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Pathology of the Chest Wall and Diaphragm

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Abnormalities of the chest wall and diaphragm frequently affect pulmonary function. In some cases, these effects may be asymptomatic and clinically irrelevant; in others, they may contribute to, or be the most important factor in, the development of respiratory failure. The main disorders of the chest wall and diaphragm and their effects on respiratory function are discussed in this chapter (Display 76-1).

SYSTEMIC SCLEROSIS OR SCLERODERMA

The cutaneous manifestations of scleroderma are well known. Sir William Osler vividly described the disease in 1898:

> In its more aggravated forms, diffuse scleroderma is one of the most terrible of all human ills. Like Tithoneous to 'wither slowly' and like him to be 'beaten down and marred and wasted' until one is literally a mummy, encased in an ever shrinking, slowly contracting skin of steel, is a fate not pictured in any tragedy, ancient or modern.[1]

The most important abnormalities in scleroderma resulting in respiratory compromise involve the lung and are discussed in Chapters 31 and 67. Extensive involvement of the chest wall is rare. The term "diffuse systemic scleroderma" was coined by Tuffanelli and Winkelmann to describe those cases with generalized cutaneous sclerosis, usually beginning centrally, and often sparing the extremities, and involving the trunk rather than the face and hands.[1] The gender ratio in this small group (5.4% of all cases) was equal; these patients did not have Raynaud phenomenon and had a rapid course and poor prognosis.[1,2] In addition to intrinsic lung disease, involvement of the skin by scleroderma limits expansion of the thoracic cage and effectively contributes to a situation of restrictive lung disease.[1,2]

OBESITY

Respiratory complications of obesity are well known.[3] The pathogenesis of these complications is manyfold; moving an obese body requires additional muscle work and imposes high metabolic demands. It has been demonstrated that this increased mechanical work may be two to four times that required for nonobese subjects.[3] This is reflected in the fact that oxygen consumption and carbon dioxide production in obese subjects are higher at rest and during exercise than in normal people. In addition, accumulation of fat in the subcutaneous tissue around the ribs and intercostal muscles, the diaphragm, and the abdomen, along with the increased pulmonary blood volume, decreases respiratory compliance to as little as one third of normal. This effect is increased during recumbency.[3] If ventilation-to-perfusion ratio abnormalities result in hypoxia but not hypercapnia, such individuals are said to have only simple obesity. If, on the other hand, hypercapnia is also present, they are said to have the obesity hypoventilation syndrome (*i.e.*, pickwickian syndrome).

Many persons with obesity hypoventilation syndrome have diminished ventilatory responsiveness, but it is not clear whether it precedes obesity or is acquired. Furthermore, hypercapnic acidemia contributes to pulmonary arterial vasoconstriction and hypertension, and, ultimately, right heart failure.[3]

BONE ABNORMALITIES

Spinal deformity resulting in kyphosis and scoliosis may be idiopathic or secondary to other conditions, such as poliomyelitis, tuberculosis, hemivertebrae, hyperparathyroidism, Paget disease, and arthrogryposis multiplex congenita.[4] Kyphoscoliosis in severe cases of osteomalacia due to vitamin D deficiency or low intake of

DISPLAY 76-1. DISEASES OF THE CHEST WALL AND DIAPHRAGM

Chest Wall

Systemic disorders
- Systemic sclerosis (*i.e.*, scleroderma)
- Obesity

Bone diseases
- Kyphosis
- Scoliosis
- Kyphoscoliosis
- Ankylosing spondylitis

Tumors
- Malignant peripheral neuroectodermal tumor
- Pleuropulmonary blastoma
- Ewing sarcoma
- Rhabdomyosarcoma

Diaphragm

Paralysis
- Unilateral
- Bilateral

Malformation
- Congenital diaphragmatic defects and accessory diaphragm

Trauma
- Traumatic rupture

Tumors and tumorlike conditions
- Endometriosis
- Fibromas
- Lipomas
- Angiofibromas
- Nodular fasciitis
- Fibrosarcoma
- Liposarcoma
- Rhabdomyosarcoma
- Malignant schwannoma
- Leiomyosarcoma

calcium has been documented in human skeletal remains and is still observed in geographic areas under poor economic conditions.[5] The deleterious effects of chest wall deformities on lung volumes are well documented; abnormal lung development, in severe cases,[6] and reduction in lung volumes occur at an early stage of the deformity, become more evident with the more severe curve, and may result in cardiopulmonary symptoms, usually in the late teens.[7]

