Lymphoedema in bariatric patients

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Obesity continues to rise in Western and developing countries and the prevalence of morbid obesity in the US has reached 5% (Arterburn et al, 2005). Obesity is linked to leg oedema, and morbid obesity certainly appears to be a factor in the development of chronic venous insufficiency (CVI), a condition seen in many patients with secondary lymphoedema. It is also becoming clearer that the association between obesity and lymphoedema is two-way: obesity being a risk factor for lymphoedema, while the condition itself predisposes individuals to become obese, thus creating a vicious feedback loop.

Key words

Morbid obesity
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Leg oedema among the obese is almost ubiquitous by clinical observation, but conspicuous by its absence in papers discussing management of obese patients. However, a number of questions arise with regard to the aetiology of oedema in those who are suffering from obesity. For example, does chronic venous insufficiency (CVI) and its accompanying oedema raise the odds of having lymphoedema? (The mechanism of CVI in obesity is thought to be related to reduced venous return from obstruction by abdominal fat, reduced calf muscle pumping resulting from inactivity, changes in Starling forces due to increased blood pressure and capillary filtration, increased dependency resulting from limited mobility, and the frequent comorbid condition of sleep apnoea requiring patients to remain upright at night.) Is obesity itself the most important risk factor for developing lymphoedema among the obese population (and therefore the level of obesity), or is it a question of encountering a 'triggering' type of event for a patient that has certain genotypes, whom we might describe as having chronic subclinical lymphoedema? Furthermore, does having lymphoedema increase the odds of becoming obese, which then worsens the situation?

In attempting to answer these questions, it is worth first noting that oedema in patients who are obese is a clinical spectrum that has been poorly defined in the literature. We often think of the typically obese patient as one who sits most of the day, overeats, takes little exercise, and suffers from oedema of dependency. Using the body mass index (BMI) as an indicator of the degree of obesity severity, overweight is defined as 25.0–29.9 kg/m^2, obese as ≥30 kg/m^2, and morbidly obese as ≥40 kg/m^2. In a recent survey of 18,584 non-institutionalised individuals aged ≥50 years (the Survey of Health, Ageing and Retirement in Europe [SHARE] study), using normal BMI individuals as a reference, Peytremann-Bridevaux and Santos-Eggimann (2008) found that overweight men and women had an adjusted odds ratio (OR) of 1.8 and 1.9 respectively for self-reporting swollen legs. However, the OR for self-reporting swollen legs in men and women who are obese was 5.0 and 4.4, respectively. Not only are these results the beginnings of a weight-dependent relationship, but of all the self-reported disease conditions and health complaints (totalling 29 in number) in the obese category, swollen legs had by far the highest OR. These results should not be surprising; once obesity is attained, higher BMIs lead to less mobility because it takes more effort to carry the extra mass around. Less mobility means less exercise of the calf muscles and potentially poorer venous circulation and lymph return.

Obesity also causes a variety of cardiovascular diseases, the most profound of which is hypertension, as well as microangiopathies (de Jongh et al, 2004). Risk estimates from population studies attribute 55–75% of all hypertension to obesity (Krauss et al, 1998; Pischon and Sharma, 2001). Elevated blood pressure by itself does not necessarily mean the development of oedema, but if the left ventricle is sufficiently stressed by hypertension this can lead to left-sided heart failure and pulmonary hypertension, which will produce bilateral leg oedema (Blankfield et al, 2000). However, if visceral adiposity is exceptionally high, a common occurrence in morbidly obese patients, breathing difficulties and obstructive sleep apnoea can cause periodic hypoxia and leg oedema. For example, a recent

study conducted by Iftikhar et al (2008) suggests that as many as one-third of all individuals suffering from obstructive sleep apnoea have leg oedema, and interestingly tend to be older, more obese, and more likely to have type II diabetes or hypertension, and higher hypoxia.

