Morphological and Histochemical Analysis of the Ileal Orthotopic Neobladder Mucosa Transformation

Introduction and Objective: Radical cystectomy and urinary diversion is the gold-standard treatment for muscle invasive bladder cancer. The progress achieved in reconstructive operations on the urinary bladder today leads to enlargement of prescriptions for enterocystoplasty (neobladder). However, the consequences of using parts of the intestinal tract for different types of urinary diversion are not widely appreciated. The aims and background: to assess the long-term histological, apoptotic and proliferating alterations of the intestinal mucosa of ileal orthotopic neobladders in patients with cystectomy.
Material and Methods: We prospectively studied the histological modifications in the mucosa of ilea neobladder and conduit in 23 patients who where followed for 2 years. Furthermore we studied differentiation, proliferation apoptotic mechanisms by evaluating Cdx2, Ki-67, bcl-2, p53 and TUNEL as relevant markers. Sections stained with alcian blue and periodic acid-Schiff reagent, which differentially stain mucosubstances. The performed technique was the method of “Double-U” pouch, which has been worked out in our clinic. In all patients, two random ileal biopsy specimens were obtained during surgery from the proximal 5 cm of the ileal segment used for the controls. Postoperatively, 3, 6, 12, and 24months later, cold-cup random mucosal biopsies were obtained during endoscope of the neobladder.
Results: Compared with normal ileal mucosa (there was reduction in villous height starting already during the first 6 postoperative months. This reduction was concomitant with an increase in crypt depth and a slightly increased inflammatory reaction in the lamina propria and submucosa. The goblet cells appeared to have increased in number in biopsies obtained after 3 months and remained increased in number at later times. The ileal epithelium shows changes toward a colonic aspect with villous atrophy and increased goblet cell number although, as in normal ileum, sialomucins are the most abundant secretory products. The overall proliferation rate of the mucosa, calculated as the ratio positive/total nuclei for Ki67, was moderate in groups up to 24 months ($P > 0.05$). No changes in expression of Cdx2, bcl-2, p53 were revealed in our investigation.
Conclusion: According to morphological changes of ileal mucosa of neobladder we determined 3 phases of adaptation: reactive and inflammatory – up to 6 months, compensatory- protective 6-12 months and atrophic – 12 months and more). Despite progressive atrophy, reduction of enterocytes, the ileal neobladder retains cambial compartment peculiar to intestinal phenotype with apoptosis activity that may be evidence of low degree of neoplastic transformation. These changes show that the mucosa of the ileum adapted well to the new environment, i.e. neobladder expansion and contraction as a urinary reservoir.