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Pathology of the Mediastinum

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The existence of a pathologic process of the mediastinum secondarily affecting the airways and lungs should always be considered in the clinical evaluation of patients with respiratory symptoms. More concrete evidence of mediastinal pathology is usually provided by radiographic techniques, including tomograms, computed tomography (CT) scan, angiography, and visualization of the esophagus with contrast media. Most frequent are inflammatory processes and neoplastic conditions primarily in the anterior mediastinum (Display 74-1).

INFECTIOUS AND REACTIVE INFLAMMATORY CONDITIONS

Mediastinitis Caused by Infectious Agents

Aerobic and anaerobic bacteria such as β-hemolytic streptococci, *Staphylococcus aureus*, and *Bacteroides* species have been implicated in the development of acute mediastinitis.[1,2] This is frequently the sequelae of esophageal perforation or thoracic surgery. The symptoms include fever, pain, dysphagia, and respiratory distress. Severe dyspnea may also result from airway compression or from massive pleural effusion or pneumothorax. In infectious mediastinitis, chest roentgenograms usually show mediastinal widening with ill-defined borders and pleural effusion.

A variety of fungal organisms may be responsible for the development of chronic mediastinitis. The most frequently implicated etiologic agent in the United States is histoplasmosis, which produces a fibrosing inflammation.[3–6] Other fungi, such as *Aspergillus*, *Cryptococcus*, and *Mucor* species, are also recognized as causes of mediastinal inflammation and fibrosis.[7–9]

Histologically, the lesions are characterized by diffuse infiltration by fibrous tissue admixed with chronic inflammatory cells and a prominent granulomatous reaction. Special stains such as Gomori methenamine silver and periodic acid-Schiff are useful for the detection of the fungal organisms. Other agents responsible for granulomatous mediastinitis include mycobacteria, and *Nocardia* and *Actinomyces* species.[10–12] Special stains and cultures of mediastinal aspirates and biopsies are mandatory for diagnosis.

Noninfectious Sclerosing Mediastinitis

In a significant number of cases, a specific infectious etiologic agent cannot be identified in patients with chronic fibrosing mediastinitis. Such cases have been variously designated as idiopathic fibrous mediastinitis, sclerosing mediastinitis, or granulomatous and fibrous mediastinitis of unknown etiology (Fig. 74-1). The pathogenesis of these lesions is controversial, and the entity itself is badly in need of a more adequate definition. It has been considered by some as an exaggerated fibrous response secondary to rupture into the mediastinum of granulomatous lymphadenitis, or as an abnormal host response to histoplasmosis involving mediastinal lymph nodes.[3,13,14] Other cases have been associated with sarcoidosis, rheumatic fever, traumatic hemorrhage, and drugs such as methysergide, or have been considered part of a systemic manifestation of a familial, multifocal process.[15,16] In the majority of instances, however, a specific etiologic agent cannot be identified.

Histologically, the lesions consist of bundles of relatively acellular, hyalinized connective tissue admixed with inflammatory cells and often with lymphoid follicles at the periphery of the lesion. The fibrous process infiltrates adjacent structures, invading and encasing the walls of veins and bronchi (Fig. 74-2).[17]

Clinically, the most frequent presenting complaints include cough, dyspnea, chest pain, wheezing, dysphagia, and hemoptysis. Superior vena cava syndrome is also a frequent complication. Invasion of pulmonary veins usually occurs around the left atrium and results in a clinical syndrome that closely mimics mitral valve stenosis with pulmonary hypertension.[18] Thrombosis of pulmonary arteries or veins may also lead to pulmonary infarcts. Infiltration of the trachea and bronchi may be accompanied by vascular ectasia causing hemoptysis, dyspnea, and markedly abnormal pulmonary function tests.

DISPLAY 74-1. PATHOLOGY OF THE MEDIASTINUM

Infections and Reactive Inflammatory Conditions
Infectious mediastinitis
Noninfectious sclerosing mediastinitis

Benign Tumors
Thymoma
Mature teratoma
Solitary fibrous tumor
Neurogenic tumors

Malignant Tumors
Malignant thymic epithelial neoplasms
Neuroendocrine neoplasms
Germ cell tumors
Mediastinal sarcomas
Malignant lymphomas
Tumors metastatic to or invading mediastinum

Cysts and Non-neoplastic Tumorous Conditions
Congenital cysts
Acquired cysts
Angiofollicular lymphoid hyperplasia (*i.e.*, Castleman disease)
Thymolipoma

The lung may exhibit secondary changes of venous or arterial obstruction by the fibrosing process, including medial hypertrophy and intimal proliferation of small and medium-sized arteries and arterioles, and intraalveolar accumulations of hemosiderin-laden macrophages.[19] A complication of sclerosing mediastinitis is pulmonary interstitial fibrosis, which mimics usual interstitial fibrosis clinically and radiographically.[20]

