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).1,2

Iwase and colleagues3 divided FV into localised and diffuse types using MDCT angiography. This classification resembles the findings obtained by investigation of resected or autopsied stomachs.3 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).3

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 colleagues4 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 evaluating the effect of treatment of FV.5 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.3,6

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 shuntangiography (TIPS), which represents the efferent vein of gastric varices.6 Although FV with a high risk of bleeding can 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,7 this patient underwent endoscopic sclerotherapy.

J K Willmann, D Weisheit, T Böhm, T Pfammatter
Institute of Diagnostic Radiology, University Hospital, Zurich, Switzerland
P Bauerfeind
Division of Gastroenterology, University Hospital, Zurich, Switzerland

Correspondence to: Dr D Weisheit, Institute of Diagnostic Radiology, University Hospital, Rämistrasse 100, 8091 Zurich, Switzerland; dominik.weisheit@dmg.usz.ch

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 neutropenia 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 anticardiolipin antibody (1 in 468) and her extractable nuclear antigens and dsDNA were negative, as was her anti-neutrophil cytoplasmic autoantibody and her antimitochondrial and antismooth muscle antibodies. Her thrombophilia screen was negative but her IgG anticardiolipin antibodies were positive at 22.3 (0–5.8).

A diagnosis of antiphospholipid syndrome was made. She was treated with heparin and warfarin and subsequently made a good recovery.

Discussion

Primary antiphospholipid syndrome is defined as the presence of antiphospholipid antibodies (lupus anticoagulant or anticardiolipin antibodies) in association with thrombosis or recurring miscarriage, but in the absence of an associated connective tissue disorder such as systemic lupus erythematosus (SLE).1

SLE has previously been described as an unusual cause of acute autoimmune pancreatitis. In the literature there are a small number of cases of pancreatitis in association with SLE and antiphospholipid syndrome.2,3

A single case of pancreatitis associated with lupus anticoagulant but without anticardiolipin antibodies has also been described.4 However, to my knowledge this is the first reported case of primary antiphospholipid syndrome associated with anticardiolipin antibodies causing acute pancreatitis.

In the antiphospholipid syndrome, vascular occlusion is due to thromboembolism whereas in SLE the primary abnormality is vasculitis. In a single post mortem case of pancreatitis due to antiphospholipid syndrome associated with SLE, the pathological abnormality was vascular occlusion due to thromboemboli.5 Oral anticoagulation rather than steroids is therefore the treatment of choice for antiphospholipid syndrome.6

The patient described fulfills the criteria for a diagnosis of primary antiphospholipid syndrome. While there is no histological 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 thrombosis 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 acute pancreatitis.

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

H L Spencer

Correspondence to: Dr H L Spencer, Sheffield Teaching Hospitals, Herries Rd, Sheffield, UK, happyhal@cheerful.com

References


Author’s reply

Autoimmune pancreatitis is a recently described clinical entity in which autoimmune mechanisms are involved in the pathogenesis. As Etemad and colleagues1 described that autoimmunity was one of six risk 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.7 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 other 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.

T Kamisawa, N Funato, A Okamoto

Correspondence to: T Kamisawa, Department of Internal Medicine, Tokyo Metropolitan Komagome Hospital, 3-18-22 Komagome, Bunkyo-ku, Tokyo 113-8677, Japan; kamisawa-t@komagome-hospital.bunkyo.tokyo.jp

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.6 Earlier studies with antiviral amantidine, which has been used in influenza, had shown promising results.7 Now, Adinolfi et al (Gut 2001;48:220–5) 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 subcutaneously 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.8 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.

N Khokhar

Correspondence to: Professor N Khokhar, Division of Gastroenterology, Department of Medicine, Shifa International Hospital and Shifa College of Medicine, Islamabad, Pakistan; drnkholkar@yahoo.com

Who should perform endoscopic procedures?

We read with great interest the report of Smale et al. on upper gastrointestinal endoscopy performed by nurses (Gut 2003;52:1090–4). This work shows a limited experience with specific endoscopy trained nurses that had no significant effect on diagnostic yield, patient comfort, or patient satisfaction compared with medical staff. Many experiences, some of them mentioned in this report, have shown that nurses can successfully perform endoscopic procedures.

