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PRIMARY LYMPHEDEMA OF LOWER EXTREMITIES.
I. LYMPHANGIOGRAPHIC AND HISTOLOGICAL STUDIES OF
LYMPHATIC VESSELS AND LYMPH NODES IN PRIMARY
LYMPHEDEMA

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Lymphangiographic and histological examinations were carried out in 123 patients with the clinical diagnosis of primary lymphedema. All patients were classified into 4 groups according to the radiological findings. Also histological findings in some of these patients were compared with the lymphangiographic patterns. Lack of lymphatic vessels suitable for lymphangiography on the dorsum of the foot does not mean aplasia of vessels in the extremity. Histological examination of the skin and lymphangiographies performed through the retromalleolar and femoral accesses have visualized normally developed lymphatic vessels, but with secondary degenerative changes. These findings speak against the theory of inborn defect of the lymphatic vasculature.

One hundred and ninety-eight patients with various types of edema of lower extremities were treated in the Department I of Surgery, Medical Academy in Warsaw, during the period of 1965—1970. The diagnostic procedures performed in all the patients included direct lymphangiography, phlebography, histology of the skin, lymphatic vessels and lymph nodes, (7), electron microscopy of lymphatic capillaries (1), and lymphatic absorption of isotope labeled proteins (8).

In the present communication, which is a part of this complex study, radiological and histological findings will be described. Two items will be discussed: 1) classification of the primary lymphedema according to the lymphangiographic pattern, and 2) comparison of lymphangiographic and histological patterns in different groups of lymphedema.

METHODS

Lymphangiography of the lower extremities was carried out in 123 patients with the clinical diagnosis of primary lymphedema. In the majority of cases only one extremity was involved, but there were some cases with bilateral

changes. Lymphedema appeared spontaneously some to several years before admission. In most cases it was found for the first time during the puberty, with evident exacerbation in summer at high ambient temperature. Edema was accompanied by heaviness of foot and calf. Past history and thoroughful clinical investigation helped to exclude all other etiological factors except of those producing lymph stasis.



Fig. 1. Lymphangiogram of the lower extremity of a patient with aplasia of lymph vessels. No lymph vessel was found on the dorsum of the foot. Contrast medium injected through a vessel found at the knee level revealed normal anatomy of lymphatics of the thigh and pelvis.

Lymphangiography of the affected extremity was carried out according to the method of Kinmonth (4). Lipiodol ultra-fluid 38% was used as the contrast medium.

In 30 patients the specimen of lymphatic vessel was taken for histology. In 21 patients a specimen of the inguinal lymph node was taken for histology at the time of lympho-venous shunt procedure.

RESULTS

1. Classification of primary lymphedema according to the lymphangiographic findings. Patients were classified into 4 groups (Table I).

Group 1 included 46 out of 123 patients (37.4%) in which no lymphatic vessel could be found on the dorsum of the foot, or it was a very thin and tortuous vessel not suitable for cannulation. Six out of these patients signed the consent to have a lymphatic vessel dissection at the knee joint level. In all these cases normal lymphatic vessels were found in that region. They were cannulated and lymphangiography disclosed normal vessels and lymph nodes in the thigh and pelvis (Fig. 1).



Fig. 2A



Fig. 2B

Fig. 2A. Lymphangiogram in a patient with hypoplasia of lymphatic vessels. Single narrow lymphatic vessel in the calf. B. Histological pattern of the vessel seen on lymphangiogram does not show any primary abnormalities. All layers of the wall are normally developed. Lumen of the vessel is almost completely obstructed by the thickened intima. H. E., magn. $\times 250$.

In group 2 of 16 cases (13%) lymphangiography revealed single tortuous lymphatic vessel in the calf and thigh and a tiny inguinal lymph node (Fig. 2A).

In 24 cases (19.5%) of group 2 lymphangiography helped to visualize one narrow lymphatic vessel in the calf. There was also some lymph stasis in the foot with signs of dermal backflow (Fig. 3A). In other cases of the same group vessels of collateral circulation bypassing the inguinal lymph nodes could be found, and also uneven distribution of the contrast medium in the nodes. Filled with Lipiodol they had an "angora"-like appearance (Fig. 4A).



