Role of multi-detector row CT angiography in the management of gastric fundal varices

We read with great interest the article by Willmann et al (Gut 2003;52:886–92) regarding the superiority of multi-detector row CT (MDCT) angiography over endoscopic ultrasound for the detection and characterisation of submucosal gastric fundal varices (FV).

We strongly agree that MDCT angiography provides excellent visualisation of FV, as well as afferent and efferent veins, and that it provides valuable anatomical information for deciding the therapeutic strategies for FV (fig 1A, B). Iwase and colleagues1 divided FV into localised and diffuse types using MDCT angiography. This classification resembles the findings obtained by investigation of resected or autopsied stomachs. According to Iwase and colleagues, diffuse FV are more difficult to obliterate with cyanoacrylate than localised FV. Diffuse FV may be better treated with balloon occluded retrograde transvenous obliteration (B-RTO). Although FV with a high risk of bleeding have not yet been fully clarified, they are defined according to the criteria proposed by Kim and colleagues in Japan. Because high risk FV are easily detected endoscopically, it is not necessary to distinguish FV from perigastric collateral veins by MDCT angiography.

MDCT angiography can also provide useful information for evaluation of the effect of treatment of FV. Obliteration of the afferent veins as well as the actual varices is important to prevent recurrence.3 If these vessels are not visualised by MDCT angiography after therapy, FV will rarely recur.4 With regard to the treatment of FV reported by the authors, we also have some comments. Firstly, they treated a patient by transjugular intrahepatic portosystemic shunting (see fig 2 in Willmann et al). However, as the patient had a type 2 portal haemodynamic pattern, as classified by Kanagawa and colleagues, B-RTO would have been preferable if his portal pressure gradient was less than 12 mm Hg.5 Secondly, we would like to ask the authors how they treated the patient presented in fig 3? As the varices seem to be so-called GOV2, as classified by Sarin and Kumar,6 they could be treated by endoscopic sclerotherapy with the oesophageal varices.

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References

Authors’ reply

We thank Dr Matsumoto et al for their interest in our work.

Balloon occluded retrograde transvenous obliteration (B-RTO) is a recently described interventional radiology technique which allows effective treatment of gastric varices, similar to but less invasive than transjugular intrahepatic portosystemic shunt stent (TIPSS). It has recently been shown that B-RTO of gastric varices can even be performed through the left inferior phrenic vein which represents the efferent vein of gastric varices.2 There is no doubt that B-RTO through the left inferior phrenic vein would have been an option for the treatment of the patient shown in fig 2 of our article (Gut 2003;52:886–92). However, since the portal venous pressure gradient in this particular patient was 28 mm Hg, we preferred to place a 10 mm diameter TIPSS in this particular patient.

The patient illustrated by fig 3 in our study (Gut 2003;52:886–92) was classified as having gastro-oesophageal varices type 2 (GOV-2), according to the endoscopic classification proposed by Sarin and Kumar. This patient underwent endoscopic sclerotherapy.

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References
Primary antiphospholipid syndrome as a new cause of autoimmune pancreatitis

I read with interest the article by Kamisawa et al regarding the aetiology of autoimmune pancreatitis (Gut 2003;52:683–7). The cause of a significant proportion of cases of acute pancreatitis remains uncertain. I would like to describe a case of acute pancreatitis associated with antiphospholipid syndrome to highlight another potentially important cause of autoimmune pancreatitis which I believe has not been previously described.

Case report

A 30 year old woman was admitted twice in the space of three months with acute pancreatitis. She had a past medical history of anxiety and occasional migraines, for which she took alprazolam and propranolol, respectively. She had suffered two miscarriages and had one healthy child. She drank 3 units of alcohol per day. She was otherwise well and had no history of musculoskeletal problems.

On both occasions her amylase level was significantly elevated (787 and 364, respectively). Ultrasound and computed tomography of her abdomen were carried out each time and demonstrated a diffusely swollen pancreas consistent with acute pancreatitis, but with no evidence of gall stones or biliary duct dilatation.

Liver function tests were all normal with the exception of a slightly elevated gamma glutamyl transferase level. Glucose, lipids, thyroid stimulating hormone, calcium, and clotting (international normalised ratio and activated partial thromboplastin time) were all normal. Full blood count was normal except for a neutrophilia during her acute illness. Her erythrocyte sedimentation rate was raised at 78. Urine microscopy and urinary protein excretion were both normal.

On her second admission to hospital she had four generalised seizures and magnetic resonance imaging showed cortical vein thrombosis with associated venous infarction. Subsequent investigation revealed a strongly positive antinuclear antibody (1 in 640) but her extractable nuclear antigens and dsDNA were negative, as was her antineutrophil cytoplasmic autoantibody and her antimitochondrial and antismooth muscle antibodies. Her thrombophilia screen was negative but her IgG anticardiolipin antibody. Her thrombophilia screen was negative, as was her anti-dsDNA were negative, and her anticytoplasmic autoantibody was strongly positive antinuclear antibody (1 in 50).

The patient described fulfills the criteria for a diagnosis of primary antiphospholipid syndrome. While there is no historical proof that her pancreatitis was due to vasculocclusive thromboembolism, several facts make this the likely explanation. The recurrent episodes in the absence of another cause, the proven cerebral thromboembolism at the time of her second attack of pancreatitis, and her positive anticardiolipin antibodies are highly suggestive that thromboembolism of her pancreatic blood vessels was indeed the cause of her pancreatitis.

I suggest that the investigation of patients with idiopathic pancreatitis should include checking their antiphospholipid antibodies.

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References


Author’s reply

Autoimmune pancreatitis is a recently described clinical entity in which autoimmune mechanisms are involved in the pathogenesis. As Etemad and colleagues described, the aetiology was one of six factors of chronic pancreatitis, autoimmune pancreatitis is not acute but chronic pancreatitis. Patients with autoimmune pancreatitis rarely showed acute attacks of pancreatitis or marked elevation of serum amylase. Although the pancreas of autoimmune pancreatitis is swollen similar to acute pancreatitis on ultrasound and computed tomography, it is induced by dense lymphoplasmacytic infiltration with fibrosis. Obliterated phlebitis throughout the pancreas is one of the characteristic pathological findings of autoimmune pancreatitis. The lumen of the vein was filled with prominent cellular infiltrates and fibrosis. Venous occlusion was not due to thromboembolism but to phlebitis. Although the role of obliterated phlebitis is unknown in the pathogenesis of autoimmune pancreatitis, many IgG4 positive plasma cells, which might be closely related to pathogenesis, were observed in the obliterated veins. Signs of thrombosis were not observed in any organs of our patients with autoimmune pancreatitis. We think that autoimmune pancreatitis is quite different from the pancreatitis reported by Spencer.

