Lymphology 16 (1983) 217–222
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Lympho-nodal Fibrosclerosis in Primary Lymphedema
Part One: Considerations on Lympho-nodal Fibrosclerosis in Primary Lymphedema

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Summary

Segments of an inferior inguinal ganglion and of an external iliac (upper inguinal) ganglion were microscopically examined in 46 cases of bilateral primary lymphedema and 26 cases of unilateral primary lymphedema. The examination was performed bilaterally and comparatively to a set of ganglions unaffected by lymphedema, during the years 1974–1978.

In all the lymph nodes originating from the patients with lymphedema important morphopathological alternations were noticed, chiefly consisting in fibrosis, fibrosclerosis, fat loading, hyalinization processes, giganto-cellular responses, etc., leading even to an aspect of cirrhosis, lympho-nodal pseudo-cirrhosis.

These alterations were also found on the healthy side of the patients with unilateral primary lymphedema at the time of the microscopical examination. In the same patient clinical edema appeared in the following years. The degree of the morphopathological alterations was greater in the side of the greater edema and more peculiar in the cases of bulkier edema.

Since 1974 we have watched the morpho-pathological (MP) changes of the inguinal iliac lymph nodes (LN) in female patients with primary lymphedema (PL). We found significant changes consisting in various processes of nodal fibrosclerosis. The tributary lymphatics of these nodes showed important morpho-physio-pathological changes. The results of these studies were the subject matter of some preliminary papers published during the last decade (1, 2, 3).

The lympho-nodal morpho-physio-pathological changes, as well as those of the distal lymphatics make up a reciprocally influencing and determining complex. The clinical results in time, corroborated with the MP changes as well as those of the distal lymphatics make up a reciprocally influencing and determining complex. The clinical results in time, corroborated with the MP changes of the lymphatics and of the LN are the subject of this study.

Material and methods

In 72 cases of PL without any infection in antecedents, two ganglions had been extirpated: one from the inferior inguinal group and one from the external iliac group. The operation had been performed on the occasion of the lymphovenous shunt. These cases may be broken up as follows: 26 with unilateral lymphedema, of which 3 with distal trunkal (unilateral) hyperplasia, and 46 with bilateral lymphedema, cases of unequal volume, of which 9 with bilateral distal hyperplasia (others than the three above mentioned), hyperplasia localized at the shank without proximal surging back from the thigh. (In one case the hyperplasia had extended to the dorsal side of the foot, too.) The other 61 cases had radiological trunkal hypoplasia in various degrees up to superficial lymphatic anaplasia, with the deep lymphatic network becoming opaque by the lymphatic punction at the dorsum of the foot (Fig. 1).

In 23 of these cases (16 with unilateral and 9 with bilateral PL) this operation of LN extirpation was performed during the same morning as the lymphography with ultrafluid Lipiodol. At the same time we extirpated some

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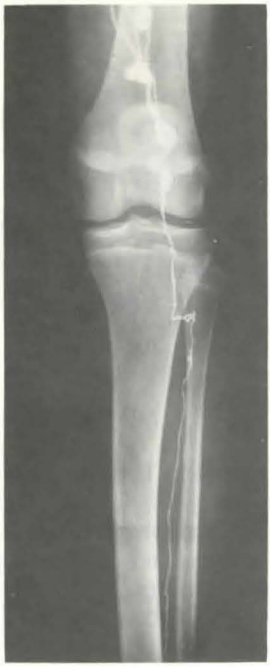

Fig. 1 Lymphangiography in a 13-year-old female patient with unilateral primary lymphedema (it is difficult to find a lymph vessel on the dorsal side of the foot). Only a deep lymphatic was opacified. No superficial lymphatic is visualized

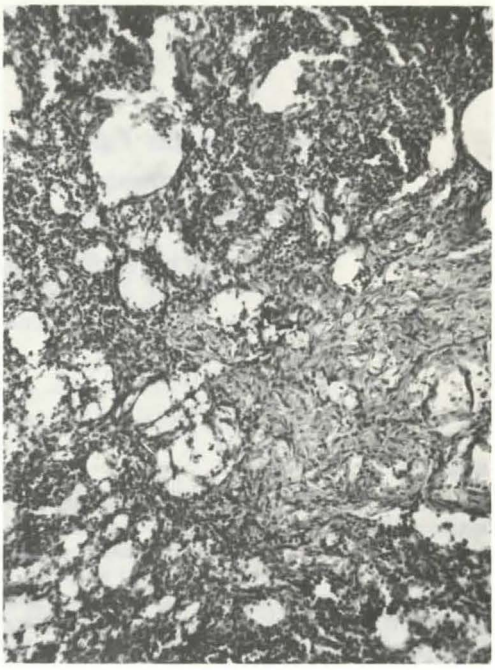

Fig. 2 Microscopical examination (260) of the same patient's ill side: fibrosis, fibrosclerosis, fat loading, hyalinization processes

