Phlebolymphedema: Neglected Outcome of Combined Venous and Lymphatic Insufficiency

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Phlebolymphedema is an unavoidable outcome of the hemodynamically unique relationship between the venous and lymphatic circulation systems as one “inseparable” system. Although these two systems run based on totally different hemodynamic principles, i.e., venodynamics and lymphodynamics, they are mutually interdependent dual outflow systems of circulation to transport used blood out of the tissue [1-4].

Therefore, the failure of one system puts an additional burden/load on the other system, and a long-term failure of one system would result in ‘total’ failure of this dual system altogether, which is called “phlebolymphedema.”

The overloading of one of these two systems would allow the other to play an auxiliary role to compensate the insufficiency/failure and assist the fluid return back to the circulation system; however, such a “mutually complementary” role/function between both systems is possible only when they are in normal functional status.

Therefore, if one of the two systems should fail in its normal function (e.g., chronic venous hypertension, lymphedema), such mutual interdependence causes a new condition that affects both systems simultaneously known as “phlebolymphedema.”

When chronic venous insufficiency (CVI) results in an excessive fluid load at the tissue level, it disrupts the “check and balance” function of the capillary system allowing additional load on the lymphatic system. When this overloading exceeds the maximum capacity of normal lymphatic compensation, the lymphatics themselves are damaged following initially enhanced function to compensate for the insufficient venous system, and a safety valve insufficiency of the lymphatic system occurs that leads to “lymphostasis” resulting in chronic lymphatic insufficiency (CLI).

Accordingly, when the venous stasis exceeds this maximum lymphatic compensatory capacity, the insufficiency becomes “phlebolymphatic,” showing characteristics of a major fibrosis of the interstitial tissue. The increased protein concentration in the tissue leads to a degenerative phlebolymphatic process resulting in dystrophic ulcers, skin infections, etc.

CLI becomes more prominent when the lymphatic drainage is “compromised” by various etiologies (e.g., surgery/radiotherapy associated with cancer treatment). Therefore, the clinical manifestation of “phlebolymphedema” is extremely variable depending upon the degree/extent of CVI and CLI and the etiology (primary and secondary) and is clinically more distinctive along the lower extremity.

For example, chronic “indolent” venous stasis ulcers on the distal lower leg have been a hallmark of “advanced” CVI as the sequelae of deep vein thrombosis (DVT) for many decades. However, they no longer remain as a venous condition as the local condition changes/advances to become a “combined” condition of CVI and CLI, i.e., phlebolymphedema, although these ulcers might have started as a single venous condition of CVI in the beginning [5,6].

Should the ulcers become intractable, resisting healing, they give rise to a new condition of secondary phlebolymphedema, that is a combined condition of phlebogenic edema (phlebo-edema) and lymphogenic edema (lymphoedema), caused by the CVI and CLI. Therefore, this new condition of “lymphatic-venous edema” actually represents the accumulation of excess intercellular fluid due to lym-
phatic failure/CLI which was precipitated by the CVI.

Indeed, CLI evolving to phlebolymphedema is rather a “safety valve insufficiency” as a combined effect of increased lymph flow and reduced drainage capacity in the diseased lymphatic system often as an outcome of advanced post-thrombotic syndrome (PTS). Therefore, it is not a simple condition of mechanical insufficiency with reduced lymph flow due to defects in the lymph vessels and lymph node system nor a dynamic insufficiency caused by increased lymph flow overwhelming the maximum load-carrying capacity of a physiologically normal lymphatic system.

Among various etiopathogenesis of such a combined condition of CVI and CLI, Klippel–Trénaunay syndrome (KTS) is best known for this unique condition of “primary” phlebolymphedema (cf. secondary PLE). As one of the multiple vascular malformation components of KTS, the “marginal vein” with venous reflux/hypertension is the most common venous malformation to cause CVI, 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 [7,8].

CLI in KTS is caused by independent lymphatic malformation (LM), one of the two major vascular malformations, i.e., primary lymphedema caused by truncular LM lesion (e.g., lymphatic dysplasia: aplasia, hypoplasia, or hyperplasia). Extratruncular LM (lymphangioma) seldom evolves into CLI.

These two combined conditions of the marginal vein (MV) and primary lymphedema exerts a synergistic impact on the mutually interdependent and inseparable venous-lymphatic system to make the limb swelling worse and further to cause an “indolent ulcer.”

MV is the outcome of a birth defect, which failed to involute following the developmental arrest during the vein trunk formation period in the “later stage” of the embryonic development. MV is often superficially located beneath the skin mimicking the ordinary varicose veins but it is not a varicose vein but an embryonic vein remnant often combined with a unique condition of avarulosis, congenital absence/lack of venous valves, which allows severe reflux resulting in chronic venous hypertension/stasis with subsequent CVI/PTS.

Secondary phlebolymphedema develops during end stage CVI mostly as the sequelae of PTS following the DVT, becoming a complicated condition to manage due to the newly developed condition of local/regional lymphedema. CLI in such case generally presents as regional/local lymphedema that develops secondarily following the steady progress of local tissue damage (e.g., ulcer) by the CVI/PTS. Occasionally, the hidden condition of primary lymphedema in clinical/subclinical status becomes the cause of CLI accelerating the deterioration of the underlying benign primary venous disorder (e.g., reflux) to result in CVI.

CONCLUSION

Venous and lymphatic systems are “inseparable” dual outflow systems. Although they are run by two entirely different independent fluid dynamic principles, maintaining the critical differences of the rheologic characteristics between venous (low fluctuating flow) and lymphatic (peristaltic flow) system, they maintain a ‘mutually complimentary’ function.

Therefore, the failure of one system leads to an additional burden/load on the other system. When this overloading exceeds the maximum capacity of the compensatory function of the other system, it results in the failure of both systems together.

Long-term failure of one system results in “total” failure of this mutually interdependent dual system altogether, which gives rise to a new condition called “phlebolymphedema” as the combined condition of CVI and CLI.

CONFLICTS OF INTEREST

Byung-Boong Lee has been a member of the editorial board of Vasc Specialist Int since 2019.

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