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Treatment of interferon non-responsive chronic hepatitis C with triple therapy with interferon, ribavirin, and amantidine can be encouraging

Patients with hepatitis C virus infection who do not respond to treatment with interferon alone or its combination with ribavirin present a serious clinical challenge and there is no clear choice for treatment in these individuals. Earlier studies with antiviral amantidine, which has been used in influenza, had shown promising results. Now, Adinolfi et al (Gut 2001;42:425–30) have shown 68% end of treatment response with induction therapy using daily interferon for four weeks (and then three injections weekly) in combination with ribavirin and amantidine hydrochloride.

We had used interferon in doses of 3 million units given scubutaneously thrice weekly with ribavirin 800–1200 mg/day and amantidine hydrochloride 100 mg orally twice a day in a small group of chronic hepatitis C patients who had not responded to a combination of interferon and ribavirin. We found a 50% end of treatment response after a treatment period of 12 months (see table 1). Half of the patients showed no effect on alanine aminotransferase or hepatitis C virus RNA, and in these patients treatment was discontinued after three months.

There are reports of good results with the use of amantidine in combination with interferon. Therefore, although the mechanism of action of amantidine in this setting is unclear, it is becoming obvious that there is an encouraging situation for these hard to treat patients and there may be light at the end of the tunnel. Due to lack of major sponsorship for amantidine from a large
pharmaceutical company however, it may take a while before this happens.

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References


4 Nakamura H, Uyama H, Enomoto H, et al. The combination therapy of interferon and amantidine raises many other simple questions: (1) When to stop? (2) The main goal of this work was to have cheaper endoscopists, so why not to minimise costs by teaching nurses other physician tasks, such as physical examination or minor surgical procedures? (3) Should we begin teaching endoscopy to non-resident in our endoscopy wards? (4) Why not begin to teach nurses other endoscopic procedures, such as endoscopic retrograde cholangiopancreatography or endoscopic ultrasound and, in this event, what is the future role for physicians?

In summary, we believe our efforts should be directed towards better clinical practice, defining indications for different medical procedures, limiting costs in the many other aspects of endoscopy and gastroenterology, and trying to perform our specific role, nurse or medical, as scientifically based and accurate as possible.

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The diagnostic dilemmas in discrimination between pancreatic carcinoma and chronic pancreatitis

Early diagnosis to distinguish between malignant pancreatic tumours and chronic pancreatitis is still difficult, despite significant progress in imaging techniques. Moreover, patients with chronic pancreatitis have a higher risk of pancreatic cancer development.

The study of Malka et al (2002,51:849–52) clearly confirms these difficulties, independently of rigorous selection criteria of patients with chronic pancreatitis. To exclude the possibility that chronic pancreatitis may be caused by early potentially premalignant lesions, the authors eliminated from their investigations even patients with chronic pancreatitis in whom pancreatic cancer was recognized during the first two years of follow up.

Several studies indicate the value of circulating tumour marker evaluation as a simple, sensitive, and reliable test facilitating the differential diagnosis between chronic pancreatitis and cancer.10 To improve the effectiveness of serological diagnosis of patients with pancreatic tumours, different tumour markers have been assessed, including CEA, CA 242, CA 50, and CA 72-4.7 8 However, the sensitivity and specificity of these markers appeared to be insufficient for differentiation of pancreatic carcinoma from chronic pancreatitis. In 1996, CAM 17-1 was described as a new useful diagnostic marker in pancreatic carcinoma. It showed a sensitivity similar to that of CA 19-9 but higher specificity, giving only 10% false positive results in patients with chronic pancreatitis.

Tissue polypeptide specific antigen (TPS) is a different type of antigen that does not correlate with tumour mass but reflects tumour proliferative activity.4 Our study revealed that elevated levels of TPS detected preoperatively 100% of patients with pancreatic carcinoma. The introduction of 200 U/l as a decision criterion for TPS level allowed an increase in the specificity of this marker to 98% and eliminated all but 2% of the false positive results in patients with chronic pancreatitis. Moreover, TPS is useful for detection of the early stages of clinical advancement of pancreatic carcinoma.

It seems that measurement of TPS, using 200 U/l as the cut off value, should facilitate more precise discrimination between the early stages of pancreatic carcinoma and chronic pancreatitis.

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References


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Table 1 Patients treated with interferon, ribavirin, and amantidine

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*Normal alanine aminotransferase and undetectable hepatitis C virus (HCV) RNA.
Small bowel malignancy in coeliac disease

We were interested to read the case report by Rampertab et al on small bowel neoplasia in coeliac disease [Gut 2003;52:1211–14]. The findings are very much in accord with ours from the British Society of Gastroenterology (BSG) National Survey published earlier this year.1 Over a two year period (1998–2000), we collected details of 175 cases of primary small intestinal adenocarcinoma, of which 13% were associated with coeliac disease and 7% with Crohn’s disease.

With regard to coeliac associated adenocarcinomas, similar to Rampertab et al, we found a predominance of males (2:1) and an equal distribution between the duodenum and jejunum. Age range was 47–80 years. Fifty per cent presented acutely, predominantly with obstruction, and 45% chronically with anaemia, weight loss, or abdominal pain. Mean time of symptoms prior to diagnosis was 14 months, which was reflected in a relatively poor 30 month overall survival of 58%. In 63%, coeliac disease had been diagnosed a mean of 8.2 years prior to the diagnosis of adenocarcinoma; in almost all of these patients there had been a good clinical and mucosal response to a gluten free diet. In 37%, coeliac disease was diagnosed at the same time as adenocarcinoma.

Although 13% of small bowel adenocarcinomas being associated with coeliac disease implies that the risk of these cancers in coeliac disease is very high, such an increase translates into a very small absolute life time risk of less than 1%, as these tumours are rare. Nevertheless, we agree that coeliac patients require long term follow up for this and other complications. However, the best means of surveillance needs to be determined.

Of most concern is the long delay in the diagnosis of small bowel adenocarcinoma, irrespective of whether or not coeliac disease is present. This leads to poor survival as 40% have metastasised by the time the diagnosis is made. A high index of suspicion is required by all gastroenterologists for this rare, but eminently treatable, type of adenocarcinoma.

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References


Submucosal “dissection” in collagenous colitis

We were fascinated to read the paper by Cruz-Correa et al [Gut 2002;51:600] describing cases of mucosal tearing at colonoscopy in patients subsequently found to have collagenous colitis. We were particularly interested in their postulated mechanism for these tears being a disruption of colonic mural integrity by the submucosal collagen layer. We would like to present two cases which add further weight to this theory as well as possibly providing information as to the pathogenesis of diarrhoea in this condition.

