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SHORT COMMUNICATION

Oedema in obesity; role of structural lymphatic abnormalities

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Oedema is a common finding in obesity and its cause is not always clear. Possible causes include impairment of cardiac, respiratory and/or renal function, chronic venous insufficiency and lymphatic problems. Lymphoscintigraphy is the best method to detect structural lymphatic abnormalities that can cause lymphoedema. We reviewed 49 female subjects with pitting oedema who had undergone lymphoscintigraphy, divided in three groups. The first group was comprised of severely obese patients in whom cardiorespiratory causes for oedema had been excluded. The second group consisted of non-obese patients with recognized causes for oedema and the third group was non-obese patients with 'idiopathic' oedema. A standard classification was used to interpret lymphoscintigraphy results. The frequency and severity of lymphoscintigraphic abnormalities was greatest in patients with clinical diagnoses of oedema related to 'recognized causes' (any abnormality in 50% of legs with obstruction in 22%). Obese patients and those with 'idiopathic'oedema had fewer ($P=0.02$ for both) and milder lymphoscintographic abnormalities (any abnormality 32 and 25%, respectively, obstruction 5 and 3%, respectively), and although the clinical oedema was invariably bilateral, the lymphoscintigraphy abnormalities were usually unilateral. In conclusion, structural lymphoscintigraphic abnormalities are uncommon in obesity and do not closely correlate with the clinical pattern of oedema. *International Journal of Obesity* (2011) **35,** 1247–1250; doi:10.1038/ijo.2010.273; published online 25 January 2011

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Introduction

Oedema is much commoner in obese compared with lean age-matched subjects[1] and can be marked.[2] Much of the extra oedema is due to cardio-pulmonary and renal disease, but formal cardio-pulmonary tests are not abnormal in the majority of patients.[3–5] Some oedema in obesity may be because of lymphatic abnormalities,[6,7] but this has not been extensively studied. Lipoedema is a specific, recognized cause of bilateral enlargement of the legs in obesity[8] because of abnormal deposition of subcutaneous fat, but there is debate as to its definition and cause,[8] and it has several clinical features distinguishing it from lymphoedema.[8,9]

Lymphoedema means oedema due to lymphatic dysfunction. It may be subdivided into primary or secondary: primary lymphoedemas include the congenital type (for example, Milroy's disease). Secondary lymphoedema may be due to obstruction of the lymphatic vessels (malignant infiltration, infection or radiotherapy) or lymphatic interruption (for example, surgery).[10–12]

Lymphoscintigraphy, introduced in 1953, is the standard method for evaluation of lymphatic structural abnormalities. It is relatively non-invasive, well-tolerated and technically simple to perform.[13,10] The results generally correlate with clinical severity,[13] provide diagnosis within 3 h, and guide therapy.[14,11] Several studies have reported a specificity of 100% and sensitivity values in the range 90–95% (see refs. 14–17) Lymphoscintigraphy can identify various patterns of lymphatic obstruction.[14,11,18] Abnormal lymphoscintigraphy is a predictor of response to treatment.[12,19] An authoritative review[7] regarded oedema in morbid obesity as 'a condition worthy of special consideration' and showed examples with and without abnormal lymphoscintigraphy. However, studies examining the value of lymphoscintigraphy have not specifically considered severely obese patients.

We reviewed recent lymphoscintigraphs on patients with pitting oedema of the lower limb in whom cardiorespiratory causes had been excluded. We hypothesized that: (a) lymphoscintigraphy would correlate with clinical findings in obesity (b) patients with other known causes, such as previous deep venous thrombosis and pelvic surgery, would show the consistent changes reported in previous studies.

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Patients and methods

Patients

Patients from the obesity clinic with oedema underwent cardiorespiratory evaluation, including sleep studies and echocardiography (usually trans-esophageal). In those with moderate/severe pitting oedema (typically bilateral to the knee, occasionally above) and no evidence of cardiorespiratory disease, we undertook lymphoscintigraphy. Lipoedema was excluded on clinical grounds.

We compared the obese patients with others undergoing lymphoscintigraphy in our Nuclear Medicine department.