segments of the lymphatics from the dorsum of the foot, that had been treated in the same manner as the ganglions prepared for examination under the optical microscope. In the other cases the lymphography had been performed previously (one week – 16 months). After the injection of the patent blue V dye no dorso-pedal lymphatic changed its colour in 37 (6 bilateral) legs of the 144 (72 cases). In these cases catheterization and injection of ultrafluid Lipiodol into the lymphatics were not performed. In 19 of these (10 with primary unilateral and 3 with bilateral lymphedema) the lymphography was carried out bilaterally by means of Au 198.

At the same time in all the cases protein analysis, electrophoresis and immunophoresis of the serum (of the lymph in 16 cases, and of the pre- and postganglionary lymph in 9 cases) were performed.

After extirpation the ganglions were examined by touch; the sections were examined with the naked eye and with the magnifying glass. Half of each ganglion was fixed in formol, included to paraffin, cut and coloured with eosin haematoxylene.

In 19 cases fragments of these ganglions were prepared and examined under the electron-microscope.

The patients' age ranged between 8 and 19 years: 4 males and 68 females.

The LN used for comparison were obtained from 14 patients (8 males and 6 females, aged 14–24) without lymphedema, with inguinal or femoral hernia, during surgery of hernia. The lymphatic ganglions were extirpated and processed according to the same technique as for the examination under optical or electron-microscope (in six of the cases).

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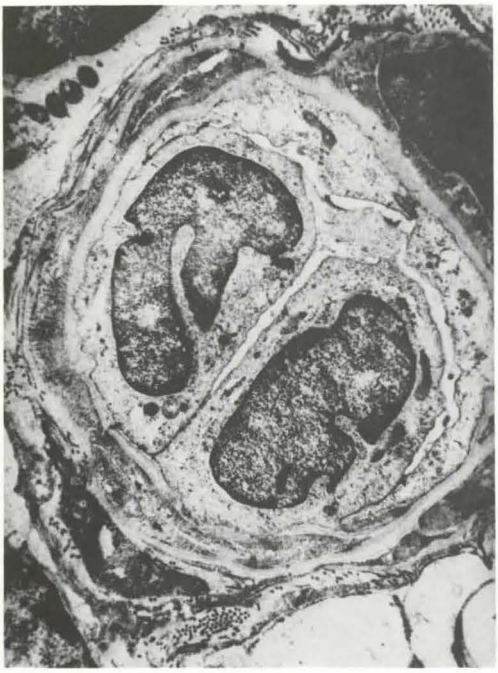

Fig. 3 The electron-microscopical image of the same case: a distinct hypertrophy of the endothelial cells obliterating the capillary lumen

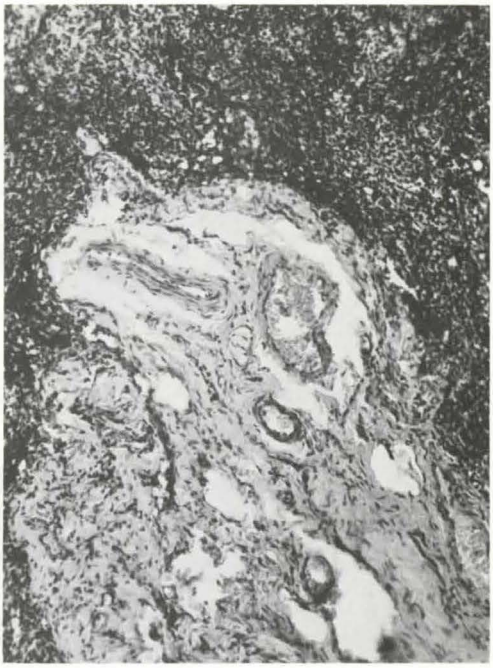

Fig. 4 Microscopical examination of the same patient's edema-free side: fibrosis and fibrosclerosis

We fixed and coloured the dorso-pedal lymphatics in 14 cases of secondary posttumoral lymphedema after lymphography had been performed. The extirpation of LN and lymphatics were made with the patients' consent.

Results

In all the case of PL the lymphatic ganglions had an increased induration and had a more reduced volume with 16–38 % than the patients who had no lymphedema.

