Platelet count/spleen diameter ratio as a predictor of oesophageal varices in alcoholic cirrhosis

We read with great interest the article by Giannini et al (Gut 2003; 52:1200–5) regarding platelet count/spleen diameter ratio as a non-invasive parameter to predict the presence of oesophageal varices in patients with liver cirrhosis. In patients with liver disease due to alcohol, platelet count is reduced due to the myelotoxic effect of alcohol. In the study, only 16.5% (24/145) of patients had liver cirrhosis due to alcohol. In the UK, alcohol is the commonest cause of liver cirrhosis.

We retrospectively studied endoscopy, haematology, and radiology reports of 40 patients who had been treated for alcohol induced cirrhosis at Homerton Hospital, London. Of these, 30 had oesophageal varices at endoscopy and 10 did not. The platelet count/spleen diameter ratio was calculated within two months of endoscopy.

The median platelet count/spleen diameter ratio in patients with varices was 537 (range 371–670) and with no varices 2229 (range 1542–3174). A platelet count/spleen diameter ratio of <909 had 100% sensitivity and specificity for the prediction of oesophageal varices in patients.

We have shown that this non-invasive method of predicting the presence of oesophageal varices through platelet count/spleen diameter ratio is reproducible in alcoholic cirrhosis patients.

References


Diagnosis of hereditary non-polyposis colorectal cancer (HNPCC)

The original Amsterdam criteria were not developed to serve as the diagnostic criteria for HNPCC but merely to introduce a uniform approach to the selection of families for collaborative studies. It was originally considered that the criteria would be relatively specific rather than sensitive. However, colorectal cancer is a common disease, and the finding of three close relatives affected by bowel cancer within a single large family would not necessarily equate with a specific autosomal dominant disorder, even if one of the subjects happened to be aged below 50 years. Ponz de Leon and colleagues (Gut 2003; 53:115–22) show in table 3 that families meeting the Amsterdam criteria but having cancers that are DNA microsatellite stable do not display the clinical features of HNPCC (see below). This is not altogether surprising. In fact it was shown nearly 10 years ago that colorectal cancers in such Amsterdam positive kindreds were often very frequently DNA microsatellite stable and that the clinical and pathological features of these families were unlike HNPCC (see below). Of course, the latter findings do not preclude a genetic basis for such clustering of colorectal cancer within a family.

The diagnostic features of HNPCC have accumulated and been refined over time. HNPCC is now defined by a set of clinical, pathological, and molecular features that encompass: a family history of colorectal cancer, a particular spectrum of extracolonic neoplasms, multiple colorectal neoplasia, early onset neoplasia, particular histological features among colorectal cancers, the presence of DNA microsatellite instability, loss of expression of DNA mismatch repair proteins as shown by immunohistochemistry, and a germline mutation in a DNA mismatch repair gene. It may not be possible to identify the germline mutation in all families, even when cancers show evidence of deficient DNA mismatch repair. This is merely the result of technical limitations which should not preclude a diagnosis based on other clinical features.

Now that there is international agreement that the term HNPCC equates to a specific clinicopathological entity, there would seem to be little merit in applying the diagnosis when only the limited set of clinical features encompassed by the Amsterdam criteria is met. Reporting of a family history of colorectal cancer has been shown to be unreliable. What would we think of a judge who chose to base his verdict only on hearsay and rumour and to ignore all evidence of a scientific nature? Why should a family be burdened unnecessarily with the label HNPCC and all its ramifications and how may epidemiological research be advanced by the application of a vague and unreliable diagnostic label?

J R Jass

Correspondence to: Professor J R Jass, Department of Pathology, Duffus Building, McGill University, 3650 University st, Montreal, Quebec, Canada H3A 2A4; jeremy.jass@mcgill.ca

Author’s reply

In reply to the letter of Dr Jass we would like to make the following points.

We agree with Dr Jass that since the new discoveries and advances in our knowledge of hereditary non-polyposis colorectal cancer (HNPCC), the diagnosis of the syndrome has become a matter of conscience. The Amsterdam clinical criteria are useful but not definitive in the diagnosis of the disease, and other parameters (pathological, biological, molecular) must be taken into account. Besides, family history is not reliable in every case. So, what should we do?

We believe that, as a first step, the classical clinical approach of tracing a genealogical tree focused on malignancies in the family should be pursued for each proband to attempt to estimate the probability of disclosing an hereditary form of colorectal cancer. In doing this, we do not label a family as HNPCC on clinical grounds alone, but we think that such families should be studied and followed with particular attention to obtain other clues and proof of the syndrome and to provide appropriate counselling measures.

