytometry have significant impact on treatment regimen, thus sufficient diagnostic material need to be obtained prior to the initiation of chemotherapy. Recent advancement in molecular genetic testing utilizing fluorescent in situ hybridization and polymerase chain reaction may allow diagnosis with smaller amounts of tissue obtained from percutaneous fine needle aspiration or core biopsies [15, 16]. An open procedure with excision of the entire lymph node provides the best approach for adequate tissue diagnosis and assessment of nodal architecture [11]. However, the risk of anesthetic complication from the mass effect of the large mediastinal mass should be carefully assessed prior to any procedure as discussed in section "Anesthetic consideration for patients with mediastinal tumors".

In patients without extra-thoracic disease, pretreatment with steroids or radiation prior to biopsy may reduce tumor size rapidly and allow for safer anesthesia. However, radiation may significantly alter pathology making the correct diagnosis difficult. In some cases the radiation field can be adjusted to spare an area for later biopsy. Pretreatment with

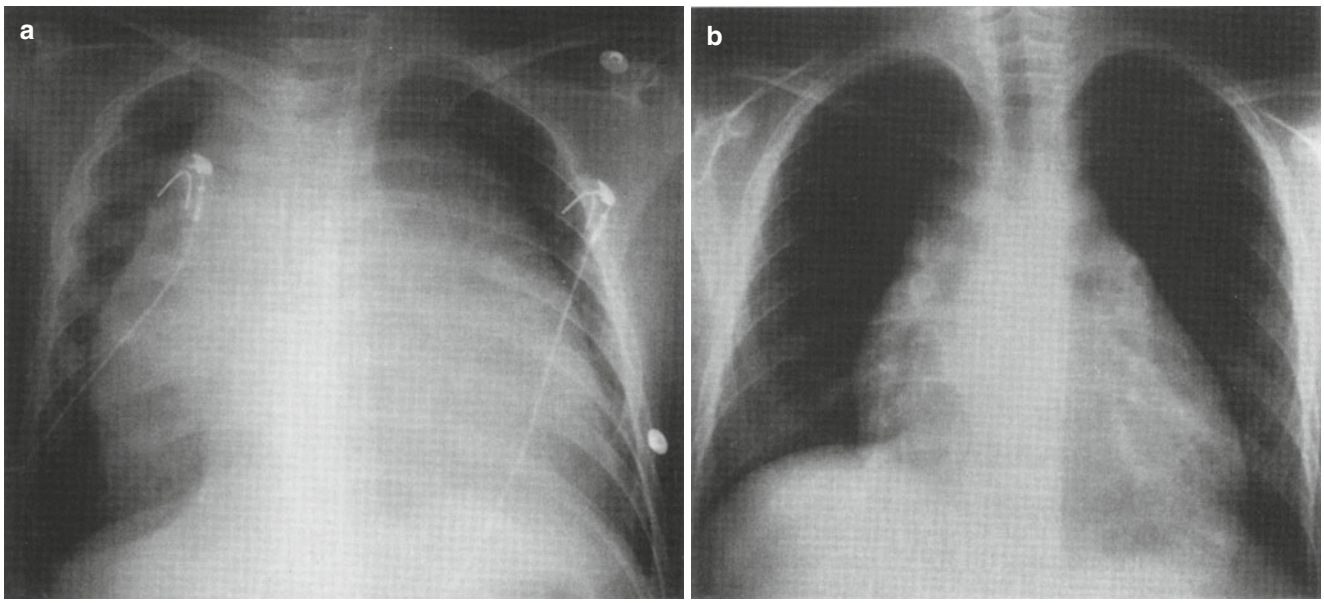

Fig. 27.3 (**a**) Chest radiograph of an 8 year old girl who presented with a 3 week history of wheezing, cough, anorexia and weight loss of 3 kg. The pleural effusion was tapped to avoid biopsy and the diagnosis of acute lymphoblastic lymphoma was obtained. (**b**) Chest radiograph 1 week after the first course of prednisone, vincristine, doxorubicin, methotrexate, and intrathecal cytosine arabinoside (ara-C) demonstrates a dramatic response to therapy

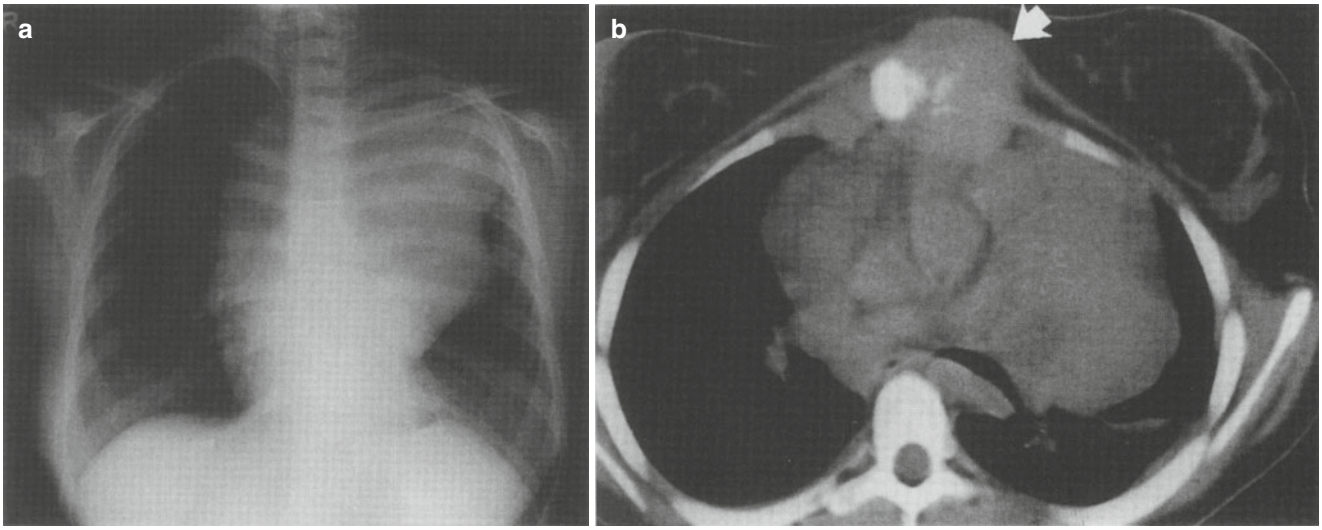

Fig. 27.4 (**a**) Chest radiograph of a 12 year old girl obtained because of mild left pleuritic chest pain demonstrates a large anterior mediastinal mass. (**b**) The CT scan revealed that the mass was eroding through the chest wall and sternum (*arrow*). Because of significant tracheal compression a biopsy was obtained under local anesthesia and Hodgkin's disease was diagnosed

steroids may also ablate tumor and cellular architecture as well as cytogenetic markers, leading to inaccurate diagnosis [17, 18] but may be necessary in the face of overwhelming anesthetic risk.

The staging, treatment and prognosis for lymphomas are discussed in Chap. 20.

Teratomas and Germ Cell Tumors

Germ cell tumors account for 6–18 % of pediatric mediastinal neoplasms [19]; they are the second most common tumor of the anterior mediastinum in children. They are believed to derive from primordial germ cells that missed their "target" during migration and remained in the mediastinum. Eighty-six percent are benign mature teratomas containing all three germinal layers, and the rest contain various malignant components including seminomas and non-seminomas.

Teratomas

Overall, 7–10 % of all teratomas are mediastinal, making this the third most common site after the sacrococcygeal and gonadal primaries [20]. Teratomas may present at any age from infancy to adolescence. The majority are benign, but after adolescence mediastinal teratomas have a high incidence of malignant behavior, which is usually indicated by elevated levels of tumor markers (alpha fetoprotein and beta-HCG) [20]. Immature elements are not of prognostic significance in children under 15 years, but they are associated with local aggressiveness and distant metastases above that age [21, 22]. Most mediastinal teratomas are located in the anterior mediastinum and frequently have large cystic components (Fig. 27.5), but a few have been described in the posterior mediastinum, some with epidural extension. Intrapericardial and intracardiac lesions are also described, the former presenting in utero or at birth with fetal hydrops or massive pericardial effusion [20]. Infants and toddlers with an anterior mediastinal teratoma commonly present with respiratory distress, but in older children, the teratoma may be an incidental finding on chest radiograph. It may also present as a chest wall mass with erosion through the soft tissues (Fig. 27.6), with hemoptysis or trichoptysis from bronchial erosion, with rupture into the pleural cavity, or with cardiac failure [20, 22]. CT scan is the imaging technique of choice in the evaluation of these lesions. It can define the extent of the lesion and possible tracheal compression. A heterogeneous anterior mediastinal mass containing calcification and varying tissue densities including fat is highly suggestive of the diagnosis [23]. Surgical resection via anterior thoracotomy, median sternotomy or thoracoscopy [24] is usually curative, although if present, malignant elements in the tumor will require further therapy.

