ABSTRACT

The aim of the presented thesis is to summarize a benefit and limitations of histopathological assessment of bioptic samples for diagnostics and prediction of complicated course of the disease in children with inflammatory bowel diseases (IBD). We would also like to outline a potential benefit of more sophisticated histopathological methods in these domains.

In the first phase of our research, we aimed at correlation of microscopical disease activity in children with Crohn's disease (CD) with activity assessed endoscopically and clinically. We also examined a histopathology as a possible predictor of development of complications, since previous works on adult cohorts indicate only a limited predictive value of microscopy. Our study confirmed this premise also for pediatric patients, since histopathological findings correlated weakly with endoscopy, didn't correlate with clinical activity of the disease and did predict none of the defined complications. On the other hand, endoscopy appeared to be a reliable predictor of complicated course of the disease.

In the next part of our research, we were searching for other, more precise methods of assessment of histopathological disease activity that could serve as predictors of complications. We focused at immunohistochemical assessment of tissue calprotectin (CPT). As a product of neutrophils, this substance is released into mucosa and lumen of the gut in case of active inflammation. Therefore, we speculated, that direct visualization of this substance could pecify the assessment of acute inflammation in children with IBD. The first study was performed on cohort of pediatric patients with ulcerative colitis (UC), the second on children with CD who underwent ileocecal (IC) resection. In the second study, we assessed the tissue CPT in resection margins of resected bowels. In the first study, we demonstrated a good correlation of levels of the tissue CPT with microscopic activity of the inflammation established by standard histopathological scores, but a poor correlation with endoscopy and no correlation with clinical activity of the disease. The tissue CPT had no predictive value for complications development, much like histopathology itself. On the other hand, levels of the fecal CPT and moderate clinical activity of the disease (defined as Pediatric Ulcerative Colitis Activity Index > 40) predicted a necessity to initiate a systemic 5-aminosalicylic acid therapy and corticotherapy. Neither the second study confirmed that immunohistochemical detection of the tissue CPT could predict a complicated course of the disease, in this case an endoscopic recurrence in 6 months after ileocecal resection. However, a presence of acute and chronic peritonitis in resection margins appeared to be a predictor, as well as a low serum albumin and

elevated CRP at the time of diagnosis and high level of the fecal CPT at the time of endoscopic control.

The third domain of our research focused at improvement of diagnostics of pediatric IBD. We aimed at immunohistochemical assessment of CD30+ lymphocytes in intestinal mucosa in children with CD, UC and IBD unclassified (IBDU). Since the current knowledge about IBD immunopathogenesis indicate that children with UC could have higher levels of CD30+ lymphocytes in serum and intestinal mucosa, we decided to use this detection as a possible marker of UC differentiation. Our work showed a significant difference in numbers of mucosal CD30+ lymphocytes in almost all bowel segments, with maximal difference in rectum. Children with UC showed significantly higher counts of mucosal CD30+ lymphocytes compared to children with CD. We also found a cut-off that was able to differentiate UC from CD with almost 90 % sensitivity a specificity. These results are promising also for a future targeted anti-CD30 therapy. Apart from that, we focused at detection of CD30+ lymphocytes in children with IBDU. A significant difference between UC and IBDU we found could shed a light on biology of IBDU and select IBDU patients with possible future differentiation towards UC.