From an epidemiological point of view, we agree that estimation of the frequency of the syndrome based on clinical criteria should be considered with caution, but it is the only practical way. When a population approach was used, defining the microsatellite status of all registered tumours in a period and then searching for constitutional mutations in patients with unstable tumours, as high as 2.7% of patients with colorectal tumours were labelled as HNPCC. These values are similar to those obtained with clinical criteria (Gut 2003; 53:115–22) although not confirmed in other settings. Therefore, we believe that it is not a burden for the family if we choose to follow them with special care. Moreover, it has been demonstrated that active follow up can reduce the number of newly developed carcinomas in families with HNPCC (not all with a molecular diagnosis) and reduce cancer mortality.
Bone density loss in Crohn’s disease: role of TNF and potential for prevention by bupropion

We note with interest the demonstration by Card et al. that the increased hip fracture rate in Crohn’s disease (CD), and by inference the diminished bone density commonly noted in CD, is only to a minor degree secondary to iatrogenic corticosteroid use (Card et al. 2004;33:231–5). The subject of bone mineral density loss in CD has been recently reviewed; tumour necrosis factor α (TNF-α) is suspected of being an important mediator of this loss. 1 Evidence has been published for localised overproduction of TNF-α being largely responsible for the bone loss seen in rheumatoid arthritis, 2 psoriatic arthritis, 3 multiple myeloma, 4 hip prosthesis loosening, 5 peritendinous disease, 6 and spondylarthropathies. 7 Anti-TNF-α antibody has been shown to slow the bone loss of spondyloarthropathy and rheumatoid arthritis. 8

We have found that the commonly used antidepressant bupropion can induce remission in CP 9 and have found that bupropion can lower TNF-α levels. 10 If bupropion is found to be effective in CD and to lower TNF-α levels in large trials, it might be considered for use in bone loss and osteoporosis, in CD or otherwise.

R E Kast, E L Altschuler
Department of Psychiatry, University of Vermont, Burlington, Vermont, USA

Correspondence to: Dr R E Kast, Department of Psychiatry College of Medicine, University of Vermont, 2 Church St, Burlington, Vermont 05401, USA; rekkast@email.com

References

Poor bowel preparation: a poor excuse

In the article by Bowles et al (Gut 2004;53: 277–83), poor bowel preparation is cited as the cause of 19.6% of failures to achieve complete colonoscopy. Similarly high values of up to 35% have been quoted elsewhere.

In a personal series of 1195 procedures, only 19 of 197 (9.6%) failures were attributed to this cause. This difference was highly significant (p<0.001).

As choice of laxative agent and population demographics are similar, one could conclude that either Guerney patients are more compliant with or responsive to bowel preparation or that minimal faecal residue present is a sufficient test of irrigation of the colon (excusia?) for what is basically a technical failure.

I suspect the same applies to “patient discomfort” which, at 34.7%, is also significantly higher (p<0.001) than my own values of 31/197 (15.7%). My typical sedation is 5 mg midazolam and 10 mg nalbuphine.

1 confess that my usage of these excuses presumably relates to the fact that both series are relatively small and the confidence intervals are likely to be wide, much as they found.

Unfortunately, Murray et al provide no follow up data relating to the duodenal adenomas in their series. We have clinical data for all our cases, with a median duration of follow up of four years. Seventeen of 18 duodenal adenomas were removed (six surgically, four by endoscopic mucosal resection (EMR), three snared, three during biopsy, and one by argon photoagulation), and of these, two patients had a recurrence. Unfortunately, EMR, the other kept under surveillance, and all were alive at the time of review (median time from diagnosis 58 months). Among the 28 patients who had no therapy for their polyp, 10 died (median length of follow up 43 months). One patient who had a tubulovillous adenoma with high grade dysplasia developed a 3 cm adenocarcinoma of the first part of the duodenum five months after initial diagnosis and underwent a Whipple’s procedure but died 12 months later from metastatic disease. The other patients died from unrelated causes.

Sporadic duodenal adenoma and colorectal neoplasia

We read with great interest Murray et al’s article concerning the association between sporadic duodenal adenoma and colorectal neoplasia (Gut 2004;53:261–5). We have also noted a lack of published literature regarding sporadic duodenal adenomas, with the exception of the two reports identified by the authors, 1 as well as a more recent case series, 2 and therefore welcome the addition of their large case series and comparison group. Although there is the potential for bias in the detection of colorectal neoplasia in their duodenal adenoma cases, as the indications for colonoscopy were somewhat different between cases and controls (with almost one third of cases of duodenal adenomas being endoscoped for investigation of anaemia or melanoma), overall their data support a clinically relevant association between duodenal and colonic adenomas.