Malignant Germ Cell Tumors

The mediastinum is the primary site in 4 % of malignant germ cell tumors [25]. These are complex tumors of varied histology with frequent coexistence of benign elements [26]. Malignant components include yolk sac tumors (also known as endodermal sinus tumors), seminomas, dysgerminomas, embryonal carcinomas, and choriocarcinomas [27]. They are more common in boys than girls (3:1). A strong association is found in patients with Klinefelter's syndrome, who often present with precocious puberty from the choriocarcinoma elements [20]. AFP and β-HCG should be obtained preoperatively, as for suspected germ cell tumors in other loca-

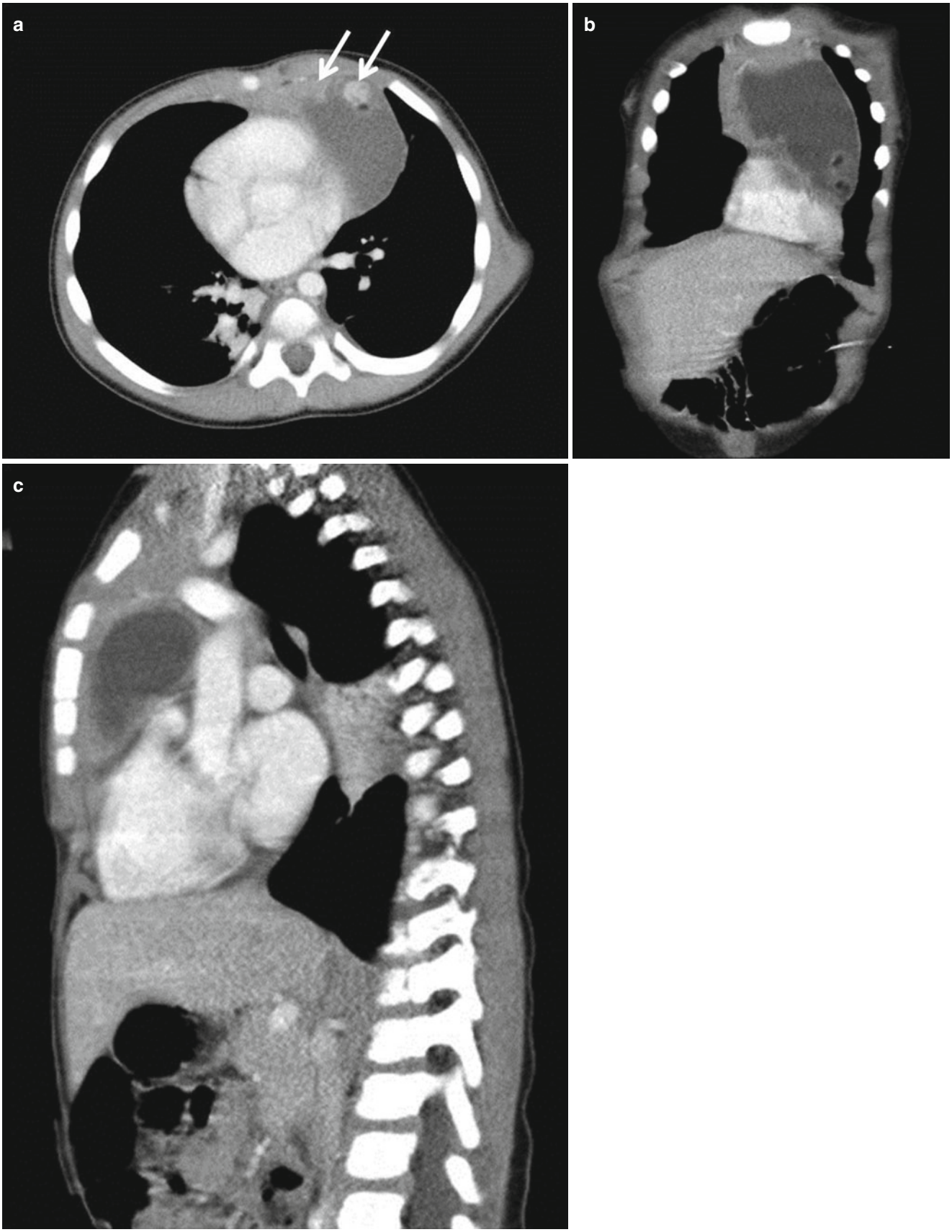

Fig. 27.5 (**a**) Axial, (**b**) coronal, and (**c**) sagittal CT scan of a 22 month old boy presenting with fever, cough, and weight loss. The anterior mediastinal mass is predominately cystic, with small solid components containing calcifications and fat densities (*white arrows*), arising from the thymus. This is highly suggestive of a benign cystic teratoma. The patient underwent complete surgical resection via median sternotomy without additional therapy

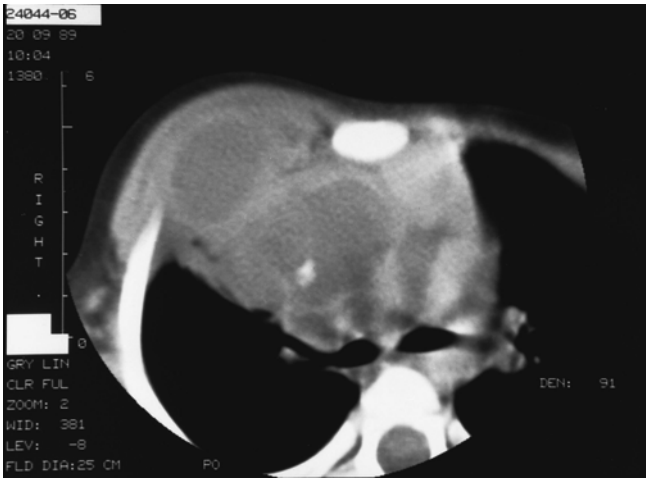

Fig. 27.6 A 2 year old was referred for a 5 cm by 5 cm hard fixed right chest wall mass that appeared suddenly during an upper respiratory infection. The computed tomography scan shows a bilobed lesion that extends through the chest wall and contains a small area of calcification. An incisional biopsy revealed pus-like material, containing ghost cells and calcified debris. Serum markers were normal. Complete excision of the mass required a right anterior thoracotomy and partial resection of an adherent right middle lobe. Pathologic examination revealed a ruptured mature teratoma with marked inflammatory reaction, containing foci of enteric, respiratory, and squamous mucosa; smooth muscle; salivary glands; pancreas; neuroglial tissue; and bone (Reproduced with permission from page 983 of: Laberge et al. [90])

tions. Elevated serum AFP will lead to suspicion of malignant yolk sac component, and high serum β-HCG is likely from the choriocarcinoma elements. Diagnostic biopsy should be obtained for large tumors considered difficult to resect either with image-guided core needle biopsy or via an anterior mediastinal approach [27]. Both can be safely performed under local anesthesia should the patient present with significant respiratory symptoms. The prognosis for patients with malignant germ cell tumors arising in the mediastinum was regarded previously as dismal with only occasional survivors in the pre-chemotherapy era [28, 29]. The POG/CCSG intergroup study demonstrated successful reduction in tumor bulk with neoadjuvant chemotherapy, which allowed complete resection of tumors with malignant components in 82 % of patients [27]. With the combination of multiagent chemotherapy (cisplatin, etoposide and bleomycin) and aggressive surgical resection, the POG/CCSG intergroup study reported 83 % 5-year overall survival and 79 % event-free survival in patients with extragonadal malignant germ cell tumors [29]. Similar results were reported by the United Kingdom Children's Cancer Study Group and the French MGCT study, utilizing carboplatin instead of cisplatin to minimize renal toxicity and hearing loss [30, 31]. However, children older than 12 years of age with thoracic primaries had a six times higher risk of death compared with younger children with other primary sites. An alternative high dose cisplatin regimen offered better event-free survival than standard dose cisplatin, but at the cost of increased treatment related toxicities and secondary malignancies [32].

The management of primary mediastinal germ cell tumors should be conservative at diagnosis, with biopsy only for large tumors. Patients with elevated tumor markers or histologic confirmation of malignancy should receive neoadjuvant chemotherapy prior to attempt at resection. Benign tumors and masses persisting after chemotherapy (often due to coexisting benign teratomatous elements) should be resected aggressively, and an excellent outcome can be expected [33].

Thymic Tumors

Tumors or tumor-like lesions arising from the thymus include thymic hyperplasia, thymic cysts, thymomas, and thymolipomas. These lesions represent less than 5 % of resected mediastinal tumors in children.

Thymic hyperplasia may take the form of lymphoid follicular hyperplasia with or without thymic enlargement. These are often present in autoimmune diseases such as myasthenia gravis and Grave's disease, and associated with a favorable response to thymectomy. True thymic hyperplasia can present as massive hypertrophy in children; surgical resection is only indicated in symptomatic patients when the diagnosis is unclear (Fig. 27.7); otherwise a short course of steroids will shrink the lesion. Thymic rebound hyperplasia is seen in children who have received systemic chemotherapy, usually within 2 years of initiation. It is a self-limited process and spontaneous resolution is expected [34, 35]. The diagnostic dilemma in patients who have been treated for mediastinal lymphoma is to distinguish thymic rebound from recurrent or metastatic tumor. Thymic rebound hyperplasia appears as diffuse enlargement with a fine mixture of fat and lymphoid tissue, a smooth contour, and normal appearing vessels on imaging studies. Recurrent neoplasia usually has a nodular contour and often contains necrotic or calcified foci [36]. Recovery from recent stress such as thermal burn or systemic illness can also result in thymic hyperplasia.

Thymic cysts are thin-walled, usually unilocular cysts containing thymic tissue in the cyst wall. They often extend from the mediastinum to the neck and are benign. Most are asymptomatic but hemorrhage into the cyst cavity or secondary infection may lead to tracheal compression and respiratory distress. Surgical excision is curative in symptomatic patients and is recommended in asymptomatic patients with large cysts to prevent complications.

