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Saccular intracranial aneurysm rupture leads to subarachnoid hemorrhage and is preceded by chronic inflammation and atherosclerotic changes of the Saccular intracranial aneurysm wall. Increased lymphangiogenesis has been detected in atherosclerotic extracranial arteries and in abdominal aortic aneurysms, but the presence of lymphatic vessels in saccular intracranial aneurysm (sIAs) has remained unexplored. Huuska et al. studied the presence of lymphatic vessels in 36 intraoperatively resected sIAs (16 unruptured and 20 ruptured), using immunohistochemical and immunofluorescence stainings for Lymphatic endothelial cells (LEC)markers. Of these LEC-markers, both extracellular and intracellular LYVE1, podoplanin, VEGFR-3, and Prox1-positive stainings were detected in 83%, 94%, 100%, and 72% of the 36 sIA walls, respectively. Lymphatic vessels were identified as ring-shaped structures positive for one or more of the LEC markers. Of the sIAs, 78% contained lymphatic vessels positive for at least one LEC marker. The presence of LECs and lymphatic vessels were associated with the number of CD68+ and CD163+ cells in the sIA walls, and with the expression of inflammation indicators such as serum amyloid A, myeloperoxidase, and cyclo-oxygenase 2, with the presence of a thrombus, and with the sIA wall rupture. Large areas of VEGFR-3 and  $\alpha$ -smooth muscle actin ( $\alpha$ SMA) double-positive cells were detected in medial parts of the sIA walls. Also, a few podoplanin and  $\alpha$ SMA double-positive cells were discovered. In addition, LYVE-1 and CD68 double-positive cells were detected in the sIA walls and in the thrombus revealing that certain CD68+ macrophages are capable of expressing LEC markers. This study demonstrates for the first time the presence of lymphatic vessels in human sIA walls. Further studies are needed to understand the role of lymphatic vessels in the saccular intracranial aneurysm pathogenesis 1).

Huuska N, Netti E, Lehti S, Kovanen PT, Niemelä M, Tulamo R. Lymphatic vessels are present in human saccular intracranial aneurysms. Acta Neuropathol Commun. 2022 Sep 5;10(1):130. doi: 10.1186/s40478-022-01430-8. PMID: 36064651.

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