

Morphometric analysis of lymphatics vessels in fibrotic human lung

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In pulmonary fibrosis, the usual interstitial pneumonia (UIP) pattern is characterised by heterogeneous, patchy fibrosis, with areas of normal lung adjacent to areas of complete destruction (honeycombing) and by fibroblastic foci (FF). The NSIP pattern which is characteristic of systemic sclerosis, is characterised by a more homogeneous involvement of the lung without honeycombing and FF. Little is known on lymphatic vessels in lung fibrosis. Defective lymphatic clearance could lead to prolonged exposure to pathogenic antigens and/or pro-inflammatory/pro-fibrotic mediators. We evaluated the distribution and morphology of lymphatic vessels in lung biopsies of 6 patients with UIP, 6 NSIP and 5 controls. Consecutive sections were stained with Movat's pentachrome and with double immunostaining for von Willebrand factor and podoplanin (D2-40). Area, perimeter and position were recorded for vessels with a diameter $> 5\mu\text{m}$. We investigated separately in intralobular, sub-pleural, and interlobular spaces. Lymphatics were consistently larger in subpleural spaces and in interlobular septa than in intralobular tissue. In the latter, the density of lymphatic vessels was significantly reduced in NSIP and in UIP (both $21\pm 1\text{ mm}^{-2}$) compared to controls ($35\pm 4\text{ mm}^{-2}$). In controls, $85\pm 6\%$ of the intralobular lymphatics were close ($< 100\mu\text{m}$) to a blood vessel, and only $5\pm 4\%$ were in the proximity of bronchoalveolar spaces, while in the disease groups they were less frequently perivascular (NSIP $55\pm 3\%$, UIP $56\pm 2\%$) and more frequently associated with the bronchoalveolar lumen (NSIP $85\pm 3\%$, UIP $69\pm 2\%$). By contrast, in interlobular septa, lymphatic density was significantly increased in NSIP ($303\pm 28\text{ mm}^{-2}$) and in UIP ($286\pm 124\text{ mm}^{-2}$) compared to controls ($96\pm 69\text{ mm}^{-2}$). No differences in lymphatic density was seen in subpleural spaces. Thus, our data show a marked redistribution of lymphatic vessels within the lung in pulmonary fibrosis, without noticeable differences between the NSIP and UIP patterns.

Key words

Lymphatic vessels, lung, systemic sclerosis.