Radiologic findings include asymmetric widening of the mediastinum with distortion of tissue planes, or the presence of a mass with lobular contours. Tomograms and CT scans are useful in defining areas of narrowing in the trachea and bronchi, and angiograms are helpful for detecting compression of arteries and veins by the fibrosing process. Many cases of idiopathic sclerosing mediastinitis will follow a slow, self-limited course, whereas others will show a progressive course and death due to pulmonary and vascular complications. Antifungal agents and steroids do not appear to play any role in the management of this condition.[20] Surgery will be indicated in most patients, both for establishing a pathologic diagnosis and for relief of symptoms of vascular and airway obstruction.

BENIGN NEOPLASMS

Benign neoplasms of the mediastinum may lead to respiratory symptoms due to compression of airways. They enter in the differential diagnosis of pulmonary lesions when they appear radiologically as hilar or intrapulmonary masses. Histologically, they are both epithelial and nonepithelial.

Thymoma

The most common benign epithelial neoplasm of the mediastinum is thymoma. Approximately 95% of cases present in the anterosuperior mediastinum; the majority (60%–80%) are entirely encapsulated and histologically benign (Color Fig. 74-1).[21] In about one half of the cases, the tumor is found incidentally on routine chest x-ray films of asymptomatic patients. In a significant number of cases, however, the patients will demonstrate local signs and symptoms due to compression or invasion of adjacent structures, such as cough, chest pain, dysphagia, hoarseness, and superior vena cava syndrome. Infrequently, they may simulate radiologically such conditions as pulmonary stenosis[22] and constrictive pericarditis.[23]

Thymomas are also notorious for their association with myasthenia gravis and a variety of other neuromuscular, hematologic, autoimmune, and neuroendocrine disorders.[21] Rare cases have been described of thymomas arising within pulmonary parenchyma,[24] or in the pleura, resembling a mesothelioma.[25] Occasionally, thymomas may undergo extensive cystic degeneration and present grossly and radiographically as multiloculated cystic

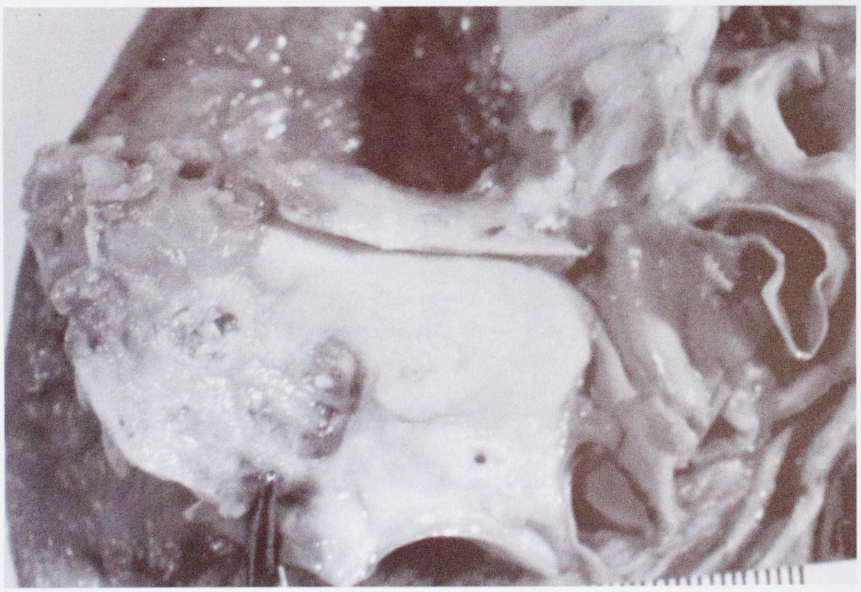

FIGURE 74-1. In idiopathic fibrosing mediastinitis, the pearly white fibrotic tissue produces obstruction of a pulmonary vein and extends around the main bronchus. (Contributed by the editor.)

