Multipotent mesenchymal progenitor cells are present in endarterectomized tissues from patients with chronic thromboembolic pulmonary hypertension.

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Public Summary:
Factors contributing to the development of a fibrotic vascular scar and pulmonary vascular remodeling leading to chronic thromboembolic pulmonary hypertension (CTEPH) are still unknown. This study investigates the potential contribution of multipotent progenitor cells and myofibroblasts to the development and progression of CTEPH. Histological examination of endarterectomized tissues from patients with CTEPH identified significant neointimal formation. Morphological heterogeneity was observed in cells isolated from these tissues, including a network-like growth pattern and the formation of colony-forming unit-fibroblast-like colonies (CFU-F). Cells typically coexpressed intermediate filaments vimentin and smooth muscle alpha-actin. Cells were characterized by immunofluorescence and quantitated by fluorescent-activated cell sorting (FACS) for the presence of cell surface markers typical of mesenchymal progenitor cells; cells were >99% CD44(+), CD73(+), CD90(+), CD166(+); >80% CD29(+); 45-99% CD105(+); CD34(-) and CD45(-). Cells were capable of adipogenic and osteogenic differentiation, determined by Oil Red O and Alizarin Red staining, respectively. Additionally, a population of Stro-1(+) cells, a marker of bone marrow-derived stromal cells (4.2%), was sorted by FACS and also capable of adipogenic and osteogenic differentiation. In conclusion, this study is the first to identify a myofibroblast cell phenotype to be predominant within endarterectomized tissues, contributing extensively to the vascular lesion/clot. This cell may arise from transdifferentiation of adventitial fibroblasts or differentiation of mesenchymal progenitor cells. The unique microenvironment created by the stabilized clot is likely a factor in stimulating such cellular changes. These findings will be critical in establishing future studies in the development of novel and much needed therapeutic approaches for pulmonary hypertension.

Scientific Abstract:
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