

Characterization of lymphatic vessels in human peripheral neuropathies

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Immunohistological studies on lymphatics' topography in human peripheral nerve are few and recent. By D2-40 immunohistochemistry, we previously described lymphatics in epineurium of human sural nerve. Lymphangiogenesis is described in inflammation. In angiopathic and vasculitic neuropathies proliferation of epineurial blood capillaries is reported. The aim of our study is therefore to investigate the topography and the density of lymphatics in human peripheral nerve and to search possible correlation with blood capillary neovascularization in different neuropathies. We examined biopsied sural nerves of patients suffering from CIDP (chronic inflammatory demyelinating polyneuropathy), vasculitic neuropathy and non inflammatory axonal neuropathy. Immunohistochemistry for detection of lymphatic marker podoplanin (D2-40 antibody) and for general endothelial marker CD31, as well as for Schwann cells protein S-100, was carried out on serial cryostat sections. Morphometric analysis was performed. Lymphatic capillaries were detected in epineurium, most consistently in adjacency of main blood vessels. Occasionally lymphatics were dilated and repleted with mononuclear cells. Podoplanin was also expressed by perineurium and by Schwann cells. No lymphatics were observed endoneurially. Lymphatics showed a far lesser density than blood capillaries and increase of epineurial vascularization resulted significantly associated with higher density of lymphatics. Density variations of epineurial lymphatics, accompanying blood capillaries proliferation, suggest that lymphangiogenesis may occur in neuropathies, in response to inflammation/ischaemia. Lymphatics' responsiveness to molecular microenvironment is indicated by their expression of growth factor receptors, such as VEGFR3. Lack of lymphatics in closed endoneurial environment is in agreement with analogous findings in brain. Non lymphatic expression of podoplanin is reported in several cell types of nervous system: normal and tumoral ependymal cells, perineurium and Schwann cells. As biological functions of podoplanin, involved in cell migration and cytoskeletal reorganization, are uncompletely understood, its localization on non lymphatic structures of peripheral nerve needs to be defined.

Keywords: Lymphatic vessels, peripheral neuropathies epineurium, inflammation.