Surgical reduction of the spinal deformity, in severe cases, may prevent progression of the respiratory impairment, and it improves the parameters of respiratory function by an average of 10%.[8] Hypoxemia and anatomic restriction of the pulmonary vascular bed result in pulmonary hypertension.[6] Acute respiratory failure in these patients may be precipitated by respiratory infections, and this was formerly a preterminal event with a median survival of 1 year.[4] With treatment, most patients can be successfully managed conservatively, without mechanical ventilation, with a median survival of 9 or more years.[4] The use of bracing may be effective in progressive curves of 30° to 40°. Idiopathic scoliosis beginning after the age of 11 years does not appear to carry the risk of cardiorespiratory failure that was hitherto believed.[9] Anesthetic management of these patients poses special considerations.[10]

Ankylosing spondylitis (*i.e.*, Marie-Strümpell disease) is a progressive inflammatory disease that affects the diarthrodial joints of the spine, the costovertebral joints, and the sacroiliac joints. It predominates in males by a ratio of 9:1. Its etiology is unknown, but it is associated with HLA B27.[5] Examples of this disease have been documented in skeletal remains from the neolithic period and predynastic Egypt, and in ancient skeletons from Nubia and other archaeological sites.[5] Ankylosing spondylitis results in fusion of the costovertebral joints, severely limiting expansion of the chest because of decreased thoracic wall compliance; however, this seems to cause little disability.

The incidence of pleuropulmonary involvement varies in published reports from 0 to 30%.[11] A review of 2080 patients with this condition revealed an incidence of 1.3%; the most common abnormality was upper lobe fibrobullous lesions. Secondary infection of the bullous spaces with *Aspergillus* species (*i.e.*, aspergilloma), atypical mycobacteria, and other organisms can occur.[11] Other lesions observed include apical pleural thickening, pleural effusion and empyema, and pneumothorax; cor pulmonale is uncommon. The arthritis precedes the onset of pleuropulmonary abnormalities by 15 years or more and is almost always inactive when pleuropulmonary manifestations appear.[11]

TUMORAL PATHOLOGY OF SOFT TISSUES AND BONY CAGE

Malignant Peripheral Neuroectodermal Tumor

In 1979, Askin and colleagues described a series of 20 cases of malignant small cell neoplasms arising in the thoracopulmonary region in children.[12] These neoplasms may present early in life or later in childhood and adolescence, or, rarely, in adult life, as a palpable mass in the chest wall that may involve the adjacent lung; occasional examples are exclusively pulmonary. Failure of local control, rather than metastatic spread, results in a median survival of only 8 months.[12] These tumors measure 5 to 10 cm in greatest dimension.

Malignant peripheral neuroectodermal tumors (MPNTs) are solid, circumscribed masses with a uniform gray-white surface. Necrosis, hemorrhage, and cystic areas may be present (Color Fig. 76-1). Microscopically, sheets or anastomosing profiles of uniform, hyperchromatic cells are separated by fibrovascular septa. Lobules of tumor cells may be present; dystrophic calcification is uncommon (Fig. 76-1). Cytoplasmic glycogen may be detected with periodic acid-Schiff stain.[13] These tumors can be diagnosed by fine needle aspiration cytology.[14] Evidence of neuroectodermal differentiation has been provided by ultrastructural, immunohistochemical, cell culture, and cytogenetic observations. With the electron microscope, these tumors show cytoplasmic neurosecretory granules, a filamentous cytoskeleton, and neuritic-type cell processes that contain microtubules, filaments, and dense-core granules; intercellular junctions are present.[15]

Immunohistochemically, these tumors are invariably reactive for neuron-specific enolase.[16,17] Cytogenetic analysis by Seemayer and colleagues showed a reciprocal translocation (11;22) (q24; q12); these markers are commonly identified in neural crest–derived neoplasms.[15]

These neoplasms are therefore in the "primitive neuroectodermal tumor" category, along with peripheral neuroblastomas

