

Lympho-nodal Fibrosclerosis in Primary Lymphedema Part Two: Consequences of Lympho-nodal Fibrosclerosis on Lymph Stasis in Primary Lymphedema

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Summary

The inguinal-iliac lympho-nodal fibrosclerotic processes appearing in female patients with primary lymphedema bring about an obvious tendency of reduction of the circulatory flux in the afferent lymphatics at some distance from the lympho-nodal area: at the foot or at the shank.

The inguinal lympho-nodal morphopathological alterations (examined in 72 cases of primary lymphedema) were followed, by distal lymph stasis at the level of the foot and of the leg, without sensibly affecting the lymph flow in the thigh. These aspects of the lymph stasis adjacent to the lympho-nodal areas are striking in the patients with secondary lymphedema.

In the topical literature there are sporadic remarks on these changes at the level of the nodes or of the lymphatics (1, 2, 3, 4, 5, 6). Numerous researchers have avoided extracting such nodes in order not to aggravate the evolution of the edema. We had obtained the first fragments of nodes before 1974 from cases in which we had performed shunts of lymphatic nodes to the vein. Later on we extended this morphopathological (MP) examination to the cases that did not change the colour of the lymphatics on the dorsal side of the foot and we performed lymphography by direct nodal puncture also in the cases in which the Servelle operation was carried out. This time we were surprised by the intensity of the existing fibrosclerotic changes and by the lymph-flow consequences that these changes might bring about. We delivered a paper about these consequences at the 1978 Prague Con-

gress (7) when our remarks were based on an appreciable number of investigations. After having made sure that these ganglions extirpated for MP examination were not aggravating the evolution of the edema, we investigated morphopathologically the inguinal iliac nodal chain, discovering the presence of these changes in all the nodes of this chain.

The existence of this kind of fibrosclerosis is certain; it is to be found in all the nodes of the limbs having primary lymphedema (PL) (1, 2, 3, 4, 5,6) and it has characteristics that are different from the nodes of the patients who had several episodes of erysipelas where the hyalinization processes are predominant. These MP changes also differ from those occurring in the inguinal nodes of the patients with postthrombotic syndrome, when hypertrophy with nodal hypercellularity is produced.

At the clinical examination of female patients with PL we may reveal an inguinal microadenopathy having significant hardness, nodes of a more reduced volume on the lymphadenogram.

At the MP examination of the dorsal pedal lymphatics, as well as of those at the leg, in all the cases of lymphedema, we found on obvious fibrosis of the tunica media and the proliferation of the tunica intima without the hypertrophy of the muscular layer, as it had been remarked by other authors (*Kinmonth*) (2, 3).

At the same time one may discuss the different aspects of the dilatation of the lymphatics

cal and electron-microscope in 46 female patients with unequal bilateral lymphedema without infectious inflammation at the date of the examination. In all the cases we remarked a process of fibro-lipo-sclerosis which was more intense, greater and more extensive on the side of the bulkier edema. Since the LN alterations precede the clinical beginning of the edema and since they are greater on the side of the bulkier edema, we think that these alterations determine the evolution of the edema as well as its clinical beginning. On the other hand, it is not out of the question that the presence of the distal edema should have consequences on these LN.

3. Why is it that in some cases a trunkal hypoplasia occurs and that in other cases a distal vascular hyperplasia occurs in the presence of the quasi-identical MP changes of the LN? All the cases of PL that we are referring to reveal an inguinal iliac LN hypoplasia with the above mentioned macro- and microscopic changes. Of the 73 cases of PL that were microscopically examined during the present study, 12 cases had lymphatic vascular hyperplasia. The trunkal hyperplasia was localized at the leg in all the 12 cases and, in one case even on the dorsal side of the foot with a radiologically visible reflux as far as the digital lymphatics. In these vessels of the leg the Lipiodol stagnates for 2–3 days and it can be made to flow in the direction we want by exerting compressions on different points of the legs. In these cases the lymphatics at the level of the thighs have a normal aspect and they are provided with functional valves. The LN are permeable to Lipiodol. If in some cases a delay appears in the opacifying of the ilio-aortic LN, this delay may be due to a prolonged stagnation of a considerable quantity of Lipiodol in the dilated, sinusoid and valveless vessels at the leg.