Thymomas are rare in children as compared to adults, with only 2 % presenting in the first two decades of life. They are usually benign and arise in the upper anterior mediastinum or at

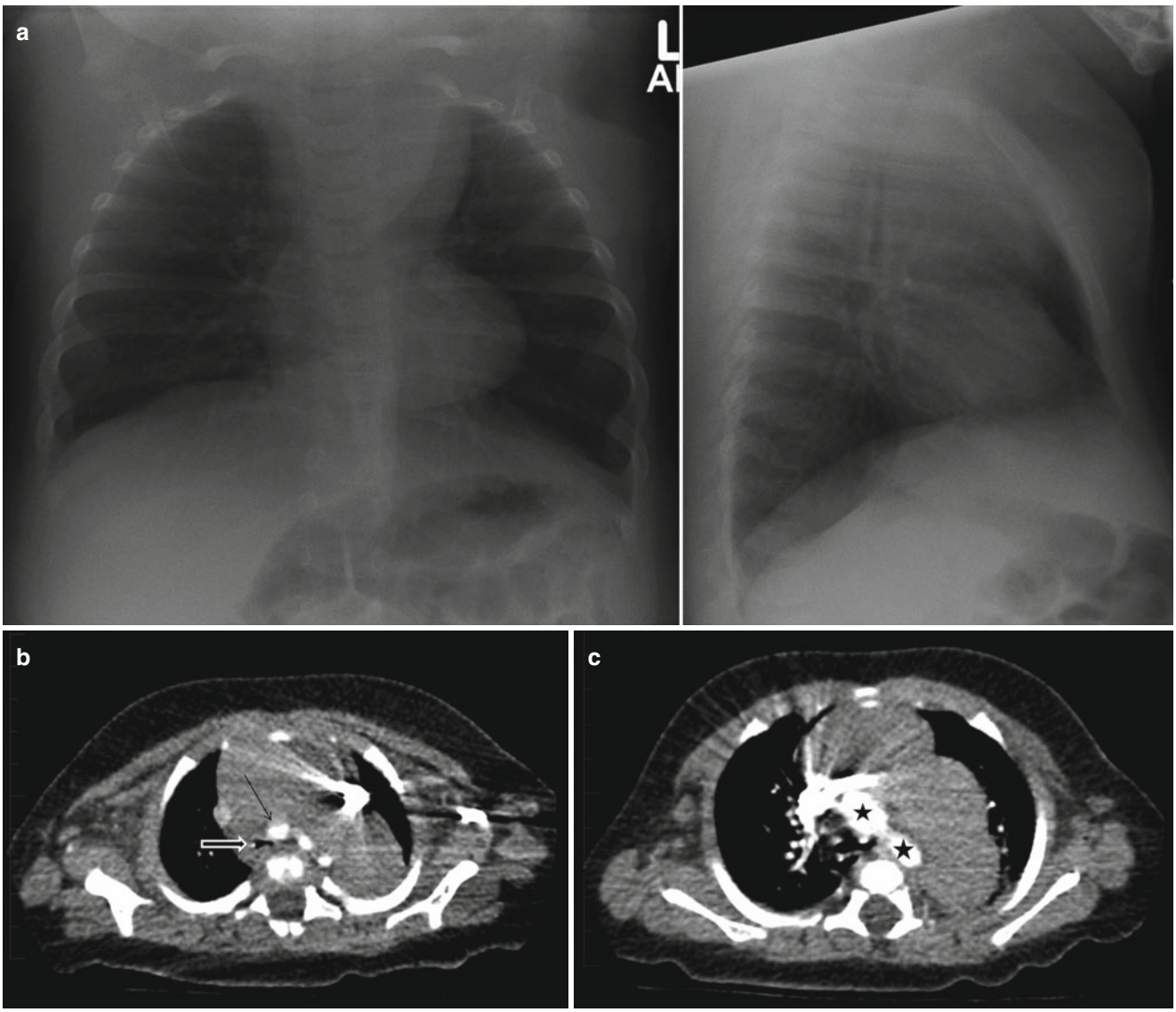

Fig. 27.7 A 4 month old girl presented with stridor and wheezing. (**a**) The chest radiograph showed an anterior mediastinal mass. (**b**) CT scan showed marked compression of the trachea (*thick arrow*) at the level of the brachiocephalic artery (*thin arrow*); artefacts are due to contrast injection in the left arm. (**c**) The mass extended posteriorly, and inferiorly past the level of the aortic arch (*stars*). Repeat CT scan after 2 days of steroids (not shown) showed mild improvement; thymic hyperplasia was suspected but because of diagnostic uncertainty and persistence of symptoms, a thoracoscopic excision was carried out without complications. Pathology confirmed thymic hyperplasia

the base of the neck. Although they may be massive in size, they generally compress adjacent structures rather than invade them. Respiratory distress and superior vena cava syndrome may occur [37]. They are occasionally associated with myasthenia gravis. Surgical resection is curative and recurrence is rare (2 %) [38]. Malignant thymomas are epithelial in nature and invasive as in adults. Aggressive surgical resection is critical as response to chemotherapy and radiotherapy is limited. Resection of lung, pleura, diaphragm, superior vena cava and pericardium may be required to achieve complete surgical extirpation.

Thymolipoma is a rare benign tumor of the thymus that often attains gigantic proportions in clinically asymptomatic patients (Fig. 27.8). Associated conditions such as myasthenia gravis [39], aplastic anemia [40], Graves' disease [41], and Hodgkin's disease [42], although possibly coincidental, have been reported in adult patients. One case of erythrocyte hypoplasia and hypogammaglobulinemia has been reported in a child [43]. Thymolipomas show fatty attenuation mixed with fibrous septae and normal thymic tissue on CT scan; on MRI, they demonstrate high signal intensity on both T1 and T2 weighted images along with strands of lower signal intensity at the fibrous septae [36]. Histologically a thymolipoma is composed of thymic and mature adipose tissue. The tumor usually extends inferiorly to either side of the medias-

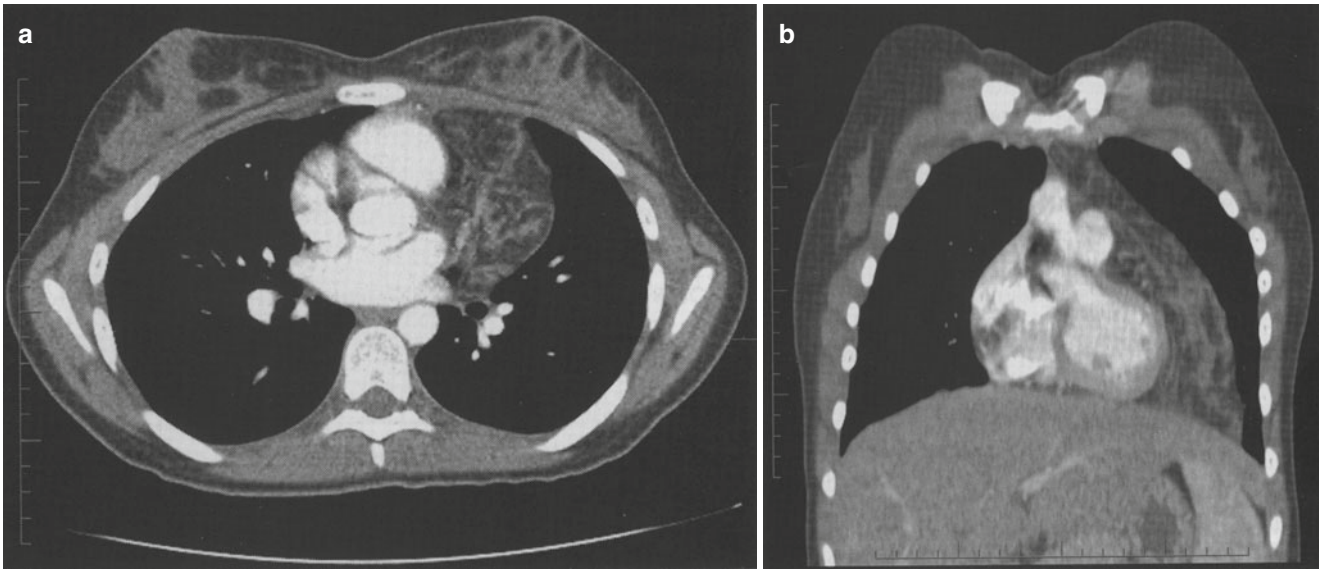

Fig. 27.8 Thymolipoma. This 17 year old girl had an incidental finding of a heterogenous anterior mediastinal mass during investigation of Crohn's disease. (**a**) This axial cut on CT scan shows the soft tissue mass with fat infiltration, to the left of the aortic arch. (**b**) The extent of the mass to the costo-diaphragmatic angle can be appreciated on this coronal reconstruction. A thoracoscopic resection was performed (Courtesy of Dr. Ken Shaw)

tinum. Surgical resection is necessary for definitive diagnosis and can be accomplished thoracoscopically as these tumors tend to be pliable and rarely invade neighboring structures [43, 44].

Lymphangiomas

Lymphatic malformations are the most common vascular anomalies found in the anterior mediastinum. Isolated lymphatic malformations of the mediastinum are rare and can be found in all three compartments. Most mediastinal lymphangiomas are in fact extensions of cervical, axillary or chest wall lesions. These lesions are congenital in nature and are usually asymptomatic; spontaneous resolution is uncommon but has been observed. Symptoms often develop as a result of infection, hemorrhage, or cyst expansion, leading to the need for intervention. Complete surgical resection can be difficult and lead to significant morbidity as these lesions tend to infiltrate between vital structures. Percutaneous aspiration and sclerotherapy has been gaining popularity for both primary and recurrent lesions. Several sclerosing agents have been reported to yield good results, including OK-432, alcoholic solution of zein (Ethibloc), bleomycin and doxycycline [45, 46]. OK-432 is the most commonly reported agent in the literature, favored by Japanese and European surgeons with good to excellent outcomes, but is not clinically available in North America. Alcoholic solution of zein is widely used in Europe and Canada with favorable results as well. However, there is no standardized regimen in the administration of sclerosing therapy as the literature is comprised of mostly case reports and expert opinions [34, 47], and there is limited experience with large mediastinal lesions. Surgical resection remains an excellent option for macrocystic lesions without infiltration of vital structures. A combined thoracoscopic drainage and sclerotherapy is also a viable option for lesions not accessible percutaneously (Fig. 27.9).

Others

Angiofollicular or giant lymph node hyperplasia (also called Castleman's disease) is usually a benign condition, which most commonly affects mediastinal nodes. The grossly enlarged nodes are very vascular on imaging studies. Excisional biopsy is required to differentiate this from lymphoma. The disease sometimes takes a systemic form, in which case the course is complicated with anemia and growth failure. These manifestations sometimes improve with excision of the enlarged node(s) if easily accessible, but aggressive surgical resection should be avoided [48].

Langerhans cell histiocytosis in the mediastinum is usually part of a multifocal systemic disease, but rarely may present as an isolated thymic mass. Superior vena cava syndrome has been described. The prognosis for unifocal mediastinal disease is excellent [37].