CVI generally results from ambulatory venous hypertension, or an inability to reduce venous pressure with exercise, and produces bilateral leg oedema. Although there is still some debate regarding exactly how chronic venous hypertension causes CVI, it is thought that a number of inflammatory responses are responsible for the associated skin changes. As this paper is focusing on obese populations, it is reasonable to ask whether obesity is a factor in the development of CVI. A review of environmental factors in the development of CVI suggests that obesity and lack of physical activity are strongly associated with CVI in women, but less so in men (Jawein, 2003). In a retrospective cross-sectional study (including 20 ambulatory patients with a mean age of 62 years, a mean BMI of 52, and a mean weight of 164 kg; 39 limbs under study), Padberg et al (2003) also found that morbidly obese patients had severe symptoms typical of CVI in limbs, but approximately two-thirds of the limbs had no anatomic evidence of venous disease, i.e. duplex ultrasound scan examinations were negative. However, two-thirds of the limbs experienced ulceration and over half of the ulcers recurred over a three-year period after initial healing. Moreover, the association of increasing limb symptoms with increasing obesity suggested that obesity itself contributes to CVI morbidity. Thus, it appears obesity also plays a role, although an undefined one, in the development and severity of CVI.

Lymphoedema is another cause of leg oedema (Ely et al, 2006). In classical differential diagnosis of leg oedema, the healthcare professional studies the clinical picture and attempts to define the aetiology of the oedema, supported by appropriate testing. In the patient who is obese, because leg oedema is common, it can be harder to confirm lymphoedema in the initial stages because the oedema

may be multifactorial. While several studies have been able to delineate an operational definition of lymphoedema in arms following axillary node dissection, or in lower limbs following inguinal or ilio-inguinal dissection for melanoma using classification and regression tree analysis (CART) (volume changes of 16% and 15% respectively, compared to the contralateral limb), these causes of lymphoedema can be seen as 'pure' (Starritt et al, 2004; Spillane et al, 2008). These operational definitions are harder to apply in the obese because oedema may have been long-standing and untreated, and the separate contributions of lymphoedema and oedema due to obesity in leg oedema cannot always be teased out, even if a positive Stemmer's sign is apparent.

When patients present with later stages of lymphoedema, diagnosis becomes much easier. This is because in the advanced stages of lymphoedema, the physical findings of a positive 'Stemmer's sign', fibrosis, and even elephantiasis are so characteristic that the diagnosis of lymphoedema is an easy one to make, even if the exact cause is not clear. However, the presentation of the obesity itself must always be considered. For example, lipoedema, sometimes known as 'fat leg syndrome', primarily affects women and causes deposition of fat around the buttocks and legs but never the feet, which can give rise to a 'pantaloon' appearance (Warren et al, 2007). Its onset is gradual and is often confused with obesity. Additionally, lymphoedema can be absent or present; if present, the condition is often referred to as lipolymphoedema, particularly when the patient is morbidly obese.

Finally, a phenomenon termed massive localised lymphoedema (MLL) can present in the morbidly obese. Originally thought to be rare, case reports are increasingly being reported in the literature (Jensen et al, 2006; Modolin et al, 2006; McCrystal and O'Loughlin, 2007; Asch et al, 2008; Bogusz et al, 2008; Berenji et al, 2009), which parallels the overall increase in incidence of morbid obesity in Western nations in recent years. Originally described by Farshid and Weiss (1998), histological findings

of MLL enable clinicians to differentiate this phenomenon from its cousin, liposarcoma. Typically it appears in the lower limbs, but abdominal, suprapubic, and inguinal sites are not uncommon. Masses are typically large with a mean weight of 7kg, although masses exceeding 20kg are not uncommon. Morphologically, these fibro-fatty masses show dermal sclerosis with prolific ectatic lymphatic vessels intertwined with chronic inflammatory cells and interstitial oedema (Bogusz et al, 2008). While the exact cause of MLL remains a mystery, it is thought that the presence of a massive amount of adipose tissue can result in lymphatic obstruction, ectasia, and the reactive changes visualised in pathological findings (Bogusz et al, 2008).

Thus, a broad spectrum of oedematous conditions can be seen in bariatric patients from which true lymphoedema has to be carefully identified.