In the cases of tumoral, post-radiotherapeutical, inflammatory, etc. secondary lymphedema (SL), which are the consequence of the appearance of a LN obstacle or of a trunkal compression in the lymph flow, an obvious dilatation lymphatics in the close vicinity of the obstacle occurs, but only in the presence of a valvular trunkal lymph system with maintained function. These

dilatations do not exceed in diameter the functional capacity of the valvular system because as soon as the trunkal dilatation is greater than the surface of the valves the latter remain open and contractility of the intervalvular system (20) (lymphangions) without the valvular participation and support is ineffective. At the same time we may see some lymphatics by which a collateral by-pass of the circulation can be effected, thus avoiding the LN obstacle. In SL the dilatation concerns the vessels in the upper third of the thigh, while at the leg they have a normal aspect. In the cases of PL the vascular dilatation appears in a small number of cases (17 %) and it occurs distally at the leg far from the lymphographically mechanically-free LN in front of the lymph flow. The difference between the two kinds of vascular dilatation in PL and SL is very obvious, but very difficult to explain in the case of PL. In these cases should there be alterations in the structure of the lymphatics at the level of the shanks with a displasia of the intravascular muscular or nervous tissue? !

The metastatic tumoral localization brings about LN changes that are different from those in PL. They consist in the stoppage of the trans-LN circulation in the case of LN metastases as well as after X-ray therapy, and they determine, as we have already mentioned, a trunkal dilatation in the upper third of the thigh and the opening of the collateral circulation; these aspects become evident on lymphography. Comparatively, in the patients with PL, the circulation through the LN takes place without any obstacle, and the distal lymphatics (plantar, at the shank) are very few and very thin in most of the cases (83 %), the distal intralymphatic resorption being very reduced. The same aspects may be revealed especially on lymphography with Au 198.

The fact that in most cases of PL a distal trunkal hypoplasia appears in the presence of some hypoplastic LN with fibrosclerosis and liposclerosis, the LN that are permeable by the lymph and the contrast dye without the alteration of the lymphatics near the LN make us assume that the secret of this evolution is to be found in these LN. The axillary LN, that were investigated in, or extracted from, those female pa-

in the patients with tumoral lymphedema, or after X-ray therapy (9, 9, 10), when this dilatation is compared to PL. In the case of tumoral invasions the lymph vessels are dilated in the vicinity of the neoplasically invaded lympho-nodal (LN) obstacle. The dilatation is materialized in the opacification of a very numerous lymphatic vascular network, but without reaching a monstrous caliber of these vessel that have valvular continence, which supplies a support to the functional integrity of the intervalvular segments. In the female patients with PL most frequently a hypoplasia of the distal lymphatics appears, but without the possibility of asserting or inferring that this aspect is a consequence of the obliteration of the lymphatics (11, 12). In female patients with PL if a dilatation of the lymphatics occurs, this dilatation is distal, at the leg, far from the nodal area with nodes permeable to Lipiodol (13). In such cases the lymphatics are very large, sinuous, dilated, their diameter reaching 2–3 mm, with an incompetent valvular system without the hypertrophy of the muscular coating that has an obvious fibrosis. Thus these vascular changes in the cases of trunkal hyperplasia and PL are not the consequence of the LN obstacle, but the consequence of the LN and lymph vessel circulatory alterations, the indication of inguinal surgical therapy becoming disputable (13, 14, 15). On the basis of these remarks we may assert that the edema is the consequence of the reduction of the vascular and LN functional capacity in which the fibrosclerotic alterations are to be found (2, 16). The more intense these changes are, the bulkier and with a shorter evolution the edema is, the more intense the MP changes are. These remarks on the regional LN in female patients with PL were revealed many years ago by lymphography with Au 198 (17). These alterations denote a reduction in the capacity of fixing of phagocytosis in the reticular-endothelial LN tissue and a reduction of resorption.

In the femal patients with PL two situations may mainly arise after the injection of the contrast dye. In most of the cases the dye diffuses laterally on the dorsal side of the foot, which is due to the diminishing of the local

resorption; the lymphography of these cases showed a vascular hypoplasia. In the least of the cases were found coloured spots or areas, on the legs, the dissection and catheterization of the dorsal pedal lymph vessels being very easy.