Among the less common mediastinal tumors, there are reports of lipomas and lipoblastomas, and rare instances of liposarcoma. Other sarcomas such as rhabdomyosarco-

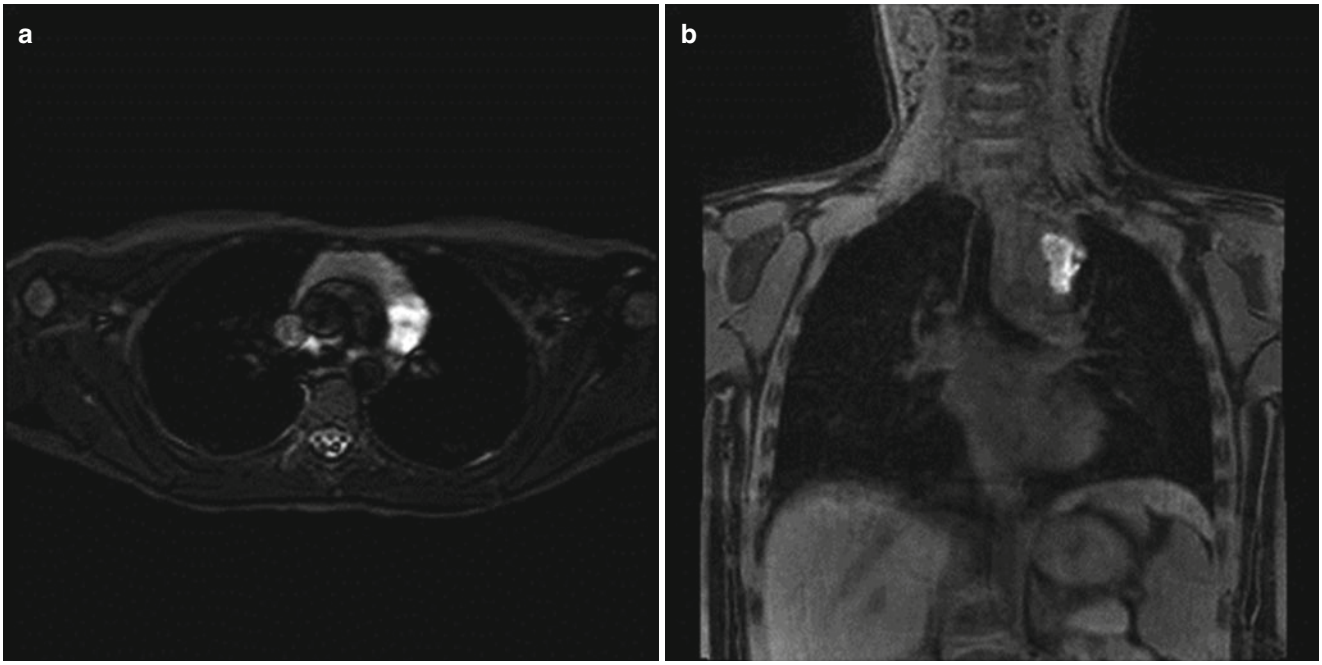

Fig. 27.9 (**a**, **b**) A 7 year old girl had cervical lymphangioma resected 4 years previously. She had remained asymptomatic until she recently presented with prominent left neck and chest wall vessels. A MRI was performed to demonstrate the superior mediastinal mass compressing the left subclavian and innominate veins, with mild tracheal deviation. The lesion was treated with left thoracoscopic drainage and doxycycline sclerotherapy with satisfactory resolution of symptoms (Courtesy of Dr. Wolfgang Stehr)

mas, Ewing tumors, mesenchymomas and other unusual neoplasms may also occur [37]. Rare cases of fibromatosis have also been described in the mediastinum.

Middle Mediastinal Tumors

The middle mediastinum is also known as the visceral compartment, containing the trachea and mainstem bronchi, the heart and the great vessels. Lymphoid tissues are also abundant in this region, thus lymphomas are the most common tumors, often involving both the anterior and middle mediastinum. Benign vascular tumors and lymphatic malformations are also found here. Gorham's disease is worth mentioning; even though it is not a tumor per se, it behaves as one. Gorham's disease or "vanishing bone disease" is a rare disorder of unknown etiology, characterized by proliferation of vascular channels that results in the destruction and resorption of the osseous matrix [49]. Some consider it as an extreme form of lymphangiomatosis [50]. The shoulder and the pelvis are the most commonly affected sites; however, various locations in all of the other areas of the skeleton have also been reported. The disease may present with pain from lytic bony lesions and pathological fractures, or with chylous pericardial or pleural effusions, which may be life-threatening. These effusions may be due to mediastinal extension of the disease process from the involved vertebrae, scapulae, ribs or sternum, or may represent a direct lymphangiomatous involvement of the mediastinum. In general, mediastinal and spinal involvement are associated with a poor prognosis. The treatment is mostly supportive, with isolated trials of radiation therapy, anti-osteoclastic and anti-angiogenic medications including pamidronate, zoledronic acid and alpha-2b interferon [51]. Pleurodesis and pleuroperitoneal shunts may be useful for symptomatic relief. The disease occasionally becomes quiescent after adolescence.

Bronchogenic cysts are benign congenital lesions that can present with symptoms of tracheal compression or recurrent pulmonary infections. The treatment is complete surgical excision [52] (Fig. 27.10).

Posterior Mediastinal Tumors

Neurogenic Tumors

Tumors of neural crest origin are the most common posterior mediastinal lesions. They arise from the sympathetic chain and range from benign ganglioneuroma to malignant neuroblastoma. Twenty percent of neurogenic tumors are located in the mediastinum. Neuroblastoma is the most common tumor and occurs mostly in infants and young children (Table 27.2). Ganglioneuromas present in older

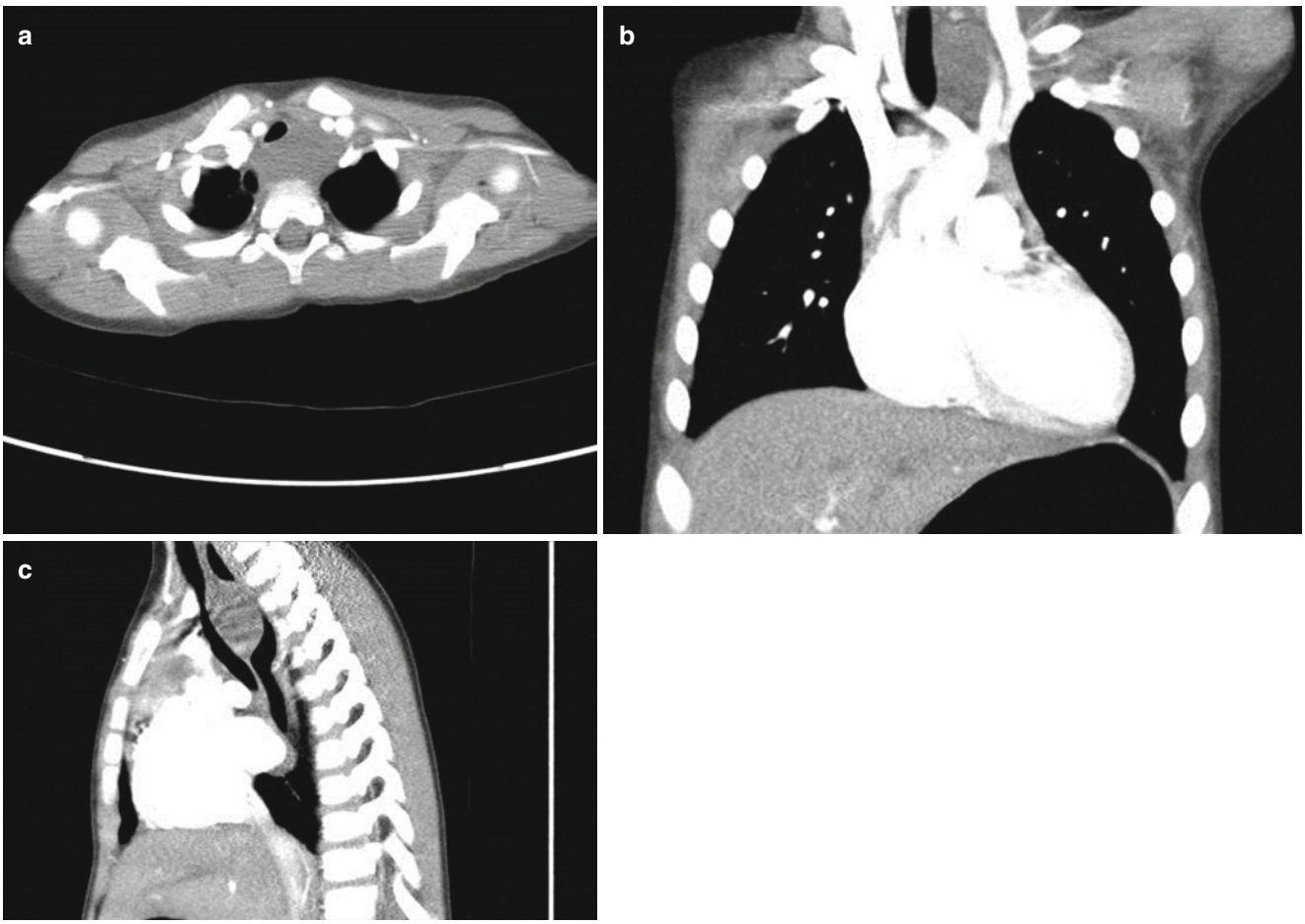

Fig. 27.10 (**a**) Axial, (**b**) coronal, and (**c**) sagittal view. A 2 year old boy presented with chronic cough and mild dysphagia. CT scan revealed a cystic mass in the superior mediastinum partially compressing the trachea anteriorly and the esophagus posteriorly. The patient underwent stepwise general anesthesia, starting with intravenous ketamine and propofol. Once easy masking was established, a fiberoptic intubation was performed and the airway was secured. Patient underwent a left thoracoscopic resection of the lesion and pathology confirmed it to be a bronchogenic cyst

children and teenagers as asymptomatic lesions, which are identified incidentally on chest radiographs obtained for unrelated reasons. Radiographically they appear as paraspinal spindle-shaped lesions and are frequently calcified. Neurogenic tumors may occur anywhere along the paraspinal sulcus from the thoracic inlet to the diaphragm. They can present as incidental paraspinal mass on routine chest radiograph, or can be identified on investigations performed for Horner's syndrome, ataxia or opsoclonus myoclonus. When the tumor extends into the spinal canal, it may present with signs and symptoms of cord compression. Investigations for paraspinal posterior mediastinal masses should include a CT scan or MRI prior to surgical resection to better define the relationship to surrounding structures and assess possible spinal extension (Fig. 27.11). Spot urinary catecholamines should also be obtained. A preoperative MIBG scan is recommended to determine local tumor extent and presence of distant metastases, and will be a useful modality for postoperative monitoring when the tumor is MIBG avid.

