

Methods Purified *C difficile* toxin A was labelled with Alexa Fluor 488 (toxin A⁴⁸⁸) and its biological activity and specificity of fluorescence were confirmed using Vero cells and anti-toxin A antibody, respectively. Peripheral blood mononuclear cells (PBMNCs) were obtained from 20 patients [13 female, 7 male; median age 67 yrs (range 32–96 yrs)] with *C difficile* infection, within 10 days of diarrhoeal onset. For flow cytometry, PBMNCs were incubated on ice in the dark for 1 h in the absence or presence of toxin A⁴⁸⁸. After washing, cells were labelled with anti-CD19-ECD (B cell marker) and anti-IgD-PE (to identify antigen-activated IgD-negative cells). PBMNCs were also polyclonally stimulated in vitro for 6 days to induce differentiation of memory B cells to antibody secreting cells (ASCs). Enzyme-linked immunospot (ELISPOT) assays were used to quantify toxin A-specific IgG ASCs and expressed as percentage of total IgG ASCs. Toxin A-specific IgG antibody levels in sera were studied by ELISA. Data are expressed as median (range).

Results Compared to control buffer, a significantly greater proportion of events (flow cytometry) were seen in the CD19-positive, IgD-negative gate in PBMNCs exposed to toxin A⁴⁸⁸ [0.09% (0%–0.54%) vs 0.92% (0.09%–1.78%); $p<0.001$]. In four patients studied at the same time as flow cytometry, toxin A-specific ASCs were detected by ELISPOT assays (0.04%–2%). In studies over 4 (1–10) months after infection, toxin A-specific ASCs were observed [0.33 (0.07–2.12)%]. Serum anti-toxin A antibodies were detectable in eight patients at the time of clinical disease and in four patients, the antibody levels increased over the following 6 (2–10) months.

Conclusion (1) A small population of toxin A-specific, antigen-activated B cells can be detected in the circulation soon after *C difficile* infection. (2) In addition to circulating antibody, toxin A-specific memory B cells can be detected over many months after *C difficile* infection. (3) Future studies can investigate the relationship between the development of B cell responses to *C difficile* toxins and the nature of clinical disease.

Competing interests None declared.

PWE-109 SHOULD CT COLONOSCOPY REPLACE FLEXIBLE SIGMOIDOSCOPY EXAMINATION AS FIRST LINE INVESTIGATION IN PATIENTS WITH SUSPECTED COLORECTAL CANCER?

doi:10.1136/gutjnl-2012-302514d.109

¹U D Simoniuk, ²A Milewska, ¹C Kiire. ¹Department of Gastroenterology, Southport Hospital, Southport, UK; ²Medical University of Białystok, Białystok, Poland

Introduction It is recommended that all patients undergoing barium enema have a flexible sigmoidoscopy to exclude disease in rectum and sigmoid colon. With the introduction of CT colonoscopy (CT colon) is sigmoidoscopy still required for the investigation of patients with suspected colorectal cancer (CRC).¹ We reviewed CT colon and flexible sigmoidoscopy results in our patients who underwent both procedures with a view to answering this question.

Methods The findings of CT colon in 520 consecutive patients were reviewed by a GI radiologist blinded to the findings at flexible sigmoidoscopy. The mean age of the population was 65 years old. Patients with inadequate bowel preparation for flexible sigmoidoscopy, colonoscopy, polypectomy, abnormal MRI or CT colon as first line investigation and more than 6 months period between CT colon and flexible sigmoidoscopy were excluded. Statistical analysis was performed with χ^2 and Fisher test.

Results 332 patients were excluded for the reasons stated above. 188 patients were analysed. In 88% of these there was concordance between the results of CT colon and flexible sigmoidoscopy. Statistically significant ($p<0.001$) association was shown between detecting cancer by flexible sigmoidoscopy vs CT colon. The sensitivity and specificity of flexible sigmoidoscopy was 74% and 99%

respectively [ppv=0.93, npv=0.94]. Flexible sigmoidoscopy did not identify six cancers which were revealed on CT colon. CT colon did not detect two cancers due to collapse colon and further investigation was recommended. There was statistical significant ($p<0.05$) association between bowel symptoms such as PR bleeding and iron deficiency anaemia and the diagnosis of bowel cancer in patients undergoing flexible sigmoidoscopy.

Conclusion CT colon should replace flexible sigmoidoscopy especially in elderly patients as first line investigation. Flexible sigmoidoscopy still has a role in those patients who found on CT colon to have a collapse left colon.

Competing interests None declared.

