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H.H. Lien, M.D., Dept. of Diagnostic Radiology, The Norwegian Radium Hospital, Montebello, Oslo 3, Norway.

Lymphography 9 (1976) 28-35

Diffuse Lymphangiomyomatosis

G.P. Pouliadis, J. Wellauer, W. Wirth

Central Roentgendiagnostic Institute, Cantonal Hospital, University of Zurich
(Direktor: Prof. Dr. J. Wellauer), Zurich, Switzerland
Roentgendiagnostic Institute, Buergerspital, Cantonal Hospital
(Director: PD Dr. W. Wirth), Zug, Switzerland

Summary

A case of diffuse lymphangiomyomatosis with involvement of the large veins of the body is reported. The clinical, pathologoanatomic and especially the roentgenologic findings are described. Interstitial lung thickening, pleural effusions and spontaneous pneumothorax are findings which together with a stasis in the lymphatic system strongly suggest the diagnosis. The extensive involvement of the venous system supports the theory of a hamartomatous nature of the disease.

Lymphangiomyomatosis is a condition characterized by smooth muscle proliferation in the lymph vessels and lymph nodes, especially those of the retroperitoneum and posterior mediastinum, and more often than not through similar changes in the perilymphatic regions throughout the lungs.

The disease has been encountered only in middle-aged females. There are two main forms: a localized one with mediastinal or retroperitoneal lymphangiomyoma but no involvement of the pulmonary parenchyma and a diffuse form with lymph node disease and pulmonary parenchymal lymphangiomyomatosis.

Silverstein et al. (17) differentiate a third group which includes patients with stigmata of tuberous sclerosis and diffuse lymphangiomyomatous changes.

The clinical picture of the diffuse form of lymphangiomyomatosis is dominated by respiratory symptoms due mainly to interstitial lung disease frequently accompanied by recurrent chylous pleural effusions.

In this paper we present a case of diffuse lymphangiomyomatosis with some exceptional findings. To date, including this case (12, 13), 35 cases of diffuse lymphangiomyomatosis have been reported.

Fig. 1 Dilated and tortuous retroperitoneal lymphatic vessels. Immediate post-injection film.

Case report

K.I., a 39 year old female with an unremarkable clinical history, developed painfull swelling of the left arm and left cervical region without any apparent reason. The symptoms subsided within three weeks without any medical treatment.

Two years later the patient was admitted to the hospital with dyspnea, coughing, weight loss and general weakness. A chest roentgenogram revealed bilateral pleural effusions and some accentuation of the lung markings.

Thoracentesis yielded a milky fluid which was found to be chyle. Lymphangiography was performed and showed dilated and tortuous retroperitoneal lymphatic vessels (Fig. 1). The thoracic duct was well visualized and no fistula could be seen (Fig. 2a). There was however an atypical opacification of axillary, cervical and mediastinal lymph nodes (Fig. 2b). Interesting was the paucity and small size of the visualized retroperitoneal lymph nodes (Fig. 3a). A phlebogram of the thoracic outlet demonstrated obliteration of the left subclavian and brachiocephalic vein and a partial occlusion of the right brachiocephalic vein, with development of considerable collateral circulation (Fig. 4).

The patient was treated with multiple thoracenteses, a high-calory, high-protein, low-fat diet and was placed on anticoagulants. She left the hospital in fair condition only to return several months later. During this interval and in spite of anticoagulation she had developed thrombosis of the inferior vena cava and both iliac veins. Again there was a massive chylothorax, lip- and acrocyanosis and the patient experienced dyspnea.

A second phlebography of the thoracic outlet revealed a peripheral extension of the thromboses while the phlebographic examination of the inferior vena cava and the lower extremities demonstrated postthrombotic changes in the left superficial femoral vein, both iliac veins and the inferior vena cava. All laboratory examinations were normal except proteins: 3.9 g% and total lipids which were diminished.