A 60 year old woman presented to her general practitioner with a two month history of profuse watery diarrhoea. A barium enema examination was reported as showing evidence of a mild colitis only. The general practitioner commenced corticosteroids resulting in complete resolution of her symptoms. On referral to our department, a gastrointestinal radiologist reviewed her radiographs. It was noticed that throughout the films there was a radiolucent border outlining the colonic mucosa (see fig 1) suggesting the presence of a submucosal layer of gas for which no explanation could be found. Although endoscopic examination of the colon was macroscopically normal, serial biopsies revealed the presence of a subepithelial collagen band up to 100 μm thick and a diagnosis of collagenous colitis was made. There was no evidence of pneumatosis or of submucosal barium on the small amount of submucosa included. She has since remained well on mesalazine.

The second patient was a 68 year old woman with a four week history of profuse watery diarrhoea. An emergency admission was required as a result of deranged clotting secondary to warfarin, which she was taking for a mechanical aortic valve. Following correction of her coagulopathy she underwent a colonoscopy. The instrument was advanced to the caecum without difficulty by a very experienced endoscopist who had performed in excess of 10 000 procedures. Macroscopically, there was evidence of a mild colitis. Standard serial biopsies were taken. Shortly following the procedure she complained of right shoulder tip pain. On examination she was neither distressed nor haemodynamically compromised. Her abdomen was soft. Chest and abdominal radiographs showed significant free gas under the diaphragm and in the peritoneum. At laparotomy she was found to have pneumoperitoneum without faecal contamination. No perforation was identified but there was considerable emphysema within the cecal wall extending proximally along the terminal ileum and distally to the mid ascending colon. No further operative procedure was performed. Endoscopic biopsies showed mild active inflammation and a subepithelial collagen band. None of the biopsies was full thickness. A diagnosis of collagenous colitis was made and her symptoms settled on a short course of corticosteroids.

We suggest that the complications seen in the investigation of these two patients result from a weakness within the colonic wall caused by the collagen layer. In the first case it appears that cleavage or dissection of the colonic wall alongside the collagen layer may have occurred. It is unclear whether this happened as a result of air insufflation at the time of examination or whether it was already present. In the second case we postulate that air insufflated at the time of the colonoscopy tracked alongside the collagen layer perforating into the peritoneum remote from its original point of entry; possibly a proximal biopsy site.

If a true weakness in the integrity of adhesion of the elements of the colonic wall does exist and such “dissection” can happen spontaneously, then it may provide some insight into the pathogenesis of diarrhoea in this condition, especially as there appears to be no correlation between the width of the collagen band and the severity of symptoms.

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Responses to endothelin-1 in patients with advanced cirrhosis before and after liver transplantation

I read with interest the article of Vaughan et al [Gut 2003;52:1505–10] and was pleased to...
see my novel studies 4,5 partially reproduced in patients with decompensated cirrhosis. I disagree with some of the results as the study involves a substantial design, methodological, and analysis problems.

The authors said that advanced cirrhotic patients have ‘generalised vasodilatation’. Vasodilatation does occur in these patients but only in the splanchic and pulmonary beds. Indeed, studies by me and others have shown vasocstriction in the brachial, femoral, cerebral, and renal territories, especially in advanced cirrhosis. 6 Therefore, I would like to stress the point that with advancing cirrhosis, further activation of the neurohumoral systems occurs, with consequent peripheral vasocstriction. However, blood pooling, particularly in the splanchic bed, lowers systemic vascular resistance.

A major criticism of the study of Vaughan et al is that they measured forearm blood flow (FBF) in only one arm. Changing levels of akeness and external stimuli produce similar fluctuations in blood flow of both arms, and lead to significant misleading alterations in the measured responses if unilateral measurements are used. Thus responses to intra-arterial infusions should have been measured in both arms with the results expressed as ratios of concurrent FBF in the infused and non-infused arms, where the latter serves as a contemporaneous control for the drug effects in the former. Further, enhanced FBF ratios are significantly more reproducible than unilateral FBF measurements both at rest and following infusion of vasoconstrictors.

The authors demonstrated a surprising increase in FBF (33–40%) in response to infusion of a locally active dose of the potent vasoconstrictor endothelin-1 (ET-1), which reached its maximum within five minutes from the start. They attributed their finding to enhanced ETB receptor mediated vasodilatation. This needs to be tested by selectively blocking ETB receptors, using BQ-788. To date, upregulation of ETB receptors has been reported in the splanchic and pulmonary vascular beds but not in the forearm. 7 How can the maximum response to the slowly acting ET-1 be reached within five minutes? Also, dose-response curves of the effects of ET-1 and BQ-123 should have been performed.

In the present study, ETA receptors were unaltered while those mediated by the ETB receptor were enhanced in patients with decompensated cirrhosis. Thus one would expect that blocking ETB receptors with BQ-123 would allow ET-1 to act unopposed on ETB receptors and produce enhanced vasodilatation. However, this was not the case (fig 2 in the article). What adds to my surprise here is that BQ-123 inhibited ET-1-induced increased FBF by 33–40%. How can infusion of ET-1 produce the same action as ET-1 continued to be infused in the forearm, while ET-1 or preproendothelin mRNA concentrations (4) examined the responses to an ETB receptor antagonist; (5) performed a dose-response curve; and (6) selected a comparable control group on similar medications as the patients.

References
1 Helmy A, Newby DE, Jalan R, et al. Enhanced vasodilatation to endothelin antagonists is not affected by the biological precursor ET-1. Due to its autocrine, paracrine, and endocrine nature, plasma concentrations of ET-1 alone do not reflect the activity of the endothelin system or the status of ET-1 production. 8 This should have been stated by the authors. I also recommend collecting samples in tubes containing 1000 IU aprotinin and EDTA.

In conclusion, the scientific contents of this article would have been greater if the authors had: (1) measured FBF in both arms; (2) presented their data as per cent change in the ratio of flows in both arms at every time point; (3) assessed plasma big ET-1 or preproendothelin mRNA concentrations; (4) examined the responses to an ETB receptor antagonist; (5) performed a dose-response curve; and (6) selected a comparable control group on similar medications as the patients.

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Germline testing of mismatch repair gene testing is not aided by prescreening tumours for allelic loss

Immunostaining and microsatellite testing of tumours is increasingly being used to guide germline testing in individuals with suspected hereditary non-polyposis colorectal cancer (HNPCC). 9 While the aim of these prescreening tests is to test for and maximise the chance of identifying a pathogenic germline change, it is clear that neither alone is ideal. In clinical practice, germline testing can often only be justified where an individual has developed a tumour which is microsatellite unstable, and which fails to express a mismatch repair protein. Clearly, this approach is imperfect as not all pathogenic germline mutations are associated with failure of expression of the mismatch repair proteins. The aim of this pilot study was to retrospectively assess the utility of loss of heterozygosity studies in predicting the matched mismatch repair gene.

