abnormality. Fifty consecutive patients (29 F; age range 20-69 yrs), with normal serum biochemistry, CBC, thyroid function, EMA, and normal ileum-colonoscopy were evaluated. Patients matched the symptom-based diagnosis of IBS (n=27), of functional diarrhea (FD n=7), and unspecified functional bowel disorders (UBFD n=16). Biopsies of the terminal ileum (n=2) cecum (n=1), ascending (n=1), transverse (n=1), descending (n=1), sigmoid (n=1) colon, and rectum (n=1) were stained with H-E for microscopic assessment by a pathologist unaware of the clinical diagnosis.

Results: Histological abnormalities were found in 14 (28%) patients: 4 IBS-D, 4 functional diarrhea and 6 UBFD. Increased lymphoplasmacytic infiltrate and granulocyte clusters were present at the level of a) the ileum only in 1 IBS patient, and in 2 UBFD patients; b) the cecum only in 1 IBS patient, Altered crypt architecture was present in the rectum only in 1 UBFD. Microscopic colitis was present in 1 IBS-D, 3 functional diarrhea, and 1 UBFD, patients.

Conclusions: Mucosal biopsies at multiple sites of colon, rectum, as well as terminal ileum are required to detect non-specific microscopic inflammatory abnormalities and specific microscopic collagenous colitis that may be equally present in patients with different clinical presentation of endoscopy negative symptom-based diagnosis of functional bowel disorders.

P183 TREATMENT WITH ANTI-TUMOR NECROSIS FACTOR ALPHA ANTIBODIES AND SUB-OBSTRICTIVE SYMPTOMS IN CROHN’ S DISEASE: PROSPECTIVE LONGITUDINAL STUDY

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Background: The development of strictures has been reported using anti-TNFα monoclonal antibodies (MoAbs) in Crohn’s Disease (CD). The possible correlation between anti-TNFα therapy and development of symptomatic stenosis is unknown.

Aim: The main purpose was to assess, in a prospective longitudinal study (and in a retrospective analysis), the frequency of sub/obstructions in CD pts treated with different anti-TNFα therapies. Secondary end point was to evaluate possible changes of sonoographic findings after anti-TNFα therapy.

Methods: Prospective longitudinal study. From Jan 2004 to Oct 2007, 20 CD pts (11 M, median age 41.5 yrs, range 17-69 yrs) were treated with anti-TNFα MoAbs including Infliximab (n=11), Cetolizumab (n=4), Adalimumab (n=5) according to standard protocols. At baseline, the pattern of the lesions was fibrostructuring in 8, fistulizing in 4 and inflammatory in 8 pts. The median follow up was 47 weeks (range 22-47) in the Infliximab, 134 wks (range 32-134) in the Cetolizumab and 21 weeks (range 19-23) in the Adalimumab group. Clinical assessment (CDAI), including the development of sub/obstructive symptoms after biological therapy was recorded at each drug administration. Small Intestine Contrast Ultrasonography (SICUS) was performed before and after anti-TNFα MoAb therapy in 11 pts (Infliximab n=8, Cetolizumab n=3). Sonographic parameters were considered bowel wall thickening (≥3 mm), sub/obstructive fibrostructuring (diameter ≥1 cm) with or without pre-stenotic dilation (≥25 mm), fistulae, abscesses, lesion extent (cm). Retrospective analysis. Clinical records of CD pts in follow up from Jan 1999 to 2007 showed that additional 60 consecutive CD pts (24 M, median age 45 yrs, range 21-71) were treated with Infliximab. Sub/obstructive symptoms after treatment were considered.

Results: Prospective longitudinal study: 4/20 pts (20%) treated with anti-TNFα MoAb developed sub/obstructive symptoms (2 with Infliximab, 2 with Cetolizumab). All these pts were treated with steroids and 2 pts (Infliximab group) required surgery after 8 and 4 mths. Subobstructive symptoms were observed after therapy in 4/8 pts with fibrostructuring disease before treatment. The median time from the first anti-TNF therapy and subobstructive symptoms was 21 mths (range 6-23). Sonographic findings did not significantly change after treatments. Retrospective analysis. Development of sub/obstructive symptoms was observed in 10/60 pts (16.6%) treated with Infliximab; 9/10 received steroids and 5/10 pts required surgery.

Conclusion: Prospective and retrospective analyses suggest the possible role of anti-TNFα therapies in inducing sub/obstructive symptoms in CD.

P184 OUTCOME OF POUCH SURGERY FOR ULCERATIVE COLITIS: SINGLE CENTER EXPERIENCE

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Aim: The purpose of the present study is to present the experience and evaluate the outcome of pouch surgery for patients with ulcerative colitis (UC), Materials and Methods: Fifty eight patients underwent surgery for UC between 1996 and 2007 at Mansoura Gastroenterology Center. A retrospective analysis has been done of all patients with UC undergoing surgery which includes details of the patient’s history, indication of surgery, type of operation, postoperative morbidity, and functional outcome.

Results: The main indication for operation was failed medical treatment (n=42, 72.4%). Pouch surgery was performed in 25/58 patients (43.1%). The majority of patients, 23/25 (92%) had J-shaped pouch and most patients, 19 (76%), underwent a stapled anastomosis. Twenty patients (80%) had a defining ileostomy. There was one postoperative small bowel obstruction. Early complications after pouch surgery included pelvic sepsis (n=4), small bowel obstruction (n=2), pouch hemorrhage (n=1), wound sepsis (n=3). Long-term follow-up data were available for 14 patients. The most common long-term complication was anastomotic stricture (n=9, 42.6%). Five patients (35.7%) presented with pouchitis. Median daytime stool frequency was 5.1. Three patients (21.4%) presented with fecal incontinence.

