Abstract

Background. P-Glycoprotein (P-gp), a product of the MDR-1 gene, is a transmembrane efflux pump involved in drug transport, first described in cancer refractoriness. In the normal bowel, P-gp is detectable on superficial epithelial cells, but has not been described in crypt epithelium. The role of P-gp and its intestinal expression in steroid-refractory ulcerative colitis (UC) are controversial. Aim. to compare P-gp immunostaining pattern in colonic epithelial cells of steroid-refractory versus steroid-responder UC patients. Methods. P-gp was assessed by immunohistochemistry in rectal biopsies obtained from 19 patients with active UC, including pre-surgical samples from 11 refractory patients who underwent colectomy, and 8 responders. We devised a 5-point (0-4) score, according to the percentage of epithelial surface with positive immunostaining in the superficial and crypt epithelium (apical, lateral and cytoplasmic areas). Results. Compared with responders, steroid-refractory patients had significantly higher immunostaining scores in the superficial epithelium, both in apical (2.8±0.5 versus 1.1±0.5, \( p=0.023 \)) and cytoplasmic cellular areas (2.7±0.5 versus 1.2±0.5, \( p=0.032 \)). Positive immunostaining of the superficial epithelium was frequently detected in refractory patients (apical: 9/11 cases, cytoplasmic: 10/11 cases) but was only observed in 4/8 responders. P-gp was also detected in similar areas of the crypt epithelium in 6/11 refractory patients, while it was infrequent in the group of 8 responders (1 apical 1 case, cytoplasmic 2 cases). Samples from the mucosa of normal ileal pouch-anal anastomoses obtained several years after the surgical procedure had a P-gp immunostaining pattern which was similar to that of rectal samples from patients with refractory UC. Conclusions. These results suggest a critical role of P-gp overexpression in steroid-refractory UC.

Keywords

Ulcerative-colitis, Steroidresistance, Inflammatory-Bowel-Diseases, MDR1, PGlycoprotein