The peripheral lymphatics have a very important natural tendency to atrophy after the ablation of the LN to which they drain, as well as after the reduction of the functional circulatory capacities of the lymphatic nodes (5, 11, 12, 18, 19). The situation which arises in PL may suggest the conclusion that the first aggression occurs on the inguinal iliac lymph nodes and, secondarily, changes appear in the functionality and aspect of the lymphatics.

The presence of MP changes in the LN is certain in the case of PL. These changes consist in various degrees of fibrosis, sclerosis, early loading with fat, aspects that were also mentioned by *Kinmonth, Olszewski* (2, 3), conjunctive proliferative processes leading as far as genuine 'nodal cirrhosis' in which the lymph tissue is isolated in solitary nodes dispersed among the non-tumoral proliferative tissue.

Several questions may appear in connection with these aspects:

1. Do these LN M changes precede or follow PL? — We watched and thoroughly studied 26 female patients aged 5–19 with unilateral PL at the time when they entered our records. Beside other explorations of the lymphatic system, in these cases we performed examinations of the bilateral inguinal LN under the optical and the electronmicroscope. The processes of fibrosclerosis were noticed both on the clinically healthy side and on the edematous one. During the following 2–5 years the edema appeared on the opposite side, too, and in 7 of these cases on the side where it appeared later, the edema being bulkier at this time. These remarks made us think that the appearance of these MP LN changes preceded the clinical beginning of the edema.

2. To what extent do the MP LN changes influence the evolution of the edema or to what extent are they influenced by it? — We carried out investigations of LN under the opti-

tients who had no edema at the upper limb, do not show particular changes when compared to the patients who had no lymphoedema.

The lymph flow is the result of some very complex processes which take place along the lymphatic vessels (20, 21) and especially at the level of the lymph nodes (16). The LN are situated at the confluence points of the lymph streams. Within these LN the lymph is recapillarised in the sinusoid capillary system in a manner that grossly resembles the way in which the blood from the portal vein is capillarised in the liver. During this process, the lymph is subject to numerous transformations concerning mainly its protein and cellular composition. The reduction of the functional capacity, i.e. of processing the lymph in the regional LN, may determine various changes in the distal lymphatics that are tributary to these LN (5, 7, 8, 10, 11).

We had also noticed some changes in the sinusoid capillaries which appear as 'strange body response', sometimes considered as a consequence of the Lipiodol being phagocytosed after lymphography. However, these remarks had also been found in the female patients with PL with an obvious trunkal hypoplasia, which allowed the catheterization of the dorsal pedal lymphatics into which no Lipiodol was injected.

In all the observed cases we found an important increase of gammaglobulin in the serum and the lymph of the patients with PL (7, 13, 23, 24), an aspect to be dealt with in another paper. At the same time we noticed an increase and change in the pattern of the immuno-globulins, more obvious in the post-nodal lymph, closer to the type appearing in the reaction of the rejection of transplant. After general treatment with cortisone (25), that was performed in some of the female patients with PL, lasting improvements appeared after their release from hospital. The good results obtained after the intralymphatic treatments with cortisone support the discovery of these MP changes (25).

The fibrosclerotic changes, and the macrophagous

gigantocellular processes that were observed in the cells of the LN sinusoid capillaries, may underlie some disturbances in the physiology of these LN. The electro- and immunoelectrophoretic changes may find their reason in the above mentioned proliferative processes.

Conclusions

In all the cases of PL, MP LN changes occur; they consist mainly in fibrosclerotic changes. The MP changes are consistent with the clinical evolution of the case, being more important in the more advanced and more critical cases.

The MP changes precede the appearance of the edema. They are absent in healthy individuals. When these MP changes are present in female patients, they may cause and generate edema. These changes are accompanied by physiopathological and MP changes of the lymphatics at the level of the leg and at the dorsum of the foot.

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Editorial Note

These two papers are published because the work has been performed and it is our belief that the information is valuable and that it would be wrong to allow it to be lost. However, this publication does not imply that the Editors necessarily approve of the methods used. Neither should this note be taken to mean that they disapprove; a number of workers, apart from the authors of these papers,

have excised lymph nodes from patients with lymphoedema. Nevertheless, it is our opinion (and that of experts in the field, whom we have consulted) that such a procedure is very likely to worsen the lymphoedema. Hence it should only be performed when the information which will be gained is essential for the correct treatment of the patient.