Secondary Lymphedema Of The Lower Extremities

Stanley G. Rockson, M.D.

Lymphedema is, broadly speaking, the condition in which interstitial protein-rich fluid accumulates as a consequence of impaired lymphatic drainage. This reduction of lymphatic flow can result from either congenital (primary) or acquired (secondary) anomalies of lymphatic outflow. Although the impact of lymphedema can sometimes be detected in the viscera, the pattern of either upper or lower extremity edema will often be integrally tied to the pathogenesis of edematous condition and predictive of its natural history. Thus, when one considers the substantial, growing prevalence of acquired (e.g., secondary) lymphedema of the lower extremity, it is noteworthy that these are ascribable, almost exclusively, to the large number of patients who undergo pelvic cancer surgery and that these cases are due, paradoxically, to the increasingly successful outcomes after oncologic therapy. In addition, there are several other predisposing disease categories which can be implicated in the pathogenesis of secondary lower extremity edema and which can thereby play a predictive role in the development of the edema and its response to therapy.

Secondary lymphedema develops as the consequence of a disruption or obstruction of lymphatic pathways, induced by surgery or other disease processes (Table 1). Secondary lymphedema is much more common than the primary form. Globally, the most important acquired lower extremity lymphedema can be ascribed to filariasis, which accounts for over 90 million afflicted individuals world-wide. Nevertheless, in Western society, lymphedema arises most often as a consequence of neoplastic disease, either through direct lymphatic invasion by tumor or through the iatrogenic long-term effects of the neoplastic therapy. Disruption of the lymphatic pathways may be caused by surgery and/or radiation therapy. Both forms of therapy can produce fibrosis. Surgical disruption of lymphatic pathways may be intentional (lymph node dissection for cancer surgery) or accidental (for example, during iliopelvic revascularization). In Western society, the most common examples of secondary lymphedema of the leg would be that which is seen after inguinal and pelvic lymph node dissection for pelvic neoplasms.

Edema of the leg is comparably common after pelvic or genital cancer surgeries, particularly when there has been inguinal/pelvic lymph node dissection and/or irradiation. The reported frequency varies between 1.2–47%. Pelvic irradiation correlates with an increase in the frequency of leg lymphedema.

Lymphedema has also been observed following other surgical techniques, such as ilio-femoral bypass, which can produce traumatic or fibrotic disruption of the major lymphatics.

Trauma represents another important predisposing factor. Injury of the lymphatic channels can lead to obstruction and the development of lymphedema. Curiously, however, some patients with otherwise clear-cut primary lymphedema report injury as an initiating event.

In addition to filariasis, the incidence of which is comparatively uncommon in Western life, more commonly encountered bacterial pathogens have also been implicated in the pathogenesis of secondary lymphedemas. In an early series of 300 patients with lymphedema, inflammatory lymphedema was observed in 41 of the cases (13.7%). The investigators described single or recurrent attacks of streptococcal cellulitis or lymphangitis which result in chronic swelling of the limb. These attacks have a sudden onset and are accompanied by high grade fever, chills and general malaise. The involved extremity is swollen, hot, tender, and erythematous, and the proximal lymph nodes are swollen and tender. After resolution, which requires 4-14 days, the edema of the limb persists and will worsen after subsequent attacks. In a subsequent patient series, it was reported that 43 of 80 patients with secondary lymphedema had swelling as a consequence of infection. In 21 of these cases the edema was ascribable to recurrent cellulitis and lymphangitis and in 14, active trichophytosis. Affected patients were usually between 30 and 59 years old, with near gender balance. Our own experience is similar to Kinmonth’s: the primary inflammatory edema originally described by Allen has apparently become rather rare. This shift in etiology may perhaps be attributed to the widespread usage of potent antibiotics; nevertheless, secondary recurrent lymphangitis and cellulitis, which punctuate and aggravate the course of preexisting lymphedema, remain difficult to control.

Given the global prevalence of filariasis, it is, indeed, the most common cause of lymphedema in the world. It is estimated that approximately 78.6 million people are infected. Most of the symptomatic patients have lymphedema. In a recent study from India, the predicted incidence exceeds 85 percent. Filaritic lymphedema can affect up to 11% of the population in the endemic areas, to be found in tropical zones throughout the world. Wuchereria bancrofti, Brugia malayi and Brugia timori are the organisms responsible for human filariasis. Many other species of Wuchereria and Brugia have been described in animals, with the potential to cross-infect humans. Various pathological mechanisms have been implicated in the lymphatic destruction from this disease: direct toxic effects of the worm, host immune response and superimposed bacterial infection have all been proposed. The parasite is transmitted by a mosquito vector which carries the infective larvae. The acute clinical manifestations of filariasis include episodic attacks of adeno-
lymphangitis, with fever. In most of the cases, lymphedema of the lower extremities develops and progresses after these recurrent attacks of adenolymphangitis.

Neoplastic obliteration of lymphatic vessels, lymph nodes (metastases), and lymphatic ducts (external compression or carcinomatous lymphangitis) is also a major cause of secondary lymphedema. The most frequent cause in the leg is prostate cancer.

Observations of acquired lymphedema in patients with arthritis are quite numerous. Lymphedema can accompany both rheumatoid and psoriatic arthritis. The upper extremity is more likely to be affected, but lower extremity involvement has been described. The lymphedema is most likely attributable either to lymphatic obstruction or the aftermath of lymphangitis.

Lymphatic dysfunction also contributes to other types of mixed, chronic edema, such as chronic venous insufficiency and lipedema.