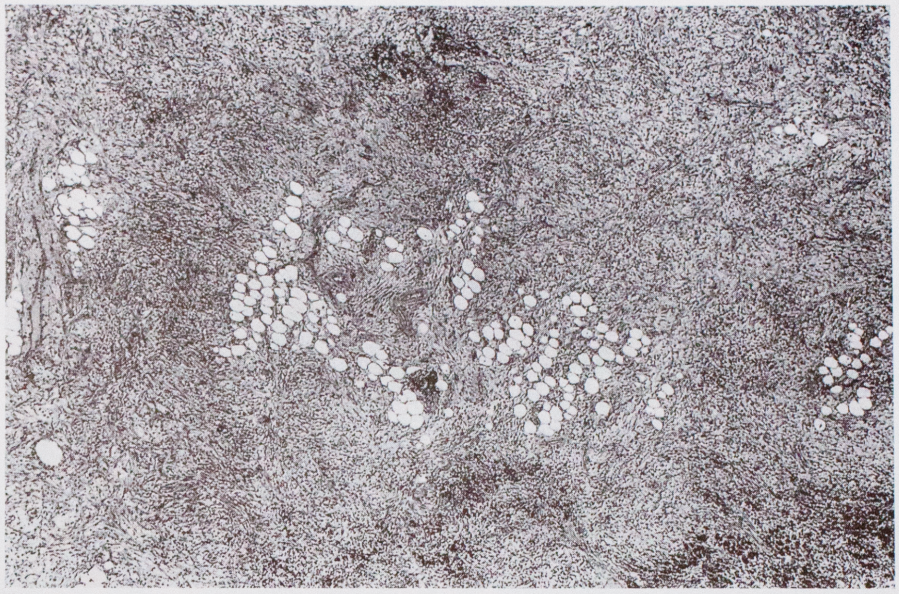

FIGURE 74-2. Infiltration of fat and soft tissues is seen at the periphery of this lesion of sclerosing mediastinitis. (H & E stain; low magnification.)

masses[26]; these generally give rise to symptoms due to compression of the adjacent lung and other mediastinal structures.

Microscopically, thymomas display a wide variety of histologic appearances. Traditionally, three main histologic variants are described: lymphocyte-rich (Fig. 74-3), epithelial-rich (Fig. 74-4), and spindle cell thymoma. The morphologic hallmark of these tumors is their biphasic cell population featuring an admixture of epithelial cells and small lymphocytes in varying proportions. Other histologic features useful for diagnosis are the distinctive lobulated growth pattern both on gross examination and under low-power magnification, the perivascular spaces, and the areas of medullary differentiation.[27]

Immunohistochemical assay plays an important role for diagnosis in equivocal cases, particularly in lymphocyte-rich thymomas, in which keratin stains will help highlight the scattered epithelial cells admixed with the lymphoid infiltrate. Electron microscopy may serve to identify the elongated cell processes of the epithelial cells and the abundant tonofilaments inserting into well-formed desmosomes. Benign, well-encapsulated thymomas have an excellent prognosis, and surgical excision is generally curative.

Mature Teratomas

These benign neoplasms account for up to 75% of all mediastinal germ cell tumors. They can occur at all ages but are more frequent in young adults.[28] Mature teratomas may be found incidentally on chest x-ray films, or may present with symptoms due to compression of mediastinal structures and lung, such as cough, dyspnea, or chest pain.[29] A case characterized by life-threatening hemoptysis has been reported.[30]

Radiographically, benign teratomas appear as large, lobulated mediastinal masses that displace and compress adjacent structures such as the trachea, lungs, carina, and great vessels.[31] Mature teratomas may be predominantly solid but are more often cystic (Color Fig. 74-2). On cut section, the cystic cavities will be

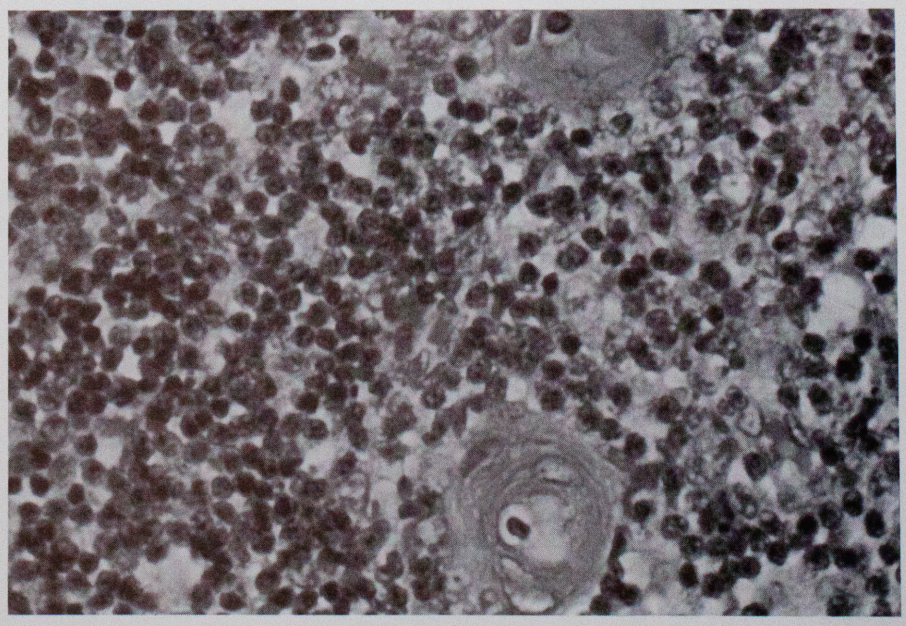

FIGURE 74-3. Notice the presence of thickened and hyalinized vessels in lymphocytic thymoma. (H & E stain; intermediate magnification; contributed by the editor.)