Most mediastinal neurogenic tumors are well encapsulated and readily resectable, unlike their abdominal counterparts. Surgical resection is the treatment of choice and is curative for benign lesions such as ganglioneuromas. Several recent series have reported successful thoracoscopic resections, but removal within an endobag is essential to prevent tumor spillage [24]. The tumor can be closely adherent to the posterior part of the ribs and necessitates removal of part of the periosteum. Often it is impossible to avoid leaving small amounts of residual disease along the sympathetic nerve roots as they emerge from the foramina. These areas are simply marked with small titanium clips for future imaging. For upper thoracic neuroblastomas, a temporary or permanent Horner's syndrome is a normal postoperative "complication", especially when present preoperatively. Adequate sampling of ipsilateral lymph nodes is essential to determine

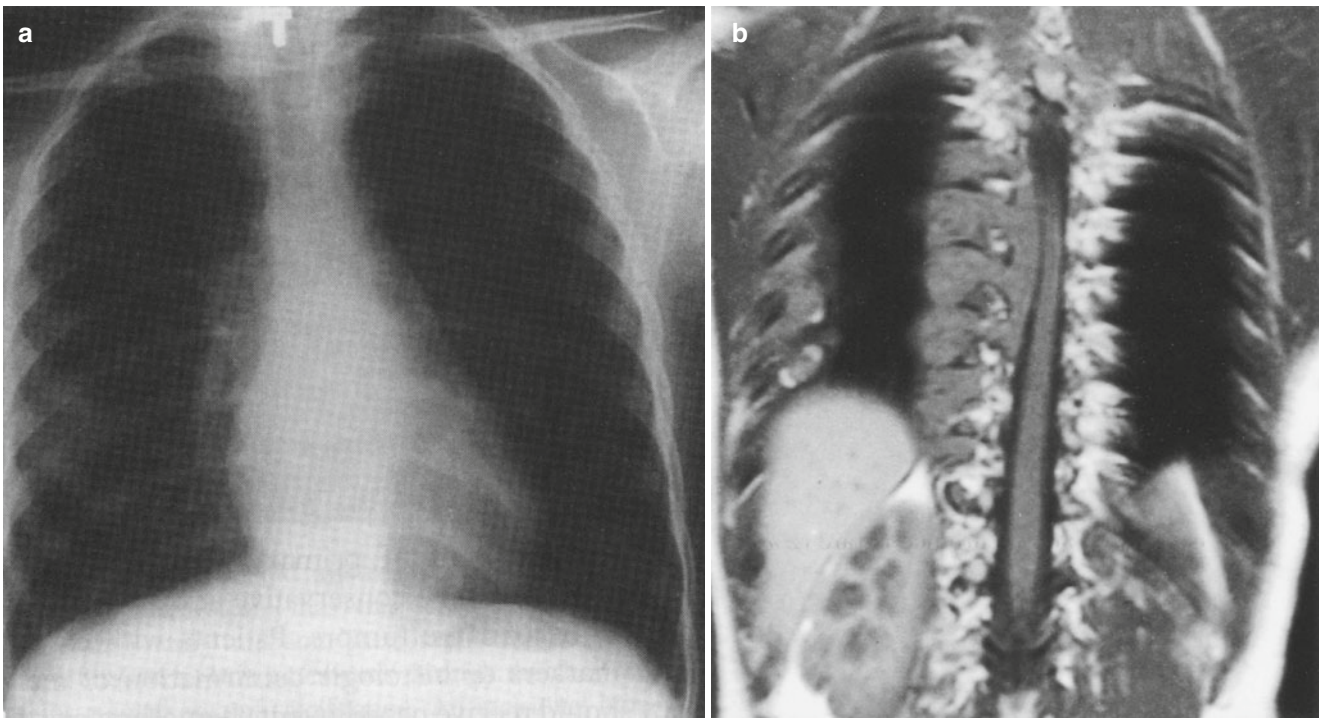

Fig. 27.11 (**a**) Chest radiograph of a 5 year old girl referred for back pain, which demonstrated a minimal right paraspinal mass, but on the MRI scan (**b**) a dramatic extension of the tumor was demonstrated through the spinal foramen, and was compressing the spinal cord, although she had no significant neurological symptoms. A percutaneous needle biopsy demonstrated the tumor to be a neuroblastoma

surgical staging in neuroblastomas, as patients with stage L1 disease according to the International Neuroblastoma Risk Group Staging System (INRGSS) may be observed after a macroscopically complete surgical excision. Ipsilateral nodes are excised if any are visible, but extensive sampling, including contralateral nodes, is not required for thoracic neuroblastomas, unlike for their abdominal counterpart. Patients with thoracic neuroblastomas tend to have a better prognosis (see Chap. 13 for a complete discussion on neuroblastoma).

The optimal treatment for patients presenting with symptomatic spinal cord compression at diagnosis has evolved. Treatment of the so called 'dumbbell' lesions with significant extension into the spinal canal must first involve control of the spinal lesion by laminectomy/laminotomy, radiation, or chemotherapy [53]. Initial resection of the thoracic component entails the risk of potential swelling of the spinal tumor with worsening of neurologic compression and paralysis [6, 54]. Recent studies from France, Italy and the Pediatric Oncology Group all demonstrated equal efficacy between laminectomy, radiation, and chemotherapy to relieve or improve neurologic deficits. However, patients treated with chemotherapy usually did not require additional treatment and have less orthopedic sequelae, whereas patients treated either with radiotherapy or laminectomy commonly did [55–57]. Although laminotomy may be a worthwhile alternative with fewer sequelae than laminectomy, the current trend is to use chemotherapy for debulking, now that the fear of inducing tumor necrosis, resulting in edema and increased cord compression, has been dispelled. Surgical decompression is reserved for patients who show progressive neurologic deterioration after initiation of chemotherapy [58]. The frequency of complete neurologic recovery in children with intraspinal neuroblastoma inversely correlates with the duration and severity of the presenting neurologic deficits [56], and up to 44 % have permanent disabilities [55].

Prognosis in neuroblastoma is age-dependent, with a better prognosis for infants compared to older children. Intrathoracic neuroblastomas have a more favorable prognosis than abdominal primaries of comparable stage [58, 59]. This is most likely related to the favorable biology of most thoracic neurogenic lesions [60, 61]. In the presence of a maturing ganglioneuroblastoma, it is important to remember that the tumor is as malignant as its most malignant component. A small proportion of older children with thoracic neuroblastoma appear to have a protracted course, with late recurrences and death.

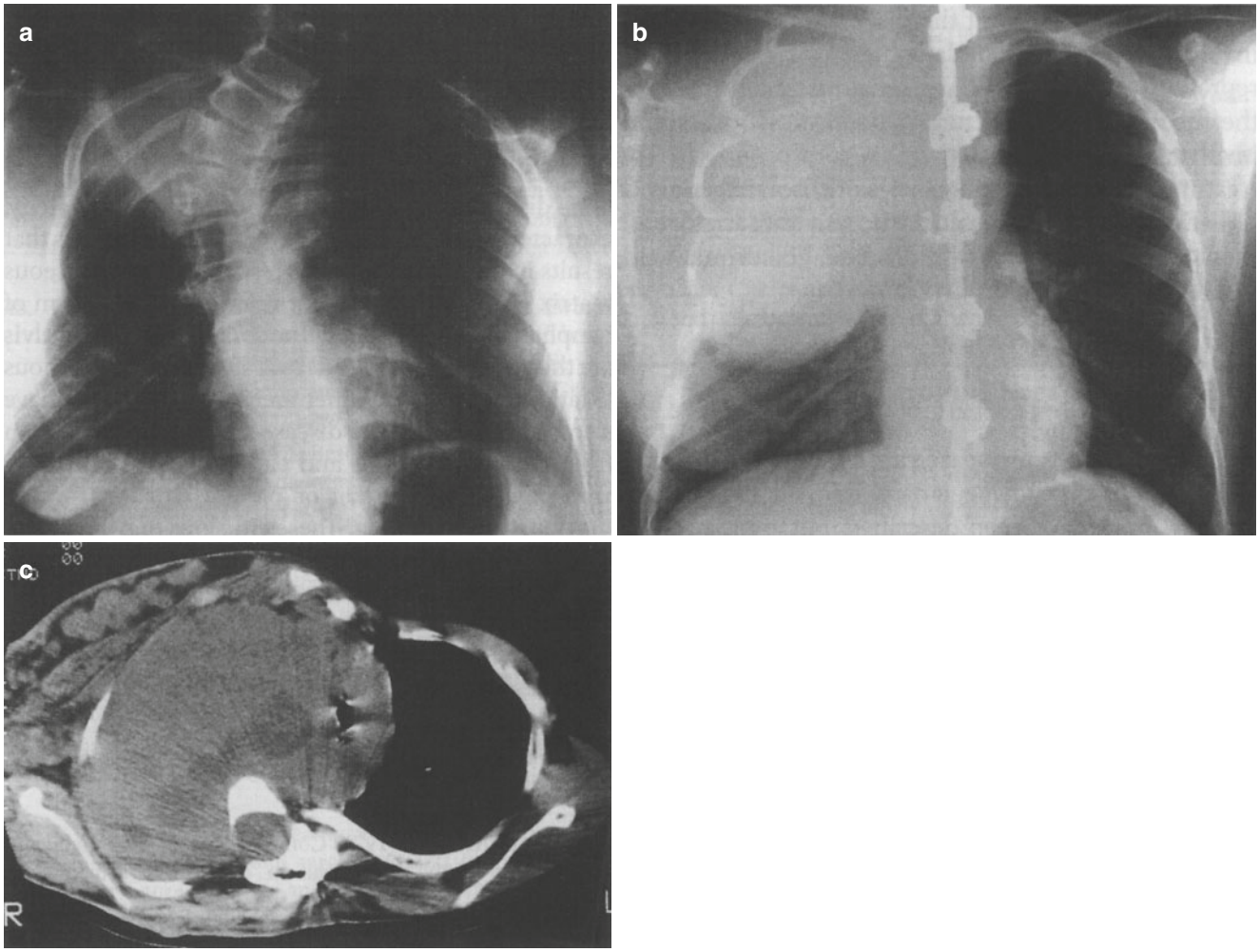

Fig. 27.12 (**a**) Chest radiograph of a 10 year old boy with neurofibromatosis obtained immediately prior to fusion of his spine. The right apical mass had been stable in size. (**b**) Dramatic increase in the size of the apical mass was noted 9 months later. At resection, malignant degeneration into a neurofibrosarcoma was found. Note thinning of the upper ribs as a result of the long-standing neurofibroma. (**c**) CT scan obtained prior to resection demonstrates the large mass displacing the mediastinum to the left, but not compressing the trachea. Multiple subcutaneous neurofibromas are seen in the subcutaneous tissues of the right chest