These results are corroborated by our own recent experience at Leeds General Infirmary where we have studied the natural history of duodenal adenoma. We also examined histopathology records and case notes for patients with sporadic duodenal adenomas between 1990 and 2002 (excluding familial adenomatous polyposis and hereditary non-polyposis colorectal cancer). We identified 35 cases; 16 males and 19 females (mean age 65 years). The majority of these were noted incidentally at upper gastrointestinal endoscopy or endoscopic retrograde cholangiopancreatography, with a similar range of indications for examination as those noted by Murray et al. Using the criteria stipulated by the authors, 25 (71%) of the adenomas were advanced. Of the 35 patients in our series, 11 underwent colonoscopic examination. This revealed a synchronous colonic adenoma in four patients (36%), three of which were tubulovillous adenomas and therefore advanced according to the aforementioned criteria, and the fourth a tubular adenoma.

Unfortunately, Murray et al do not provide follow up data relating to the duodenal adenomas in their series. We have clinical data for all our cases, with a median duration of follow up of four years. Seventeen of 18 duodenal adenomas were removed (six surgically, four by endoscopic mucosal resection (EMR), three snared, three during biopsy, and one by argon photoagulation), and of these, two patients had a recurrence. Unfortunately, EMR, the other kept under surveillance, and all were alive at the time of review (median time from diagnosis 58 months). Among the 18 patients who had no therapy for their polyp, 10 died (median length of follow up 43 months). One patient who had a tubulovillous adenoma with high grade dysplasia developed a 3 cm adenocarcinoma of the first part of the duodenum five months after initial diagnosis and underwent a Whipple’s procedure but died 12 months later from metastatic disease. The other patients died from unrelated causes.

Despite published literature that suggests duodenal polyps have no prognostic importance, 3 we believe that the optimal management of duodenal adenomas is early excision and follow up. We also concur that there is an association between sporadic duodenal adenomas and colorectal neoplasia, and agree entirely that all patients found to have sporadic duodenal adenomas should undergo colonoscopy. However, owing to reasons of study size and bias in the comparison groups, the magnitude of this association cannot be accurately determined. Furthermore, the reasons for this association are as yet unclear, and
molecular studies are required to further investigate.

A C Ford, O Rotimi, S M Everett
Centre for Digestive Diseases, Leeds General
Infirmary, Leeds, UK
Correspondence to: Dr A C Ford, Centre for Digestive
Diseases, Leeds General Infirmary, Great George St,
Leeds LS1 3EX, UK; aford12399@yahoo.com

C Neut
Laboratoire de Bacteriologie, Faculté de Pharmacie,
Lille, France, and INSERM EP11 14, CHU Lille, France

P Desreumaux, J F Colombel
Service d’Hepatogastroenterologie, Hopital Huriez,
and INSERM EP11 14, CHU Lille, France
Correspondence to: Dr C P Tamboli, Division of
Gastroenterology, University of Iowa Hospitals and
Clinics, 200 Haskins Dr, Iowa City 52242, USA;
cyrus-tamboli@uiowa.edu

Dysbiosis as a prerequisite for IBD

We thank Dr Szligayli for his very interesting
comments in his letter regarding dysbiosis in
inflammatory bowel disease (IBD).1

The main question remains as to why
beneficial bacteria such as bifidobacteria
might be lacking in IBD (Gut 2004;53:1–4). Dr Szligayli describes an interesting hypoth-
thesis of colonic prebiotic deficiency as a
possible mechanism for dysbiosis. A sugges-
tion made in this deficiency could be
linked to increased proximal small intestinal
dysfunction with enhanced absorption of
prebiotic substrate, causing a relative deficiency of prebiotics distally. Certainly, the phenomen-
on of increased small bowel permeability has been documented in Crohn’s disease; its importance in ulcerative colitis is less
however. As lactulose is not a major compo-
nent of the normal human diet, long term
epidemiological dietary trends should also have to be consistent with a significantly decreased intake of common prebiotic substrates, if this hypothesis is correct.

Unfortunately, there is currently little clinical
evidence to support or refute this theory, as
dietary studies in IBD have been subject to
many biases inherent in their study design.

Bifidobacteria are strongly glucidolytic and
show nearly no growth in the absence of
fermentable sugars or polyaccharides. One
group of good substrates are mucins, which
are often increased in Crohn’s disease. Perhaps differences in ease of glycosylation
between some substrates affect the ability of the flora to metabolise them. This has not
been well studied in IBD. There are also likely
to be other influences on the host’s dominant
flora, including genetic factors. Observations among some of our healthy cohorts with low
levels of bifidobacteria have revealed highly variable responses of bifidobacterial counts
to prebiotic treatments. Whether a poor response might represent a risk factor for
IBD is also an interesting question.