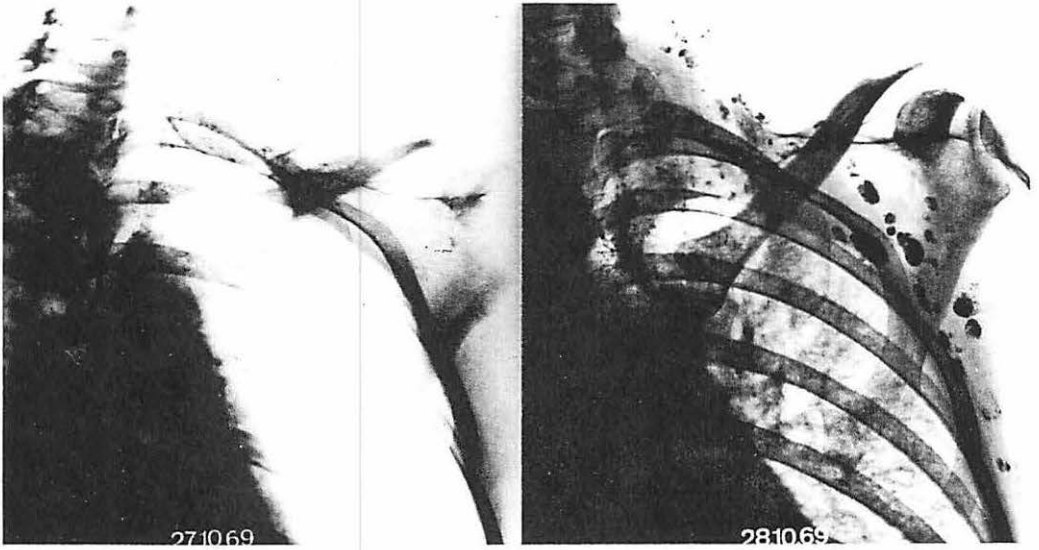
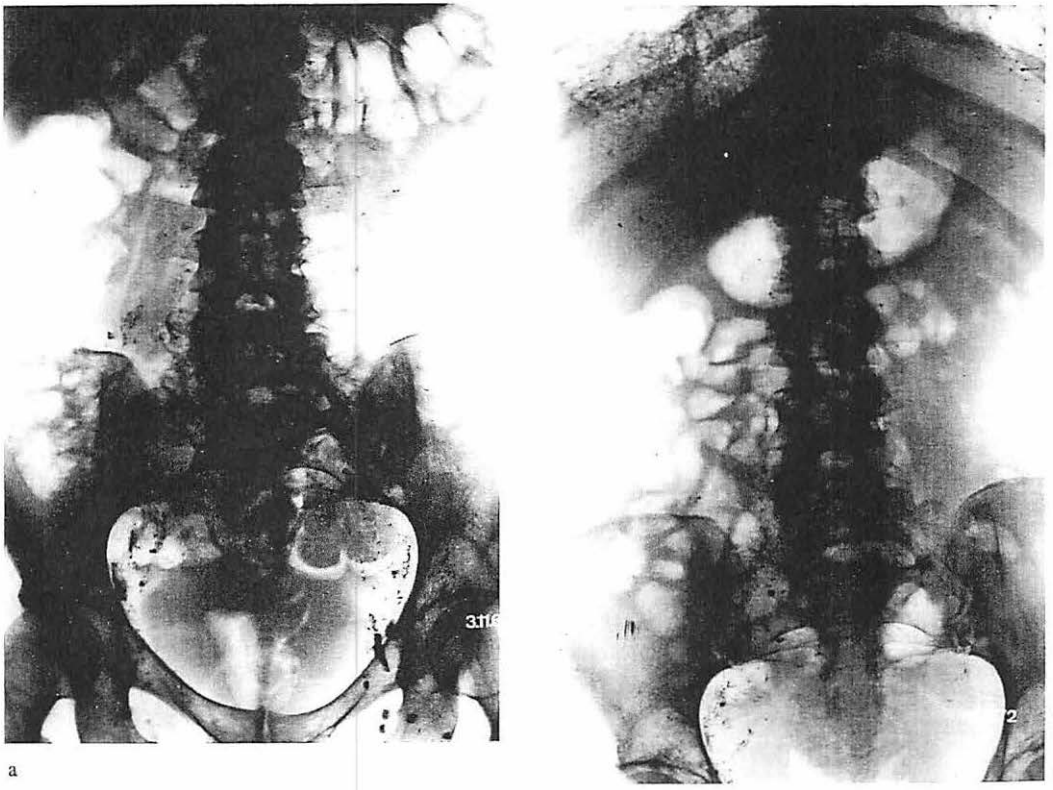


