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EDITORIAL

LYMPHATIC IMAGING

A major stumbling block in understanding lymph dynamics has been the difficulty of depicting lymphatics in living patients. In this regard, the introduction of direct oil contrast (conventional) lymphography by Kinmonth and his associates in the early 50's was a milestone advance. Expanding on the pioneering efforts of McMaster who used intracutaneous injection of vital dyes to follow lymph flow and Kaindl and Servelle who directly cannulated pathologically dilated lymphatics and injected them with iodinated contrast for radiographs, Kinmonth *et al* combined these efforts to display radiographically both lymphatic trunks and draining nodes routinely in a wide variety of lymphedemas. Over the ensuing 30 to 35 years, an extensive experience accumulated in both patients and experimental animals using the Kinmonth technique and a multitude of congenital and acquired patterns of lymphatic dysplasia and dysfunction were systematically catalogued. Despite this monumental achievement, lymphatic visualization by conventional lymphography had notable limitations. It was time-consuming, required an incision for exposure of a peripheral lymphatic, was typically a one-time procedure, occasionally accompanied by pulmonary oil embolism and local wound infection, and the poppyseed oil itself was irritating (albeit mildly) to the lymphatic endothelial lining. Accordingly, with the introduction of computed scanning and magnetic resonance imaging to visualize visceral lymph nodes along with the continued frustration to reconstruct lymphatics reliably, the use of conventional lymphography for other than tumor staging virtually disappeared.

While these developments unfolded, a number of clinics around the world have begun to explore alternative approaches to visualize lymphatics. Among these are better water-soluble (as opposed to oil) lymphography, fluorescent microangiography, and isotope lymphography. Whereas each shows promise, the refined update of isotope lymphography as whole body lymphangioscintigraphy (LAS) is consistently providing vivid images of peripheral lymphatics and insight into lymph flow dynamics. Indeed, where the necessary and expensive collimators and sophisticated gamma cameras are available, there is universal agreement that LAS is not only the initial preferred test for depicting lymph dysfunction but also that there is rarely need nowadays for oil contrast lymphography.

Yet, despite a wealth of articles in support of this viewpoint, it is surprising how few institutions, including university hospitals, especially in the United States, have incorporated this technology and particularly its refinements into everyday clinical practice, and how infrequently patients with idiopathic edema syndromes undergo LAS despite absence of a clear diagnosis. Most patients either receive no diagnostic study (i.e., they remain with a presumptive diagnosis of lymphedema, or in effect a negative image) or more disconcerting they are subject to the incommodious largely outmoded conventional lymphogram or unwarranted contrast venography.

What can be expected of LAS and what are its shortcomings? In the upper limbs which have notoriously been technically difficult to

study even using oil contrast lymphography, LAS provides excellent images of truncal-paraaxillary nodal anatomy. After radical and more limited operations and/or irradiation for treatment of breast cancer, a wide spectrum of arm swelling (lymphedema) ensues that ranges from none, mild to severe. Rather than such post-treatment lymphedema representing the "whims of lymph dynamics", preliminary experience with LAS suggests that disruption of axillary truncal continuity is quite variable from patient to patient despite ostensibly similar ablative treatment. LAS, therefore, seems to be a promising indicator as to whether lymphedema is likely to appear (or progress) and whether massage or application of elastic stockinettes (or pneumatic compression) are appropriate prophylactic or therapeutic remedies.