Seven individuals with germline mutations in hMSH2 were identified from the family cancer clinic at St Vincent’s Hospital, Sydney. The tumours from each of these individuals were microsatellite unstable and failed to express hMSH2, but demonstrated normal expression of hMLH1. For loss of heterozygosity (LOH) analysis, we used microsatellite markers D1S180 and D1S235 (for Exon 1), D1S5, D3S2158, and D1S2555 (for D1S5), D2S21153, D2S2156, D2S2292, D2S2369, and D2S378 (for hMLH1). Only heterozygous loci were regarded as informative and LOH was scored when there was a major reduction (at least 50%) or total loss of one allele in the tumour compared to normal tissues.

Of the seven tumours examined in this study, six showed allelic loss of hMSH2, suggesting that the residual normal allele was silenced by LOH. In five tumours, allelic loss of hMSH2 occurred in association with LOH in at least one other mismatch repair gene. Only one tumour had retained heterozygosity at all assessable loci, possibly indicating that a mutation had caused the second hit in this tumour.

Allelic loss of hMSH2 often occurs in association with germline mutations but it is clear that loss of the other mismatch repair genes is also a frequent finding. Screening tumours for LOH should not be employed to select patients for mutation analysis of mismatch repair genes. The use of immuno-histochemistry and microsatellite testing remain the best available prescreening tools.

Figure 1 Loss of heterozygosity analysis of four mismatch repair gene tumours from seven individuals with germline mutations in hMSH2.

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PostScript

Figure 1

Gene	 marker	 Exon
D1S180	 D1S235	 PM1S1	 D2S118	 D2S155	 D2S21153	 D2S2156	 D2S2292	 D2S2369	 D2S378	 D3S1447	 D3S3685
1	 2	 3	 4	 5	 6	 7
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Reference


Mild respiratory distress after wireless capsule endoscopy

A 74 year old male patient was seen in our clinic for chronic diarrhoea. Duodenal biopsies revealed the presence of coeliac disease; upper and lower endoscopies were otherwise unremarkable. As he also presented with marked anaemia and weight loss, he underwent wireless capsule endoscopy (M2A capsule; Given Imaging) in order to exclude additional small bowel pathology.

On the second day after application of the capsule (and before analysis of the pictures), he complained of mild respiratory distress while walking, which had started “right after swallowing the capsule”. Physical examination revealed quiet inspiratory and expiratory wheezing, most audible over the central part of the right lung. A chest X-ray was obtained (fig 1) which showed aspiration of the video capsule since this diagnostic method has first been published case of aspiration of an M2A capsule.1 It underlines the recommendations of the manufacturer for cautious use in patients with known or possible swallowing disorders (http://www.given imaging.com).

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Reference


Late development of cholangiocarcinoma after hepaticojejunostomy due to ampullary carcinoma

We read with great interest the article by Bettschart et al (Gut 2002;50:128–9) which found an increase in cholangiocarcinoma incidence after biliary-enteric drainage for benign disease.

In their hypothesis, changes in biliary epithelium were induced by toxic carcinogenes due to reflux of intestinal contents and bile stasis. However, this chronic irritation and carcinogenesis of the biliary mucosa after biliary-enteric anastomosis has not been reported after surgery for malignant disease. We present a case of a 65 year old woman who developed a cholangiocarcinoma eight years after duodenopancreatectomy for an ampullary carcinoma, stage I. The patient was referred to our department because of obstructive jaundice and cholangitis. Computed tomography scan showed that the patient was disease free. Percutaneous transhepatic cholangiography showed biliary-enteric anastomosis stricture and a diffuse biliary stenosis.

Percutaneous transhepatic anastomosis dilatation was performed but was ineffective. The patient was operated on and extensive fibrosis and inflammation of the biliary-enteric anastomosis and biliary duct were detected (fig 1). Resection of the stricture and hepatojejunostomy were performed. In addition to fibrotic and inflammatory tissue, histological examination showed a poorly differentiated cholangiocarcinoma with invasion of all levels of the right hepatic duct wall. Surgical margins were free of disease. The patient was discharged on the 10th postoperative day. She died 10 months after surgery.

In common with the authors, we support the hypothesis that reflux of intestinal contents, bacterial translocation, and pancreatic juice can trigger biliary mucosal changes and the carcinogenesis process.1,4 We believe that apart from those predisposing factors causing chronic cholangitis, there must be susceptibility in these patients due to genetically altered enzymes that are involved in detoxifying carcinogenic products.3 This is the first case report of malignant transformation in the biliary epithelium after biliary-enteric anastomosis for malignant disease. As there are no markers to identify patients in the early stage of development of malignant transformation, we agree with the authors2 about monitoring all patients who develop cholangitis after biliary-enteric anastomosis for benign disease and also patients with malignant disease who are in remission.

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References


Figure 1 Chest x ray showing aspiration of the video capsule into the right main bronchus (Courtesy of Professor G Kaufmann, Heidelberg, Germany).

Figure 1 Anastomosis stricture and diffuse biliary stenosis. Cholangiocarcinoma (arrow) on the right hepatic duct can be seen.
Adoptive transfer of genetic susceptibility to Crohn’s disease

We read with interest the stimulating case report on fulminant Crohn’s colitis following allodonor transplantation performed by Sonwalkar et al. (2003;52:1518–21) and the respective editorial.1 The authors and the editorialists hypothesised on whether the colitis might be ascribed to the adoptive transfer of stem cells displaying genetic alterations which are associated with Crohn’s disease. However, the ileal sparing disease localisation and course of the colitis which finally necessitated urgent colectomy is rather unusual for Crohn’s disease. In addition, the genetic mismatch between donor and recipient is hardly compatible with the outlined hypothesis.

According to the cited study by Lesage and colleagues,2 the allele difference at position −156 of the TLR4 polymorphism of the NOD2 gene is not regarded as “a disease causing mutation”. In line with this concept is the fact that the donor and his first degree relatives did not suffer from Crohn’s disease. Apart from this observation, the authors did not describe in detail which particular genetic mutations or polymorphisms differed between the donor and recipient. However, some of the described genes are simply not associated with inflammatory bowel disease. As shown by some of the authors1 and ourselves,3 polymorphisms in the MICB gene (which is not situated within the HLA class III but the HLA class I region) are not associated with Crohn’s disease. The same holds true for polymorphisms of the HSP70 gene which were weakly associated with a more severe course of Crohn’s disease in Japanese patients but not with the disease itself.4 To date, most of our knowledge, data on possible associations between mutations of the LMP2, LMP7, and NOTCH4 gene and Crohn’s disease are completely lacking. In conclusion, at best only an extremely weak genetic predisposition can be extracted from the extensive genotyping and thus the postulated transfer of genetic susceptibility remains highly speculative.

