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Number of CD68(+) macrophages and FasL expression in colon mucosa of patients with inflammatory bowel disease as prognostic factors of colon carcinogenesis

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Colorectal cancer (CRC) is observed in 5.5-13.5% of patients with ulcerative colitis (UC) and in 0.4-0.8% of patients with Crohn's disease (CD). Gut mucosa of patients with CD, but not with UC, and the stroma of CRC have elevated numbers of CD68(+) macrophages. CRC is the second among 20 types of cancer in the number of CD68(+) cells in tumor tissue, though in 33% of tumor samples of CRC patients and in all samples of normal tissue this protein is not expressed. The expression of Fas Ligand (FasL), representing another branch of immunoreactivity, in the lesions of CRC and UC but not of CD is upregulated. The fact that enterocyte apoptosis is increased in lesions of CD and lymphocytes in UC are resistant to Fas-mediated apoptosis can be the keypoint for understanding the counterattack hypothesis [O'Connell et al., 1999], suggesting that cells express FasL and are able to kill Fas-expressing infiltrating activated lymphocytes and escape rejection by the immune system, which can be the basis for differences in association of UC and CD with CRC. The aim of this study was to evaluate the number of CD68(+) macrophages and to analyze FasL expression in colon mucosa of patients with UC, CD and CRC in order to assess its value for prognosis of CRC.

Material and methods: The diagnosis was independently established by endoscopic, radiological, and histological criteria. Expression of CD68 (KP1 clone, Dako, 1:50) and FasL (Diagnostic BioSystems, 1:75) was analyzed immunohistochemically in the samples of colon mucosa taken from the affected areas of 4 patients with UC, 6 patients with CD and 10 patients with CRC. In addition in 7 CRC patients the samples taken from unaffected areas were analyzed. All paraffin-embedded samples were serially sectioned, deparaffinized and processed using the streptavidin-biotin technique [Hsu SM et al, 1981]. Morphometry was provided using a Leica DMR microscope, Leica DC300 digital camera, a personal computer (Intel core i3) and Leica QWin software. The relative square (percent) of immunopositive cells to the total square occupied by the cells was calculated for 5 fields for each sample.