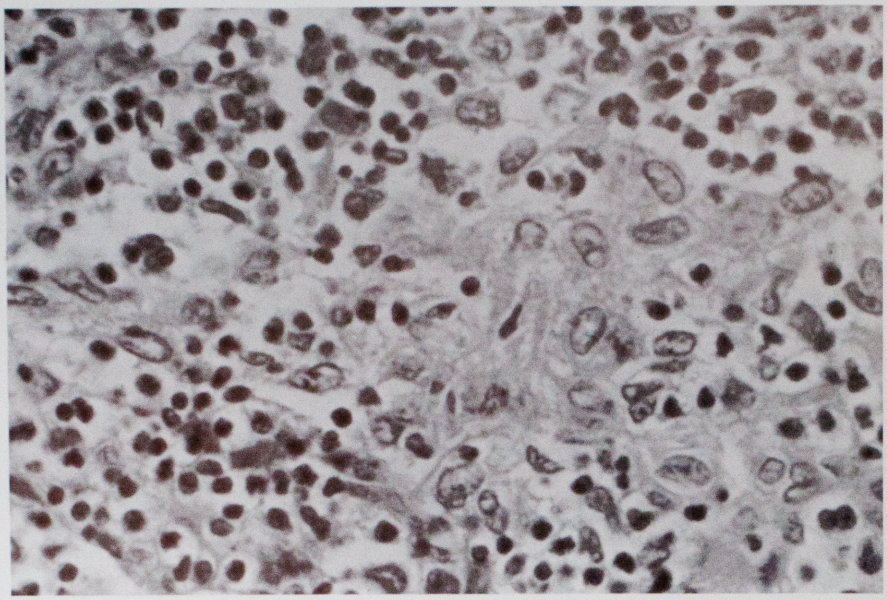

FIGURE 74-4. Characteristic microscopic appearance of mixed epithelial–lymphocytic thymoma. (H & E stain; intermediate magnification; contributed by the editor.)

filled with white or yellow sebaceous material admixed with hair. Histologically, tissues derived from all three germ layers will be present, including dermal, bronchial, and intestinal epithelium; bone; cartilage; mature neural tissue; and teeth. Mature teratomas are benign tumors that do not infiltrate adjacent organs or metastasize. Surgical excision is curative.

Solitary Fibrous Tumors

Also known as fibrous mesothelioma or submesothelial fibroma, solitary fibrous tumor is a benign neoplasm that may occur in any serosal-lined surface of the body, including the pleura, pericardium, and peritoneum. Witkin and Rosai have described a series of cases presenting as anterior mediastinal masses, presumably arising from the mediastinal pleura or pericardium.[32] Such tumors may be responsible for compression symptoms, or may be associated with hormonal manifestations such as hypoglycemia.[33,34] They are characterized grossly by their polypoid, pedunculated growth, and are usually attached to the serosal surface by a short stalk. Radiologically, they usually present as well-circumscribed, peripheral masses; occasionally, however, they may indent the pleura, because of compression by the rib cage, and grow into the lung, giving the impression of an intraparenchymatous lung tumor. Histologically, solitary fibrous tumors display a wide variety of growth patterns; the most frequently found are the fibromalike, storiform, hemangiopericytomalike, neural, and diffuse sclerosing type.[35] Although none of these histologic growth patterns are diagnostic *per se*, the presence of more than one of them within a single lesion is characteristic and highly suggestive of this neoplasm. Final diagnosis, however, rests on strict correlation of the histologic findings with the anatomic location and gross features of the lesion, namely, encapsulation, polypoid configuration, and attachment to the serosal surface by a stalk or short pedicle.

Benign Neurogenic Tumors

Such tumors most often arise in the posterior mediastinum and may grow to attain massive proportions, causing respiratory symptoms due to compression of mediastinal structures. These are tumors of peripheral nerves, such as schwannoma and neurofibroma (Fig. 74-5), and tumors of autonomic ganglia, such as ganglioneuroma (Color Fig. 74-3), gangliofibroma, and ganglioneuroblastoma.[36,37] The majority of these well-circumscribed, encapsulated masses are completely cured by surgical excision.