Of course, nurses require a training program, similar to the one usually offered to our residents and trainees. We are certain that specifically trained nurses could also perform liver biopsies, abdominal ultrasound examinations, diagnostic laparoscopies and some surgical procedures, such as appendectomy or elective cholecystectomy. Any manual (surgical or endoscopic) procedure may be learnt by anyone, medical or non-medical, in common with many other forms of manual labour or craftsmanship. Frequently, and not so long ago, GPs performed some surgical procedures, such as caesarean section and appendectomy, and barbers once performed surgery. This could be the first step towards a new perspective for medical practice in which nurses might attend our gastroenterology wards and clinics in some circumstances.

We have no doubt about the accuracy and seriousness of this report but, as the authors explain in the introduction, the main motivation for the study was economic. Public health systems, such as the British and Spanish systems, have a great deal of sanitary costs. In our day to day clinical practice, many strategies are tried with the aim of reducing costs. But some frequently overlooked ethical, scientific, and philosophical questions are implied. Nowadays, there are more restrictive conditions to teaching endoscopy to young gastroenterologists. Ethical and legal concerns make resident training more expensive and difficult, as our developed societies are increasingly demanding of healthcare quality and safety. Hence should we begin teaching endoscopy to non-medical staff? We do not believe so. We also believe that one essential function of medical practice is to provide investigation (an always limited field in terms of funds and time) in public hospitals’ busy endoscopy wards. Then, should nurses have a specific training in investigation? The excellent work of Smale et al. raises many other simple questions: (1) When to stop? (2) The main goal of this work was to have cheaper endoscopists, so why not try to minimise costs by teaching nurses other physician tasks, such as physical examination or minor surgical procedures? (3) Should we begin training nurses instead of our residents 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.

E Redondo-Cerezo, J Garcia-Cano
Digestive Service, Unidad de Endoscopías, Hospital General Virgen de la Luz, Cuenca, Spain

Correspondence to: Dr E Redondo-Cerezo, Servicio de Aparato Digestivo, Hospital General Virgen de la Luz, C/Hernando de Donantes de Sangre 1, Cuenca, 16002, Spain; eredondac@yahoo.es

References


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 (Gut 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.1–3 To improve the effectiveness of serological diagnosis of patients with pancreatic cancer, different tumour markers have been assessed, including CEA, CA 242, CA 50, and CA 72-4.4–7 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 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.

A Harlazinska-Szymarka, M Strynska-Karpinska
Department of Clinical Immunology, Wroclaw Medical University, Mikulczycz-Rodeckiweg, Street 7, Wroclaw 50-368, Poland

Correspondence to: Professor A Harlazinska-Szymarka; immuno@immuno.am.wroc.pl

References


www.gutjnl.com
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 UK 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 another 7% with Crohn’s disease.\(^2\) Of these patients there had been a good clinical and mucosal response to a gluten free diet. 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 and coeliac disease is very common. 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.

P D Howdle, G K T Holmes
Department of Medicine, Clinical Sciences Building, University of Leeds, Leeds LS9 7TF, UK

Reference

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 and her symptoms settled. 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 the diarrhoea in this condition, especially as there appears to be no correlation between the width of the collagen band and the severity of symptoms.

J D Mitchell, R Teague, R Bolton, J Lowes
Torbay Hospital, Bessemer Rd, London SE5 9RS, UK

Correspondence to: J D Mitchell; jannitch@clara.net

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

Figure 1 Erect radiographs from a double contrast barium enema series. Submucosal tracking of gas is arrowed.
see my novel studies \(^1\) partially reproduced in patients with decompensated cirrhosis. I disagree with some of the results as the study involves 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. Immobilisation by me and others have shown vasoconstriction in the brachial, femoral, cerebral, and renal territories, especially in advanced cirrhosis.\(^5\) Therefore, I would like to stress the point that with advancing cirrhosis, further activation of the neurohumoral systems occurs, with consequent peripheral vasoconstriction. 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 aleness 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, FBF ratios are significantly more reproducible than unilateral FBF measurements both at rest and following infusion of vasoconstrictors.\(^6\)

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.\(^5\) 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.

Both the authors, ET, receptor mediated responses were unaltered while blocking ETA receptors with BQ-123 would allow enhanced in patients with decompensated cirrhosis. Thus one would expect that blocking ETA 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-induced increase in FBF by −33–40%. How can infusion of ET-1 produce the same per cent change in FBF as infusion of its selective ETB receptor antagonists?\(^5\)

Many of the included patients were receiving diuretics, \(\beta\)-blockers, and immunosuppressive medications, which were withheld only on the day of testing. These medications affect circulating volume, vascular tone, and the activity of the neurohumoral systems. To eliminate these effects, drugs need to be stopped for at least five times their half life. Alternately, control subjects on the same medications should be used (for example, renal transplant recipients with a normal liver).

