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"Die-Back" in Primary Lymphedema – Lymphographic and Clinical Correlations

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Summary

Both obliteration and dilatation of distal lymphatics are seen in primary lymphedema but it is only in secondary lymphedema that the lymphographic progression of the disease has been documented. In this retrospective study the same progression was found in 13 out of 20 patients with primary lymphedema. Each of these patients had initial evidence of proximal lymphatic obstruction. In ten patients the lymphangiographic changes were associated with a clinical deterioration of the leg. These findings suggest some urgency in diagnosing those patients that may benefit from a lymph bypass procedure.

Introduction

When the lymph outflow from a limb is arrested by processes giving rise to secondary lymphedema, well documented changes occur in the lymph vessels distal to the site of obstruction.

Danese and *Howard* (1) in a series of patients with post-mastectomy edema, noted progressive dilatation of the arm lymphatics. In some patients with longstanding edema they were unable to find any lymphatics and concluded that these had become obliterated. *Jackson* (2) reviewed a series of patients who had undergone inguinal lymphadenectomy. He found tortuosity of lymphatics with dermal backflow of contrast. In some patients the lymph trunks ended blindly and in others no lymph vessels could be found. He suggested that the lymphatics had become occluded through external pressure from fibrotic subcutaneous tissues. *Battezzati* and *Donini* (3) stated that phatic obstruction is followed by dilatation the lymph capillary plexuses with subseque obliteration of collecting ducts and increas dermal backflow. All these changes have be confirmed by *Kinmonth* (4) who applied th term "die-back" to the progressive atrophy and disappearance of the main lymph trunk

Clodius (5) and *Olszewski* (6) were able to produce lymphatic obstruction in the hind of dogs. Both workers found, from lymph phy, that there was an early dilatation of phatics before clinical swelling was appare They termed this the "latent phase". Whe edema appeared the degree of dilatation in creased. In neither study was die-back or phatics reported despite follow-up period six and seven years respectively.

Pfleger and her colleagues (7) made a hist gical study of the lymphatics in the legs o 900 patients with a variety of conditions, and without edema. In 10% of patients h logical changes were found in the lymph These consisted of 1) perilymphangitis, 2 tatic lymph vessels and 3) closure of the sel lumen by swelling and proliferation of dothelial cells or by organized lymph thr bus.

These reports indicate that an initial dilat of lymph vessels takes place in secondary lymphedema which is followed by progre obliteration brought about by thrombosis organisation following stagnation of lym Many cases of primary lymphedema are to obstruction within abnormal fibrotic

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guinal and iliac lymph nodes (8) and it therefore seems likely that this progressive distal obliteration could also occur in primary lymphedema. Although die-back has been suspected in primary lymphedema there have been no studies to show whether or not it does in fact occur. Progressive obliteration of afferent lymphatics would have important implications within the general context of lymph bypass operations for primary lymphedema. This paper reports a study aimed at elucidating the course of the lymphographic and clinical changes in patients with primary lymphedema of the legs.

Patients and Methods

372 patients who attended our clinic between 1970 and 1978 were the subject of a detailed review reported elsewhere (9). In that series, twenty patients were found to have undergone lymphography on more than one occasion and they constitute the basis of the present study.

The initial lymphogram of each patient was reviewed and allocated to one of three groups "proximal hypoplasia", "distal hypoplasia" or "bilateral hyperplasia" according to our current classification (8). The subsequent lymphographic studies were then compared with the initial ones noting the numbers of vessels shown, their course and calibre, and the presence or absence of dermal backflow. The time interval between the first and subsequent lymphograms was also recorded.

The clinical course of the disease in each patient was determined by out-patient review in addition to previous recorded measurements and clinical photographs. Any evidence of increase in the size of the limb was noted. Documentary evidence of past episodes of cellulitis of the limb was also noted.

Results

Lymphography

The initial lymphograms showed proximal hypoplasia in 13 patients and bilateral hyperplasia in seven. No patient had distal hypoplasia. On the subsequent studies, no change in the lymphographic appearance was found in seven patients. The remaining 13 patients showed definite changes. Seven patients had features indicative of increasing lymphatic obstruction: increased numbers of collateral vessels in groin and pelvis, increased tortuosity and/or increased dilatation of the peripheral lymph trunks and increased backflow of contrast into the dermal lymphatics. A further six patients showed a reduction in the number of lymph vessels (Fig. 1).

Tab. 1 The initial lymphographic classification related to the comparison between first and second study

	Proximal hypoplasia 13	Bilateral hyperplasia 7
No change	4	3
Increasing distension	3	4
Die-back	6	0

Table 1 shows that die-back (decreased numbers of visualized lymphatics) was exclusively associated with proximal hypoplasia. Increasing distension was almost equally divided between proximal hypoplasia and bilateral hyperplasia.

The mean time interval in months between first and second study in each group were (with range): – no change 21.4 (1–96); increasing distension 43.3 (1–80); die-back 35.8 (5–84).

Clinical course related to lymphographic findings

Table 2 shows that where the lymphograms were unchanged, five of the seven patients did not experience any clinical deterioration. When the second lymphogram showed evidence of increasing distension or die-back, ten of the thirteen patients experienced worsening of the limb swelling. None of the twenty patients were recorded as having experienced any episodes of cellulitis.