MALIGNANT NEOPLASMS

The mediastinum is the seat of origin of a wide variety of epithelial, nonepithelial, and lymphoid malignancies. Such neoplasms most often will come to the attention of the physician because of respiratory symptoms resulting from compression of major airways, or due to infiltration of adjacent neural structures. When extensive infiltration or metastases to the lungs have occurred, it may be very difficult to assess the exact origin of the tumor.

Malignant Thymic Epithelial Neoplasms

A great deal of controversy exists in the literature regarding primary malignant thymic epithelial neoplasms. This is the result of two factors:

FIGURE 74-5. Gross appearance of mediastinal neurofibroma in a patient with neurofibromatoses. (Contributed by the editor.)

1. Primary thymic epithelial neoplasms showing the conventional, characteristically bland histology of benign thymomas have been shown in a small percentage of cases to be capable of locally aggressive behavior and metastasis; such tumors have been variously designated as invasive thymomas or as "type-I malignant thymoma" by Levine and Rosai (Color Fig. 74-4; Fig. 74-6).[38]
2. There are primary thymic epithelial neoplasms that already display cytologic features of malignancy, the thymic carcinomas or "type-II malignant thymoma" of Levine and Rosai.[38] They may exhibit such a bewildering array of morphologic appearances that they will require strict clinicopathologic correlation to rule out the possibility of a metastasis from an occult source.

In addition to these two extremes, a third category of malignant thymic epithelial neoplasms has become increasingly recognized,[39,40] which combines features intermediate between the two (*i.e.*, the gross and histologic architectural features of benign thymomas, but also a mild-to-moderate degree of cytologic atypia); such cases are best designated "atypical thymomas."[39]

The first group of tumors alluded to (*i.e.*, invasive thymomas) will require careful attention to their capsular integrity for prognostication, both on gross inspection at the time of surgery and on microscopic examination of the resected specimen.

The second group (*i.e.*, thymic carcinomas) comprises several histologic variants, including well-differentiated squamous, basaloid, mucoepidermoid, poorly differentiated squamous (*i.e.*, lymphoepitheliomalike), small cell or neuroendocrine, clear cell, sarcomatoid, and undifferentiated or anaplastic carcinoma. A recent study showed that these tumors could be divided into two prognostic groups based on their histologic features: low-grade thymic carcinoma (*e.g.*, well-differentiated squamous, mucoepidermoid, and basaloid carcinoma) and high-grade thymic carcinoma (*e.g.*, lymphoepitheliomalike, small cell or neuroendocrine, clear cell, sarcomatoid, and anaplastic or undifferentiated carcinoma).[41] The low-grade neoplasms were characterized by a relatively favorable prognosis, with 5-year survival being attained in approximately 90% of cases. The high-grade neoplasms all proved to be rapidly fatal, with survival averaging only 15 months.

FIGURE 74-6. Metastatic seeding of the diaphragm by invasive thymoma in the same patient presented in Color Fig. 74-4. (Contributed by the editor.)

Neuroendocrine Neoplasms

Thymic carcinoids were first recognized as a distinct entity separate from thymoma in 1972, by Rosai and Higa.[42] Despite their close morphologic resemblance to carcinoids in other locations, they are included here under malignant thymic neoplasms because of their marked aggressive behavior, including local invasion, frequent recurrences, and metastases to lymph nodes and distant organs.

Thymic carcinoids may be discovered incidentally on chest x-ray films, or may present with local or nonspecific systemic or endocrine symptoms. Local thoracic symptoms are the result of displacement of mediastinal structures by the tumor and include dyspnea, cough, chest pain, and superior vena cava syndrome.[43] Nonspecific systemic symptoms include malaise, fatigue, fever, and clubbing of digits. About 50% of patients present with endocrine disturbances, including Cushing syndrome, inappropriate antidiuretic hormone secretion, hyperparathyroidism, and multiple endocrine neoplasia syndrome; interestingly, no case of thymic carcinoid has yet been reported in association with the clinical development of the carcinoid syndrome.

Thymic carcinoids usually present as large, bulky, lobulated masses with infiltrative borders. Bone scans and other radiographic studies are useful in the detection of metastases, which are usually multifocal and osteoblastic.[43] Histologically, they are characterized by a highly organoid or endocrine arrangement of the tumor cells, in nests, ribbons, or festoons separated by a richly vascular stroma. Mitotic activity is invariably present, as are areas of necrosis, calcification, and capsular and vascular invasion. The diagnosis may be aided by positive immunohistochemical stains with chromogranin, or by positive reaction for peptide hormones such as serotonin, somatostatin, adrenocorticotrophic hormone, and others.[44] In equivocal cases, electron microscopic examination will demonstrate the presence of dense-core neurosecretory granules (*i.e.*, 80–400 nm) within the cytoplasm of the cells.