C P Tamboli
Division of Gastroenterology, Department of Internal
Medicine, University of Iowa Hospitals and Clinics,
Iowa City, USA

Reference
1 Szligayli A. Dysbiosis as a prerequisite for IBD
(electronic response to Tamboli et al. Dysbiosis in
would however take issue with their hypothesis, as
we indeed believe in the remarkable differ-
ences in the mode of hepatitis C virus (HCV) transmission in these two high risk groups.

Remarkable difference in the mode of HCV transmission among haemodialysis patients and IVDAs

We read with great interest the letter by Saxena et al. (Gut 2003; 52:1656–7). We would however take issue with their hypothesis, as we indeed believe in the remarkable differences in the mode of hepatitis C virus (HCV) transmission in these two high risk groups.

References

COX 2 inhibition and bowel strictures

The letter by Mir et al. (Gut 2004;53:154) caught our attention and seems to have caught the editorial staff dozing. Mir et al present a patient who had been regularly taking conventional non-steroidal anti-inflammatory drugs (NSAIDs) for 26 years for axial spondylarthropathy and ascribe the presence of distal ileal stricturing and ulceration solely to the NSAID, cyclo-
oxxygenase 2 (COX 2) selective inhibitor that caught our attention and seems to have caught the editorial staff dozing. Mir et al present a patient who had been regularly taking conventional non-steroidal anti-inflammatory drugs (NSAIDs) for 26 years for axial spondylarthropathy and ascribe the presence of distal ileal stricturing and ulceration solely to the NSAID, cyclo-
oxxygenase 2 (COX 2) selective inhibitor that

The other point to note is the fact that co-infection with HCV and HBV is common in IVDAs2 but less prevalent in HD patients. This interesting point may highlight evidence of another difference in the main transmission route of infection in these two populations.

S M Alavian, B Hajirazadeh
Tehran Hepatitis Center, Tehran, Iran
Correspondence to: Dr S M Alavian, PO Box 14155- 3651, Tehran, Iran; manager@ranjegroup.info

2 COX 2 inhibitors can cause an extraintestinal manifestation of 5–10% of cases of inflammatory bowel disease. It is difficult to exclude this as the cause of both the recent ulceration and
structuring because histology does not always show typical (for example, granulomatous) changes. To date, the only small bowel pathology reported from selective COX-2 inhibition (or absence) is of ileocecal inflammation and perforation (not structuring) in animal studies. Hence, while it is a remote possibility that COX-2 inhibition may have given rise to the lesions in this patient, these are far more likely to be due to other factors.

L P Maiden
King’s College Hospital, London, UK

I Bjarnason
Department of Medicine, Guy’s, King’s, and St Thomas’ School of Medicine, Bensheimer Rd, London, UK

Correspondence to: Dr L P Maiden, lpmaiden@doctors.net.uk

References

Intravenous pulse cyclophosphamide therapy in Crohn’s disease and ulcerative colitis

The management of refractory severe inflammatory bowel disease (IBD) is still unresolved. We read with interest the article by Stallmach et al. on the safety and efficacy of intravenous pulse cyclophosphamide in acute steroid refractory IBD (Gut 2003;52:377–82).

In common with other disease, the aims of therapy in IBD fall into three categories:

(a) induction of remission;
(b) maintenance of remission; and
(c) prevention of relapse, all of which should be undertaken with minimal mortality and morbidity either from the disease itself or from therapy.

Based on previous observations of improvement in autoimmune diseases (that is, vasculitides), cyclophosphamide can be a primary cytotoxic drug: pulse intravenous cyclophosphamide is probably equally effective as oral cyclophosphamide in inducing remission and this remission is usually maintained by continuing cyclophosphamide for 3–6 months before changing to a combination of other oral therapies. Therapy must be continued to prevent relapse and for maintenance.

We would like to report on some other cases. In our cohort, we included patients with Crohn’s disease (CD) and ulcerative colitis (UC). Four patients with CD and four with UC were diagnosed according to standard criteria. They did not respond to conventional therapy and therefore we administered pulse cyclophosphamide therapy monthly (for six months, 800 mg each time). Most patients went into remission after the second/third cyclophosphamide pulse. Disease activity decreased, there were no side effects, no toxicity, and all patients achieved long lasting remission. For maintenance, patients with CD were treated with methotrexate (10 mg/week) and patients with UC were given azathioprine (100 mg/day). Remission appears to be stable.