Fig. 3A

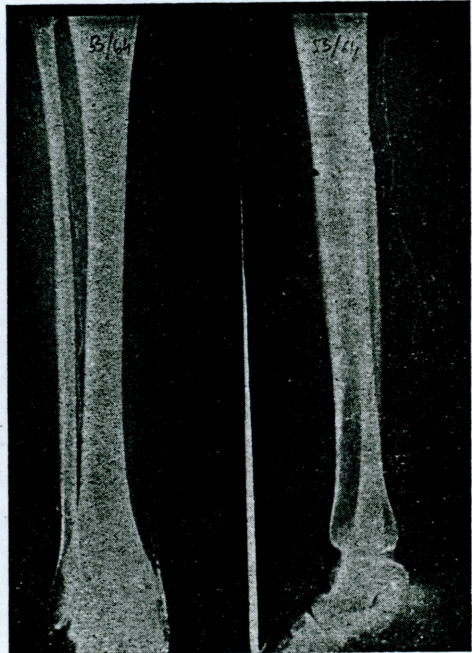


Fig. 3B

Fig. 3. Lymphangiogram in a patients with the obstructive hypoplasia. In the inguinal region collateral circulation bypassing the lymph nodes, in the foot dermal backflow (medial aspect).

In group 3 of 9 patients (7.3%) the contrast medium filled in a retrograde fashion dilated and tortuous lymphatic vessels of the foot, then it proceeded slowly to the wide calf vessels (Fig. 5A). Inguinal lymph nodes could be visualized only after 24 hours. In 6 out of these 9 patients spontaneous peristaltic movements of lymphatics could be seen with naked eye, and also at lymphangiography when droplets of the contrast medium kept moving actively to the upper part of the extremity.

In group 4 of 25 patients (20%) normal lymphatic vessels and lymph nodes were found despite of clinical diagnosis of lymphedema.



Fig. 4A

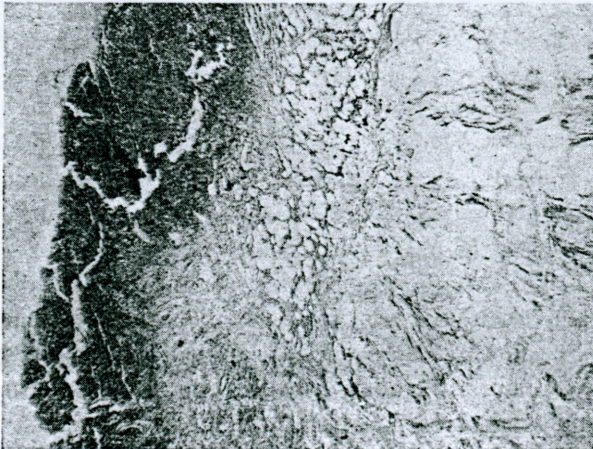


Fig. 4B

Fig. 4 A. Lymphadenogram of inguinal lymph nodes in a patient with obstructive hypoplasia, Angora-like pattern of the node. B. Histological appearance without lymphoid tissue, replaced with connective and adipose tissue. H. E., magn. $\times 250$.

2. Histology of lymphatic vessels and lymph nodes in different groups of lymphedema classified according to the lymphangiographic findings.

In group 1 (the so called aplasia) in 10 patients no lymphatic vessel could be found at the time of dissection for lymphangiography. In all these patients a thoroughful study of skin and subcutaneous tissue from the dorsum of the foot was made. In 4 cases a normally developed lymphatic vessel was found with secondary obstructive changes (Fig. 6).



Fig. 5A

In group 2 (the so-called hypoplasia) in 12 out of 13 specimens of lymphatic vessels no developmental abnormalities of the lymphatic wall could be disclosed. There were, however, secondary changes as intimal thickening, hypertrophy or atrophy of muscular fibers, organization of the lymph thrombi, and partial occlusion of the lumen (Fig. 2B).