Mechanisms of lymphoedema

Lymphoedema is traditionally differentiated in two ways: primary and secondary. Primary lymphoedema has an estimated incidence of approximately one in 6,000 individuals, and is more prevalent in females than males (Swirsky et al, 1998). It is genetically mediated and has been defined according to the age of onset, with congenital defects (sporadic or familial) appearing by the age of one year, lymphoedema praecox between the ages of one and 25 years, and lymphoedema tarda after the age of 35 years. However, this time-related classification is becoming obsolete, as we better understand how the nature of lymphatic defects become clinically apparent. Development of the lymphatic system (lymphangiogenesis) proceeds parallel to angiogenesis, and its mechanisms are similar although there is some overlap. The Prox1 homeobox is the master gene controlling the signalling responsiveness of designated cells to vascular endothelial growth factor C (VEGF-C), which binds to VEGFR-2 (and VEGFR-3 receptors), as well as Syk and SLP-76, which are haematopoietic signalling proteins that cause cells to become involved in either the lymphatic or vascular systems (Rockson, 2009).

The familial form of the congenital type is called Milroy's disease, and in some individuals is linked to autosomal inheritance mutations in the VEGFR-3 gene (more accurately termed the FLT4 gene) (Kerchner et al, 2008). The result is small or absent lymphatic vessels and lymphoedema that affects both legs, but can also affect the arms and face.

During recent years, searches for other genes associated with primary lymphoedema or other genetically-based syndromes in which lymphoedema is a component have revealed tantalising results. For example, truncating mutations in the forkhead-related transcription factor FOXC2 lead to lymphoedema and distichiasis, an additional row of eyelashes originating from the meibomian glands (Fang et al, 2000; Finegold et al, 2001), and homozygous missense/heterozygous nonsense mutations in SOX18, a transcription factor belonging to the SOX gene family that encodes for transcription factors required in pleiotropic developmental processes, cause hypotrichosis (no hair growth), lymphoedema, and telangiectasia, the development of small dilated blood vessels near the surface of the skin (Irrthum et al, 2003). Several other candidate genes have been recently identified, including fatty acid binding protein (FABP4), neuropilin-2 (NRP2), SOX17, and vascular adhesion molecule 1 (VCAM1), and the research continues (Ferrell et al, 2008).

Lymphoedema praecox, often referred to as Meige's disease, usually affects adolescent women, and mostly presents unilaterally in the calf and foot. Although often familial, and the hereditary characteristics of the disease imply genetic involvement, identification of the specific genes involved is still an ongoing process (Ferrell et al, 2008). In the authors' opinion, what precipitates the development of primary lymphoedema is likely to be multifactorial in origin. We can postulate that developmentally, a moderately dysfunctional or weakened lymphatic system is present, but due to the redundancy features observed in normal individuals (i.e. 5–10% of the lymph transport capacity is typically utilised), it is probable that individuals either may not experience any lymphatic problems or any subclinical manifestations go unnoticed. However, when a traumatic event occurs, such as that caused by mechanical injury or burn, or inflammation induced by viral/bacterial infections or stress factors produced by the hypothalamic-pituitary-adrenal axis, focal changes can occur in the lymphatics of one of the lower extremities. This results in localised lymphatic transport overload and lymphoedema (Kerchner et al, 2008).

A provocative question to understanding the phenotype of the patient with primary lymphoedema is to ask how many patients have subclinical lymphoedema as a result of acquired or congenital defects in the lymphatic system. An intriguing study that may provide a window of insight into this question was conducted by Damstra et al (2008). The authors proposed that patients who had cases of erysipelas without any clear precipitating agent might also have underlying subclinical lymphatic dysfunction. Using lymphoscinctigraphy to image both legs after one episode of erysipelas in one leg only, after having excluded other known risk factors for erysipelas, including diabetes mellitus, CVI, or overt signs of lymphoedema, they found that out of 40 patients, 33 had objective lymphatic impairment in the affected limb, and of these patients, 26 (79%) also had impaired lymph drainage in the non-affected leg. This study strongly suggests that the presence of minor or moderate dysfunction of the lymphatic system from acquired or inherited genetic defects may be a lot more common than we think. Moreover, this concept may be crucial to understanding the development of secondary lymphoedema. Rockson (2009) also encapsulates the concept this way: 'More recent attitudes surrounding lymphedema suggest that the boundaries may [be] blurred: primary cases often declare themselves after a ''secondary'' provocation, and evolving clinical data suggest that there may be a genetic predisposition to the development of lymphedema, even when the inciting secondary event(s) are easy to identify'.