Fig. 2 (a) Good visualization of the upper third of the thoracic duct. Immediate post-injection film.
(b) Atypical opacification of axillary and cervical lymph nodes on the left side. Delayed film.



a b

Fig. 3 Diminished number and small size of the visualized lymph nodes.
(a) 2 weeks after clinical onset of the disease.
(b) 32 months later. Still further decrease in number and size of the lymph nodes.

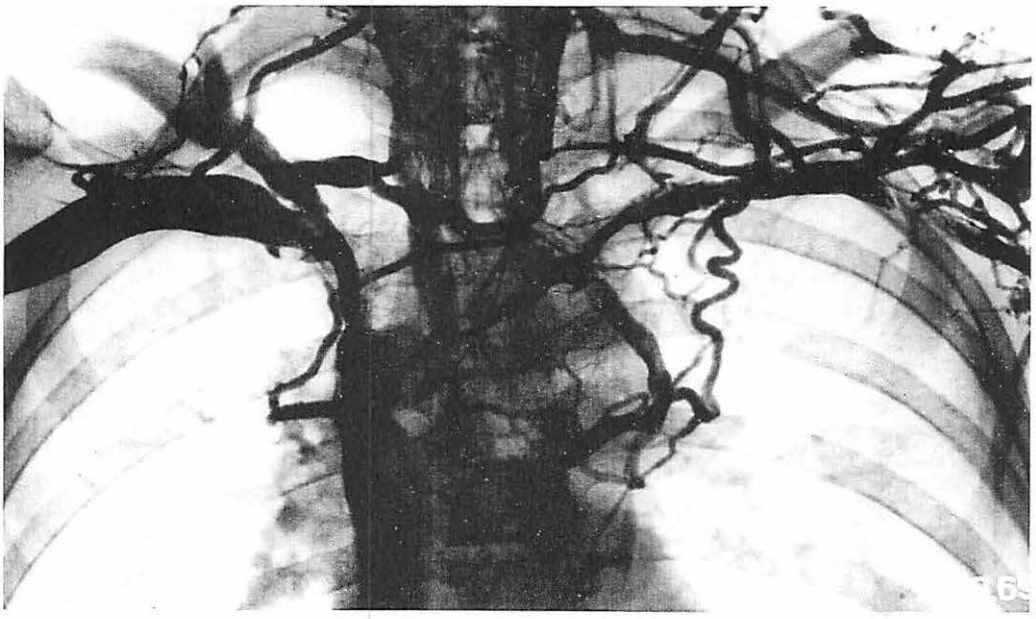


Fig. 4 Phlebography of the thoracic outlet. Obliteration of the left subclavian and brachiocephalic veins and partial occlusion of the right brachiocephalic vein.

A right sided thoracotomy and pleurodesis as well as a partial pericardectomy were performed. 1500 ml of chylous pleural effusion and 300 ml of chylous pericardial effusion were recovered. After the operation there was a successive diminution of the right sided effusion. There was still effusion on the left side. This was initially treated with thoracenteses but they had to be abandoned because of increasing coagulation of the effusion. A chest roentgenogram showed an increase of the lung markings, thickening of the right pleura and a left sided effusion (Fig. 5).