Others

Plexiform neurofibroma may occur in the mediastinum as an isolated lesion or in patients with neurofibromatosis (NF 1 or von Recklinghausen's disease). Resection is required for isolated lesions in order to obtain a histologic diagnosis [62]. In patients with neurofibromatosis, resection is required if the lesions are symptomatic. Rapid growth usually occurs if there is malignant transformation to malignant peripheral nerve sheath tumor (Fig. 27.12). MRI and PET scan are both useful to detect malignant transformation in NF 1 patients [63, 64].

Pheochromocytoma (also called paraganglioma) can also occur along the sympathetic chain in the neck and mediastinum and produce symptoms of compression as well as flushing and hypertension. This tumor has been described in the anterior mediastinum as well. Regional or distant metastases are seen in 15–20 % of patients [37]. Other rare neurogenic tumors include *neurilemmoma* and malignant *schwannoma*.

Anesthetic Consideration for Patients with Mediastinal Tumors

Risk Assessment

The majority of patients with mediastinal tumors tolerate general anesthesia well with a reported anesthetic complication rate of <10 % [65]. However, respiratory or hemodynamic collapse during induction of general anesthesia is a recognized risk in children with an anterior mediastinal mass. The increased risk is contributed by several factors, and can be understood as restrictive or obstructive ventilatory compromises, decreased venous return and

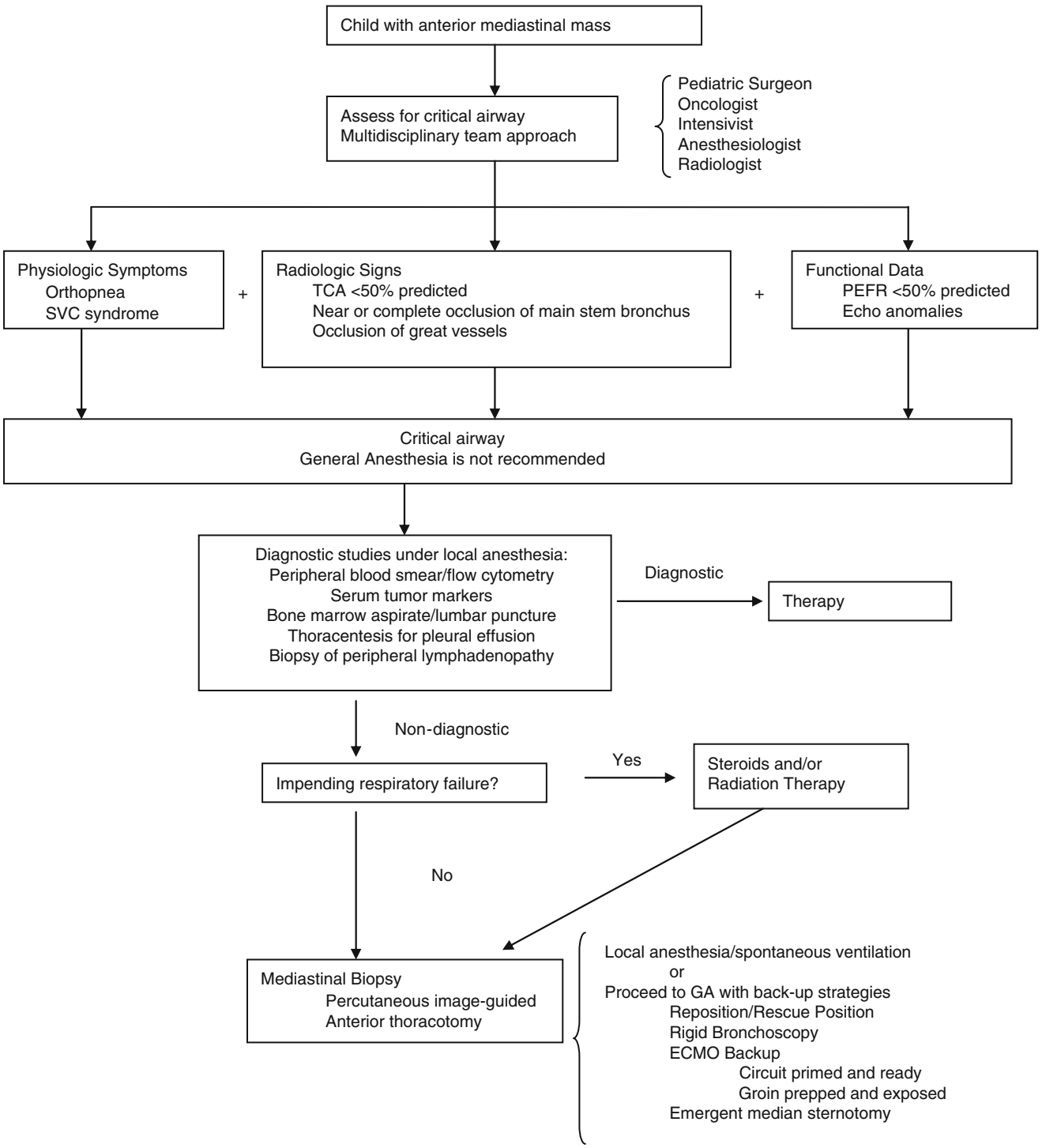

Fig. 27.13 Anesthetic risk assessment and diagnostic approaches for children with an anterior mediastinal mass. *SVC* superior vena cava, *TCA* tracheal cross-sectional area, *PEFR* peak expiratory flow rate

increased pulmonary pressure with right-sided heart failure. Restrictive compromise is contributed by decreased functional residual capacity and decreased lung compliance. Obstructive changes are evident by the decreased airway diameter and worsened under anesthesia by the loss of normal bronchial smooth muscle tone and distal airway collapse.

An algorithm depicting the assessment of critical airway and the appropriate diagnostic procedure is illustrated in Fig. 27.13 [8–10]. Anesthetic risks should be considered

with the combination of clinical, radiological, and functional data. Clinical signs and symptoms alone do not correlate well with anesthetic complications. Several recent studies have also shown that the degree of airway and vascular compression correlates poorly with actual clinical symptoms. [8, 66, 67] The only symptom that is strongly associated with respiratory collapse is orthopnea [5, 68, 69]. Thus patients presenting with orthopnea should avoid general anesthesia for either diagnostic or therapeutic procedures as a general rule.

Historically, children with a mediastinal mass less than one-third of the diameter of the thorax have a low risk of anesthetic complications, and those with a mass greater than 45 % of chest diameter are thought to have the greatest risk [1, 70]. As technology advanced, CT scans became routinely used to define the cross-sectional area of the trachea to assess the relationship to anesthetic risk [69, 71, 72]. Both Azizkhan et al and Shamberger et al suggested that children with tracheal cross-sectional areas (TCA) less than 50 % of predicted should not receive a general anesthetic. A recent retrospective series in the anesthesia literature reported imaging findings of mainstem bronchus compression and great vessel compression, along with orthopnea and upper body edema, as significantly associated with anesthetic complications in children with anterior mediastinal masses [65].

Extensive pulmonary function abnormalities were identified in a group of patients with anterior mediastinal masses prospectively studied [72]. The peak expiratory flow rate (PEFR) in pulmonary function studies is the best parameter in the prediction of anesthetic problems. It provides a quantitative reflection of central airway size. It can be easily performed with a hand-held device and compared with the predicted values [10, 72]. A PEFR of less than 50 % of predicted is associated with increased anesthetic risks [69]. The measurement of pulmonary function in children with anterior mediastinal masses may add valuable information to the anatomic evaluation obtained by CT scan. In particular, it can quantitate the magnitude of pulmonary restriction in relation to the size of the mass and may identify impairment of flow related to compression of airways distal to the carina, which cannot be measured by CT scan. Thus, the clinical, functional, and radiological findings can be incorporated into a simple algorithm to assess anesthetic risk for each individual patient (Fig. 27.13).