Conclusion: Pouch surgery is a major one that attains many complications. However, the long term results and patient’s satisfaction are reasonable.
During oesophageal manometry lower oesophageal sphincter pressure (LES) mean value was normal (21.1 mmHg ± 3.2), 9 patients (30%) had a normal oesophageal corpus peristalsis but 21 (70%) had non specific oesophageal motility disturbances. Each patient with diagnosed GERD had continue baseline Crohn’s disease treatment, additionally with proton pump inhibitor (PPI) pantoprazole 40 mg/day. All the patients had a significant improvement in general feeling and decrease abdominal pain and discomfort.

Conclusions: Abdominal pain, which is a predominant symptom in patients with Crohn’s disease, could be also intensified with undiagnosed gastroesophageal reflux disease. Efficacy GERD treatment may lead to significant improvement in general feeling and better effect of Crohn’s disease treatment.

P187
COAGULATION DISORDER AFTER TREATMENT WITH CERTOLIZUMAB PEGOL

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Introduction and Aims: The anti-TNF alpha immunomodulators, represented a major advance in the therapy of inflammatory bowel disease (IBD), initially in Crohn’s disease (CD) and now also in ulcerative colitis. They have, however, secondary effects, some well known and expected and others unexpected and rare.

The authors present a case of secondary deficiency of coagulation factors after treatment with Certolizumab Pegol in a patient with CD.

Material and methods: Review of clinical records of the patient with detailed study of coagulation.

Results/Case description: A 32-year old patient, with ileo-colic CD (A2 L3 B2 P), diagnosed in 2001, with multiple perianal fistulae, with recurrent symptoms of abdominal pain and distension was admitted in 04/2007 in our Gastroenterology Department. He was on therapeutic with azathioprine, mesalamine and corticoids (multiple cycles - corticoid-dependent disease) without adequate clinical response. Infliximab was started in 2002, initially with good results but with loss of response in the last year, even with increased dosage. On admission he had no leukocytosis, anaemia or alterations in coagulation times. C-reactive protein was 14.14 mg/dl (normal-0.5) and abdominal ultrasonography revealed thickening (1 cm) of distal ileum with some peritoneal fluid. IV prednisolone (50 mg/day) was started and the patient went well. Since the disease was corticoid-dependent and refractory to infliximab we decided to start Certolizumab Pegol (400 mg at 0, 2 and 4 weeks and then every 4). Soon after induction, the patient was clinically well but we noticed a marked elevation in activated partial thromboplastin time (51.2 seconds to a control of 29.5 s and a maximum of 34 s). A study of coagulation disorders was performed and a significant decrease of Factor XII time (51.2 seconds to a control of 29.5 s and a maximum of 34 s). A study of coagulation disorders was performed and a significant decrease of Factor XII time (51.2 seconds to a control of 29.5 s and a maximum of 34 s). A study of coagulation disorders was performed and a significant decrease of Factor XII time (51.2 seconds to a control of 29.5 s and a maximum of 34 s). A study of coagulation disorders was performed and a significant decrease of Factor XII time (51.2 seconds to a control of 29.5 s and a maximum of 34 s). A study of coagulation disorders was performed and a significant decrease of Factor XII time (51.2 seconds to a control of 29.5 s and a maximum of 34 s).

Concentration: Certolizumab Pegol is a new anti-TNF alpha, with some potential in patients refractory to infliximab but, in our only patient submitted to this drug, a rare and undocumented secondary effect occurred. We must be alert to potential adverse events of this new kind of drugs.

P188
REDUCED METALLOTHIONEIN EXPRESSION IN COLONIC CROHN’S DISEASE: EVIDENCE FOR A NEW DISEASE-MODIFYING GENE

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Background: The identification of genetic determinants of Crohn’s disease (CD) remains a challenge. This study aimed at identifying new candidate susceptibility genes for CD by integrating known disease loci with gene expression in unaffected colon biopsies of CD patients. We focused on characterizing one of the candidate genes, metallothionein (MT), which belong to a family of highly conserved stress proteins comprising immunomodulating properties.

Methods: June CD patients and 11 controls were subjected to microarray analysis using a focus microarray (VIB Crohn 7K2) containing 6,779 expressed sequence tags. The expression of MT was analyzed by quantitative PCR and immunohistochemistry. To model lowered MT expression in vitro, a colon carcinoma epithelial cell line expressing small interfering RNA against MT was generated. The gene for MRE-binding transcription factor 1 (MFTF1) was screened for mutations in 96 CD patients and the influence of a polymorphism on transcriptional activity was assessed in a luciferase reporter assay.

Results: Eighteen differentially expressed genes were identified. Metallothionein mRNA expression was reduced in colon biopsies (P=0.008) and in PBMCs (P=0.026) of patients with colonic involvement. This observation was confirmed in realtime by immunohistochemistry (P=0.046). MT-knockdown HT29 cells showed a reduced IL8 secretion in response to bacterial challenge. Sequence analysis of the main transcriptional regulator of MTs, MTF1, revealed two coding mutations: Asp63Glu in 5 patients and Gln335Arg in 2 patients. In addition, a frequent (29%) polymorphism at the splice site junction between exon 8 and 9 (c.1270A>G) was found. An intronic polymorphism (IVS1-128A>T) was significantly associated with colonic disease (Chi-square: 8.297, P=0.004). Moreover, this polymorphism was shown to influence the transcription of a reporter gene, suggesting allele specific transcription of MTF1. This could be responsible for the reduced MT expression observed in colonic CD.

Conclusions: We showed that deficient basal MT expression in CD patients with colonic involvement is, at least in part, genetically determined. We identified MTF1 (located within the IBD7 locus) as a new disease-modifying gene.