The increased incidence of inflammatory bowel disease in patients with congenital immune defects and the recently described increased adherence of bacteria to the intestinal mucus, which might particularly be facilitated in the presence of mutated NOD2 protein, suggest that the initial event in the complex pathophysiological process in Crohn’s disease is compatible with impaired mucosal clearing function which precedes an excessively large T cell driven immunological activity. This hypothesis is further sustained by various genetically engineered animal models which are protected from the development of enterocolitis under germ free conditions, and therapeutic approaches, such as the use of immunomodulatory substances or anti-TNF therapy (for overview see Folwaczny and colleagues’). Thus a complementary explanation for the described phenomenon might be the persistent immunosuppressive therapy the donor had received.

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BOOK REVIEWS

Self Assessment Colour Review of Hepatobiliary Medicine


Roger Chapman and Henry Bodenheimer have produced a useful addition to the libraries of gastroenterologists with an interest in liver disease. Hepatobiliary Medicine provides 189 questions and answers in 190 pages covering a wide range of hepatobiliary problems. The book will fit in a white coat pocket and is printed on high quality glossy paper. The questions comprise case histories illustrated with laboratory test results and photographs of histology and imaging investigations. Unfortunately, the reproduction does not allow readers to recognise some of the histological and imaging abnormalities referred to in the text, but most can be discerned with the benefit of hindsight (and the answers). The authors have done an excellent job in assembling a diverse collection of cases with relevant images and laboratory data. The questions are presented on one side of the page and the answers are on the reverse, allowing the reader to formulate their own responses without “cheating.”

The subject matter of the book encompasses the full range of liver diseases, including a fair smattering of rarities that are only likely to be encountered more than once by specialist hepatologists. Indeed, the current Oxford liver cases will test experts. Hepatobiliary Medicine fulfils the remit of the series, as declared in the book’s header, to help readers “learn, revise, reinforce.” Inclusion of a number of paediatric cases will be particularly helpful to adult gastroenterologists/hepatologists who are occasionally asked to see paediatric cases.

The authors have included an index and a list of cases classified by diagnosis. This is extremely useful when using the book for revision or reinforcement. Apart from this observation, the classification of cases reveals some surprising choices of emphasis. Eight questions on primary sclerosing cholangitis, seven on Wilson’s disease, and one on fatty liver diseases hardly reflects the distribution of cases that the general gastroenterologist might encounter but the selection of cases will educate and inform, and the choices reflect the difficulty of diagnostic conundrums rather than disease prevalence.

Publication of this short textbook is timely with the growth of hepatology as a subspecialty and the shortening of training programmes reducing the opportunities for trainees to “learn by nonsmoking case based experience. This book will be particularly useful for trainees in gastroenterology and hepatology.

However, there are a few caveats and some things that could have added value. The inclusion of a number of paediatric cases will be particularly helpful to adult gastroenterologists/hepatologists seeking reinforcement of problems they rarely encounter. Self Assessment Colour Review of Hepatobiliary Medicine does not claim to be a textbook but the authoritative voice used in the answers carries an air of certainty. In the vast majority of cases, little fault can be found with the information contained in the answers although the level of knowledge assumed by the authors and that offered to the readers is variable. As a result, some of the information contained in the answers is superficial and some is out of date. Inclusion of key references and a recommended reading list would have been helpful. A compact disc or website presenting the photographic images might enhance the visual aspects of the book.

This book will be useful to trainees in gastroenterology and hepatology, to specialists who are asked to consult on difficult hepatobiliary cases, and even to specialist hepatologists seeking reinforcement of problems they rarely encounter. Self Assessment Colour Review of Hepatobiliary Medicine is a useful addition to the gastroenterologist’s library.

W Rosenberg

The Inflammatory Bowel Disease Yearbook 2003


This is the first in a planned yearly series of updates on the latest topics in inflammatory bowel disease clinical practice and research. I was initially sceptical that the hard backed book format could provide a useful reference text when using the book for revision or reinforcement of current knowledge but was pleasantly surprised that the reviews were topical and cited papers from early 2003 (including for example, the natalizumab trial and wireless endoscopy data). These are aimed at the general gastroenterologist, and those with a more in depth clinical or research interest in inflammatory bowel disease.

Six key current areas are reviewed by experts in the field: conventional drug therapy, the newer biological therapies, serodiagnosis, genetics, imaging developments, and...
probiotics. These topics are written by authors expert in the field, and there is little overlap between the chapters—often a problem in the multi-author format. I would have preferred more detail in a few areas (for example, pharmacology/adverse response prediction with azathioprine) and a bit less in others (for example, some of the genetics chapter is too detailed, and it was not easy to differentiate replicated from preliminary findings). All chapters are well referenced, with good tables and figures of key points providing clarity.

The Yearbook disappeared once from my shelf while I was trying to review it—to provide preparation for a colleague’s brush with the media spotlight—so I would definitely recommend it as a useful update. It might be especially helpful if one had missed out on attending a recent gastroenterology conference. Finally, Remedia might be able to further promote the Yearbook with a prize for guessing the nature and relevance of the weird industrial plumbing on the cover.

D van Heel

Fast Facts: Irritable Bowel Syndrome, 2nd edn


Functional gastrointestinal disorders in general, and irritable bowel syndrome in particular, have long been a minefield of misunderstanding and mismanagement which has caused confusion not only to clinicians but also to patients.

In recent years, an international working team have attempted to resolve this babel-like tower of confusion by forming the now famous Rome group and producing Rome criteria which have served to harmonise clinical terms and facilitate trials of therapy. However, in general, ex cathedra statements and weighty tomes from the Vatican have rarely changed the understanding of the gospel for the average cleric or parishioner, and a simpler interpretation is usually required. This little “hymnal” provided by two experienced practitioners with many decades of practical experience and a “cardinal” understanding of the issues of irritable bowel syndrome, now provides just what is necessary to bring the word to the people.

The book’s mission is to review in a simple and balanced way what we know (and what we do not know) about the nature of symptoms, and their causes, and how, in an equally simple and practical way, both the primary care practitioner and patients can help themselves to cope with what is often a disturbing chronic set of problems. Their communication style is clear and concise, and without any tendency to pontificate. While its target readership is stated to be the “family doctor”, I am sure that it is equally relevant for the gastroenterologist and for the trainee in gastroenterology for whom the standard textbooks on the subject do not offer much practical guidance in the clinic.

Broadsheet reading patients would also benefit from the balanced view provided by the authors and with luck might in turn reduce their uptake of the increasingly bizarre non-orthodox therapies which are now appearing.

The books first edition appeared in 1999, and has now, by popular demand, been republished in an extensively updated version. It clearly reflects current understanding of the condition and provides a balanced and pragmatic view of its management.

In short, an excellent and up to date pocket palter for the practitioner.

D Thompson

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.

