Phlebolymphedema: Hall Mark Of Combined Insufficiency Of Venous-Lymphatic System

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DISCLOSURE OF CONFLICTS OF INTEREST
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I do not have any relevant financial relationships with any commercial interests.

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Phlebolymphedema (PLE) is a combined condition of phlebogenic leg edema (=phlebo-edema) and lymphogenic leg edema (=lympho-edema).

Phlebolymphedema = lymphatico-venous edema

Phlebolymphedema represents the accumulation of excess intercellular fluid in the legs and feet due to lymphatic obstruction as the result of chronic insufficiency.

Lymphedema secondary to CVI has been called ‘phlebolymphedema’ for the last two decades! Indeed, Phlebolymphedema refers to lymphedema caused by CVI to compensate for venous insufficiency: valvular failure of lymphatic vessels by lymphatic overloading.

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This CLI becomes more prominent especially among the ‘compromised’ lymphatic drainage condition of various etiologies (e.g. surgery/radiotherapy associated with cancer treatment).

Clinical manifestation of the PLE is therefore, extremely variable depending upon the etiology (primary and secondary) and the degree/extent of the CVI and CLI, and clinically more distinctive along the lower extremity.

Clear understanding on the interrelationship between the venodynamics and lymphodynamics is mandated for the proper management of PLE.

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When the lymphatics themselves are damaged following initially enhanced function to compensate for the insufficient venous system, a safety valve insufficiency of lymphatic system occurs with resulting ‘lymphostasis’.

When the venous stasis exceeds this maximum lymphatic compensatory capacity, the insufficiency becomes ‘phlebo-lymphatic’, showing characteristics of a major fibrosis due to increased interstitial protein concentration.

Degenerative phlebolymphatic process is mandated for early aggressive management to avoid dystrophic ulcers and skin infections, etc.
The venous point of view - ‘phlebolymphedema’ along the end stage of chronic venous insufficiency is much complicated condition due to newly added condition of local/regional lymphedema. It therefore, becomes a major additional burdening to the clinical management due to the complexity of local circulation.

The lymphatic point of view - lymphatic system/abnormality seldom becomes clinically significant burdening to the venous system while lymphatic system often becomes visibly strained as a victim of abnormal venous condition, especially when the lymphatic system is in marginally compensated condition (eg. Klippel-Trenaunay Syndrome).

The assessment of the extent/severity of the CVI should be based on Duplex ultrasonography and may include various plethysmographies in addition to ascending/descending phlebography per indication.

For the CLI, the functional status of the lymphatic system should be measured with lymphoscintigraphy to delineate excessive fluid accumulation in the tissues of the limb or affected lymphatic territories.

Appropriate appraisal of the CVI and also CLI should include differential diagnosis between ‘primary’ PLE of congenital origin and ‘secondary’ PLE with various backgrounds.

Diagnosis
- The assessment of the extent/severity of the CVI should be based on Duplex ultrasonography and may include various plethysmographies in addition to ascending/descending phlebography per indication.
- For the CLI, the functional status of the lymphatic system should be measured with lymphoscintigraphy to delineate excessive fluid accumulation in the tissues of the limb or affected lymphatic territories.
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Differential diagnosis – systemic causes
- Cardiac failure
- Hepatic failure
- Renal failure
- Thyroid failure – myxedema
- Idiopathic cyclic edema
- Drugs - methyl dopa, nifedipine, hydralazine, hormones, antinflammatory drugs

Differential diagnosis – local or regional causes
- Venous origin: Chronic venous insufficiency
- Lymphatic origin: Chronic lymphedema – primary & secondary
- Mixed condition: Phlebolymphedema
- Congenital vascular malformation
- Lipedema
- Factitious edema (Dependent edema)
- Post-revascularization edema
- Hemihypertrophy

Laboratory evaluation for Venous System
- Venous duplex ultrasonography – test of choice
- Air plethysmography: functional assessment
- CT scan with/without contrast
- MRI study, standard & MR venography (MRV)
- Radioisotope venography
- Ascending & Descending venography
- Percutaneous direct puncture phlebography
- Volumetry
- Whole body blood pool scintigraphy (WBBS)*
- Transthoracic lung perfusion scintigraphy (TIPS)*
* For the congenital vascular malformation assessment

Laboratory evaluation for Lymphatic System
- Lymphoscintigraphy - test of choice
- CT scan - exclude underlying malignancy
- Standard MRI - potentially most useful
- Lymphangiography (oil contrast): optional for the candidate of venolymphatic reconstructive surgery
- Volumetry
- MR lymphangiography: optional
- Ultrasonographic lymphangiography: optional
- Miscellaneous: dermascan, tonometry, ultrasonographic measurement of subcutaneous edema: optional
Management of phlebolymphedema (PLE) should aim at BOTH conditions of chronic venous insufficiency (CVI) and chronic lymphatic insufficiency (CLI) as an outcome of simultaneous ‘dual’ outflow system failure.

