

A loss of telocytes accompanies fibrotic remodelling of the colonic wall in ulcerative colitis

Mirko Manetti, Irene Rosa, Luca Messerini, Lidia Ibba-Manneschi

Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy

Crohn's disease (CD) and ulcerative colitis (UC) are complex diseases in which the interaction of genetic, environmental and microbial factors drives chronic relapsing and remitting intestinal inflammation that finally leads to extensive tissue fibrosis. In UC, this results in a stiff, fibrotic colon unable to carry out peristalsis or to resorb fluids. Colonic dysmotility is often observed in UC patients and has been linked to severe damages of the enteric neural structures and a reduced density of interstitial cells of Cajal (ICC). Telocytes (TC), a peculiar type of stromal cells, have been recently identified in a variety of human tissues and organs, including the gastrointestinal tract. Several roles have been proposed for TC, including mechanical support, spatial relationships with different cell types, intercellular signalling and modulation of intestinal motility by spreading the slow waves generated by the pacemaker ICC. We have recently demonstrated that a loss of TC accompanies the fibrotic remodelling of the intestinal wall in CD patients. The aim of the present work was to investigate the presence and distribution of TC in colonic specimens from UC patients compared with controls. Archival paraffin-embedded full-thickness samples of the left colon from UC patients who underwent elective bowel resection and controls were collected. Tissue sections were stained with Masson's trichrome to detect fibrosis. TC were identified by CD34 immunohistochemistry. Double immunofluorescence for CD34 and CD31 (vascular endothelial cells), alpha-SMA (smooth muscle cells, myofibroblasts) and c-kit (ICC) was also performed. In early fibrotic UC cases, fibrosis affected the muscularis mucosae and submucosa, while the muscularis propria was spared. In advanced fibrotic UC cases, fibrosis extended to affect the muscle layers and the myenteric plexus. Few TC were found in the muscularis mucosae and submucosa of both early and advanced fibrotic UC colonic wall. Conversely, numerous myofibroblasts were observed in the submucosa of all UC cases. In the muscle layers and at the myenteric plexus of early fibrotic UC, TC were preserved in their distribution. In the muscularis propria of advanced fibrotic UC, the network of TC was reduced or even completely absent around smooth muscle cells and myenteric plexus ganglia, paralleling the loss of the ICC network. In UC, the loss of TC accompanies the fibrotic remodelling of the colonic wall and might contribute to colonic dysmotility.

Keywords

Telocytes, ulcerative colitis, colonic wall, fibrosis.