Unusual Diffuse Pulmonary Lymphatic Proliferation in a Young Boy


We describe a 4-year-old boy who died of an unusual generalized pulmonary lymphatic proliferation. His condition cannot clearly be categorized with any of the previously described pulmonary lymphatic disorders.

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Several rare disorders may affect the pulmonary lymphatic vessels of children, including lymphangioma, lymphatic dysplasia, and congenital pulmonary lymphangiectasis. An additional disorder of pulmonary lymphatics, lymphangioleiomyomatosis, has been reported only in women of childbearing age. We report the case of a 4-year-old boy who died of a pulmonary lymphatic disorder, the clinical and pathologic characteristics of which seem to share features with several of these disorders.

CASE REPORT

A 3-year-old boy with an uncomplicated perinatal course was reported by his mother to have had a "rattle in the chest" since birth. Pneumonia was diagnosed at age 8 months and treated with antibiotics given orally. At age 18 months, frequent coughing and wheezing episodes developed and asthma was diagnosed. He was treated with bronchodilators and occasionally with prednisone, which produced significant improvement. A second case of pneumonia was diagnosed at age 36 months and again treated with antibiotics given orally. Three months later, the patient had increasing cough, and a chest roentgenogram revealed an enlarged cardiac shadow, bilateral pleural effusions, and interstitial densities (Fig 1). An echocardiogram demonstrated pericardial effusion but normal cardiac anatomy. He underwent pericardiectomy; however, the pericardial effusion reaccumulated and thoracotomy was performed. A large mediastinal mass was identified and resected and pericardiectomy was performed. The tissue from the pericardium and mediastinum aggregated to 6.5 × 5.5 × 1.3 cm. This tissue was characterized histologically by adipose and fibrous tissue of varying density, containing multiple poorly delimited spindle cell aggregates arranged asymmetrically around ectatic lymphatic channels and blood vessels. The nuclei were cytologically bland, and mitoses were rare. Occasional lymphoid follicles and a moderate number of hemosiderin-laden macrophages were scattered throughout the tissue. A biopsy specimen from the pulmonary trunk demonstrated an identical lesion of spindle cells and ectatic lymphatic channels. A normal 6-g thymus was removed.

Postoperatively, he continued to have bilateral pleural effusions and pulmonary infiltrates, and a second thoracotomy was performed for lung biopsy and pleurodesis. Histologic study of the lung biopsy specimen demonstrated poorly demarcated spindle cell aggregates subpleurally, along interlobular septa, focally within alveolar walls.

REFERENCES

adjacent to pulmonary blood vessels, and adjacent to bronchioles distally to the level of respiratory bronchioles. The lesions were associated with ectatic lymphatic channels at all sites. A small amount of hemosiderin deposition was present in the pulmonary interstitium and in intra-alveolar histiocytes, although the intervening pulmonary parenchyma was normal (Fig 2). He was treated with a low-fat diet and diuretics with a subsequent decrease in pleural effusion but persistence of pulmonary infiltrates. He continued to have significant respiratory distress and wheezing. His airway obstruction was partially reversible, and he was treated with bronchodilators and diuretics.

At age 3 years 5 months, hemoptysis developed. Treatment with
prednisone decreased the frequency and severity of the hemoptysis. Several attempts to taper the prednisone dose resulted in increased hemoptysis. At age 4 years 6 months, he continued to have daily hemoptysis and required daily prednisone. Therefore, he was treated with interferon alfa in an attempt to control the lymphatic proliferation in the lungs. He subsequently had a marked decrease in hemoptysis. However, this treatment was discontinued after 3½ weeks because his platelet count had decreased to 53 × 10^9/L. One month later, his platelet count had recovered to 94 × 10^9/L.