**DIAGNOSIS**

In most cases of advanced, sustained lymphedema of the lower extremities, a typical history and characteristic clinical presentation will establish the diagnosis of lymphedema with near certainty. Nevertheless, in cases where the clinical presentation is more subtle, or where the potential for mixed etiologies exists, additional tests will be helpful to ascertain the presence of impaired lymphatic flow and/or the typical pattern of abnormal fluid distribution within the tissues. The diagnosis of lymphedema is more difficult to confirm in the early stages of the disease, particularly when edema is mild or intermittent.

**Isotopic Lymphoscintigraphy** — When utilized in conjunction with the standard consultative methods at the bedside, isotopic radionuclide (indirect) lymphoscintigraphy is a reliable and reproducible method to confirm the diagnosis of lymphedema. In secondary lymphedema the channels can be seen to be dilated, and the level of obstruction can be determined. In lymphedema of any cause, the proximal advance of the radionuclide is delayed, and its accumulation distally in the dilated channels of the dermis is manifested as a “dermal back-flow” pattern. The radio-labeled macromolecular tracer (99mTc-filtered sulfur colloid) is injected intra- or subdermally within one of the inter-digital spaces of the affected limb. The lymphatic transport of the macromolecule is tracked with a gamma camera. The rate of tracer appearance within the lymph node is quantifiable. Although various routes of administration may be utilized, intradermal injection has been recommended for optimal evaluation of the epifascial lymphatic transport. It has been advocated that evaluation of both epifascial and subfascial lymphatic compartments be performed to provide an accurate assessment of lymphatic transport in the lower extremities. Lymphoscintigraphy enables adequate assessment of lymphatic function, visualization of major lymphatic trunks and lymph nodes. Typical abnormalities observed in lymphedema include dermal back-flow, absent or delayed transport of tracer, crossover filling with retrograde back-flow, and either absent or delayed visualization of lymph nodes.

For the functional evaluation of the lymphatic system, lymphoscintigraphy is probably the best of the readily available methods. Nevertheless, the technique does require standardization for the type and amount of injected tracer, the site of injection (intradermal or subdermal), and the stress protocol, if such is utilized.

The techniques of magnetic resonance imaging (MRI) and computerized tomography (CT) can also be useful in the differential diagnosis of lower limb edema.

**THERAPEUTIC OPTIONS IN SECONDARY LOWER EXTREMITY LYMPHEDEMA**

The mainstay of therapy in this disorder should be the aggressive and uninterrupted use of conservative physiotherapeutic interventions (i.e. decongestive lymphatic therapy) to achieve and maintain volume reduction in the limb(s). Once volume reduction of the lower limbs has been accomplished, the long-term maintenance of edema reduction requires the prescription of compressive garments fitted to the patient’s anatomic contours and disease requirements. Adjunctive, continued utilization of physiotherapy is certainly acceptable and often quite desirable.

Relatively inelastic stockings and panties that transmit high grade compression (40-80 mm Hg) will prevent re-accumulation of fluid after successful decongestive treatments.

To provide the requisite degree of compression, the garments should be carefully chosen on the basis of meticulous limb measurements. Such garments lose their compressive capabilities after 3-6 months and must be replaced with great regularity.

**NATURAL HISTORY OF LYMPHEDEMA**

In the vast majority of cases, the knowledgeable application of complex lymphatic therapy (CLT) will result in the amelioration of edema and long-term clinical stability. However, it must be noted that chronic lower extremity lymphedema can be complicated by repeated episodes of lymphangitis/cellulitis and, in long-standing disease, neo-plastic complications have also been described.

**Lymphangitis/Cellulitis** — Accumulated fluid and proteins serve as a perfect culture medium for bacterial growth. Impaired lymphatic drainage impedes the local immune response, which, in turn, promotes bacterial and fungal invasion. The infection further impairs lymphatic drainage and the aggravation of the edema usually persists after the infection resolves. With recurrent infections there is progressive damage of lymphatic capillaries. The various types of lymphedema display a variable propensity to the development of cellulitis. In secondary lymphedema, infection has been reported in 41% of breast cancer patients. The most common cause is streptococcus. In a recently reported series of cellulitis complicating lymphedema, Staphylococcus and Micrococcus species were more often identified as the infective agents. In general, it is difficult to identify the infectious factor in lymphedema patients with cellulitis. Blood cultures, skin biopsy cultures and needle aspirates are rarely...
CONCLUSION

Secondary lymphedema of the lower extremity is an all-too-frequent accompaniment of our growing success in the control of pelvic tumors and other life-threatening modalities. The well-documented efficacy of conservative treatment strategies provides practitioners with therapeutic maneuvers to improve patients' quality of life and maintain lower extremity function. It is to be hoped that aggressive research efforts will continue to provide answers for the unanswered questions in the pathobiology of lymphedema.

TABLES:

**Secondary Lymphedema of the Lower Extremities**

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<td>Recurrent infection, e.g. erysipelas</td>
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<td>Idiopathic (autoimmune?)</td>
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Selected References

1. Kinmonth JB, Taylor GW, Tracy GD, Marsh JD: Primary Lymphoedema. Clinical and lymphangiographic studies of a series of 107 patients in which the lower limbs were affected. British Journal of Surgery 1957; 45:1-10

For a complete list of references for this article, call the NLN office, 415-921-1306.

Dr. Rockson is Co-Director of the Stanford Lymphedema Center, Division of Cardiovascular Medicine, Stanford University School of Medicine, Stanford, California.