Summary

Patients with inflammatory bowel disease (IBD) have an elevated risk of developing colorectal carcinoma (CRC). IBD-dysplasia is regarded as a conventional precursor for IBD-associated carcinoma. (1–2) Other types of non-conventional mucosal changes with serrated and villous hypermucinous morphology have also been reported but their preneoplastic potential is still not well elucidated. (3–4)

The aim of the study was to retrospectively review samples from IBD patients focusing on detection of mucosal lesions including non-conventional lesions and evaluate their relationship and immunohistochemical and molecular properties. Surgical specimens and/or endoscopical biopsy samples of IBD patients examined during a 10-year period were reviewed. Mucosal lesions were divided into three groups - group 1 of non-conventional lesions, group 2 of true serrated polyps, and group 3 of IBD-dysplasia and colorectal carcinoma. Detailed morphological evaluation, immunohistochemical analysis of mismatch repair proteins and/or MLH1, p53 and O^6-methylguanine DNA methyltransferase (MGMT) expression, and molecular analysis for *KRAS, NRAS* and *BRAF* gene mutation was performed in all lesions. Overall, samples from 309 IBD patients were reviewed. A total of 88 mucosal lesions were found in 51 patients. Most common were lesions from group 1 with serrated epithelial change seen in 41 samples (46.6 %) and villous hypermucinous change in 6 (6.8 %). Lesions from group 1 were characterized by loss of MGMT expression in 44.6 %, aberrant p53 expression, and by mutations in *KRAS* gene in 42.9 % of cases. Group 2 consisted of 15 true serrated polyps. Six conventional IBD-dysplasias and 11 carcinomas were seen in group 3. IBD-dysplasia was characterized by aberrant p53 expression in half of the cases. IBD-associated carcinomas were morphologically heterogenous and characterized aberrant p53 expression in 54.5% of cases. Seven CRC cases harbored mutation of *KRAS*/*NRAS* and one case of *BRAF* gene. Six lesions from group 1 were associated with invasive carcinoma and two of them shared the same mutation. More than one type of lesion from different groups was found in 19 patients. Our results prove the existence of mucosal changes other than conventional IBD-dysplasia in mucosa of IBD patients and extend the knowledge about their immunohistochemical and molecular properties and relation to carcinoma. Awareness of these changes is necessary to prevent their missing and under-reporting due to their potential role in IBD-related carcinogenesis.