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.ulcf.ac.uk

PET/CT and SPECT/CT Imaging in Medical, Radiation, Surgical and Nuclear Oncology

This continuing medical education programme will take place on 19-20 March 2004 at Johns Hopkins University School of Medicine, Baltimore, Maryland, USA. Further details: Office of Continuing Medical Education, Johns Hopkins University School of Medicine, Turner 20, 720 Rutland Avenue, Baltimore, Maryland 21205-2195. Tel: +1 410 955 2959; fax: +1 410 955 0807; email: cmnet@jhmi.edu; website: www.hopkinscmc.org

39th Annual Meeting of the European Association for the Study of the Liver

This meeting will be held on 15-19 April 2004 in Berlin, Germany. Further details: Secretariat, c/o Kenes International, 17 rue du Cendrier, PO Box 1726, CH-1211 Geneva, Switzerland. Tel: +41 22 908 0488; fax: +41 22 732 2850; email: info@easl.ch; website: www.easl.ch/easl2004

14th International Workshop of Digestive Endoscopy, Ultrasonography and Radiology

The 14th International Workshop of Digestive Endoscopy, Ultrasonography and Radiology will be held in Marseille on 27-28 May 2004. For further information, please contact: Nathalie Fontant, Atelier Phenix, 41 rue Docteur Morruzi, 13006 — Marseille (tel: (33) 04-91-37-50-83; fax: (33) 04-91-57-15-28; e-mail: nfontant@aphexin.com).

European Postgraduate Gastro-surgical School (EPGS) Courses 2004

The EPGS at the Academic Medical Center of the University of Amsterdam will be holding the following courses during the year: ‘Benign Hepato-Biliary Disorders’ will be held on 22 & 23 April 2004, ‘Endosonography live in Amsterdam’ will be held on 2, 3 & 4 June 2004, and ‘Update in Coloproctology’ will be held on 28 & 29 October 2004. For further information, please contact: J Gooedkoop (tel: (31) 566 3926; fax: (33) 267 5594; e-mail: j.goedkoop@amc.uva.nl; website: www.epgs.nl).
IPTA genotyping test does not improve detection of Crohn’s disease patients at risk of azathioprine/6-mercaptopurine induced myelosuppression

The thiopurine drugs azathioprine (AZA) and 6-mercaptopurine (6-MP) are effective for the treatment of inflammatory bowel disease (IBD) and their prescription is increasing. Haematotoxicty, which can lead to potentially life threatening bone marrow suppression, represents the most serious side effect of thiopurine therapy. It has been attributed to the accumulation of active cytotoxic metabolites of AZA/6-MP, collectively called 6-thioguanine nucleotides, resulting from a deficiency in thiopurine catabolism specifically catalysed by the thiopurine S-methyltransferase (TPMT) enzyme. Genotyping tests are now available to identify deficient and intermediate methylators who are, respectively, homozygous and heterozygous for non-functional alleles of the TPMT gene. As pointed out by Lennard in the leading article, homozygous and heterozygous for the TPMT gene. Our population comprising 41 patients with CD has been described in detail previously. Briefly, all patients had either leucopenia (white blood cell count <3000/mm²; n = 24) or thrombocytopenia (platelets <100 000/mm²; n = 30), or both (n = 14), leading either to discontinuation of treatment or reduction of dose by 50% or more during AZA (n = 33) or 6-MP (n = 8) treatment. Patients were genotyped for the IPTA 94C>A and IVS2+21A>C mutations according to a previously described procedure based on endonuclease digestion of polymerase chain reaction products. Distribution of the 41 patients according to their IPTA genotype is presented in table 1 and compared with that of a previously published control population of 100 healthy Caucasians. Allele frequencies in the CD population were 0.085 for the 94C>A mutation and 0.12 for the IVS2+21A>C mutation, similar to frequencies observed in the control population (0.06 and 0.13, respectively). There was no significant difference in the genotypes distribution between the two populations, which confirmed the lack of association between IPTA deficiency and myelosuppression during thiopurine therapy. Due to the retrospective nature of the study, no correlation with other side effects could be investigated. In conclusion, application of IPTA genotyping tests does not seem to improve the identification of patients at risk of myelosuppression with AZA/6-MP therapy. Although we believe that conventional TPMT genotyping tests should still be applied before the initiation of thiopurine treatment, further work is needed on the role of other candidate genes that may be involved in thiopurine haematotoxicity.

Acknowledgements
We thank N Ferrari and A Vincent for their assistance in performing the study and the members of the GETAID for recruiting patients in the study.

Table 1

<table>
<thead>
<tr>
<th>IPTA genotype</th>
<th>CD patients (n = 41)</th>
<th>Control population (n = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/A</td>
<td>26 (0.63)</td>
<td>64 (0.64)</td>
</tr>
<tr>
<td>A/C</td>
<td>6 (0.15)</td>
<td>10 (0.10)</td>
</tr>
<tr>
<td>C/C</td>
<td>7 (0.17)</td>
<td>24 (0.24)</td>
</tr>
<tr>
<td>94C&gt;A/21A&gt;C</td>
<td>0 (0.00)</td>
<td>0 (0.00)</td>
</tr>
<tr>
<td>IVS2+21A&gt;C/IVS2+21A&gt;C</td>
<td>1 (0.02)</td>
<td>0 (0.00)</td>
</tr>
<tr>
<td>94C&gt;A/IVS2+21A&gt;C</td>
<td>1 (0.02)</td>
<td>2 (0.02)</td>
</tr>
</tbody>
</table>

*Values in parentheses represent genotype frequencies.
†The control population comprised 100 healthy Caucasians who were genotyped in a previous study.

References

Small bowel malignancy at diagnosis of coeliac disease

We were very interested in the paper by Rampertab et al (Gut 2003;52:121–14) and the correspondence by Hawdle et al (Gut 2004;53:470–7). Their data are quite similar to ours, from the Italian Registry of Complications of Coeliac Disease.

We collected information on 1968 patients over 18 years of age (mean age at diagnosis: 36.7 years; female/male ratio 3.1), diagnosed with coeliac diseases between January 1982 and December 2002 at 20 Italian clinical centres specialised in gastrointestinal disease. The diagnosis was made according to revised ESPGHAN criteria. We found five (0.25%) patients with a small bowel malignancy at the time of diagnosis of coeliac disease. Age range was 49–69 years (mean 59 years) with a predominance of females (4:1). Survival rate was very poor as three patients died within 36 months of diagnosis.

These results indicate that there is an increased risk of developing small bowel malignancy in patients with coeliac disease. This correlation was confirmed with the female/male ratio. In fact, while small bowel neoplasms are usually more frequent in males, in our population four of five cases were female. Moreover, mean age at diagnosis of these cases was higher than that of patients overall, emphasising that the risk of a neoplasm increases with longstanding coeliac disease.
In conclusion, early diagnosis of coeliac disease should be made to prevent small bowel neoplasms from developing, and screening for this cancer should be carried out at diagnosis of coeliac disease, especially in patients diagnosed during adulthood.