Secondary lymphoedema is the result of many different factors that either cause lymphatic obstruction or lymphatic interruption (Kerchner et al, 2008). In the developing world, lymphatic filariasis due to the nematode *Wuscheria bancrofti* is still the most common cause (Kerchner et al, 2008), while in industrialised nations malignancy, and sequiturs of treatment, such as radiotherapy and surgery, particularly radical lymph node dissection, are the most common causes (Kerchner et al, 2008). Other common causes include trauma, recurrent bacterial infections, CVI, and thyroid dermopathy, which leads to pretibial myxoedema (Ely et al, 2006; Kerchner et al, 2008; Kröger, 2008; Mortimer, 2000; Rockson, 2009).

While there may be distinct agents such as nematodes that cause secondary lymphoedema, in many cases we do not know why one patient seemingly at high risk for the condition does not develop lymphoedema and the next patient does. This harks back to our genetic linkage idea and the prevalence of subclinical lymphatic system defects. If these defects are much more common than we think, what other genes could be responsible besides the ones that have been discussed? One clue comes from a genetic study conducted by Finegold et al (2008). By sequencing the exons and flanking regions of the hepatocyte growth factor/high affinity hepatocyte growth factor (HGF/MET) genes in 145 lymphoedema probands, 59 unrelated women with secondary lymphoedema following treatment for breast cancer, 21 patients with lymphoedema and intestinal lymphangiectasia, and 159 unrelated ethnically matched controls, the authors concluded that mutations in the HGF/MET pathway are causal for, or alter the susceptibility to a broad range of lymphoedema phenotypes. This investigation is remarkable for two reasons. First, these mutations are shared by patients with primary or secondary lymphoedema. Second, the patients are a diverse group. Both these points support the contention that certain defective genes may be one common factor in patients with seemingly diverse causes of lymphoedema.

The role of obesity in lymphoedema

It would be interesting to know the relationship of lymphoedema, primary

or secondary, with regard to BMI. This would require assessing BMI and the prevalence of lymphoedema in a cross-sectional survey of the general population, and to date this has not been done. Such epidemiological data might infer an increase in prevalence of the condition as BMI increases. The authors have reported some preliminary data on lymphoedema patients with regard to obesity (Fife and Carter, 2008). For example, whereas only a minority of their primary lymphoedema patients were morbidly obese (7.5%), in contrast, 29% of their secondary lymphoedema patients were morbidly obese (Fife et al, 2008). Moreover, a five-year retrospective review of data from the authors' clinic (2000–2005) showed that 75% of morbidly obese patients had, or have lymphoedema. These data might suggest a connection between a certain level of obesity and the development of lymphoedema, as the prevalence of morbid obesity in the US general population is approximately 5% and rising (Arterburn et al, 2005), with similar situations developing in other Western countries. An ongoing study by Reid (obesity survey with regard to lymphoedema; Peninsula Medical, Inc; available online at http://lymphedema.com/obesity1.htm) also sheds some interesting light. Dividing the patient data into four groups based on weight (means: 133, 175, 224, and 337lbs), it was found that the perceived severity of lymphoedema increased dramatically with weight, despite the observation that in regard to the actual amount of swelling, patients reported far less severity in each weight group, although perceived swelling increased progressively in each weight group. In other words, a patient of normal weight with some swelling perceived the effects were less significant compared to another patient with the same amount of swelling but higher weight. This implies that increasing obesity is associated with increasing debility from oedema, perhaps because the effect of obesity and oedema are additive. In addition, whereas self-reported infection and antibiotic treatment rates were relatively constant for the first three groups, in comparison, they more than doubled in the last group,

Table 1

Demographics of the lower extremity lymphoedema population

Characteristic	n	Value (%)
Age (year)	792	58
Gender (%)	790	
▸▸ Male		36.2
▸▸ Female		63.8
Race (%)	710	
▸▸ African American		32.5
▸▸ Arabic		0.15
▸▸ Asian		0.3
▸▸ Caucasian		64.2
▸▸ East Indian		0.15
▸▸ Hispanic		2.7
Weight (kg)	122	115.7
Height (m)	113	1.72
BMI	113	38.0
Diagnosis of obesity (%)	792	
▸▸ Yes		27.7
▸▸ No		72.3
Obesity type	792	
▸▸ None		72.4
▸▸ Simple		3.3
▸▸ Morbid		1.6
▸▸ Localised*		22.7
Patient ambulatory (%)	792	
▸▸ Yes		62.8
▸▸ No		37.2

NB: The number of patients (n) is different for some characteristics due to available data for each patient.