REFERENCE

1. NICE clinical guideline. "The Diagnosis and Management of Colorectal Cancer". Issued: November 2011.

PWE-110 WHAT IS THE SIGNIFICANCE OF "DIMINUTIVE" COLONIC POLYPS IN PATIENTS SCREENED FOR COLON CANCER AFTER A POSITIVE FAECAL HUMAN HAEMOGLOBIN TEST (FHH)?

doi:10.1136/gutjnl-2012-302514d.110

V Mahesh, ^{*}A Lim, K Pietris, J Argyrides. Department of Gastroenterology, Royal Adelaide Hospital, Adelaide, Australia

Introduction By definition "diminutive" colonic polyps are ≤ 5 mm in size. Improvements in optical imaging modalities and image resolution coupled with increased operator awareness have resulted in a higher detection rates at colonoscopy. Although such polyps are low risk for malignancy, studies suggest that high grade dysplasia may occur up to a rate of 4% in these polyps. There is an ongoing debate regarding the natural history and prognostic relevance of these polyps including suggestions for non-resection/to resect and discard.

Aim To analyse the significance of "Diminutive" colonic polyps in patients screened for colon cancer after a positive Faecal Human Haemoglobin test.

Methods Patients referred to a single tertiary institution in South Australia for screening colonoscopy after detection of a positive FHH. All patients referred between 2007 and 2010 were included in this retrospective study. The patients were referred either through the National Bowel Cancer Screening Program (NBCSP) or through GP initiated screening. Polyps were measured after the tissue was placed in formalin (histological size). For each colonoscopy the predetermined aim was to resect all polyps and assess histologically.

Results A total of 384 patients had colonoscopy. NBCSP referred (n=173, 45%) and GP initiated FOBT (n=211, 55%). 228 M: 156 F with mean age of 61.8 ± 0.6 yrs, 305 polyps in total. Majority of the polyps (57%, n=173) were ≤ 5 mm compared with 6–9 mm (23%,

Abstract PWE-110 Table 1 Histology of polyps ≤ 5 mm in size

Tubular adenoma—low grade dysplasia	86	48%
Tubular adenoma—high grade dysplasia	1	0.6%
Serrated adenoma	8	4.6%
Tubulovillous adenoma—low grade dysplasia	10	5.8%
Tubulovillous adenoma—high grade dysplasia	0	0%
Villous adenoma—low grade dysplasia	1	0.6%
Villous adenoma—high grade dysplasia	0	0%
Adenocarcinoma	0	0%
Hyperplastic polyps	66	38.1%
Total	173	

$n=69$; $p<0.001$) and ≥ 10 mm polyps (21%, $n=63$; $p<0.001$). The histological features of the polyps ≤ 5 mm were predominantly tubular adenomas (TA) (80%, $n=86/107$), please see Abstract PWE-110 table 1 for rest of histology. Only 38% ($n=66$) of polyps ≤ 5 mm were hyperplastic in nature. In polyps ≤ 5 mm in size, one TA with high grade dysplasia (0.6%) was seen but no carcinoma compared to 11 (3.6%) carcinomas/high grade dysplasia in ≥ 6 mm size polyps ($p<0.001$). Three cancers were seen, two in polyps ≥ 10 mm size and one in the 6–9 mm size. 51% were left sided, 14% were right sided, location not specified in 35%, this difference was not statistically significant.

Conclusion In patients who are positive for FHH the incidence of diminutive polyps is considerable and importantly there is a significant proportion of adenomatous polyps. Based on these findings we believe that diminutive polyps should be resected, histologically evaluated and followed-up appropriately.

Competing interests None declared.

Small bowel II

PWE-111 LIPOPOLYSACCHARIDE INDUCES SMALL INTESTINAL EPITHELIAL CELL APOPTOSIS AND SHEDDING WHICH IS REGULATED BY NF κ B SIGNALLING

doi:10.1136/gutjnl-2012-302514d.111

J M Williams,* C A Duckworth, B J Campbell, D M Pritchard. *Department of Gastroenterology, University of Liverpool, Liverpool, UK*

Introduction The gut barrier is formed by a single cell thick, simple columnar epithelium consisting of intestinal epithelial cells (IECs) held together by tight junctions. In the small intestine, IECs are generated in the crypt, migrate up the crypt-villus axis and are shed at the villus tip. When IECs detach from the villus during the process of shedding, discontinuities occur in the epithelium. IEC shedding increases in response to pro-inflammatory cytokines, resulting in larger discontinuities and increased intestinal permeability. Understanding the mechanisms which regulate IEC shedding may allow development of therapeutic strategies which ameliorate its detrimental effects on gut barrier function in intestinal disease states.

Aims To investigate whether IEC apoptosis and shedding are increased during induction of endotoxemic shock, and the genetic regulation of this process.