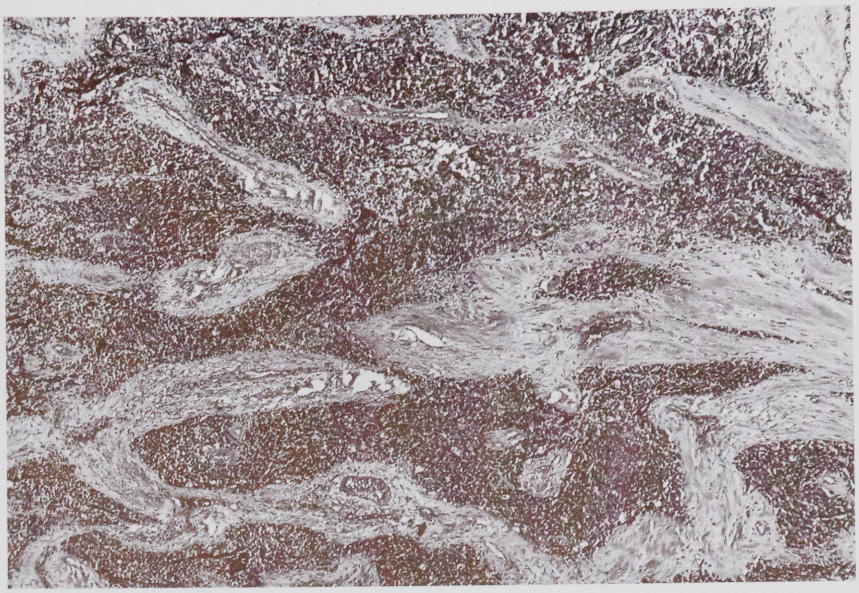

FIGURE 76-1. In a malignant peripheral neuroectodermal tumor of the thoracopulmonary region, sheets and lobules of small cells are separated by a rich fibrovascular stroma (see Color Fig. 76-1). (H & E stain; low magnification.)

and Ewing sarcomas[16–19]; however, important differences exist. Only 27% of cases of Ewing sarcoma occur in the thoracopulmonary region; by contrast, 47% of MPNTs are located in this region.[17] Disease-free survival in patients with Ewing sarcoma is 7.5 years in 60% of cases, compared with 45% for MPNT.[17] Schmidt and colleagues have suggested the following criteria in the differential diagnosis of these tumors:[17]

MPNTs are characterized by the presence of Homer-Wright rosettes or the immunohistochemical expression of at least two neural markers.

Ewing sarcomas lack Homer-Wright rosettes and express no neural markers, or only one by immunohistochemistry.

Protooncogene expression in both entities is the same.

In contrast to patients with neuroblastomas, which are primitive neural tumors derived from the autonomic nervous system and are associated in most cases with increased catecholamines (95%), patients with MPNTs do not have elevated catecholamine metabolites.[16] Virtually all neuroepithelioma cell lines are cholinergic, whereas neuroblastoma cell lines are adrenergic.[19] The cholinergic phenotype of neuroepithelioma and Ewing sarcoma[18] cell lines indicates that the cells are committed to mature into parasympathetic phenotype because high levels of choline acetyltransferase are expressed in the postganglionic parasympathetic system.[19] In contrast to neuroblastomas, however, ganglion cell differentiation is never observed in peripheral neuroepitheliomas. MPNTs of the thoracopulmonary region probably arise from intercostal nerves and, at least in some series, predominate in girls. These tumors are responsive to radiation and chemotherapeutic agents; however, in contrast to neuroblastomas, complete surgical resection is an important step in tumor management.[19]

Pleuropulmonary Blastoma

A recently described entity in children may present as a pleural-based mass, or as a mediastinal or intrapulmonary tumor.[20] Age at presentation ranges from 30 months to 12 years; equal numbers of males and females are affected. Presenting complaints include cough, fever, and chest pain. Chest x-ray films reveal partial or complete opacification of a hemithorax. The tumors are usually large (average, 572 g), multilobar, and partially surrounded by a glistening capsule; hemorrhage and necrosis are common.

Microscopically, these tumors display variable patterns, but a consistent feature is the presence of small to medium-sized cells with a high nucleocytoplasmic ratio, granular chromatin, one or two inconspicuous nucleoli, and a scanty pale eosinophilic to clear ill-defined cytoplasm. The cells grow in poorly formed nests separated by spindle cells. This component is remarkably similar to the blastematous elements of Wilms tumor (Fig. 76-2). In addition, rhabdomyosarcomatous, chondrosarcomatous, liposarcomatous components, and areas of undifferentiated spindle cell sarcoma are variably present (Figs. 76-3 and 76-4); immunoreactivity is that of the specific line of differentiation (Fig. 76-5). Entrapped epithelial elements from the lung or mesothelial cells from the pleura lack anaplastic features and do not represent neoplastic components, in contrast to pulmonary blastomas, in which both mesenchymal and epithelial components are malignant.