In the lower extremities, depiction of truncal anatomy and regional nodes (as "hot spots") is also excellent. Parailiac collectors are also usually seen, and sometimes the cisterna chyli and even the thoracic duct are imaged. However, once the radiopharmaceutical reaches the bloodstream, it is rapidly picked up by the lungs, heart, liver and spleen, the images of which tend to obscure the upper abdominal and mediastinal lymphatics. Despite this limitation, it has been possible on occasion to detect the leakage site from the thoracic duct using LAS as, for example, after disruption from blunt or surgical trauma. Unlike oil contrast, which delineates characteristic intranodal architectural patterns (as in Hodgkin and non-Hodgkin lymphoma), LAS only displays node sites as dense radioactive "spots". Accordingly, at this stage, use of LAS for illustrating lymph nodal abnormalities is limited to either their presence or absence (e.g., after radical axillary or groin dissection) and substantial enlargement. A great value to LAS besides its accuracy in depicting lymphatic collectors and the transport of tracer as a rough gauge of lymph flow, is that the procedure is safe and easy to perform repeatedly as a simple intradermal injection of radiolabeled tracer (e.g., ^{99m}Tc-human serum albumin). As such, it is an excellent modality to show changes before and after treatment including lymphatic reconstructive operations and the tracer is harmless to the vascular endothelium.

Besides the obvious advantage of providing a positive image of the lymphatics (instead of a presumptive diagnosis based solely on history, physical examination, and "deduction"), LAS may negate the clinical impression of lymphatic dysfunction to explain idiopathic edema. For example, patients with lower limb disuse (e.g., wheelchair ridden from hip arthritis or longstanding poliomyelitis) or with marked fat accumulation (e.g., so-called "lipedema") may grossly resemble patients with lymphedema, but study with LAS documents intact truncal anatomy and uninterrupted tracer transport. Even when therapy is not likely to be altered by performing LAS (as in lymphatic hypoplasia), a patient may feel immeasurably better psychologically having a positive visual image of the lymphatic abnormality rather than just a theoretical description or schematic outline of his or her disability.

Another great potential advantage of LAS is that where the imaging equipment is available, it is now possible to examine the peripheral lymphatics in a wide variety of poorly understood disorders characterized by edema without restriction because of methodology. Early experience suggests that patients with similar clinical diagnoses may in fact have dissimilar lymphatic abnormalities. For example, whereas most patients with lymphedema precox display a hypoplastic truncal pattern, some patients show segmental nodal dysplasia (similar to a radical groin dissection) with an "obstructive" pattern suggesting an acquired rather than a congenital etiology.

A related but distinct scintigraphic technique involves depiction of neoplastic

lymph nodes and distant tumor metastases after regional interstitial or intravenous injection of radiolabeled immunoconjugates or monoclonal antibodies directed against tumor-associated antigens. Known as *immuno*scintigraphy, in contradistinction to *lymphangio*scintigraphy, this method holds promise for identifying tumor deposits not ordinarily seen on plain radiographs or computer tomography. If perfected to a high degree of accuracy, this imaging method may render staging operations, such as axillary dissection for cancer of the breast, obsolete and someday permit tumoricidal drugs to be targeted selectively to the neoplastic foci.

Although costly, magnetic resonance also shows promise as an imaging tool of the lymphatic system. T_2 weighted images in particular depict pathologic dermal lymphatics without added contrast as well as more proximal nodes and obstructing masses. Refinement of intracutaneous injected superparamagnetic agents, such as iron oxide, to enhance the internal or architectural image of regional lymph nodes (by reduction in signal intensity) may in the near future revolutionize the use of this modality for studying lymphatic and lymph nodal disorders. Indeed, therapeutic intervention may even be designed and monitored using MR and CT imaging as, for example, obliteration of a chylous fistula or bulky lymphangioma.

In summary, peripheral lymphatics can now be visualized as easily as arteries and veins have been for several decades. Following the tracer uptake and transport may also allow functional and quantitative insight into lymph flow kinetics.

Because LAS can readily be applied before and after treatment, it should become an integral part of evaluating physical methods, drugs and operations designed to facilitate lymph flow such as surgically constructed lymphatic-venous or lymph-nodal venous shunts. As therapeutic techniques continue to evolve, it is increasingly desirable that lymphatics be seen in patients in their natural state to shed light on the underlying pathophysiology. In this context, all patients who carry the provisional diagnosis of peripheral lymphatic dysfunction or idiopathic edema are appropriate candidates for diagnostic lymphangioscintigraphy.

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