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Competing Interests: None declared.

Reference

Hypergastrinaemia in patients infected with Helicobacter pylori treated with proton pump inhibitors

We read with interest the commentary by McColl on Helicobacter pylori infection and long term proton pump inhibitor (PPI) therapy (Gut 2004;53:5–7). It is remarkable that he did not mention gastrin although hypergastrinaemia is a result of reduced gastric acidity as well as Helicobacter pylori infection, and that patients with H pylori infection treated with PPI have additive hypergastrinaemia. Hypergastrinaemia predisposes to gastric carcinoids in animals and humans as well as to malignant ECL cell derived tumours (gastric carcinomas) in animals and humans.

Interestingly, the carcinogenic effect of H pylori infection may be completely explained by its hypergastraeinemic effect, a work where McColl was one of the authors. Furthermore, the increased gastric cancer frequency in moderate hypergastrinaemic INS-GAS mice concomitantly infected by H pylori infection may also be caused by increased hypergastrinaemia in infected mice.

To conclude, it is odd that gastrin was not taken into consideration when discussing the risk of gastric cancer following treatment with PPI in patients infected with H pylori. Animal as well as human studies linking gastrin to gastric cancer give support for a strategy where H pylori is eradicated in patients on long term PPI treatment.

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Competing Interests: None declared.

References

Terminal ileal biopsies should not be used to document extent of colonicoscopic examination

We commend the British Society of Gastroenterology and the authors for the excellent publication of guidelines for the management of inflammatory bowel disease in adults (Gut 2004;53(suppl V):vi1–16). However, we feel that their recommendation for routine terminal ileal biopsy is inappropriate. Although it is important to biopsy the terminal ileum if there is macroscopic evidence of an abnormality, their statement that “a terminal ileal biopsy performed at colonoscopy documents the extent of examination” is not recommended practice, due to the potential risk of variant Creutzfeldt–Jacob disease transmission from prion proteins which are prevalent in the lymphoid tissue of Peyer’s patches in the ileum. Although the use of disposable forceps may reduce the risk of transmission, there could still be contamination of the intubation channel of the colonoscope and prion protein is resistant to the standard endoscopic cleaning process. If the extent of examination needs to be documented, then a photograph of the ileocecal valve or ileal mucosa is preferable.

It is worth emphasising that prion protein may be present in any part of the gastrointestinal tract and random biopsy of gastro-intestinal mucosa for reasons other than confirming an endoscopic abnormality or excluding microscopic colitis is not accepta-

ble. Similarly, for surveillance colonoscopy where multiple biopsy is recommended, the risk benefit ratio of this policy must be supported by the clinical indications.

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References

IgG food antibodies should be studied in similarly treated groups

The recent paper by Atkinson and colleagues (Gut 2004;53:1459–1464) regarding IgG food antibodies and irritable bowel syndrome (IBS) fails to compare like with like. Regardless of the IgG results, the treatment group excluded significantly different foods to the control group, particularly those foods which appear to exacerbate symptoms of IBS. Of particular concern is the “yeast exclusion” diet. A low yeast diet is not a recognised diet in standard textbooks of dietetics and nutrition. However, alternative practitioners offering such a “yeast exclusion diet” sometimes recommend exclusion of a wide range of foods, such as: bakery products, alcoholic beverages, many other beverages including commercial fruit juices, cereals, condiments, dairy produce, fungi, meat products (ham, burgers, sausages, and cooked meats made with bread or breadcrumbs), yeast extracts (Bisto, Marmite, Oxo, Bovril, Vegemite, gravy browning, and all similar extracts), all B vitamin preparations, and, in most worrying, “sugar foods” (sugar, sucrose, fructose, maltose, lactose, glycogen, glucose milk, sweets, chocolate, sweet biscuits, cakes, candies, cookies, puddings, desserts, canned food, packaged food, hamburgers, honey, manitol, sorbitol, galactose, monosaccharides, polysaccharides, date sugar, turbino sugar, molasses, maple syrup, most bottled juices, all soft drinks, tonic water, milk shakes, raisins, dried apricots, dates, prunes, dried figs, and other dried fruit).

Therefore, regardless of IgG antibody status, the dietary restrictions in one group are not controlled for by the other group, and hence the conclusion may not be valid. It would also be helpful to know if any of the patients with IgG antibodies to a particular antigen also had IgE antibodies to the same antigen.

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Competing Interests: None declared.
IgG antibodies to foods in IBS
We read with interest the article by Atkinson et al (Gut 2004;53:1459–64). The authors describe an important advance in our understanding of the putative role of inflammation in irritable bowel syndrome (IBS). However, we wonder whether their conclusion that assay of IgG antibodies may have a role in identifying candidate foods for elimination to treat patients with IBS may be a step too far. The four foods to which the patients most commonly formed antibodies and hence the four foods most commonly eliminated from the “true diet” were yeast (86.7%), milk (84.3%), whole egg (58.3%), and wheat (49.3%). The “sham diet” involved eliminating foods to which the patients had not formed antibodies and, therefore, in the sham group the exclusion rates, for yeast, milk, whole egg, and wheat were very low (0%, 1.3%, 26.7%, and 8% respectively). It is therefore difficult to assess whether a diet excluding these foods would have led to symptomatic improvement in all patients, regardless of their antibody status.

Furthermore, the foods to which the study group did form antibodies were similar to those already identified as leading to symptomatic benefit in patients with IBS when excluded from their diet. In a review cited by Atkinson and colleagues,1 it was noted that in eight trials of exclusion diets in IBS, seven identified dairy products and five identified wheat as worsening symptoms. It is not clear whether the difference in improvement in symptoms seen in the current study by comparing true and sham groups can be explained simply by the omission of these foods. This could in practice eliminate the need for antibody testing.

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Competing Interests: None declared.

Reference

Influence of dietary factors on the clinical course of inflammatory bowel disease
Jowett et al reported in their elegant study on the role of diet in maintaining remission in patients with ulcerative colitis (Gut 2004;53:1479–84). Surely the effect of diet has an essential, but often forgotten, role in altering the course of disease in all types of inflammatory bowel diseases. This role does not necessarily act by maintaining patients in remission clinically, but perhaps more importantly by modifying the activities of the disease and rendering it quiescent.

We have recently reported a case of active strictureing Crohn’s disease in an adult female patient with high stoma output.1 We were struck by the importance of the case, because the case included a patient with high stoma output. We also considered that the case could have been a potential patient with active Crohn’s disease. Another possible mechanism is that this formula may have a role as a prebiotic by stimulating the activity of bacteria which are already present in the gut.