Germ Cell Tumors

Primary malignant germ cell tumors analogous to those found in the gonads may present in anterior and posterior mediastinal locations and include seminomas (Fig. 74-7), embryonal carcinomas (Color Fig. 74-5), teratocarcinomas, choriocarcinoma, yolk sac tumors, and admixtures of these.[45,46] The majority exhibit a relatively poor prognosis and will be symptomatic at the time of presentation. Patients usually suffer from weight loss, cough, dyspnea, fatigue, and chest pain. Additionally, they may develop gynecomastia, or may have the clinical and chromosomal abnormalities of Klinefelter syndrome.

Determination of serum levels of human chorionic gonadotropin and α-fetoprotein are often useful in diagnosis and for clinical follow-up because they are usually elevated preoperatively and will fall to normal levels following surgical resection of the mass. On chest x-ray films, these tumors generally appear as large, lobulated anterior mediastinal masses that displace and infiltrate adjacent structures. Occasionally they may be cystic with areas of calcification within the cyst walls.

Histologically, germ cell tumors of the mediastinum resemble their gonadal counterparts; thymic tissue can usually be found within them or their capsules. Primary thymic germ cell tumors, also like their gonadal counterparts, may be associated with sarcomatous components, such as angiosarcoma or rhabdomyosar-

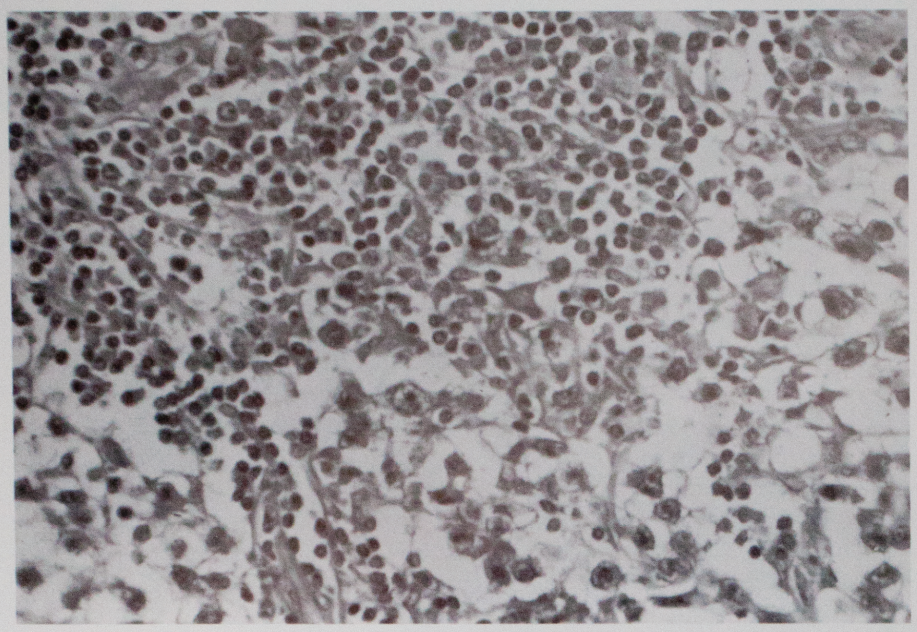

FIGURE 74-7. Clear germ cells admixed with lymphocytes are characteristic of seminoma. (H & E stain; intermediate magnification; contributed by the editor.)

coma.[47] The possibility that a mediastinal germ cell tumor may represent a metastasis from an occult gonadal primary tumor must always be ruled out by appropriate clinical evaluation.

From the standpoint of differential diagnosis, the germ cell tumor that will most likely be mistaken for a thymoma, thymic carcinoma, or large cell lymphoma is thymic seminoma. Making this distinction is of importance, because thymic seminoma may exhibit an excellent prognosis when properly diagnosed and treated.[48]

Mediastinal Sarcomas

Such tumors are rare and account for less than 5% of all mediastinal neoplasms. Mediastinal sarcomas most often arise in the posterior compartment of the mediastinum and present as large masses on routine chest x-ray films. They may be accompanied by cough, stridor, dyspnea, hoarseness, chest pain, dysphagia, superior vena cava syndrome, and neurologic symptoms secondary to compression of the spinal cord.[49] Virtually all histologic types of sarcomas may be seen in the mediastinum, including angiosarcoma, fibrosarcoma, malignant fibrous histiocytoma, liposarcoma, leiomyosarcoma, rhabdomyosarcoma, osteosarcoma, and chondrosarcoma. However, the most frequently encountered are neurogenic tumors.[50]

Malignant tumors of peripheral nerve sheath origin affect patients of both genders in their third through fifth decades of life. They may present as isolated mediastinal masses or as a manifestation of neurofibromatosis.[50] In general, mediastinal sarcomas are aggressive neoplasms that tend to recur locally and metastasize to the lungs and other organs. Histologic diagnosis depends on the recognition of the characteristic morphologic features pertaining to the different cell types. Immunohistochemical studies and electron microscopy are helpful tools for diagnosis, because these tumors may exhibit frequent overlap in their histologic growth patterns and cytologic appearances.