Pleuropulmonary blastoma is thought to arise from the thoracic splanchnopleural or somatopleural mesoderm. The prognosis of these patients is grave, and response to radiation and multidrug therapy is poor; pulmonary, skeletal, and central nervous system metastases have occurred in the majority of patients within 12 to 15 months of diagnosis (see Chap. 54).[20]

Other Chest Wall Tumors

As previously mentioned, Ewing sarcoma may arise in a rib and present as a chest wall tumor in 27% of the cases[13,17]; rhabdomyosarcoma may arise in the soft tissues of the chest wall.[13] Pseudotumors, such as nodular fasciitis, can also occur in the chest wall (Color Fig. 76-2; Fig. 76-6).

DISEASES OF THE DIAPHRAGM

The mechanical coupling of the rib cage, abdomen, and diaphragm through their area of apposition has been reviewed.[21]

FIGURE 76-2. In pleuropulmonary blastoma, small-to-medium-sized cells grow in sheets and nests. (H & E stain; low magnification.)

Paralysis of the Diaphragm

Paralysis of the diaphragm may be unilateral or, less common, bilateral. In bilateral paralysis, inspiration is achieved by intercostal and accessory muscles; the flaccid diaphragm moves cranially as the intrathoracic pressure decreases. The abdominal pressure becomes more negative rather than more positive, as occurs during diaphragmatic contraction. Accessory muscles include some that are normally expiratory.[22] Because of the limited projection of fibers from one hemidiaphragm to the contralateral, each half can operate relatively independently.

Bilateral paralysis of the diaphragm usually occurs in the context of severe generalized muscle weakness, but it may be specifically, or disproportionately, affected.[23–26] Table 76-1 includes conditions associated with bilateral diaphragmatic paralysis. Patients have dyspnea, orthopnea, tachypnea, and abdominal wall paradox in the supine position. Chest x-ray films may show elevation of both hemidiaphragms and basal atelectasis. Fluoroscopy may show decreased movement. Management is determined by the nature of the underlying condition, but often the paralysis is irreversible. Pacing of the distal phrenic nerves may be appropriate when the cause is situated in the upper cervical cord or brain stem.[22]

Unilateral diaphragmatic paralysis is more common than bilateral paralysis. The cause is often evident from the history or chest x-ray films. Therapeutic phrenicotomy for tuberculosis is no longer practiced. The most common cause is infiltration by a tumor; most often bronchial carcinoma. Approximately one third of patients have a history of neck operations resulting in phrenic nerve injury. In the remaining cases, the cause is trauma, infection, or neurologic disease (*e.g.*, phrenic nerve cold injury, cannulation of subclavian vein, pneumonia, herpes zoster of cervical nerve roots). Causes of bilateral paralysis may present as unilateral paralysis.[22,27,28] As expected, ventilation and perfusion of the lower lobe on the affected side are decreased. Diaphragmatic plication,