Remission induced in our case study highlights the part played by a base composed of the formula in the management of adult Crohn’s disease. The encouraging result demonstrates the need to treat similar cases with dietary measures first. This opportunity should not be missed as it may well obviate the need for surgical intervention or administration of potent pharmacotherapeutic agents which carries the risk of several comorbidities.

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Competing Interests: None declared.

References

Identification of ferroportin disease in the Indian subcontinent
Haemochromatosis is a common inherited disorder of iron metabolism, characterised by excessive iron absorption and deposition in tissues. The majority of cases are associated with mutations in the HFE gene and inherited in an autosomal recessive manner.1 Autosomal dominant forms of haemochromatosis have been reported, mainly associated with mutations in the ferroportin 1 gene.2 This syndrome, termed type 4 haemochromatosis or more recently ferroportin disease,1 is usually characterised by an early increase in serum ferritin with normal transferrin saturation. Iron accumulation is most prominent in Kupffer cells and other macrophages, in addition to hepatocytes. Some patients do not tolerate venesection therapy well and can develop anaemia. Hereditary iron overload disorders appear to be uncommon in Asia. Secondary iron overload due to beta thalassaemia is relatively common in the Indian subcontinent. However, primary iron overload disorders and HFE mutations appear to be rare and cases have not been well characterised in this region.3 We identified a patient from the Indian subcontinent with features typical of ferroportin disease.

A 36 year old female of Sri Lankan origin presented for a routine medical examination in December 2003. She was found to have an elevated serum ferritin of 4148 μg/l and transferrin saturation (29%) were normal. Liver function tests, blood glucose, and thyroid studies were all normal. Physical examination was normal and she had no significant past medical history or risk factors for iron overload.

C282Y, H63D, and 56C HFE gene mutations were all negative and she had no family history of iron overload. Her mother and three siblings all had normal serum ferritin levels. Her father died of ischaemic heart disease aged 48 years.

A magnetic resonance imaging scan showed hepatic iron overload. Liver biopsy showed grade 3–4 iron deposits in Kupffer cells and hepatocytes and Kupffer cells; no fibrosis or cirrhosis was evident (fig 1). The hepatic iron concentration was 17 700 μg/g dry weight and hepatic iron index was 9.1.

Venesection therapy was initially poorly tolerated with the development of anaemia following the first two 500 ml venesections. Her haemoglobin is now stable on a programme of 300–500 ml venesections every three weeks.

The features of ferroportin disease in this patient led us to sequence the ferroportin gene, as previously described.4 Analysis of the DNA sequence revealed a heterozygous three base pair deletion (TTG) in exon 5. This is the same deletion, V162del, described by us and others in haemochromatosis patients from Australia, the UK, Italy, and Greece.3

This is the first report to identify V162del or indeed any ferroportin 1 mutation in an individual from the Indian subcontinent. Identification of V162del in an Asian patient confirms that this mutation is likely to be the most common mutation of ferroportin 1 and the most common cause of non-HFE associated haemochromatosis. The wide geographical distribution of this mutation suggests that it is a recurrent mutation that has repeatedly arisen in distinct populations, probably by slippage mispairing.

Iron overload in this patient was typical of ferroportin disease. At the time of diagnosis she was asymptomatic and had no fibrosis on liver biopsy. Whether fibrosis or clinical complications will develop with age if iron stores are not depleted is unknown. In conclusion, we have identified the V162del mutation of ferroportin 1 in a fifth geographical location, emphasising that this mutation is the most common and widely distributed mutation which causes non-HFE haemochromatosis. We have identified V162del in a region where iron overload disorders have not been well characterised.

Analysis of this and other ferroportin 1 mutations may be useful in iron overload disorders in this region and may be the basis of hitherto unexplained cases of iron overload.
Figure 1 Liver biopsy sections from our patient stained with (A) haematoxylin and eosin and (B) Perls’ Prussian blue (magnification 100 x). Grade 3–4 iron is prominent in hepatocytes and Kupffer cells.

Acknowledgements

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Competing Interests: None declared.

References


BOOK REVIEW

Morson and Dawson’s Gastrointestinal Pathology, 4th edn


Why do people buy a book such as this, which involves a not inconsiderable financial outlay (even if you box clever and make it tax deductible)? I think for two main reasons—firstly, for use as a bench book, and secondly, for information on the pathological basis of gastrointestinal disease for interest, teaching, or indeed research purposes.

On the first criterion, this book succeeds, usually quite brilliantly. As a vade mecum on gastrointestinal pathology it should be on the shelf of every pathologist who engages in the reporting of such material. In my view, the book is more user friendly than the competition—Fenoglio-Preiser and Goldman to name but two—and is certainly more readable. I would therefore extol its virtues unreservedly in this respect.

On the second criterion, as a source book, I suppose the correct word is patchy. Some sections, for example that on colorectal tumours, is admirable in this respect, whereas other sections are more limited in scope and even cursory in their treatment of the pathobiology. There is also the problem of the unavoidable intrinsic delay in producing such a book, resulting in reference lists which are some years away from the publication date. I am aware however that my personal outlook is not that of most individuals who will purchase this volume so I am probably being over critical. It is, after all, quintessentially a bench book, and excellent at that.

However, I do have one real beef. In any multi-author work there is bound to be variation, but here we are not told which one of the stellar cases were responsible for which section or chapter. Of course we can make informed guesses about the Barrett’s or colorectal carcinoma sections, but who did the GIST bit? Because of some (minor) errors in the criteria for the diagnosis of malignancy, I have tried to generate a number of authors who have all denied responsibility, and blamed someone else—usually the author(s) absent at the time. Not good enough.

I have to concede however that the authors have succeeded in producing perhaps the test in gastrointestinal pathology, which is a credit to both themselves and the discipline in the UK. I congratulate them.

N A Wright

CORRECTIONS

doit: 10.1136/gut.2003.025494corr1

In the January 2005 issue of Gut, one of the author’s names of the paper entitled Human peripheral and gastric lymphocyte responses to Helicobacter pylori NapA and APhC differ in infected and uninfected individuals (H J Windle, Y S Ang, V A Morales, R McManus, and D Kelleher. Gut 2005;54:25–32) was cited incorrectly. V A Morales should read V Athie-Morales. The journal apologises for this mistake.

doit: 10.1136/gut.2003.026807corr1

In the December issue of Gut fig 1 in the paper by AJG Bell et al (Human lymphocyte stimulation with pachomins flora is greater than with flora from a healthy pouch but is suppressed by metronidazole. Gut 2004;53:1801–1805) is incorrect. The labels for fig 1C are inverted; the squares should have been labelled HetNon and the triangles HetPM. The legend is also incorrect because the label for flora grown on agar without metronidazole is HetNon, not HetP as stated.