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Muscle and vascular remodelling in inflamed, fibrotic colon of patients with ulcerative colitis

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Background. Intestinal fibrosis is a common complication of inflammatory bowel diseases, affecting patients with both Crohn's disease and ulcerative colitis (UC). Of note, the progression of intestinal fibrosis has been recently considered to depend on distinct processes from those involved in inflammation [1]. In this context, angiogenesis is currently regarded as a good candidate of active gut disease, closely related to fibrogenesis [2]. Therefore, studies on the multifactorial pathways promoting these processes are needed for understanding the pathophysiology of fibrosis, and thereby identifying anti-fibrogenic therapies. **Aim**. The present study was performed to evaluate the distribution of fibrotic tissue, the behaviour of smooth muscle cells and the presence of neovessels in the colon of UC patients. **Patients and Methods**. Full-thickness left colonic samples were studied, from patients with established and pharmacologically unresponsive UC for the following parameters: collagen and elastic fibers by histochemistry; fibrotic and profibrotic factors [type 1 and 3 collagens, elastin, fibronectin, vimentin, alpha-smooth muscle actin (α-SMA), proliferating nuclear antigen (PCNA), RhoA] by immunohistochemistry and western blot; vascular networks [CD31, CD105, nestin] by confocal microscopy immunofluorescence. **Results**. A significant increase in collagen fibers and decrease in elastin content were detected in the colon from UC patients as compared with controls. The increment of type 1 and 3 collagens, fibronectin, vimentin, PCNA and RhoA expression was associated with alpha-SMA decrease in the *tunica muscularis* of UC colon. A relevant rearrangement of vascular networks was observed in the fibrotic *tunica muscularis*, with neovessels displaying both proliferating $CD105^+$ endothelial cells and activated $nestin^+$ pericytes. **Conclusion**. The present data show that a significant muscle and vascular remodelling occurs in inflamed colonic tissues from UC patients, suggesting that, under these conditions, smooth muscle cells and vascular cells may be involved in fibrogenic processes by cell transition to mesenchymal phenotype.

References

[1] Cromer WE et al. *Curr Opin Gastroenterol* 2011, 17:578**;** [2] Lawrance IC et al., *J Crohn's Colitis* 2015, in press

Keywords

Ulcerative colitis; human; fibrosis; tunica muscularis; smooth muscle cells; vascular remodelling.