* 'Localised obesity' is a term used by the International Classification of Diseases (ICD-9) system and in this database means 'lipoedema'

Characteristics of lower extremity lymphoedema patients

Since 1998, the Memorial Hermann Center has maintained all clinical data in an electronic health record (EHR) provided by Intellicure, Inc (The Woodlands, Texas), designed specifically for the documentation needs of wound and lymphoedema patients. These programmes, collectively known as the Intellicure Clinical Documentation and Facility Management Software (ICDFMS), are not only used to manage clinic operations, but to document all aspects of patient medical data, including limb volumes. Using the SQL (structured query language) associated database with the ICDFMS, the authors undertook a retrospective study to assess the relationship between obesity and lower extremity lymphoedema among patients treated at this centre. Thus, to find out more about the characteristics of the authors' patients with lower extremity lymphoedema, all EHRs for patients attending the Memorial Hermann Center for Wound Healing and Lymphedema Management between 1 July, 2003 and 15 June, 2009 were retrospectively analysed. Of 4,826 patients, 4,034 that had either wounds (3,754) or upper extremity lymphoedema (280) were excluded, leaving 792 patients for analysis.

Women made up almost two-thirds of this typical urban population and the racial make-up was reasonably representative of the national population,

Table 2

Comorbid characteristics of the population (n=792)

Characteristic	Value (%)
Venous disease present (%)	
▶▶ Yes	23.5
▶▶ No	76.5
Wound/ulcer present (%)	
▶▶ Yes	31.4
▶▶ No	68.6
Diabetes present (%)	
▶▶ Yes	27.9
▶▶ No	72.1
Antibiotics prescribed during care (%)	
▶▶ Yes	27.4
▶▶ No	72.6
MLL present (%)	
▶▶ Yes	1.3
▶▶ No	98.7

MLL: massive localised lymphoedema

except for under-representation of Hispanics (*Table 1*). A diagnosis of obesity was made in over a quarter of the patients and the mean BMI for the population was 38. Interestingly, over a third of the patients were non-ambulatory.

Comorbid conditions relevant to lymphoedema were common: CVI and diabetes were present in 23.5% and 27.9% of the patients, respectively (*Table 2*). Most surprisingly, 1.3% of patients had MLL. The authors would not categorise this percentage as 'rare', as usually stated in the lymphoedema literature. In the US, the legal definition of rare disorders is <200,000 Americans affected, which is approximately 0.07%; in the European Union, five per 10,000 (0.05%) is the commonly accepted definition (Meyers, 2003). Given that the prevalence of obesity is only slightly higher in the authors' lymphoedema population

compared to the general population (22–24%; Finkelstein et al, 2004), this prevalence of MLL is significant.

In terms of lower extremity involvement, 71.5% of patients were affected bilaterally (*Table 3*), with only a few patients experiencing concurrent lymphoedema in other locations. Several other related conditions were noted from the EHRs that could be involved in the development of lymphoedema. Obesity (31.7%), CVI (24.7%), and cancer (14.7%) were the three most common factors; 'other' factors included chronic heart failure, bites (insect and animal), organ transplantation, and renal failure.

Breast cancer-related lymphoedema

Development of lymphoedema in the arm months to years after surgery with or without adjuvant radiotherapy treatment for breast cancer is unfortunately a common complication with a prevalence of 20–42% (Armer et al, 2004; Mansel et al, 2006). Thus, this model of secondary lymphoedema is a much-studied one. Several investigations have attempted to determine the risk factors involved in developing lymphoedema, and although other factors such as age, a history of hypertension, degree of dissection, previous inflammation/infection were identified as affecting risk, obesity was a risk factor in every study (Hayes et al, 2008; Johansson et al, 2002; Mak et al, 2008; Meeske et al, 2009; Ridner and Dietrich, 2008). Just being obese (i.e. a BMI ≥30) increased the OR to 2.48 (Meeske et al, 2009).