We identified 82 subjects with pitting oedema, who underwent lower limb lymphoscintigraphy after clinical assessment at a vascular surgery, lymphoedema/dermatology or obesity clinic. Patients with oedema clearly related to malignancy or its treatment were excluded as these causes are usually easily distinguished from the oedema of obesity. As the vast majority was female, we excluded the eight men from this study. We excluded those with rare conditions, such as lymphangioleiomyomatosis, Milroy's disease and renal transplant, and also those known to have multiple causes for oedema (for example, previous deep venous thrombosis and obesity). This left a remainder of 49 patients described in Table 1. Further clinical information on the patients (co-morbidities such as diabetes and hypertension) and medication taken is available from an archived file lodged with the publisher.

The subjects were classified clinically into: (1) severely obese, (2) oedema secondary to recognized causes such as previous surgery for benign conditions (for example, joint replacement) and/or venous disease and (3) 'cyclical' or 'idiopathic' oedema. These latter diagnoses were sometimes reached by exclusion (although lymphoscintigraphy was not part of the exclusion process).

Lymphoscintigraphy methods

In all, 20 mBq of Tc99m labelled NanoColloid in a 1 ml shielded syringe were injected subcutaneously into the interdigital web spaces between the second and third toes, on both feet, creating a wheal. The volume of each individual injection did not exceed 0.3 ml. A Siemens (Camberley, UK) E-Cam gamma camera with a low energy all-purpose collimator was used. An immediate image was acquired over the injection site for 200 s on a 64×64 matrix. After 30 min, anterior images were taken of the injection site, knee (popliteal lymph nodes) area and groin (inguinal lymph nodes) area. Further images were sought at 60 and 180 min after injection; again including the injection site, knee (popliteal lymph nodes) area, inguinal lymph nodes and in addition, the abdomen (for liver activity). However, if the tracer clearance was slow, these time-intervals were adjusted as appropriate.

Lymphoscintigraphic classification

Lymphoscintigraphic findings were classified according to Scarsbrook *et al*.[10] as showing: (1) normal rates of lymphatic flow (good definition of the deep lymphatic pathways and prompt uptake by the inguinal lymph nodes at 30 min), (2) delayed flow in normally distributed deep lymphatic channels (no radioactivity in the inguinal lymph nodes at 30 min, but apparent later), (3) complete obstruction (activity confined to injection site), (4) subdermal flow or appearance of collateral vessels. Subdermal flow could be found with either normal or delayed flow.

Statistics

We used non-parametric statistics (χ^2-tests) to compare the frequency and severity of lymphoscintigraphic abnormalities in the different diagnostic groups. A probability value of 0.05 was considered significant.

Results

The ages and clinical diagnoses of the patients are shown in Table 1. All the obese subjects had a body mass index of $>35\,kg\,m^{-2}$. Subjects in the 'recognized causes' or 'idiopathic/cyclical' groups all had body mass indices $<30\,kg\,m^{-2}$.

Table 2 summarises the lymphoscintigraphic results from the different groups.

Table 1 Diagnoses, ages and BMI of patients included

Group	*Number*	*BMI kg m^{-2}*	*Age*
Severe obesity	22	49.4 ± 10.4	44.4 ± 11.2
Recognized causes	9	26.8 ± 5.0	45.8 ± 16.5
Previous pelvic surgery	3	27.9 ± 2.6	41.7 ± 5.2
DVT only	3	27.1 ± 6.1	44.9 ± 7.2
Joint replacement with DVT	2	24.9 ± 9.8	73.0 ± 2.0
Joint replacement	1	25.9	42.0
Idiopathic/cyclical oedema	18	25.9 ± 4.7	37.0 ± 10.7

Abbreviations: BMI, body mass index; DVT, deep venous thrombosis.
Values are means ± s.d.

Table 2 Lymphoscintigraphic findings in different clinical groups

Group	*Normal lympho-scintigraphy (%)*	*Delayed flow on lympho-scintigraphy (through deep vessels) (%)*	*Obstructed flow on lympho-scintigraphy (%)*	*Subcutaneous flow on lympho-scintigraphy (%)*
Obese	30/44 (68)[a]	8/44 (18)	2/44 (5)[a]	4/44 (9)
Recognized causes	9/18 (50)	5/18 (28)	4/18 (22)	0/14 (0)
Idiopathic/cyclical oedema	27/36 (75)[a]	5/36 (14)[a]	1/36 (3)[a]	3/36 (8)

Values are numbers of legs in each category. For definition of each lymphoscintigraphic category please see text.
[a]Indicates values different between recognised causes and other groups by χ^2, $P<0.05$.