In these cases upon examination of the section with the naked eye we found hypertrophy and induration of the medullary area. The cortical had a greasy look, ampler and more extensive aspects than the ones sporadically observed in the cases which had no lymphedema.

Under the optical microscope, in the cases of unilateral PL, on the sick side we found a process of diffuse fibrosclerosis (Fig. 2) which was present on all the sections uniformly distributed with diffuse lipomatosis, with the swelling of the sinusoidal macrophages (Fig. 3), with numerous giganto-cellular rections in the sinusoidal macrophages. No sign or sketch of these processes had been noticed in the iliac ganglions of the patients with no lymphedema. In the inguinal ganglions of the latter we also detected changes consisting in loading with fat (without fibrosclerosis) to a degree of 9–11 per cent.

For this reason we shall insist less on the changes noticed in the inguinal ganglions. However, it is worth mentioning that in the cases of PL the above-mentioned MP changes in the nodes are much more intense than in the iliac ganglions.

The same aspects, the same changes were also noticed on the counterlateral side which was

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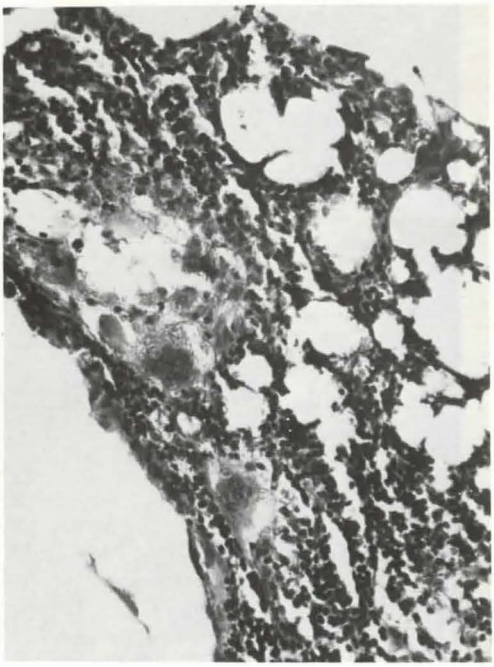

Fig. 5 Giganto-cellular reaction in a female patient with unilateral primary lymphedema

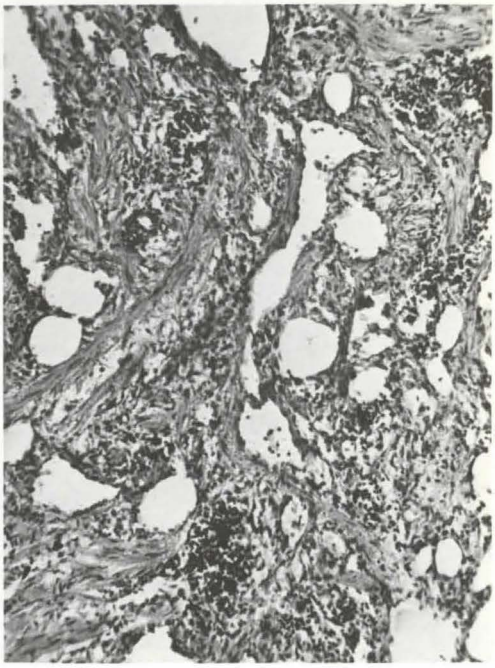

Fig. 6 Microscopical examination; greater diffuse fibrosclerotic processes, hyalinization in a female patient with bulky unilateral primary lymphedema

without edema at that time. These changes had a more reduced intensity, but they were distributed equally on all the sections and on the entire LN area (Fig. 4).

The same changes, i.e. medullar and cortical fibrosclerosis, were found in the female patients of the second group with bilateral PL. Each time we found a direct ratio, a consistency of the intensity of these changes with the clinical evolution of the edema. Thus the MP changes were greater and more extensive on the side with a bulkier edema.

According to the clinical and temporal evolution of the edema we may also classify the above mentioned changes. In the medium size edema we found processes of diffuse fibrosclerosis distributed in the medullar and cortical areas, with a central ganglionary predominance, with foci of lipomatosis and sinusoidal ectasis. These alterations are greater in the cases of intermediary edema. The lipomatosis and the ectasis of the sinusoids may lend the aspect of a honey comb. The sinusoidal macrophages are tumefied by multinucleated giant cell reactions (Fig. 5). The diffuse fibrosclerosis was present in all the cases and on the whole surface of these sections (Fig. 6). In the cases of giant edema the fibrosclerosis is accompanied by more extensive processes of hyalinization, so that the structure of the ganglion seems broken up. In these ganglions the gigantic cellular reactions are very rare in contradistinction to the ganglions originating from the more simple stages. All these ganglions were permeable to and were penetrated by Lipiodol.