Sarcomas primarily in the anterior mediastinal compartment are even rarer and usually arise as a component of mediastinal teratomas or other germ cell tumors of the thymus. Rarely, however, they may be encountered in a pure form.[51,52]

Malignant Lymphomas

The mediastinum constitutes a secondary site of involvement in a significant proportion of patients with generalized malignant lymphoma[53] and less frequently may be the primary and only site of involvement.[54,55] The main histologic types encountered in this location include Hodgkin disease, lymphoblastic lymphoma, and diffuse large cell lymphoma.

Hodgkin disease represents the most frequent form of malignant lymphoma arising in the mediastinum.[56] It is predominantly a disease of young individuals. The nodular sclerosis type is by far the most common, and it is more frequent in young women.

Clinically, they present as large anterior mediastinal masses that may develop symptoms due to compression of adjacent structures. Hodgkin disease of the mediastinum may often undergo cystic degeneration to the extent that the diagnosis may be missed both radiographically and on histologic examination. A rare complication of mediastinal Hodgkin disease is the development of hypertrophic osteoarthropathy.[57]

Lymphoblastic lymphoma of the mediastinum is mainly a disease of children and adolescents.[58] These tumors characteristically will initially present as a large anterior mediastinal mass followed by leukemic spread to bone marrow, central nervous system, and gonads. Immunohistochemical stains are helpful in diagnosis; the tumor cells will display an immature T-cell phenotype, with TdT, CD1, CD4, CD8, CD14, and CD38 positivity.

Diffuse large cell lymphomas of the mediastinum are aggressive neoplasms that most often affect women in their second and third decades of life. Although they are highly responsive to radiation and chemotherapy, they have a marked tendency to recur locally and to spread to distant sites. Clinically, these patients usually present with fever, cough, dyspnea, chest pain, and other symptoms caused by compression of surrounding mediastinal structures. Grossly, these lymphomas appear as large mediastinal masses with extensive areas of necrosis and infiltration of adjacent structures, including lung parenchyma (Fig. 74-8*A, B*).

Histologically, these lymphomas are characterized by their diffuse pattern of growth, accompanied by varying degrees of sclerosis.[59] Occasionally, malignant lymphomas in mediastinal lo-

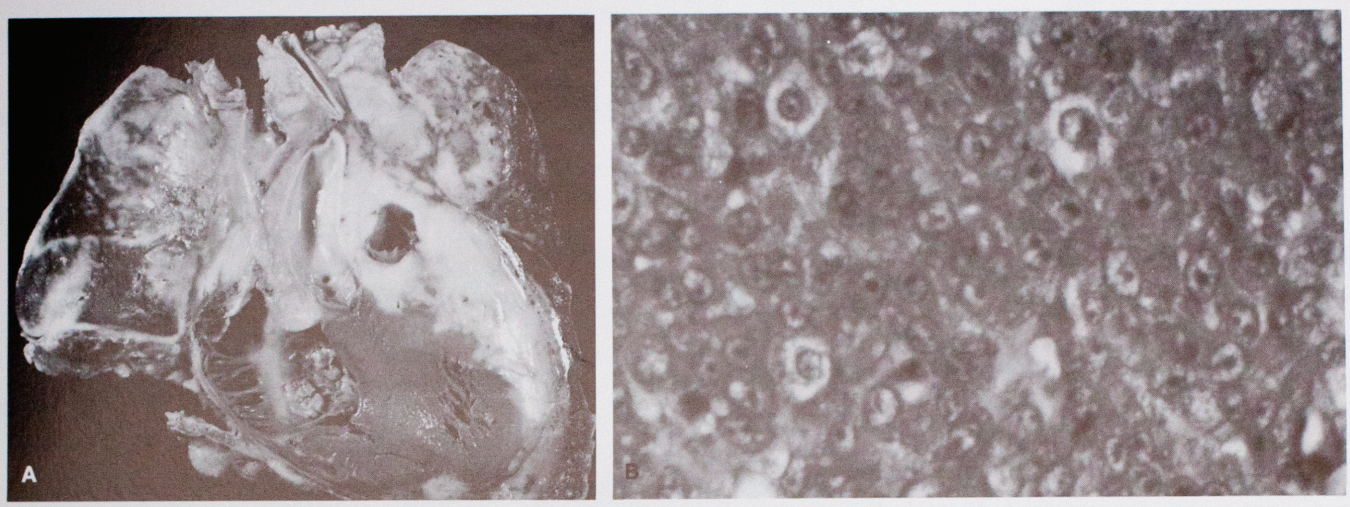

FIGURE 74-8. (A) Malignant lymphoma of the anterior mediastinum infiltrates the heart and lungs. (B) Microscopic view of large-cell lymphoma in A. Immunophenotyping revealed a B-cell lineage. (H & E stain; high magnification; contributed by the editor.)