These findings suggest that aggressive immunosuppressive therapy may be useful in some refractory patients, and further controlled study should be considered in order to fully evaluate this type of treatment as a potential therapy in IBD.

IBD continue to pose a challenge to clinicians. Over the past few years there have been significant advances in our understanding of pathogenesis and treatment. These advances will hopefully lead to more specific and targeted treatments, with consequent improvement in clinical outcomes. Intravenous pulse cyclophosphamide may be a safe and effective treatment in patients with severe IBD unresponsive to “conventional” treatment. It is also recommended as a first-line adjunct to, or replacement for, systemic corticosteroids in the treatment of IBD.

Z Barta, L Toth, G G Szabo, G Szegedi, M Zehrer
University of Debrecen, Debrecen, Hungary

Correspondence to: Z Barta, 3rd Department of Medicine, University of Debrecen, Marócz Zs krt, 22 Debrecen, Hungary; barta@iibel.dote.hu

Reference

CORRECTION

In the paper by Finotto et al (Gut 2004;53:392–400), one of the author names appeared incorrectly. The author name which was printed as R Khosravi-Fahr should have appeared as R Khosravi-Far.

NOTICES

British Society of Gastroenterology
Paul Brown Travel Fellowships

The Paul Brown Travel Fellowships are awarded by the Endoscopy Committee of the BSG. They are intended to assist trainee gastroenterologists and established consultants in visits to units outside the United Kingdom for specialist experience and training in endoscopy.

Specialist registrars who have not achieved their CCST are expected to have the approval of their Postgraduate Dean and their Regional Training Director when they apply for a Travel Fellowship. Applicants are expected to provide confirmation that they have been accepted for training in the unit that they wish to visit. Successful applicants will be expected to provide a brief written report to the Endoscopy Committee of the outcome of their visit.

Application forms are available from the British Society of Gastroenterology Office, 3 St Andrew’s Place, London NW1 4LB. Email: bsg@mailbox.ulc.erc.ac.uk

8th Southeast European Symposium of Paediatric Surgery

The 8th Southeast European Symposium of Paediatric Surgery will focus upon ‘Infectious Problems in Paediatric Surgery.’ The event will be held between 24–25 September 2004, at the University of Graz, Austria. For further information, please contact: Professor M E Hollwarth, Department of Paediatric Surgery, Medical University of Graz, Austria, Auenbruggerplatz 34, 8036 Graz; tel: +43 316 385 3762; fax: +43 316 385 3775; e-mail: kinderchirurgie@uni-graz.at.

World Congress on Gastrointestinal Cancer

The World Congress on Gastrointestinal Cancer will be held in Barcelona, Spain, on 16–19 June 2004. For further information, please contact Coleson Chase (tel: +1 770 751 7332; fax: +1 770 751 7334; e-mail: c.chase@imedex.com; website: www.worldgiscancer.com).

Advances in the Inflammatory Bowel Diseases

The conference for advances in the inflammatory bowel diseases will be held in Chicago, Illinois, USA on 8–9 October 2004. For further information, please contact: Coleson Chase (tel: +1 770 751 7332; fax: +1 770 751 7334; e-mail: c.chase@imedex.com; website: www.imedex.com/calendars/therapeutic.htm).

12th European Symposium on Neurogastroenterology and Motility

The 12th European Symposium on Neurogastroenterology and Motility will be taking place at Robinson College, Cambridge, UK. The symposium will be taking place on 15–18 September 2004.

On Wednesday 15 September, there will be a postgraduate teaching day. This will cover established and evolving assessments of esophageal, gastric and intestinal function, visceral sensitivity and brain responses. Basic science techniques including electrophysiology, imaging of gut movements and neural activation will be covered in the afternoon. Finally there will be a session on GI pharmacology covering cytokines, capsaicin and tachykinins.

On Thursday 16 September through to Saturday 18 September midday, the main meeting will be held. This will include symposia, oral free papers and poster rounds. The symposia will be designed to move from basic science to clinical practice and will include sessions on stress and the gut, appetite and obesity, serotonin and inflammation, and inflammation and GI motility. There will also be state of the art lectures and prize presentations.

For registration and further information, please see the website www.neurogastro.org and follow links for ‘12th European Symposium on Neurogastroenterology and Motility.’ Please contact the conference organizers at: Confrex, PO Box 21, Rottingdean, East Sussex, BN2 4WZ (tel: +44(0)1273 302200; fax: +44(0)1273 302334; e-mail: confrex@easyenet.co.uk).
Platelet count/spleen diameter ratio as a predictor of oesophageal varices in alcoholic cirrhosis

T A Zimbwa, C Blanshard and A Subramaniam

Gut 2004 53: 1055