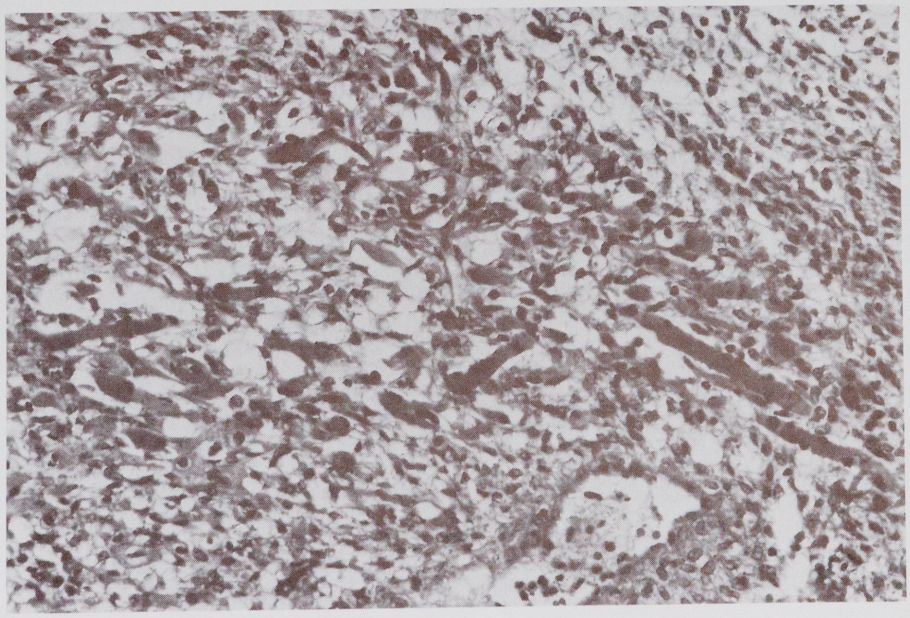

FIGURE 76-3. Focal rhabdomyosarcomatous differentiation can occur in a pleuropulmonary blastoma. (H & E stain; intermediate magnification.)

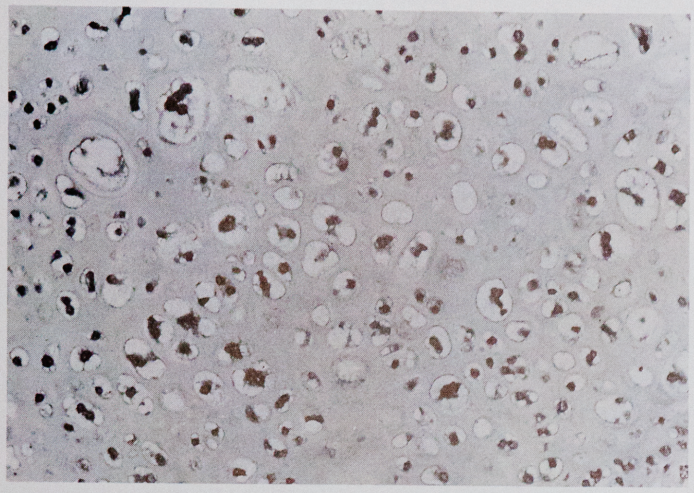

FIGURE 76-4. Focal chondrosarcomatous differentiation can occur in pleuropulmonary blastoma. (H & E stain; intermediate magnification.)

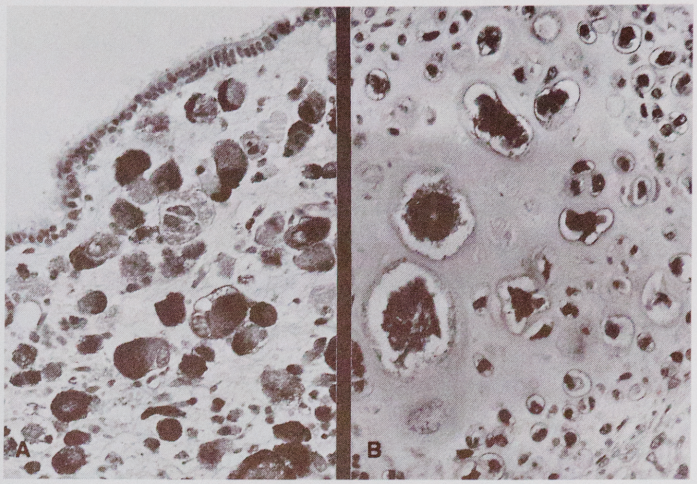

FIGURE 76-5. (**A**) Rhabdomyomatous area of pleuropulmonary blastoma is immunoreactive for desmin. (**B**) A chondrosarcomatous area is positive for S-100 protein. (Immunoperoxidase stain; intermediate magnifications.)

sometimes performed, restores a more normal position and reduces paradoxical motion, and may improve symptomatology.[22]

Other Diseases of the Diaphragm

Congenital diaphragmatic defects consist usually of partial or total failure of muscular development of the hemidiaphragm. It is usually left sided and presents in infancy. The prognosis depends on the severity of lung hypoplasia due to herniation of abdominal contents, and on associated malformations. In one series, spontaneous perinatal mortality was 61%.[29] In another study, the survival improved from 45% to 82% after institution of a treatment plan including early mechanical ventilation, muscle relaxation, judicious fluid administration, and pharmacologic support of blood pressure.[30] The rudimentary diaphragm, if present, shows normal fiber types and fibrosis.[31] Surgical repair is indicated; late complications may include thoracic cage deformity.[32,33] A thorough search for associated anomalies and karyotypic analysis are important in the management of these patients.[29,34] Accessory diaphragm is a rare congenital abnormality that is more common on the right side and is often associated with cardiovascular anomalies (see Chap. 10).[35]