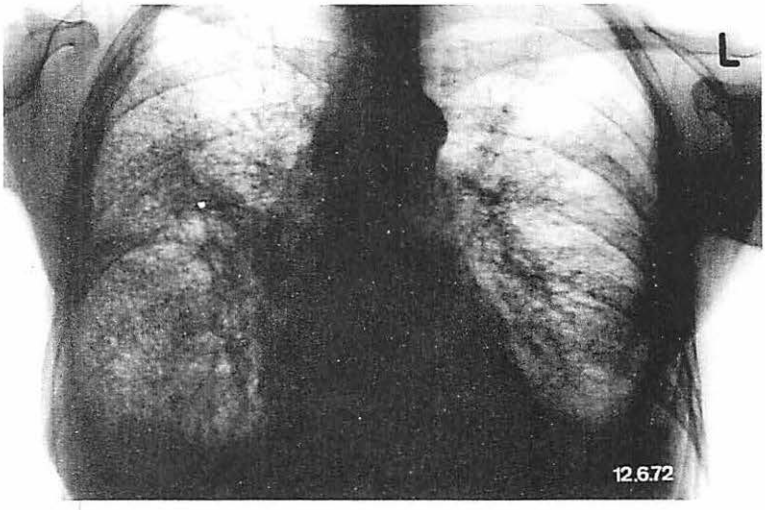


Fig. 5 Interstitial thickening in both lungs, left sided effusion and thickening of the right pleura.

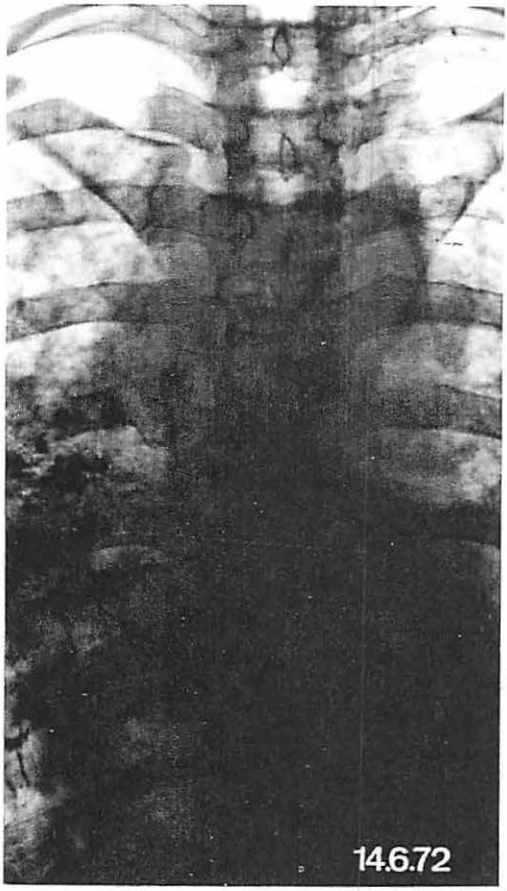


Fig. 6 Dilated mediastinal and hilar lymphatic vessels. Immediate post-injection film.

The patient noted significant symptomatic relief and left the hospital in good condition. One year later she returned with dyspnea, excessive cyanosis, superior vena cava-syndrome, a left chylothorax, chylous edema mainly of the right lung, chylous ascites and edema of the calfs.

A second lymphangiography showed on the chest film a significant dilatation of the mediastinal and hilar lymphatics (Fig. 6). The axillary and cervical lymph nodes that were opacified after the first lymphangiography were not visualized after this second lymphangiography, whereas a few small mediastinal lymph nodes could be seen this time. The 24-hour film of the abdomen revealed a decrease both in size and in number of the visualized lymph nodes as compaired to the first lymphangiography (Fig. 3b). In view of a planned second operation only a right sided lymphangiography was performed, so that the other side could be used for a preoperative, intralymphatic injection of Patent-Blue dye. A phlebogram of the inferior vena cava showed a recanalization of this vessel.

A left thoracotomy was done with the attempt to perform a lymphaticovenous anastomosis but the thoracic duct or another lymphatic vessel of sufficient size could not be found. The patient expired on the 6th postoperative day of respiratory and cardiac insufficiency, 33 months after the onset of the clinical symptoms at the age of 44.

The post mortem examination* in concordance with the clinical impression, revealed no signs of tuberous sclerosis. Honeycombing was present throughout both lungs. There was a diffuse proliferation of smooth muscle in the lymphatic vessels and lymph nodes (Fig. 7) and similar changes were seen in the pleura, pericardium and the lung interstitium (Fig. 8).