cations may assume other peculiar morphologic appearances that will cause difficulties in diagnosis, such as clear cell lymphoma and large cell lymphoma with marked tropism for germinal centers.[60,61] The diagnosis is easily established in such cases by the use of immunohistochemical stains with lymphoid markers. The majority of large cell lymphomas of the mediastinum will exhibit a B-cell phenotype.[59–62]

Metastases to and Direct Tumoral Invasion of the Mediastinum

Metastases to mediastinal lymph nodes from extrathoracic primary tumors may be the cause of respiratory symptoms due to compression of the tracheobronchial tree by tumor or by direct extension from involved lymph nodes. Numerous extrathoracic neoplasms metastasize to mediastinal lymph nodes[63] and will also be accompanied by lymphangitis and hematogenous spread to the lungs.[64] Primary neoplasms of the upper aerodigestive tract may also involve the tracheobronchial tree and lung by direct extension and invasion of mediastinal structures, particularly squamous cell carcinoma of the esophagus.

CYSTS AND OTHER NON-NEOPLASTIC TUMOROUS CONDITIONS

A variety of cystic conditions can occur in the mediastinum and may lead to respiratory symptoms by mechanical compression. Congenital cysts are the ones most frequently encountered in the mediastinum; of these, bronchogenic cysts account for up to 50% of the cases, followed by esophageal, gastroenteric, thymic, and pericardial cysts.[65]

Congenital cysts must be distinguished from acquired cysts of the mediastinum. Acquired cysts are most often multilocular and large and always accompanied by a significant amount of inflammation and fibrosis.[66,67] Those localized in the anterior mediastinum may often arise in the thymus and become adherent to mediastinal structures. Another important clinical feature is that, unlike congenital cysts, multilocular thymic cysts may recur after surgical excision, thus raising the clinical suspicion of malignancy. In a study of multilocular thymic cysts,[66] two cases were seen to recur within 2 and 4 years of initial excision. Follow-up at 3 and 8 years after reexcision of the lesions, respectively, showed no evidence of recurrence or residual disease.

Histologically, multilocular thymic cysts are characterized by the presence of multiple cystic cavities lined by squamous, columnar, or cuboidal epitheliums. Scattered nests or islands of non-neoplastic thymic tissue in the walls of the cysts are often in continuity with the cyst lining. Other cases may show cystic dilatation of Hassall corpuscles, severe acute and chronic inflammation accompanied by intense fibrovascular proliferation, necrosis, hemorrhage, cholesterol granulomas, and reactive lymphoid hyperplasia with formation of germinal centers. Occasionally, atypical changes in the cyst lining epithelium with features of pseudoepitheliomatous hyperplasia will mimic the development of carcinoma in the cyst wall.[68]

Multilocular thymic cysts must be distinguished from other primary thymic neoplasms prone to undergo secondary cystic changes, such as Hodgkin disease and thymic seminoma.[26,48] Other unusual types of cysts that may be encountered in the mediastinum include mesothelial cysts, thoracic duct cysts, mediastinal pancreatic pseudocysts, and parasitic cysts, particularly those caused by *Echinococcus granulosus* (*i.e.*, hydatid cyst).[69–72]

Other non-neoplastic tumorous conditions of the mediastinum that may give rise to compression of adjacent lung parenchyma and airways include reactive processes such as Castleman disease, and hamartomatous lesions. Castleman disease, or angiofollicular lymphoid hyperplasia, most often presents as a solitary mass involving mediastinal lymph nodes, or as part of a multicentric process. Histologically, two types are recognized: the hyaline vascular type and the plasma cell type. Mediastinal lesions may be accompanied by systemic manifestations such as fever, malaise, weight loss, anemia, and polyclonal hypergammaglobulinemia. Surgical excision is curative, and clinical and laboratory abnormalities will remit following resection of the lesion.[73]

Thymolipoma is a rare mediastinal lesion composed of an

admixture of mature fat and normal thymic parenchyma. These lesions are most often asymptomatic but may occasionally present with cough, dyspnea, or hemoptysis.[74] It is not yet clear whether they constitute a hamartoma or simply fatty replacement of a previously hyperplastic thymus. The lesions are benign, and surgical excision is curative.

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