Methods Lipopolysaccharide (LPS) from *Escherichia coli* O111:B4, was administered to adult female C57BL/6 mice at 10 mg/kg by intraperitoneal injection ($n=6$ per group). Animals were euthanased 1–6 h after LPS administration. The duodenum, jejunum and ileum were fixed in formalin. Histopathological examination of H&E stained sections, quantification of villus length, and immunolabelling of IECs for active caspase 3 was performed. Dose response experiments were performed using 0.125 to 20 mg/kg LPS, sacrificing mice ($n=4$ per group) at 1.5 h. Transgenic mice (NF κ B1–/–, NF κ B2–/– and cREL–/–) were administered 10 mg/kg or 0.125 mg/kg LPS and euthanased at 1.5 h ($n=6$). Statistical comparisons were made by t-test with Bonferroni correction.

Results In C57BL/6 mice, 10 mg/kg LPS caused a 20–50-fold increase in IEC apoptosis and shedding, with consequent villus atrophy, which was greatest in the duodenum and jejunum at 1.5 h, and in the ileum at 2 h. IEC apoptosis and shedding had subsided by 6 h after LPS administration. LPS at 0.125 mg/kg caused an attenuated response in C57BL/6 mice in terms of villus injury and amounts of apoptosis and shedding at 1.5 h, whereas at this dose NF κ B1–/– mice were severely affected, while NF κ B2–/– mice were minimally affected.

Conclusion These findings suggest that endotoxemic shock causes dynamic and hyperacute selective injury to the murine small intestine, prior to obvious pathological alterations in other organ systems. The induced apoptosis and cell shedding occurs within a well defined time period, and varies in intensity and time course in different intestinal segments. The differing sensitivity to LPS in transgenic mice implicates NF κ B signalling in the pathogenesis of this type of intestinal injury.

Competing interests None declared.

PWE-112 PREVALENCE OF OSTEOPOROSIS IN A LIVERPOOL COELIAC COHORT SUPPORTS ROUTINE USE OF BONE MINERAL DENSITY ASSESSMENT

doi:10.1136/gutjnl-2012-302514d.112

¹J Collum,* ²A Smith, ²K Martin. ¹*Department of Gastroenterology, Royal Liverpool University Hospital, Liverpool, UK;* ²*Department of Dietetics, University Hospital Aintree, Liverpool, UK*

Introduction Coeliac disease may be associated with osteoporosis and increased fracture risk. Osteoporosis is a significant public health problem with major consequences for patients and health care systems.¹ Debate exists concerning the utility of routine bone mineral density (BMD) assessment in patients with coeliac disease.² We aimed to identify the prevalence of osteoporosis in patients with coeliac disease as defined by BMD assessment.

Methods Dietitian led data sets are currently maintained for all coeliac patients under active follow-up at University Hospital Aintree. We retrospectively analysed this information to determine (1) the frequency of BMD assessment in coeliac patients and, (2) the results of BMD assessment. Osteoporosis was defined as a T score of ≤ -2.5 SDs below mean at either lumbar spine or hip.

Results The data sets for 232 patients were available for analysis. Demographics: 70% female, 30% male, mean age at diagnosis 52 (range 3–79 years). BMD assessment was undertaken in 211 (91%). The indication for this assessment in all cases was a clinicopathological diagnosis of coeliac disease. Of those undergoing BMD assessment, 26% had osteoporosis. On questioning at outpatient assessment 141 (67%) patients reported participation in regular weight bearing exercise. Of these patients 33 (24%) had osteoporosis compared to 10/30 (33%) not documented to undertake weight bearing exercise ($p=0.26$). Of those undergoing BMD assessment, 128 (61%) had been prescribed calcium supplements. 49/128 (38%) patients documented to be taking calcium supplements had BMD measurements consistent with osteoporosis compared to 4/82 (5%) patients not taking calcium supplements.

Conclusion At this UK centre, where over 90% of patients with coeliac disease underwent BMD assessment, 26% had osteoporosis. This is comparable to the rate demonstrated by Fitzgerald *et al* (25%)³ and provides further support for the routine use of BMD assessment in coeliac disease to screen for osteoporosis. A lesser proportion of patients who participated in regular weight bearing exercise had osteoporosis at BMD assessment, but this finding was not statistically significant.

Competing interests None declared.

REFERENCES

1. Lewis NR, Scott BB. *Guidelines for Osteoporosis in Inflammatory Bowel Disease and Coeliac Disease*. BSG Guidelines in Gastroenterology, 2007. <http://www.bsg.org.uk/clinical-guidelines/ibd/guidelines-for-osteoporosis-in-inflammatory-bowel-disease-and-coeliac-disease.html>
2. Lewis NR, Scott BB. Should patients with coeliac disease have their bone mineral density measured? *Eur J Gastroenterol Hepatol* 2005;**17**:1065–70.
3. Fitzgerald T, Davies H, Howdle PD, *et al*. Prevalence of osteoporosis in Leeds coeliac cohort. *Gut* 2011;**60**:A91.