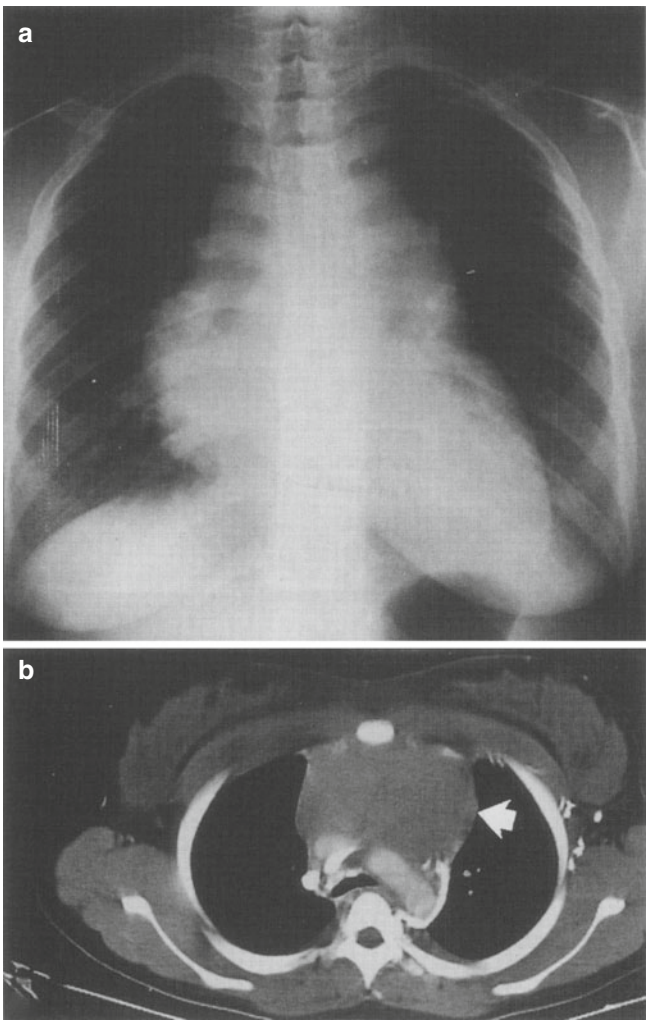

Fig. 27.14 (**a**) Chest radiograph of a 12-year-old girl who presented with facial swelling and plethora. Chest radiograph demonstrated a significant anterior mediastinal mass. Echocardiogram revealed a pericardial effusion and the CT (**b**) revealed a homogeneous anterior mediastinal mass (*arrow*). Her white cell count was 5.1 with a normal differential count. Fluid aspirated from the pericardium, however, had a white cell count of 724,000 and cytology was diagnostic of lymphoblastic leukemia

Alternatives to General Anesthesia for Diagnosis

The least invasive and lowest risk technique should be utilized first to diagnose a mediastinal mass [9]. A multidisciplinary approach in the decision making is essential for optimal patient care. An extra-thoracic approach under local anesthesia can be performed in most patients with anterior mediastinal masses to obtain diagnostic material. This includes cervical or supraclavicular excision of an enlarged lymph node, thoracentesis in the presence of pleural effusion to obtain cells for cytology and flow cytometry [14], and bone marrow aspirate and biopsy since leukemias may present as an anterior mediastinal mass (Fig. 27.14). Fine needle aspiration and core-needle biopsies of mediastinal masses under CT or ultrasound guidance is generally adequate to obtain a pathologic diagnosis, but frequently does not provide sufficient material for histologic subtyping for lymphomas [73–76]. The Chamberlain procedure (anterior thoracotomy

through the bed of the second rib) can be performed under local anesthesia even in children, and should be part of the armamentarium of the pediatric surgeon [77]. Thoracoscopic biopsy requires general anesthesia, and its diagnostic accuracy for lymphoma is still under investigation, despite excellent diagnostic yields for other thoracic lesions using minimally invasive techniques [78, 79]. Careful communication with the pathologist regarding the adequacy of biopsy material is essential when utilizing a minimally invasive technique. [80, 81]

Management of General Anesthesia

Despite the increased anesthetic risk, surgical biopsy or resection under general anesthesia remains the optimal option for some children with mediastinal tumors. Thus, careful preoperative discussion must occur between the surgeon and the anesthesiologist to provide an individualized management plan based on the child's preoperative symptoms and imaging findings (Figs. 27.15 and 27.16). Airway management maybe achieved with awake fiberoptic bronchoscopy using local anesthesia and judicious intravenous sedation. Rigid bronchoscopy performed by the surgeon may be necessary in the event of airway loss, passing the scope beyond a mid-tracheal narrowing or placing it into a patent mainstem bronchus to allow for adequate ventilation until spontaneous ventilation returns. Identifying a "rescue" position preoperatively may be helpful to minimize cardiorespiratory collapse [82].

Extracorporeal Membrane Oxygenation (ECMO) providing cardiopulmonary bypass is the final option in the management of critical mediastinal masses [83–85]. The best time to consider ECMO is prior to anesthesia induction. Cannulation options should be discussed and decided, and a circuit should be primed and ready (Fig. 27.17). A femoral approach with distal limb perfusion is the preferred method as the cervical approach would likely be compromised by the presence of the tumor [85].

Video Assisted Thoracoscopic Surgery (VATS)

Surgical biopsy and resection is essential in the management of pediatric mediastinal tumors. Anterior mediastinal masses are traditionally approached with median sternotomy or anterior thoracotomy, and posterolateral thoracotomy for posterior mediastinal lesions. Increased expertise in minimally invasive surgery has allowed VATS to be applied in the surgical management of mediastinal pathologies.

VATS offers several advantages over traditional open thoracotomy and sternotomy both for the surgeon and the patient. Thoracoscopy provides greater exposure of the entire thoracic and mediastinal compartments and wider area of access. The magnification also gives better anatomic detail. The video monitor affords the anesthesiologists and trainees a better understanding of the procedure. Patient-related advantages include less postoperative pain, less splinting, and less atelectasis [86]. The risk of skeletal deformities such as scoliosis and chest wall asymmetry is minimized with the thoracoscopic approach [87]. Shorter hospital stay and earlier return to normal activity for both patient and parents have been well documented in the literature. Conversely, potential problems with the use of thoracoscopy for biopsy include the inability to palpate lesions, the risk of intrapleural tumor spillage and the development of recurrent disease at the port sites.

Both benign and malignant conditions can be treated with VATS (Figs. 27.2, 27.9, 27.10 and 27.15). Benign mediastinal cysts and tumors can be safely resected with VATS. Biopsy, staging and even curative resection can be achieved with VATS in selected patients with malignant lesions. Even young infants tolerate VATS with few complications. In one report, 38 of 39 procedures were completed successfully using VATS [24]. Diagnosis was obtained in all cases, and complete resection was performed in 33 children who were appropriate candidates.

Relative contraindications for VATS include previous thoracotomy and significant bleeding disorder. Patients with airway compromise from large anterior mediastinal mass may require alternative diagnostic methods.

Single Lung Ventilation

A detailed discussion regarding airway management should be carried out between the surgeon and the anesthesiologist preoperatively. Single lung ventilation is essential to provide optimal exposure of the mediastinum. It can be achieved with double lumen endotracheal tubes in older children, and mainstem intubation or selective contralateral lung ventilation using ipsilateral bronchial blockers for smaller children [88]. The use of low pressure, low flow of CO_2 (3–5 mmHg) also helps to collapse the ipsilateral lung. Placement of a chest tube at the end of the procedure is procedure-dependent and at the discretion of the surgeon.

Positioning and Port Placement

Patients with anterior mediastinal masses should be positioned in a modified supine position with the affected side elevated slightly (15–45°). Patients with posterior masses are positioned in a modified prone position with a similar degree of elevation. Such positioning takes advantage of gravity to allow the lung to fall away from the lesion when the lung is collapsed. Three or four ports are placed between the ante-