In these cases of monstrous edema the Lipiodol hardly penetrates the LN structures. In these ganglions we find processes of diffuse fibrohyalinization with almost complete substitution of the lymphoid tissue by microfoci of

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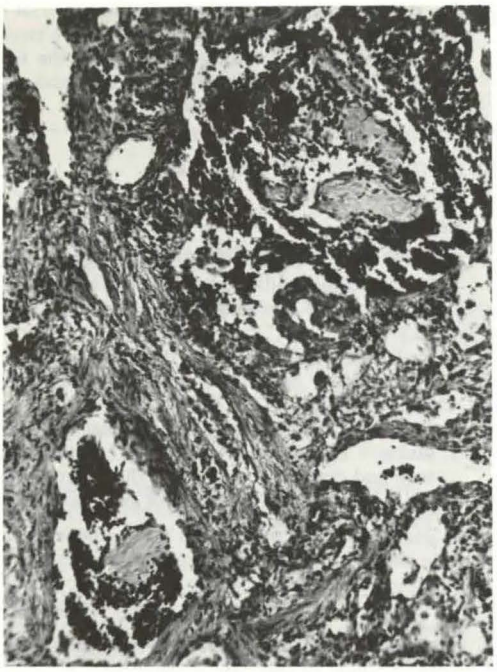

Fig. 7 Advanced fibrosclerotic processes and diffuse fibrohyalinizations, with an almost complete substitution of the lymphoid tissue, microfoci of lymphocytic infiltration in a female patient with monstrous primary lymphedema

Fig. 8 The electron-microscopical image of the same case: substantial fibrosis, lysis of collagen fibres

very frequent lymphocytary infiltration, ectasis of the lumen of sinusoidal vessels, aspects of LN pseudocirrhosis (Figures 7, 8).

In these cases, which had the described LN alterations, we found changes in the walls of the lymphatics at the thigh, at the shank and at the dorsum of the foot. In the cases of PL on the lymphogram at the level of the thigh the alterations are absent, or they are difficult to distinguish from the normal aspects. In the cases of secondary lymphedema the lymphatics of the thigh in the upper third are large, dilated and very numerous, with a collateral flow, while this collateral flow is absent on lymphography in the femal patients with PL. In the patients with PL with the hyperplasia of the lymphatics of the shank, the contractile activity of these lymphatics at the shank is reduced and sometimes it is absent, so that they stay opaque with Lipiodol even after 48–72 hours.

At a microscopic examination the dorsal pedal lymphactics in the cases with hypoplasia show changes of fibrosis and the hyalinization of the tunica media with the proliferation of the endothelium, producing shoots which proliferate in the vascular lumen (Fig. 9).

In the cases of trunkal hyperplasia at the shank the dorsal pedal lymphatics show a more intense fibrosis of the tunica media which is thickened very much by the presence of hypercellulary collagen bands with tumefied endothelium and proliferated in the lumen. In the cases of secondary lymphedema and of posttumoral lymphedema these changes are absent in the dorsal pedal lymphatics.

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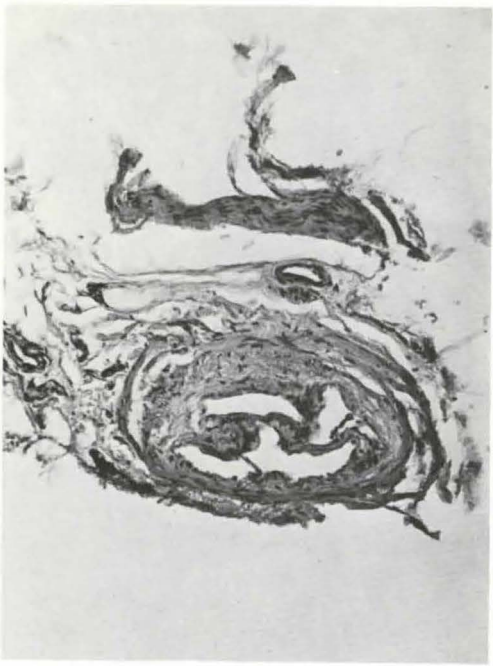

Fig. 9 Microscopical examination – transversal section in the dorsal pedal lymph vessel of the patient in figs. 1–4; fibrosis and hyalinization of the tunica media. proliferation of the endothelium producing shoots plunging into the lumen

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