At age 4 years 8 months, massive hemoptysis developed that was uncontrollable and he died. At autopsy, blood was found in the nasopharynx, trachea, and bronchi from terminal pulmonary hemorrhage. The pleural sacs and mediastinum were extensively eneased by dense fibrous adhesions. Histologically, poorly demarcated spindle cell aggregates were arranged asymmetrically around ectatic lymphatic spaces in the lung adjacent to bronchioles and blood vessels, within interlobular septa, covered the surface of the lungs, permeated the mediastinum, and were confined to the thoracic cavity (Fig 3). The spindle cells resembled vascular smooth muscle, exhibiting elongated, blunt-ended nuclei and a pattern of staining with Masson’s trichrome stain consistent with smooth muscle. Immunohistochemical studies with anti-desmin and anti-actin on formaldehyde solution-fixed, paraffin-embedded tissue obtained at autopsy were noncontributory, however, because both appropriate internal controls and the spindle cells failed to stain. The thoracic duct could not be identified. Thus, the pulmonary distribution and histologic features had remained unchanged, although the lesions had increased in size since the pericardiectomy and lung biopsy. The amount of hemosiderin deposited in the pulmonary interstitium and number of intra-alveolar histiocytes had increased, and acute intrapulmonary hemorrhage was also present. The heart and all extrathoracic viscera were grossly and histologically normal.

**DISCUSSION**

This case emphasizes the complex nature of disorders of lymphatics that may manifest as lymphangiomas (tumors of lymphatic vessels), lymphangietasis (dilatation of lymphatic vessels), or lymphangiomatosis (proliferation of lymphatic smooth muscle). When these manifestations occur together, the distinction between them is often arbitrary. Distinction between lymphangiomata and hemangiomas may also be difficult. Lymphatic disorders may occur secondary to congenital maldevelopment of, or an acquired blockage in, the lymphatic system. These conditions often lead to abnormal collections of chyle outside the lymphatic system, such as chylothorax.

Review of the literature reveals several categories of rare lymphatic disorders that can affect the lungs and that can present in childhood. The first category is lymphangiomata. This tumor may occur in the neck (cystic hygroma), axilla, subcutaneous tissue, liver, spleen, bone, lung, pleura, or mediastinum. These lesions may be isolated or may occur in association with other lymphatic dysplasia and frequently result in the leakage of chyle. A recent review of intrathoracic lymphangiomas did not describe pulmonary parenchymal involvement. However, there are rare reports of pulmonary lymphangiomata confined to one or two lobes. When multiple lymphangiomas are present, the condition is termed lymphangiomatosis. Such multiple lesions almost always involve bone in which they may cause pathologic fractures or “disappearing bones.” Lymphangiomatosis often causes chylothorax, frequently from a mediastinal lymphangioma, but to our knowledge, pulmonary parenchymal involvement has been described in only one such case.

The second category of lymphatic disorders is lymphatic dysplasia. Dysplastic or ectatic lymphatics may cause leakage of chyle where these lesions occur. Lymphedema describes a swollen extremity or body region secondary to such a lymph accumulation. A congenital form occurs in patients younger than 3 months of age; if familial, it is called Milroy’s disease. Lymphedema praecox presents in patients older than 3 months of age; if familial, it is called Meige’s disease. Intestinal lymphangiectasis describes dilatation of intestinal lymphatics with leakage of chyle into the bowel lumen. Chyloperitoneum, chylothorax, and chylopericardium represent leakage of lymphatics in those cavities. In generalized lymphatic dysplasia or lymphangiectasis, the process occurs in several sites and may cause chyle accumulations in multiple locations. Generalized lymphatic dysplasia can involve the lung. Lymphangiectasis may also be secondary to operation, trauma, infection, or neoplasm.

The third category is congenital pulmonary lymphangiectasis. This condition is most commonly associated with cardiac anomalies that cause pulmonary venous obstruction and dilated lung lymphatics. It also may occur as an isolated lesion. With or without cardiac anomalies, the disorder usually presents with severe respiratory distress at the time of birth. Congenital pulmonary lymphangiectasis is usually fatal in the newborn period whether or not it is secondary to heart lesions; however, prolonged survival has been reported.

