Histopathological damage and fibrotic remodelling of neuromuscular compartment in experimental colitis

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There is currently a scarcity of animal models of intestinal fibrosis and new methods to induce fibrosis as well as reliable parameters to evaluate fibrotic remodelling in the gut wall are highly expected [1]. The aim of this study has been to assess tissue remodelling of colonic wall in a rat model of colitis, with a particular focus on the neuromuscular compartment.

Colitis was induced in rats by intrarectal administration of 2,4-dinitrobenzenesulfonic acid (DNBS). After 6 and 21 days, the following parameters were assessed on paraffin sections from colonic samples: morphologic damage and tissue inflammatory infiltration by histology; collagen and elastic fibers by histochemistry; HuC/D, glial fibrillar acid protein (GFAP), nestin, substance P, connexin 43 and c-Kit by immunohistochemistry.

On day 6, inflammatory and ulcerative alterations were observed in all DNBS-treated rats, and they progressed towards fibrotic lesions on day 21. Colitis was associated both with a significant increase in collagen fibers and a decrease in elastic fibers throughout the whole wall thickness. Moreover, the colonic neuromuscular compartment of inflamed animals displayed a significant decrease in myenteric neuron density, a reduced density of intramuscular and myenteric interstitial cells of Cajal, a neovessel formation and an increased immunoreactivity for GFAP, nestin and Cx43.

The DNBS model of experimental colitis is characterized by a significant fibrosis of whole wall thickness, together with evident remodelling of the neuromuscular compartment. These histopathological patterns can be suitable for investigating the pathophysiology of colonic fibrosis and, therefore, to evaluate the impact of new therapeutic strategies on gut inflammation.

References


Key words

Experimental colitis, rat, colonic neuromuscular compartment, enteric nervous system, histopathological remodelling, fibrosis.