

Lymphedema Is a Disease of the Skin

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TWO OF THE ARTICLES FEATURED in this issue of *Lymphatic Research and Biology* feature original research that documents the cutaneous pathology associated with the condition of lymphedema.

In the first of these, Sun and colleagues have chosen to investigate the pathological phenomenon of cutaneous fibrosis in secondary lymphedema.¹ With the recognition that mast cells have been acknowledged to be associated with the cutaneous problem of fibrosis, they have chosen, specifically, to explore the impact of mast cell-related chymase and transforming growth factor β 1 (TGF- β 1) secretion in relationship to this process. The work was performed in full-thickness skin biopsies derived from lymphedema patients and healthy controls. Their findings suggest that increased expression of chymase in the skin is associated with fibrosis. Furthermore, since increased expression of TGF- β 1 on lymphatic vessels, endothelial cells and in the skin interstitium overlapped with chymase expression, they speculate that the chymase may facilitate the release of active TGF- β 1, which, in turn, leads to the pathological expression of fibrosis.

In the second article on this theme, Hara and colleagues have investigated the pathological attributes of acquired lymphangiectasia accompanied by lymphedema in their series

of patients.² Here, they observed universal dilation of the lymphatic vessels in the papillary dermis with inflammatory infiltration primarily of lymphocytes. They characterized these cells as predominantly CD4+ T cells and, less commonly, as CD8+ cells and CD20+ B cells. Thickened collagen was also observed in the dermis, along with acanthosis.

These two articles underscore, yet again, the important role that is played by the skin in the pathological manifestations of lymphedema. Continued scrutiny of these phenomena will be important, and may lead to very directed therapeutic manipulation of the cutaneous response to lymphatic disease.

References

1. Di S, Ziyou Y, Liu N. Pathological changes of lymphedematous skin: Increased mast cells, related proteases, and activated transforming growth factor- β 1. *Lymphat Res Biol* 2016; 14:162–171.
2. Hara H, Mihara M, Anan T, Fukumoto T, Narushima M, Iida T, Koshima I. Pathological investigation of acquired lymphangiectasia accompanied by lower limb lymphedema: Lymphocyte infiltration in the dermis and epidermis. *Lymphat Res Biol* 2016; 14:172–180.