A small randomised controlled study also demonstrated that weight loss in obese patients (BMI: 30–33) who had lymphoedema significantly reduced excess arm volume (percentage of normal arm volume) after 12 weeks (Shaw et al, 2007). In the weight-reduction group, the mean excess arm volume reduced from 24% to 15% (no change in control group).

Genetic involvement

The previous body of data indicates that obesity is intimately involved with both the development and ability to decrease the effects of lymphoedema. But does the mere presence of lymphoedema,

Figure 1. Obese 65-year-old Caucasian woman with venous insufficiency leading to lymphoedema.

Figure 2. Morbidly obese 75-year-old Caucasian woman with lipoedema, secondary lymphoedema, and pitting oedema due to congestive heart failure.

overt or subclinical, increase the risk of being obese or becoming more obese? The surprising answer appears to be yes. Harvey et al (2005) studied the effects of the Prox1 homeobox gene in mice and discovered that haploinsufficient animals, which had the least severe lymphatic alterations, survived to adulthood but became obese. In essence, the authors proposed that Prox1 haploinsufficiency led to abnormal lymph leakage due to disruption of lymphatic vascular integrity, which promoted ectopic growth of fat in lymphatic-rich regions due to

Table 3

Lymphoedema characteristics of the population

Characteristic	n	Value (%)
Lower extremity involvement (%)	754	
▸▸ Bilateral		71.5
▸▸ Left only		14.7
▸▸ Right only		13.8
Involvement of other locations (%)	754	3.8
Related conditions as a possible cause (%)	489	
▸▸ Cancer		14.7
▸▸ CVI		24.7
▸▸ Obesity		31.7
▸▸ Other		13.6
▸▸ Postphlebotic syndrome		4.3
▸▸ Postsurgical complications		5.9
▸▸ Trauma		5.1
Severity of lymphoedema; mean (SD) (Score 1–10)	492	4.37 (2.46)

NB: For lower extremity/other location involvement (n) is patient number; for other characteristics (n) is lower extremity or combined lower extremities

Figure 3. Morbidly obese 52-year-old Caucasian woman with lipoedema resulting in secondary lymphoedema.

increased lipid storage in adipocytes and increased differentiation of preadipocytes to mature adipocytes. In retrospect, this finding should not have been so surprising because chronic inflammation of peripheral lymph nodes in rats increases the number of adipocytes that surround the node (Mattacks et al, 2003), and lymph nodes in mice are most often found in close association with adipose tissue.

The genetics of lipoedema have not been studied but we can speculate that lymphatic system defects, triggered perhaps by hormone changes during puberty, could attract fat deposition to the legs. The major difficulty here is understanding why the pattern of fat deposition should be different to primary lymphoedema in which lymphoedema starts with the feet and moves upward.

Pathophysiology of lymphoedema in the patient with obesity

The four case reports that follow illustrate the difficulties in presentation and aetiology of oedema and lymphoedema involvement in those with obesity.

Case one is an obese 65-year-old Caucasian woman with venous insufficiency leading to lymphoedema (*Figure 1*). She has heart failure and is on supplemental oxygen. The haemosiderin deposits extending to the knee and lipodermatosclerosis (skin thickening) are obvious from the photograph, but obesity is evenly distributed (she has a large abdomen, which is omitted from the picture). The leg oedema is thus a combination of CVI and lymphoedema, and it is fairly certain that CVI came first. However, to what degree the obesity had a role in the development of both is unknown.

Case two is a morbidly obese 75-year-old Caucasian woman with lipoedema, secondary lymphoedema, and pitting oedema due to congestive heart failure (*Figure 2*). The patient also has characteristic venous stasis changes at the ankles, and lipodermatosclerosis, particularly of the left ankle with a 'bowling pin' deformity and fibrotic changes to bilateral feet with a positive Stemmer's sign. Without a detailed medical history, it would be difficult to know the sequence of events, but we

might postulate in this instance that lipoedema developed first, followed by secondary lymphoedema, and then congestive heart failure with venous complications because of the huge volume of the legs and thighs. Note, however, that her upper body and arms are relatively normal, which is contrary to the 'normal' pattern of obesity. Thus, obesity itself was probably not a factor, but the problems stemmed from a genetic predisposition toward lipoedema.