TRAUMATIC RUPTURE AND OTHER LESIONS OF THE DIAPHRAGM

Traumatic rupture of the diaphragm occurs most often on the left side and is frequently seen in motor vehicle accidents; associated abdominal injury is common (up to 80% of patients). A mortality rate of 19% to 31% reflects the severity of the trauma. Strangulated herniation of abdominal contents is a complication of untreated cases.[36,37]

Diaphragmatic endometriosis and primary tumors of the diaphragm are uncommon[38]; however, tumors arising in adjacent organs frequently invade the diaphragm. They include fibrous

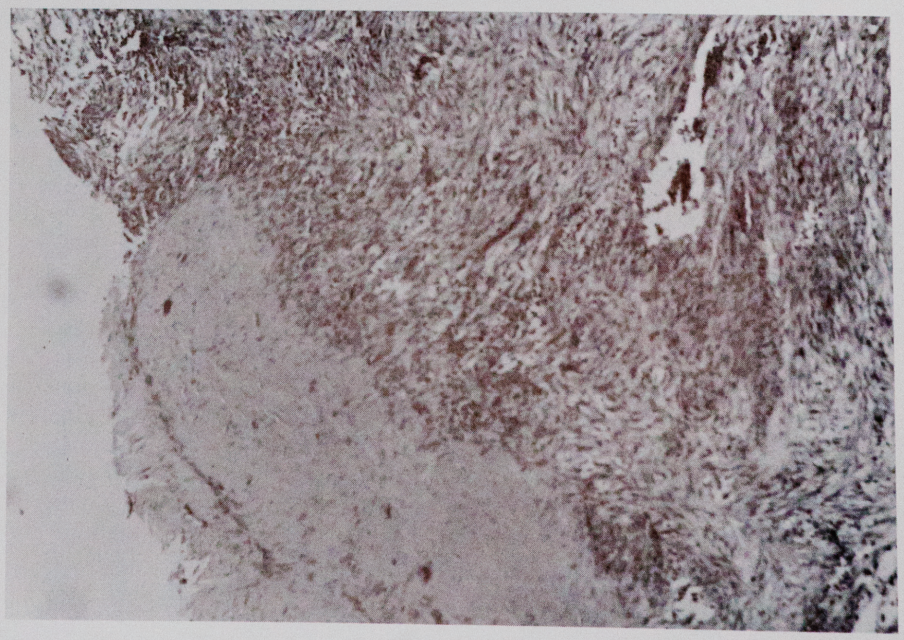

FIGURE 76-6. Spindle-cell proliferation is characteristic of nodular fasciitis of the thoracic wall (see Color Fig. 76-2). (H & E stain; low magnification.)

TABLE 76-1
Causes of Diaphragmatic Paresis and Paralysis

Site of Lesion	Condition
Spinal cord	Transection above C5
	Multiple sclerosis
Motor neurons	Poliomyelitis
	Amyotrophic lateral sclerosis
	Spinal muscular atrophy
Cervical nerve roots and phrenic nerves	Severe spondylosis
	Tetanus toxin
	Guillian-Barré polyneuropathy
	Charcot-Marie-Tooth polyneuropathy
	Neuralgic amyotrophy
	Unclassified phrenic neuropathy
	Trauma (*i.e.*, blunt chest injury, cold injury)
	Malignant invasion
	Paraneoplastic lesion
	Hypothyroidism
Diaphragmatic muscle	Limb girdle dystrophy
	Acid maltase deficiency
	Systemic lupus erythematosus
	Mixed connective tissue disease disorder
	Dermatomyositis
	Systemic sclerosis
	Amyloid infiltration

From Gibson GJ. Diaphragmatic paresis: pathophysiology, clinical features and investigation. Thorax 1989;44:960.

tumors, lipomas, fibromas, angiofibromas, and schwannian tumors. Malignant tumors include fibrosarcoma, liposarcoma, rhabdomyosarcoma, malignant schwannoma, and leiomyosarcoma.

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