In groups 1 and 2 in 14 out of 16 specimens of lymph nodes thickening of the capsule and septa together with atrophy of lymphoid tissue and proliferation of adipose tissue were found (Fig. 4B).

In group 3 in all specimens of lymphatic vessels dilatation of the lumen and hypertrophy of the muscular coat was found (Fig. 5B).



Fig. 5 A. Lymphangiogram of a patient with hyperplasia of lymphatic vessels. Multiple dilated and tortuous lymphatics. B. On histology dilated lumen and thickened muscular layer, H. E., magn. $\times 250$.



Fig. 6. Histological appearance of a lymphatic vessel from the dorsum of the foot of a patient with aplasia of lymphatics. Obstructed lymphatic vessel with fibrous thickening of intima and hyaline changes. All layers of the vessel wall fully developed. Orcein, magn. 250.

DISCUSSION

The at present widely accepted classification of lymphedema based on the lymphangiographic characteristics was suggested by *Kinmonth* (5) in 1957. This classification includes the aplasia, hypoplasia, and hyperplasia of lymphatic vessels. Aplasia of lymphatics is diagnosed in cases where no lymphatic vessel can be found on the dorsum of the foot during surgical dissection following intradermal injection of Patent Blue. It remains obscure whether all or only some of the vessels are aplastic. Hypoplasia is diagnosed when lymphangiography reveals single thin and narrow vessel in the calf and thigh and a small inguinal lymph node. In cases with hypertrophy of lymphatics the vessels are dilated, tortuous and with incompetent valves.

Some authors have modified *Kinmonth's* classification supplementing it with a group of obstructive and non-obstructive hypoplasia. In the first lymphangiography reveals dilated and thin lymphatics in the foot, calf and thigh with single narrow vessel, and in the inguinal region one hypoplastic lymph node. In some cases interlymphatic communicating vessels between the superficial and deep system can be visualized. The dilated lymphatics of the foot, and the communicating channels of the superficial and deep system appear as the result of lymph stasis. In the non-obstructive group there are no dilations of lymphatics and no radiological signs of stasis. A single lymphatic vessel in the calf and thigh is usually found.

In *Kinmonth's* statistics aplasia can be found in 14%, hypoplasia in 55%, and hyperplasia in 24% of cases. Our data are somewhat different with 37.4% for the so-called aplasia. Despite of the commonly accepted term aplasia 4 out of 10 our patients had normally developed but secondarily obstructed lymphatic vessels in the foot. Also in 6 patients lymphangiography performed through a thigh access revealed normal femoral and pelvic lymph vessels although no such vessels could be found on the foot. According to some other our studies when no vessel is found on the dorsum of the foot the medial or lateral retro-malleolar region can be dissected, a lymphatic vessel found and cannulated and lymphangiography performed successfully. All the above described findings speak against the developmental defect of the lymphatics supporting rather the theory of secondary changes in the lymphatic vessels.

The radiological findings in the group of the so-called hypoplasia revealed signs of lymph stasis in at least 50% of cases. This was dilatation of foot lymphatics, and collateral circulation around the inguinal region. Lymph stasis could be the result of mechanical obstruction to the flow at that level. Histology of lymphatic vessels disclosed normal architecture of the lymphatic wall with secondary narrowings or obstruction. Lymphadenograms of the inguinal region resemble those seen after chronic inflammatory changes in the extremity. Histological investigation of inguinal lymph nodes in that group revealed norm-

ally developed structures with some secondary degenerative changes like atrophy of lymphoid tissue and proliferation of fibrous and adipose tissue.

Our experimental studies on the post-lymphangitis changes following streptococcal infection revealed that lymphangiographic and histological patterns obtained in dogs may have some common features with those seen in patients with obstructive hypoplasia of lymphatics of lower extremities.

The hyperplasia group of lymphedema is a quite different entity and should be excluded from the primary lymphedema precox. In all patients of this group dilated and tortuous lymphatic vessels with spontaneous rhythmic contractility of their wall were observed. Histological investigations revealed hypertrophy of the muscular coat without any degenerative changes. Many of these patients had additional inborn changes as skin hemangiomas.

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