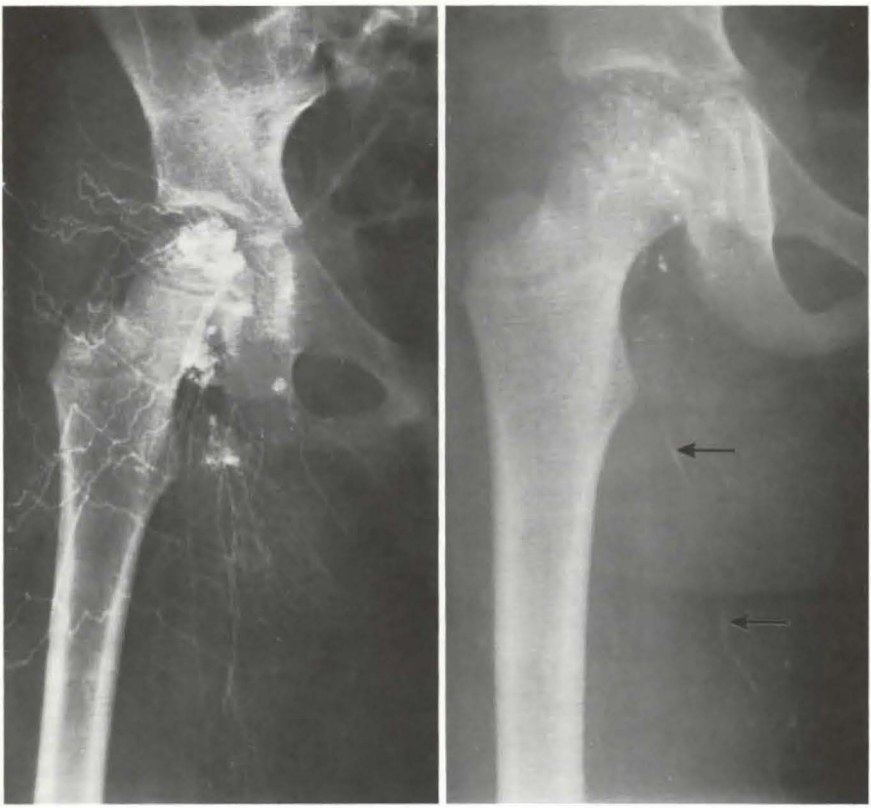

Fig. 1 Patient N.G., aged 6. Three year history of swelling of the whole of the right leg. First lymphangiogram (left) shows a severe obstruction in the inguinal region with multiple collateral pa ways. In a repeat study nine months later (right), only a single afferent lymphatic was shown after infu of the same volume of contrast (arrows). Residual contrast from the first study can still be seen in the g

Tab. 2 The clinical course related to the comparison of first and second lymphogram

Lymphogram	Clinical state: Static	Clinical state: Deterioration
Static	5 (71 %)	2 (29 %)
Deterioration	3 (23 %)	10 (77 %)

Discussion

Most patients with primary lymphedema can be managed adequately by conservative means and only those with gross incapacitating swelling require operative treatment (9). All twenty patients in this study had fairly severe ly edema and the second lymphogram was c ried out in order to assess suitability for gery. This indicates that these patients ar presentative of the more gross manifestati of the disease and explains the absence o patients with distal hypoplasia from the The latter is associated with mild edema Therefore the findings in the present gro cannot necessarily be applied to the who range of lymphedema patients.

Proximal hypoplasia is associated with fi draining lymph nodes and bilateral hype with an abnormal thoracic duct (8). All patients therefore had proximal obstruct

the flow of lymph. We have shown that this obstruction can lead to changes identical to those seen in secondary lymphedema.

Although it is likely that die-back is preceded by a stage of vessel dilatation, this is not supported by our data which in fact show a shorter mean elapsed time between the first and second lymphogram in the die-back group. However, the initial lymphograms would have been carried out at differing stages in the progression of the disease thus rendering strict comparisons between cases untenable. Furthermore, it is likely that the rate of progression is determined at the outset and varies between patients.

There is a theoretical possibility that the presence of Ultrafluid Lipiodol (UFL) within the lymph system could give rise to an impairment of lymph transit by an adverse effect on nodes and vessels. However, there exists no substantiating evidence in favour of this proposition. On the contrary, in two studies, one clinical and one experimental, on the long term effects of UFL on lymph nodes (10, 11) no irreversible histological changes were found. In the present series, seven patients showed no increase in limb swelling or change in radiographic appearances, at a mean of 21.4 months after the initial examination. This group included one patient in whom there was prolonged retention of UFL in the lymphatics because of proximal obstruction. Thus, disappearance of lymphatics cannot be ascribed to a postulated irritant effect of the contrast medium.

Nor may infection be invoked as a cause of the "die-back" of lymphatics (12) since in no patient had the lymphedema been complicated by cellulitis.

Conclusion

In obstructive primary lymphedema, atrophy or "die-back" of peripheral lymph trunks may occur secondary to obstruction in inguinal or iliac nodes, in the same way as is known to happen in secondary lymphedema. These changes are associated with an increase in the limb swelling in the majority of patients. It therefore follows that the success of any bypass procedure in primary lymphedema (13, 14, 15) depends upon early intervention before it becomes compromised by an inadequate number of remaining afferent lymphatics.

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