Primary PLE generated by the vascular malformation component of Klippel-Trenaunay Syndrome (KTS) for example, represents such complicated interrelationship between venous and lymphatic systems. KTS is therefore, mandated for multidisciplinary team management of this combined venous-lymphatic disorder because of extremely delicate mutual interdependency between venous malformation (VM) and lymphatic malformation (LM).

Clinical Management

Phlebolymphedema

 Primary Phlebolymphedema

- Primary PLE represents a combined condition of CVI by venous malformation (VM) and CLI by lymphatic malformation (LM).
- The most common VM to cause CVI is ‘marginal vein’ with venous reflux/hypertension, followed by deep vein dysplasia (e.g. iliac vein agenesis, hypoplastic femoral vein) or defective vein (e.g. web, stenosis, aneurysm, ectasia) with venous outflow obstruction/hypertension.
- CLI is mostly due to ‘primary lymphedema by truncular LM lesion (e.g. lymphatic dysplasia: aplasia, hypoplasia, or hyperplasia). Extratruncular LM (lymphangioma) seldom involved to the CLI.

Secondary Phlebolymphedema

- CVI of secondary PLE is mostly the sequellae of post-thrombotic syndrome (PTS) following the deep vein thrombosis (DVT).
- CLI of secondary PLE is generally secondary regional/local lymphedema following steady progress of the local tissue damage (e.g. ulcer) by the CVI/PTS.
- Occasionally, primary lymphedema as the cause of CLI accelerates the deterioration of the underlying benign primary venous disorder (e.g. reflux) to result in CVI.

Baseline therapy for the PLE is the compression therapy regardless of its etiology. It is a reinforced gradient compression therapy based on the CDT (complex decongestive therapy) to control the CVI and CLI together.

Primary PLE with the reflux of the marginal vein (MV) as the cause of CVI should be treated with the resection of the MV as far as the deep vein system could tolerate sudden influx of diverted blood volume.

CVI due to deep vein dysplasia occasionally requires more than conservative management when there is a clear evidence for the hemodynamic gain by the bypass surgery of hypoplastic/aplastic iliac/femoral veins to improve indolent ulcers.
The benefit of the therapy more than the basic compression therapy to the CVI for the primary PLE should be carefully weighed for the potential burdening to coexisting LM with the CLI to make the condition worse.

The CLI of the primary PLE infrequently needs additional sclerotherapy to coexisting extratruncular LM, also known as lymphangioma when it should become a burdening to the primary lymphedema as the major cause of the CLI.

Therefore, primary PLE generated by HLM as the vascular malformation component of Klippel-Trenaunay Syndrome (KTS) should be handled by a multidisciplinary team to manage such extremely delicate interdependency between VM and LM safely.

Secondary PLE with the CVI by PTS should be treated more aggressively to relieve the cause of obstruction/reflux with various forms of open surgical (e.g., bypass) and endovascular therapy (e.g., angioplasty and stenting).

When the CVI is caused by the multilevel DVT sequelae (indolent ulcer), even a minimum correction of the obstruction/stenosis is able to assist tremendous improvement of the efficacy of the compression therapy-based conservative management following successful relief of venous hypertension.

• Existing data provide convincing proof of the efficacy of endovascular recanalization procedures: recanalization of chronic iliac vein occlusions with balloon angioplasty and stenting relieves symptoms of PTS and also the condition of the CVI (e.g., swelling, pain, and stasis ulcers in the majority.

• PLE can be managed more effectively when open and/or endovascular therapy is added to the basic compression therapy to control the CVI and CLI together.

• Primary PLE with CVI by the reflux of MV can be treated successfully with MV resection, while CVI by deep vein dysplasia with the conventional compression therapy alone in its majority.

• Secondary PLE with CVI by the PTS can be further improved with correction of the venous outflow obstruction with angioplasty & stent especially when the DVT sequelae is involved to the multilevels of iliac-femoral-popliteal vein system.
Thank you for your Attention!