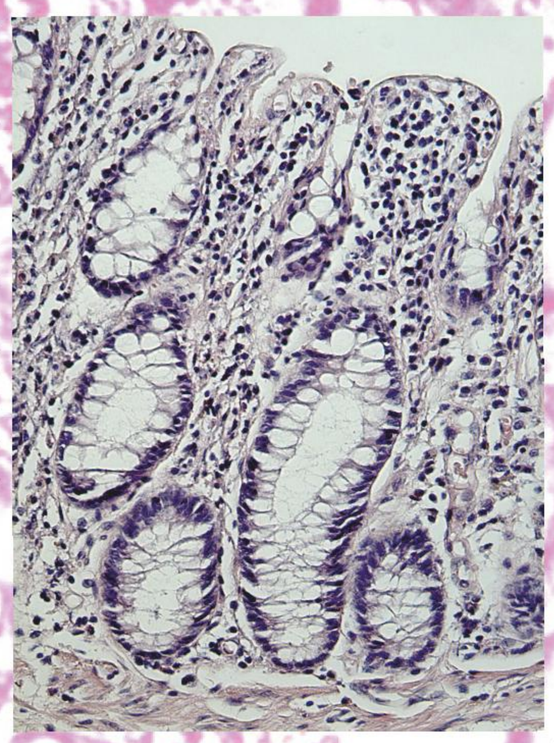


Fig.1. Inflammation changes in colon mucosa. H&E, x200

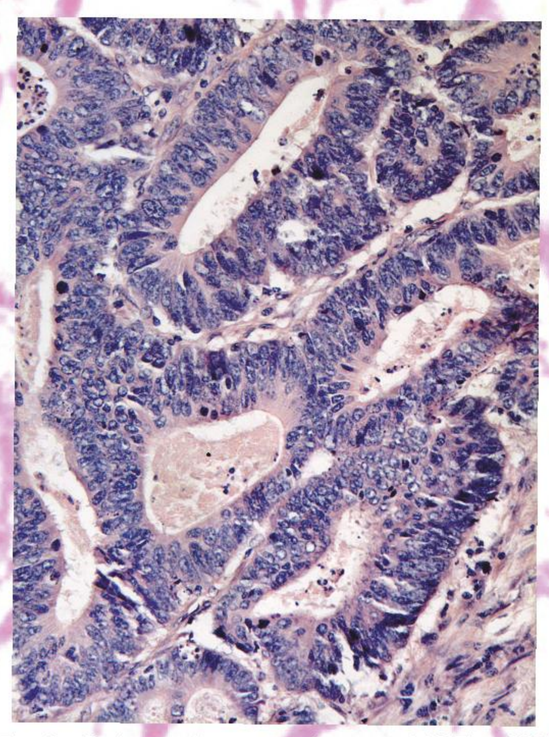


Fig.2. Colon adenocarcinoma. H&E, x200

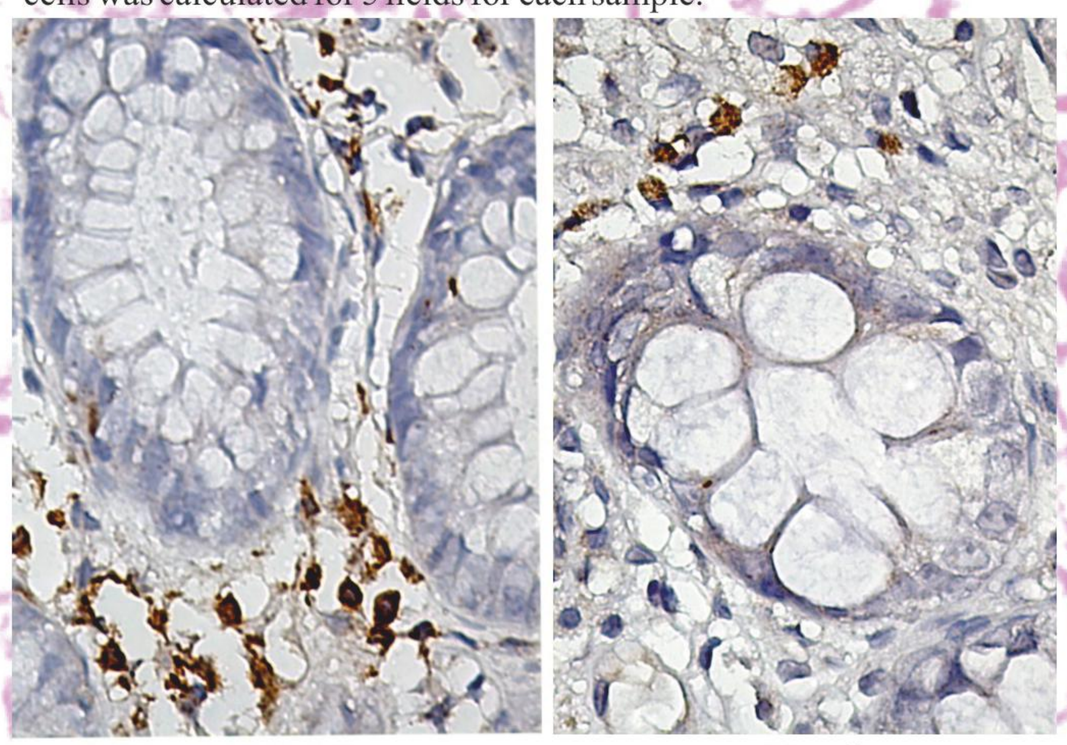
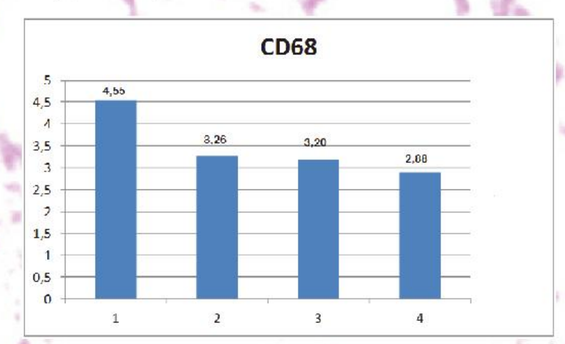
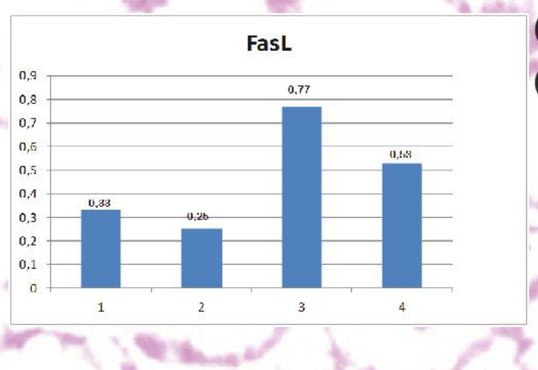


Fig.3. Expression of CD68 & FasL in cells of colon mucosa. IHC, x 400





1 - ulcerative colitis (UC)
2 - Crohn's disease (CD)
3 - Colorectal cancer (CRC)
4 - unaffected areas of CRC patients

Results:

1. We didn't find differences (p=0.19) in average numbers of CD68(+) macrophages in CD (3.26) and UC (4.55) patients,
2. We didn't find differences (p=0.17) in average expression of Fasl in lymphocytes in CD (0.25) and UC (0.33) patients,
3. Average expression of FasL in both unaffected (0.53) and affected (0.77) areas of CRC patients was higher (p=0.04, p=0.00) than in CD patients (0.25),
4. We revealed a tendency (p=0.06) to higher number of CD68(+) macrophages in UC patients (4.55) vs unaffected areas of CRC patients (2.88),
5. Average expression of FasL in affected areas of CRC patients (0.77) was higher (p=0.02) than in UC patients (0.33) and the same (p=0.23) as in unaffected areas (0.53).

Though we didn't find CD68(+) and FasL in CD and UC patients were reliable independent prognostic factors for transformation to CRC, the revealed associations support the possibility to use expression of FasL as a prognostic marker

WCGC 2015
197--P
Basic Colon Cancer
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DOI: 10.3252/pso.eu.17wcgc.2015
Poster presented at: 17th World Congress on Gastrointestinal Cancer, 1-4 JULY 2015, BARCELONA, SPAIN