A final disorder to consider is pulmonary lymphangiomatosis, which is characterized by the proliferation of smooth muscle around pulmonary lymphatics, venules, and bronchioles. The subsequent obstruction of lymphatics may lead to chylothorax and chylopericardium. Venous obstruction may cause pulmonary hemorrhage and hemoptysis, whereas bronchial obstruction may cause air trapping and pneumonothorax. Reports of this disorder have been exclusively in women of childbearing age. Some authors have noted a similarity between the lesions of lymphangiomatosis and those of tuberous sclerosis. Both estrogen and progesterone receptors have been identified in some lesions of pulmonary lymphangiomatosis.

Our patient did not fit neatly into any of the above categories. He had large mediastinal lymphangioma with lymphangiectatic involvement of pericardium, pleura, and lung parenchyma, causing chylopericardium and chylothorax. He had symptoms, including wheezing, since infancy yet had survived into childhood before severe respiratory distress developed and he ultimately died of massive hemoptysis. Clinically, his disease could represent generalized lymphatic dysplasia confined to the chest or prolonged survival from congenital pulmonary lymphangiectasis. Some clinical features are also shared with lymphangiomatosis, although our patient was a male child and thus a different sex and age than all previously reported cases of this disorder. He had no stigmata or family history of tuberous sclerosis.

Histologically, lymphatic lesions have been categorized as lymphangiectasias, lymphangiomatas, and lymphangiomatomas. The lesion described herein, although sharing some features with these entities, is distinctly different. Lymphangiectasis is characterized by dilatation and increased tortuosity of lymphatic channels. Lymphangioma is char-

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acterized by an increased number of normal-sized to cystically dilated lymphatic channels. Lymphangiectasias and lymphangiomas may possess a thin rim of smooth muscle, especially around larger spaces, although they typically lack the florid, disorganized nature of the spindle cell population demonstrated in the current case. The lesions of lymphangiomyomas or lymphangiomatosis are characterized by smooth muscle layered around a network of lymphatic spaces. The smooth muscle in lymphangio-

omyomas, however, tends to be symmetrically arranged around lymphatics, and the individual lesions have a quality of circumcision; these features contrast strongly with the asymmetric arrangement and markedly permeative, poorly circumscribed nature of the spindle cells observed in the current case.

The interpretation that the pulmonary lesion found in this patient represents a proliferative disorder of lymphatics or lymphatic-associated connective tissue is based on the clinical history of recurrent pericardial and pulmonary effusions and hemoptysis, similar to that of other progressive pulmonary lymphatic disorders; anatomic and histologic distribution of the lesion paralleling the normal course of pulmonary and thoracic lymphatic channels with relative sparing of intervening regions; and the histologic identification of open, ectatic, endothelium-lined channels within the lesion consistent with lymphatic spaces. We think that the spindle cells noted in the lesion are smooth muscle in nature based on the histologic characteristics of spindle cells with blunt-ended nuclei and an appropriate staining reaction with Masson's trichrome stain.

Our patient originally was diagnosed as having asthma because of recurrent wheezing episodes. However, his wheezing may also have been due to his pulmonary lymphatic proliferation. Wheezing or airway obstruction has been described in some of the pulmonary lymphatic disorders outlined above. As such, it seems prudent to include these rare entities in the differential diagnosis of asthma.

TREATMENT

When lymphatic dysplasia involves the lungs, the prognosis is relatively poor. Treatment is difficult and generally palliative. If chylopericardium is present, pericardiocentesis will prevent tamponade and a pericardial window will prevent reaccumulation. Similarly, thoracentesis or chest tube drainage can drain chylothorax; however, reaccumulation can be a problem. Low-fat diets may decrease the formation of chyle. At thoracotomy, a lymphangioma may be resected but recurrence is common. Closing leaks in the thoracic duct or collaterals may be attempted.

Treatment of the pulmonary parenchymal disease is also palliative. Diuretics may help eliminate excess fluid in the lungs. Wheezing from mechanical obstruction of small Airways or pulmonary edema would be unresponsive to bronchodilators. However, a trial of these medications seems warranted, nevertheless, because asthma may be coexistent. Steroids, radiation, and cytotoxic agents have been used successfully to treat hemangiomatosis and might conceivably provide some benefit in lymphangioma. Lung or heart/lung transplant may be the only hope for long-term cure and this too may be only palliative if significant involvement of other organs occurs.