Surprisingly the same changes were found in the region of the pleural scarring at the right hemithorax and in the large veins of the body (Fig. 9). Many small sized lymph nodes could be seen at the cervical, axillary, paratracheal and hilar regions but there were no lymph nodes visualized macroscopically at the abdomen and inguinal regions.

Discussion

The roentgenographic findings in patients with lymphangiomyomatosis can be quite characteristic. In cases of diffuse lymphangiomyomatosis with pulmonary involvement the chest roentgenogram may reveal interstitial lung thickening, pleural effusions and there might be a spontaneous pneumothorax (6, 8, 9, 17). Our patient did not experience a spontaneous pneumothorax but the other two main chest findings were present. Although there was honeycombing of the lungs,

* We wish to acknowledge our appreciation to Prof. Hedinger (Director of the Pathology Department, Cantonal Hospital Zurich) for contributing the pathologic material.

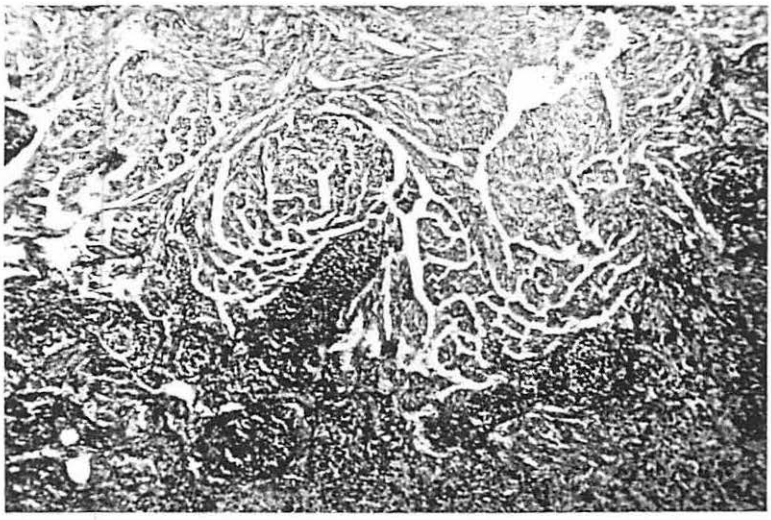


Fig. 7 Mediastinal lymph node. Hematoxylin and eosin stain. X 125. Proliferation of smooth muscle in the marginal sinus and into the lymphatic tissue.

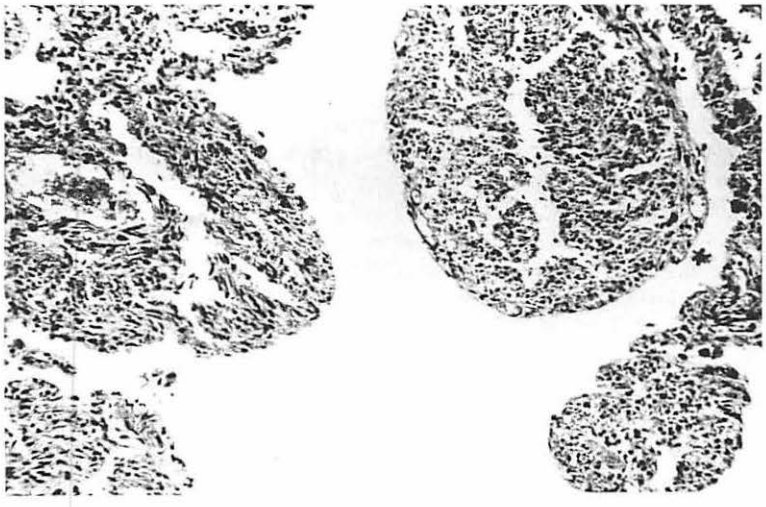


Fig. 8 Lung. Hematoxylin and eosin stain. X 125. View of a cavity with smooth muscle proliferation in the wall and nearby septa.