Case three is a morbidly obese 52-year-old Caucasian woman with lipoedema resulting in secondary lymphoedema (*Figure 3*). Note the dramatic difference between her relatively small upper body and her very large legs, and the localised fatty collections on the lateral thighs and hips. The patient also has an elevated thyroid stimulating hormone level (TSH). Compared to case two, this patient has more upper body obesity, but again we do not know what role this played.

Case four is a morbidly obese 38-year-old African American woman

Figure 4: Morbidly obese 38-year-old African American woman with lipoedema leading to secondary lymphoedema.

with lipoedema leading to secondary lymphoedema. In this instance, note the relative sparing of her feet, the bilateral symmetry of the leg enlargement, and the 'harem pants' distribution of fat deposits at the ankles whereby redundant skin folds overhang the medial and lateral malleoli (*Figure 4*).

What is perhaps striking when comparing case two to four, is how different the legs and thighs can appear, even when similar comorbidities and 'textbook' signs are present. Although one could perform various kinds of magnetic resonance imaging (MRI) or scintigraphic imaging, the treatment for all these cases is broadly the same. In the authors' opinion, while imaging studies might be of interest, they will not change the treatment plan.

Conclusions

The association of obesity with lymphoedema seems to be a two-way process: obesity increases the risk of acquiring secondary lymphoedema, but having lymphoedema also increases the risk of becoming more obese. Behind this association also lies the genetics of lymphatic dysfunction, which blurs the distinction between primary and secondary lymphoedema, as well as increasing the risk of acquiring lymphoedema. In lymphoedema-susceptible populations, an individual might successfully manage any problems or be unaware that he or she has a potential problem for many decades. The trigger for lymphoedema could be a traumatic incident or a bee sting, but it could also be the condition of being obese. However, we do not know whether the conditions that predispose

a person towards lymphoedema are multiplicative, or whether being obese combines synergistically with one or more factors to place the patient in sudden jeopardy.

The standard treatment of lymphoedema is complete decongestive therapy (CDT). CDT consists of a physiotherapy technique called manual lymphatic drainage (MLD), initially followed by compression bandaging and then the fitting of graduated compression garments, as well as therapeutic exercises and meticulous skin care. It is easy to understand why all of these components would be challenging for the morbidly obese. Patients must be able to lie supine for treatment and thus be sufficiently ambulatory to get on and off a treatment table. Patients who are minimally ambulatory obtain little benefit from exercise recommendations, and the limb distortion associated with obesity creates extreme challenges for garment fitting. Mechanical pumps can be highly beneficial for obese patients, particularly for decompressing areas such as the pannus and genitalia which cannot be bandaged, but caution must be exercised in patients with congestive heart failure. A detailed explanation of lymphoedema treatment has been well described elsewhere (Fife and Carter, 2008), but the treatment of the morbidly obese involves many unique challenges.

Although progress has been made, at present we are hampered by our understanding of the genetics involved in development of the lymphatic system, and how lymphoedema develops in the lower extremities when genes are defective. However, as cataloguing of these genes proceeds, it is likely at some point that genetic screening studies in broader populations will take place and those results will increase our ability to predict which patients are most at risk of developing lymphoedema, and perhaps give us a better understanding of the involvement of obesity. That future is hopefully far closer than we think. [JL]

Key points

▸▸ Distinction between primary and secondary lymphoedema is becoming blurred.

▸▸ In lymphoedema-susceptible populations, there are likely to be many possible triggers including obesity.

▸▸ Obesity increases risk of acquiring secondary lymphoedema, while having lymphoedema increases risk of becoming more obese.

▸▸ It remains unknown how obesity combines with other risk factors to cause lymphoedema.

▸▸ Better identification of genes involved with the development of the lymphatic system will likely lead to more screening and understanding of those patients at most risk for developing lymphoedema.

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