The prognosis in pulmonary lymphangiomatosis is also relatively poor, with most patients dying of respiratory failure within ten years. There are reports of successful therapy in women with hormonal manipulation and one such patient underwent successful heart-lung transplantation.

The course in our patient was particularly aggressive. He was treated with diuretics, bronchodilators, corticosteroids, and interferon alfa, all of which seemed to offer some temporary benefit. The use of interferon alfa was based on a report of its successful use in pulmonary hemangiomato-

sis. The age and sex of our patient made his disease unlikely to be responsive to hormonal manipulation.

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REFERENCES

3 Wagenaar SS, Swierenga J, Wagenvoort CA. Late presentation of primary pulmonary lymphangiectasis. Thorax 1978; 33:791-95
13 Corris B, Liebow AA, Friedman PJ. Pulmonary lymphangiomato-


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Granulomatous Pulmonary Zygomycosis in a Patient without Underlying Illness*

Computed Tomographic Appearances and Treatment by Pneumonectomy

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Pulmonary zygomycosis rarely occurs in the absence of underlying disease. We report a patient with granulomatous pulmonary zygomycosis without underlying disease who presented with a pulmonary mass. We present the computed tomographic findings that we believe have not been described previously. We also report the successful treatment by pneumonectomy. (Chest 1991; 100:560-61)

Pulmonary zygomycosis is an uncommon disease caused by fungi of the class Zygomycetes. These fungi are ubiquitous and are rarely pathogenic. Systemic infection in man usually occurs in the immunocompromised host or in diabetics.15 There has been one previous report of granulomatous pulmonary zygomycosis in the English language literature in a patient who was not immunocompromised or did not have diabetes.4 We report a further similar case.

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CASE REPORT

A 66-year-old retired farmer presented with a history of dry cough for one month. He had been well otherwise and had no hemoptysis, fever, or weight loss. He had stopped smoking 15 years previously. Examination revealed the following: pulse, 78 beats per minute; blood pressure, 120/80 mm Hg; no fever, cyanosis, or clubbing; no abnormalities on chest examination; and no lymphadenopathy. There was superficial thrombophlebitis at the right popliteal fossa.

Laboratory investigation showed the following results: hemoglobin, 13.1 g/dl; white blood cell count, 8,200/cu mm; raised erythrocyte sedimentation rate at 30 mm/h; serum urea, 5.7 mmol/L; sodium, 141 mmol/L; and potassium, 4.1 mmol/L. Results of liver function tests (total proteins, 70 g/L; alkaline phosphatase, 59 IU; aspartate transaminase, 20 IU; alanine transaminase, 20 IU) were normal but the respiratory function tests (vital capacity, 2.98 L; forced vital capacity, 2.44 L) were mildly reduced. A chest roentgenogram revealed a left hilar shadow and some streaky shadowing in the left upper zone (Fig 1). A computed tomogram of the chest with contrast showed an irregular soft-tissue mass at the left hilar region with areas of calcification both within the center of the mass as well as in the periphery. It appeared to surround and compress the lumen of the left pulmonary artery giving rise to shouldering and tapering of the lumen (Fig 2). The left main bronchus also appeared to be compressed. Although it appeared to be adherent to the descending thoracic aorta in some areas (Fig 2), a rim of lucency could be discerned between the aorta and the mass in other areas. Fiberoptic bronchoscopy revealed reddened and thickened mucosa in the left upper lobe bronchus extending to the apicoposterior and anterior segmental bronchi. Bronchial biopsy specimens showed only fibrous connective tissue covered by respiratory epithelium. Sputum and bronchial brushings for cytology, acid-fast bacilli, and fungi were negative.

The provisional diagnosis was bronchial carcinoma and he underwent exploratory thoracotomy. At operation a hard mass about...