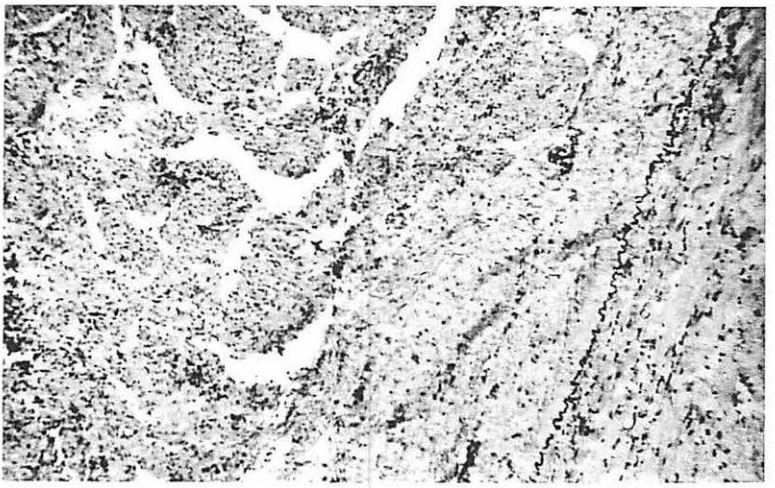


Fig. 9 Brachiocephalic vein. Elastin stain. X 125. At the lower right corner of the picture part of the vein wall is seen, adjacent to it organized thrombosis and smooth muscle proliferation in the lumen of the vein.

the interstitial thickening did not present the typical roentgenographic pattern. All these changes should strongly suggest the diagnosis of lymphangiomyomatosis whenever the effusion consists of chyle.

The contribution of lymphangiography in demonstrating an obstruction of the thoracic duct, a thoracic duct fistula or in locating a nodal mass is unquestionable. Some authors see a relative contraindication in performing this procedure in case of an impaired lung function (10, 17, 19). In our case we performed twice a lymphangiographic study within a period of two years without noticing any adverse effects. The atypical visualization of lymph nodes in the left axillary, both cervical and the mediastinal region during the first lymphangiography suggested a partial obstruction at the junction of the thoracic duct with the left subclavian vein, although this atypical lymph node visualization can be a normal variant (18). The second lymphangiography demonstrated a definite impairment of the lymphatic flow with reflux into the distended pulmonary lymphatic vessels and leakage of contrast material into the pleural space, probably by development of fistulous connections (14) and no visualization of the cervical and axillary lymph nodes. Furthermore by performing a lymphangiography shortly after the clinical onset of the disease and two years later we had the opportunity to notice a decrease both in size and in number of the visualized retroperitoneal lymph nodes during that interval.

This vanishing of the lymph nodes was also demonstrated by the postmortem examination, where no retroperitoneal lymph nodes could be visualized macroscopically. In contrast to other cases of the literature where normal sized lymph nodes or even regional lymph node enlargement has been noticed (15, 17, 20), this might be a more common finding in lymphangiomyomatosis when follow-up lymphangiographies are done.

Extraordinary in this case is the lymphangiomyomatous involvement of the venous system leading to repeated thromboses of the large veins inspite of continuous anticoagulation therapy.

The pathogenesis of this disease still remains unknown. The findings in our case might suggest the initial obstruction of the lymphatic drainage by the thrombosis of the left subclavian vein

as being the main cause of the impaired lymphatic circulation, leading to a secondary adaptation of the lymphatic system and so causing the disease (4, 5, 7, 16). This may indeed be the case although it is well known that the ligation of the thoracic duct and even the experimental ligation of the superior vena cava is not always sufficient to produce chylothorax (1, 2, 3). In this case there is a definite involvement of the veins with lymphangiomyomatosis and recurrent vein thromboses in spite of anticoagulation. No apparent explanation for the thromboses other then the lymphangiomyomatous involvement of the veins could be found.

While we cannot exclude the possibility that the diffuse lymphangiomyomatosis in this case was a secondary phenomenon, we think that the extensive distribution of the lymphangiomyomatous changes may suggest a primary involvement by a multifocal hamartomatous disease (6, 11) and that the development of the venous occlusions may then enhance the stasis in the lymphatic system.

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G.P. Pouliadis, M.D., Central Roentgendiagnostic Institute, Cantonal Hospital, 8091 Zurich, Switzerland