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Proximal and distal patterns: Different spreading patterns of indocyanine green lymphography in secondary lower extremity lymphedema

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Summary *Background:* As a clinical evaluation of secondary lymphedema of the leg, indocyanine green (ICG) lymphographic assessment has established its usefulness. In this study, we analyzed the ICG findings of patients with secondary lymphedema of the leg, focusing on the location and spreading pattern of dermal backflow (DBF).
Methods: Between April 2013 and June 2015, we investigated ICG findings performed on 90 patients with secondary lymphedema of the leg following malignant cancer resection. The patients comprised 88 women and two men; ICG lymphography was performed 12—24 h after the injection.
Results: Of the 90 patients, ICG lymphographic DBF was evident in 64 from the proximal region of the leg, termed as the proximal pattern. Of the 90 patients, DBF was found to appear in 18 patients mainly in the distal part of the leg, termed as the distal pattern.
Conclusions: In the proximal pattern, the ICG injected into the distal part of the leg propelled to the proximal part, but an obstruction after lymphadenectomy caused ICG pooling to appear first on the proximal side. In the distal pattern, the lymphatic system hypoplasia of the leg may have already been present, and lymph node dissection might be the only trigger for the development of lymphedema. This classification may reflect the pumping function and preexisting hypoplasty of the lymphatic vessels, and provides a novel approach for the pathological evaluation of lymphedema. Patients with proximal pattern on ICG lymphography may well indicate lymphaticovenous anastomosis.

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Introduction

Lymphedema occurs when lymph accumulates in the subcutaneous interstitium. The accumulation of protein-rich lymph causes inflammation, adipose tissue hypertrophy, and fibrosis, which not only causes cosmetic problems but also reduces mobility and function.[1] As the condition becomes more severe, cellulitis often develops, which in the worst-case scenario can lead to the development of fatal lymphangiosarcoma. Lymphedema is classified as primary or secondary depending on the cause: The former is believed to be due to lymphatic vessel hypoplasia, and the latter owing to obstruction of the central lymphatic system because of infection, cancer surgery, radiotherapy, or other causes.

Lymphedema is treated either surgically or conservatively. Surgery is carried out with the aim of either removing edematous tissue or restoring lymphatic vessel function. In the former case, fat resection or liposuction may be used, while, in the latter, lymphaticovenous anastomosis (LVA) or lymph node transfer may be performed.[2–4]

The methods commonly used to assess the severity of lymphedema include lymphoscintigraphy, magnetic resonance (MR) lymphography, and indocyanine green (ICG) lymphography. Lymphoscintigraphy has the advantage of providing wide-ranging images of the entire leg, but it is less useful for detailed evaluation.[5,6] Similarly, MR lymphography enables the assessment of the entire affected limb without the need for radiation exposure or drug administration, but it does not allow lymphatic vessel function to be monitored in real time.[7] ICG lymphography enables the real-time assessment of lymphatic vessel function and can be used in lymphatic vessel surgery. It is minimally invasive and accurately reflects the severity of lymphedema.[8–10]

ICG lymphography has been used previously to assess the severity of lymphedema.[8–10] In secondary lymphedema of the leg, following cancer surgery, dermal backflow (DBF) pattern occurs in the groin initially, and this descends to the thigh and lower leg; the DBF pattern may also change in tone to stardust or diffuse. In this study, we analyzed the ICG findings of patients with secondary lymphedema of the leg, and found that the findings can be broadly divided into two types according to the location of DBF. We describe these as proximal and distal patterns. This classification reflects the pumping function of the lymphatic vessels and provides a novel approach for the pathological evaluation of lymphedema. It may also be useful as an index for predicting the effectiveness of LVA.

Patients and methods

Between April 2013 and June 2015, we investigated ICG findings of 90 patients with secondary lymphedema of the leg following malignant cancer resection. This study was approved by the institutional review board of the University of Tokyo Hospital and was carried out retrospectively. Detailed patient information, including etiology, is listed in Table 1. The mean age was 59 years, and the mean duration of lymphedema was 4 years. The patients comprised 88 women and two men with a mean body mass index (BMI) of 24.2. The underlying disease was cervical cancer in 46 cases, uterine cancer in 28, ovarian cancer in 10, and prostate cancer, penile cancer, colorectal cancer, uterine sarcoma, Paget's disease of the vulva, and malignant lymphoma in one case each. Radiotherapy was administered in 37 patients, while 65 patients had a history of cellulitis. In terms of the International Society of Lymphology (ISL) staging, 28 legs were stage 0, 29 stage 1, 93 stage 2, and 30 stage 3.

Table 1 Characteristics of patients.

No. of cases	90
No. of limbs	180
Average age (range), yr	59
Sex	
Female	88
Male	2
No. of bilateral lymphedema cases	46
No. of unilateral cases	44
Etiology	
Cervical cancer	46
Uterine body cancer	27
Ovarian cancer	10
Others	6
Average duration of edema, yr	5.9
Average duration of compression therapy, yr	4.5
Radiation therapy	
Yes	37
No	53
History of phlegmon	
Yes	65
No	25
ISL lymphedema stage	
0	28
1	29
2	93
3	30
ICG location	
Proximal pattern	64
Distal pattern	18
Mixed pattern (proximal and distal pattern)	8

ICG lymphography was performed as follows: 0.2 ml of ICG (Diagnogreen 0.25%; Daiichi Pharmaceutical, Tokyo, Japan) was injected subcutaneously into both lower extremities at the first web space of the foot and the lateral border of the Achilles tendon. Imaging was performed using a Photodynamic Eye (Hamamatsu Photonics, Hamamatsu, Japan) 12—24 h after the injection. ICG lymphography images were recorded at a plateau phase of the lymphography. The diagnosis of ICG lymphographic patterns, proximal or distal, were made by plastic surgeons trained in lymphedema treatment.

Results

A pattern of fluorescent contrast from the proximal region on ICG lymphography was evident in 64 of the 90 patients. This type was termed the proximal pattern. Cases in which DBF was evident in the entire leg were also classified as