Every patient in the 'recognised causes' group had abnormal lymphoscintigraphy in their (more) oedematous leg (9 out of 18 legs, $P=0.02$ cf other groups). Complete obstruction was more commonly seen in this group (4 of 18 legs, $P=0.02$, cf other groups). Clinically in this group, six patients had a non-oedematous leg, whereas three had asymmetric oedema. In this group, the side of most oedema always matched the side of the lymphoscintigraphic abnormality.

In all obese patients, the clinical oedema was bilateral. Despite this, 10 patients had normal lymphoscintigraphic findings and among the 12 obese patients with abnormal lymphoscintigraphy, it was unilateral in 10. Only 2 out of 40 oedematous legs showed complete obstruction in the obese group, delay (with normal distribution of vessels) being the more frequent finding. The idiopathic/cyclical oedema patients were also clinically bilateral, but again the lymphoscintigraphic abnormalities were usually asymmetrical and involved delay (5 out of 32 legs) rather than obstruction (1 out of 32 legs). The frequency and severity of lymphoscintigraphic abnormalities in the obese and the idiopathic/cyclical oedema groups were similar (14 out of 44 legs and 9 out of 36 legs, respectively). Subdermal flow was seen in both obesity (4 out of 40 legs) and idiopathic/cyclical (3 out of 32 legs). In both groups, subdermal flow could be found with either normal rates of flow or with delayed flow.

Discussion

This is the first study to consider lymphoscintigraphic findings particularly in obese patients. All three groups showed a variety of abnormal lymphoscintigraphic patterns. In the group with recognized causes of oedema, most patients had unilateral oedema with 'concordant' lymphoscintigraphic abnormality. In the remainder, the lymphoscintigraphic abnormality was on the side of the more oedematous leg. In the obese group, all subjects had bilateral oedema, but 10 patients had normal lymphoscintigraphy and another 10 had only unilateral lymphoscintigraphic abnormalities. The idiopathic/cyclical oedema group showed a range of lymphoscintigraphic appearances from normal to complete obstruction. Again lymphoscintigraphic changes were rarely symmetrical despite bilateral clinical oedema. The obese and idiopathic/cyclical groups were similar in both frequency and asymmetry of lymphoscintigraphic changes, which were generally discordant with the clinical findings. Discord between clinical findings and lymphoscintigraphy is recognized as occurring in general patients,[13] but only a single case report specifically links this to morbid obesity.[6]

Our findings in obesity is at variance with previous studies suggesting lymphoscintigraphic specificity and sensitivity above 90% (see refs. 14–17). This may be because our study excluded subjects with clear-cut clinical diagnoses (for example, excluding cancer-related lymphoedema) or those with multiple factors (for example, obese subjects with history of venous thrombosis). The lack of lymphoscintigraphic abnormality in the obese group may be because of weaknesses in our lymphoscintigraphy method. This seems unlikely in view of the results in the 'recognized causes' group. More plausible is that the oedema in obese patients is not related to structural changes. Isotope lymphoscintigraphy does not give an absolute measure of lymphatic flow and is more effective at detecting structural lymphatic changes.

Our study suggests that the oedema seen in obese patients is usually 'functional' rather than a 'structural' lymphoedema. Oedema in general can be classified into 'high flow' and 'low flow' causes. High flow oedema is a feature of conditions such as nephrotic syndrome in which an increased lymph production rate at the capillaries overloads a normal lymphatic transport system. One might well expect that morbid obesity (which is associated with hyperfiltration in the kidney[20]) and raised venous pressure (for example, from raised intra-abdominal pressure) could produce a 'high flow' oedema. Local venous insufficiency would also contribute to high-lymphatic flow and oedema. Conversely, lymphatic blockage (often by surgery associated trauma) or cellulitis can cause a 'low flow' oedema. Methods of distinguishing high-lymph flow and low-lymph flow might help understand the pathophysiology(ies) of oedematous obese patients.

In conclusion, our study reveals that in oedematous obese subjects, once cardiorespiratory and obvious local causes have been excluded, lymphoscintigraphy shows abnormalities in about 35% of swollen legs. This suggests that lymphatic damage (possibly related to previous cellulitis) is not uncommon, but usually causes delayed drainage at most. Structural lymphatic abnormalities, detectable by lymphoscintigraphy are unusual in obesity and bilateral changes were very uncommon, suggesting that lymphoscintigraphy will rarely help in management.

Conflict of interest

The authors declare no conflict of interest.

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