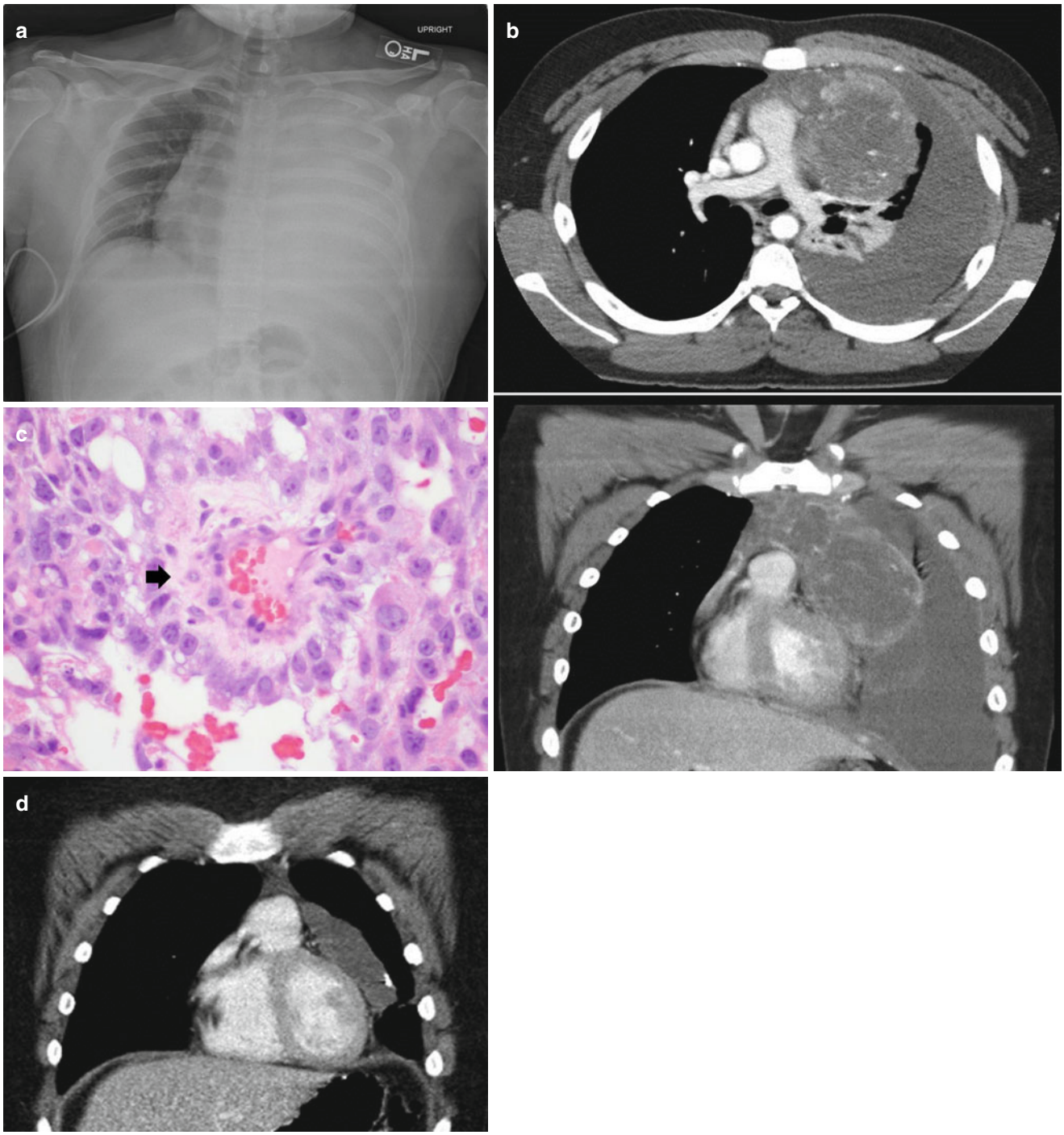

Fig. 27.15 (**a**) Chest radiograph of a 17 year old male with anterior mediastinal mass and left hemothorax presenting with respiratory distress. (**b**) CT scan demonstrating the large anterior mediastinal mass with increased vascularity and associated hemothorax. The airway is patent but the mass is compressing on the pulmonary artery and left atrium. The patient had a chest tube placed which drained mostly sanguinous fluid output; cytology was not diagnostic. After multidisciplinary discussion, thoracoscopic decortication and biopsy were done under general anesthesia. The patient received stepwise anesthetics, starting with Ketamine and propofol, followed by short acting muscle relaxant and endotracheal intubation. The patient tolerated the procedure well. (**c**) Pathology of the biopsy revealed yolk-sac tumor with pathognomonic Schiller-Duval bodies (*black arrow*). (**d**) CT scan 3 months later demonstrating significant reduction of the mass after four cycles of chemotherapy (cisplatin, etopiside, and bleomycin/VP16). The patient underwent complete thoracoscopic resection of the tumor uneventfully (Courtesy of Dr. Christopher Newton)

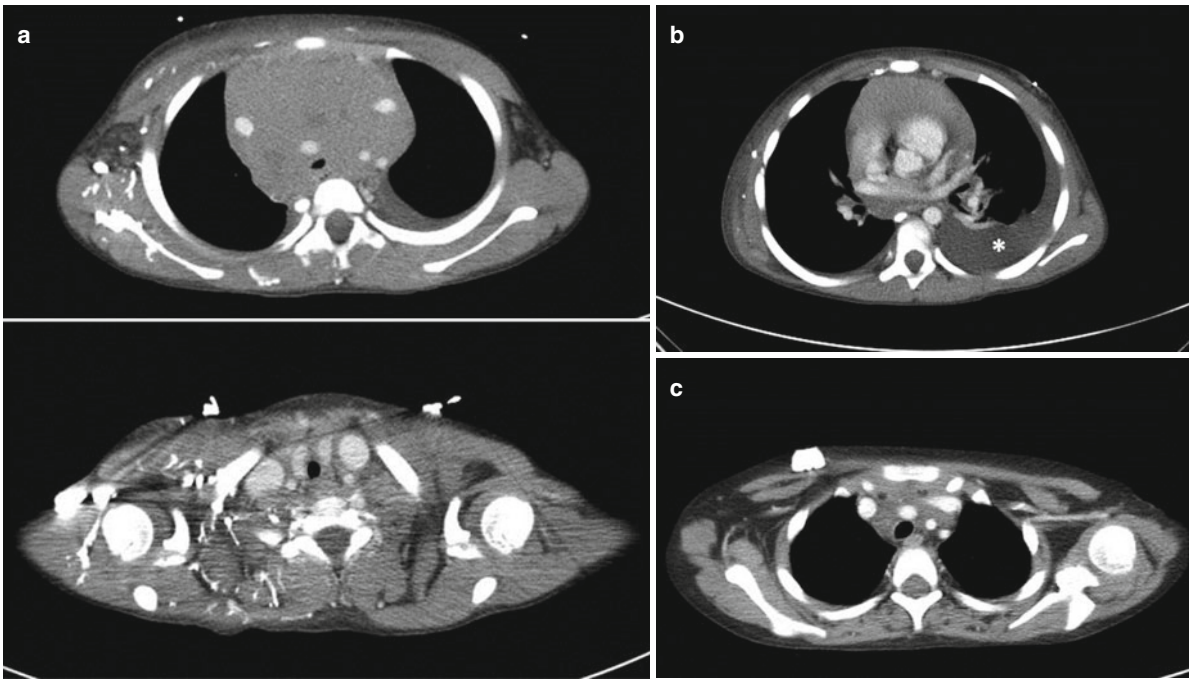

Fig. 27.16 (**a**) CT scan of a 7 year old boy presenting with facial swelling, chest wall spider angiomas, dyspnea and impending respiratory failure. Patient received intravenous methylprednisone and two sessions of radiation therapy. Note the collateral vessels indicative of SVC obstruction consistent with SVC syndrome. Tracheal cross section is 16 mm^2, 23 % of predicted value for age. (**b**) A pleural effusion developed 3 days later (*), thoracentesis was performed under local anesthesia, with child life specialist to distract the patient. However the pleural fluid cell block was non-diagnostic. (**c**) Patient's clinical symptoms improved with the pretreatment although CT finding remained unchanged. He underwent ultrasound guided core needle biopsy of the anterior mediastinal mass under local anesthesia and sedation, while maintaining spontaneous ventilation. The core needle biopsy was diagnotic for lymphoblastic lymphoma. Patient was started on chemotherapy and the CT scan at 4 weeks showed nearly normal anatomy, with tracheal cross section of 76 mm^2, 101 %of predicted

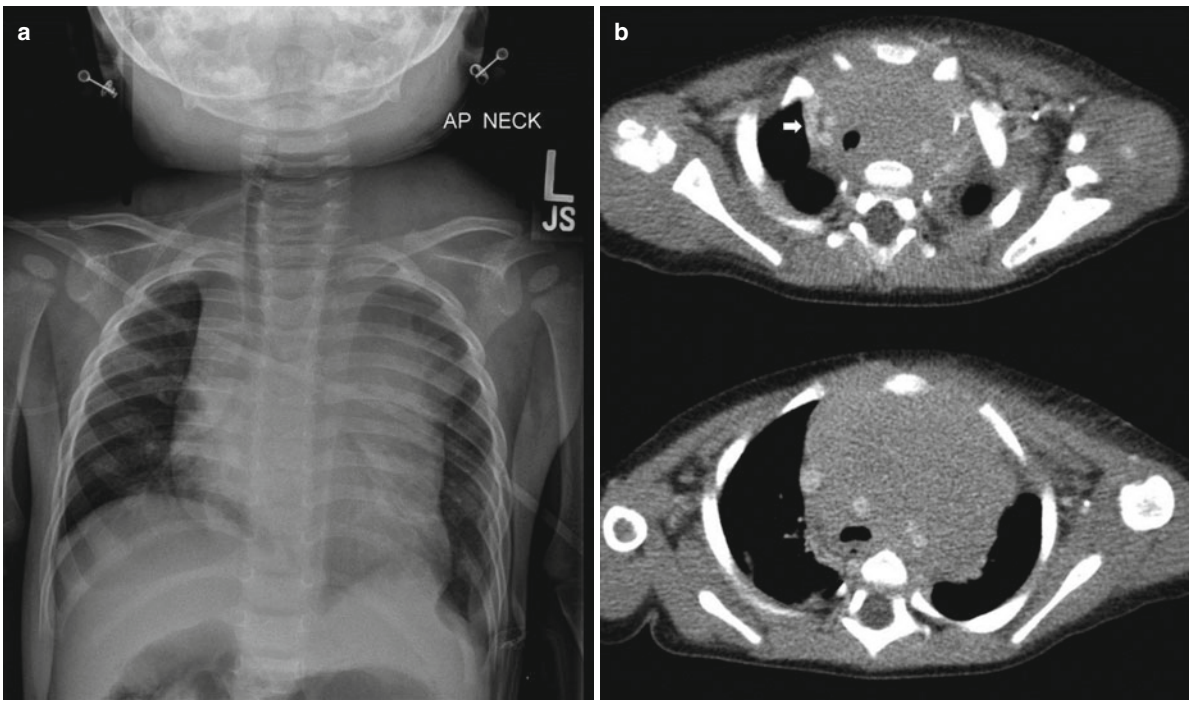

Fig. 27.17 (**a**) Chest radiograph of a 12 month old girl with a large cervical and mediastinal mass suspicious for lymphoma. Note the degree of tracheal deviation. (**b**) CT scan demonstrated significant mediastinal shift and caval compression with suspicion of a thrombus (*white arrow*). The patient underwent biopsy of the cervical lymphadenopathy under local anesthesia and IV sedation in semi-upright position. The patient tolerated the procedure well in the operating room but deteriorated in the PICU. An ECMO circuit was primed with plans for femoral cannulation but the patient tolerated intubation with positive pressure ventilation, and ECMO was eventually not needed

rior and posterior axillary lines. Entry into the thoracic cavity at the fourth or fifth interspace is optimal, as the collapsed lung from single lung ventilation may elevate the ipsilateral diaphragm.

VATS provides a safe and effective approach in the surgical management of mediastinal tumors [89]. This approach is the author's preferred method in appropriate patients with mediastinal masses, as long as basic oncologic surgical principles are upheld without compromising patient safety.

Conclusion

The majority of pediatric mediastinal masses are malignant. Anatomical assessment and knowledge of representative tissue in each compartment will provide an organized approach to the differential diagnosis. Age of the patient, imaging modalities and tumor markers (when present) are additional useful factors. Early diagnosis, resection of non-lymphomatous tumors, and adjunctive treatment can result in improved survival. Careful assessment of anesthetic risk factors in patients with large anterior mediastinal masses can avoid significant anesthetic complications. VATS offers the advantage of smaller incisions, better visualization, and faster recovery with low morbidity. VATS can be used safely in the evaluation and treatment of some mediastinal malignancies.

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