Vaughan et al reported normal plasma ET-1 concentrations in decompensated cirrhosis, without measuring preproendothelin-1 mRNA or big ET-1, the biological precursor of 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.\(^12\) This should have been stated by the authors. I also recommend collecting samples in tubes containing 1000 KIU 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 each point in time; (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.

A Helmy

Correspondence to: Dr A Helmy, Gastroenterology and Tropical Medicine Department, 6th Floor, Assiut University Hospital, Assiut 71111, Egypt. ahadamel10@hotmail.com

References


Germline testing of mismatch repair genes 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).\(^3\) While the aim of these prescreening tests is to identify those at risk 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, 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 Exo1), PMS1, D2S118, and D2S155 (for PMS1), D2S21133, D2S2156, D2S2292, D2S369, and D2S378 (for hMSH2 and hMLH1) and D3S1447 and D3S3685 (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 (fig 1). 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.

Allolic loss of hMSH2 occurs often 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.

<table>
<thead>
<tr>
<th>Gene</th>
<th>Marker</th>
<th>Tumour ID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exo1</td>
<td>D1S180</td>
<td>1 2 3 4 5 6 7</td>
</tr>
<tr>
<td>PMS1</td>
<td>D2S118</td>
<td></td>
</tr>
<tr>
<td>D2S155</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D2S21133</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D2S2156</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D2S2292</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D2S369</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D2S378</td>
<td></td>
<td></td>
</tr>
<tr>
<td>hMLH1</td>
<td>D3S1447</td>
<td></td>
</tr>
<tr>
<td>D3S3685</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 1 Loss of heterozygosity analysis of four mismatch repair genes tumours from seven individuals with germline mutations in hMSH2.
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 ankylosing spondylitis and mild upper respiratory symptoms, he underwent wireless capsule endoscopy (M2A capsule; Given Imaging) in order to exclude upper and lower GI disease. Duodenal biopsies revealed the presence of coeliac disease; upper and lower endoscopies were otherwise unremarkable. As he also presented with ankylosing spondylitis and mild upper respiratory symptoms, he underwent wireless capsule endoscopy (M2A capsule; Given Imaging) in order to exclude upper and lower GI disease.

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 into the right main bronchus. Because of the smooth surface of the capsule, its removal by flexible bronchoscopy proved to be rather difficult, but eventually it was successfully recovered from the bronchial tree. The patient made an uneventful recovery.

He had a history of ankylosing spondylitis with involvement of the cervical spine. Although he reported no symptoms of dysphagia and recalled swallowing the capsule as uneventful, it may be possible that the cervical spine disease contributed to aspiration of the capsule.

To the best of our knowledge, this is the first published case of aspiration of an M2A capsule since this diagnostic method has become available to general clinical practice. It underlines the recommendations of the manufacturer for cautious use in patients with known or possible swallowing disorders (http://www.givenimaging.com).

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 carcinogens due to reflux of intestinal contents and bile stasis. However, this chronic irritation and carcinogenesis of the biliary mucosa after biliary-enteric anastomosis may have 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 anampullary 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 bile stasis.

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 hepatojjunostomy 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. 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. 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 authors about monitoring all patients who develop cholangitis after biliary-enteric anastomosis for malignant disease and also patients with malignant disease who are in remission.


Reference


Late development of cholangiocarcinoma after hepatojjunostomy 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 carcinogens due to reflux of intestinal contents and bile stasis. However, this chronic irritation and carcinogenesis of the biliary mucosa after biliary-enteric anastomosis may have 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 anampullary 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 bile stasis.

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 hepatojjunostomy 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. 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. 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 authors about monitoring all patients who develop cholangitis after biliary-enteric anastomosis for malignant disease and also patients with malignant disease who are in remission.


Reference


Late development of cholangiocarcinoma after hepatojjunostomy 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 carcinogens due to reflux of intestinal contents and bile stasis. However, this chronic irritation and carcinogenesis of the biliary mucosa after biliary-enteric anastomosis may have 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 bile stasis.

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 hepatojjunostomy 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. 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. 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 authors about monitoring all patients who develop cholangitis after biliary-enteric anastomosis for malignant disease and also patients with malignant disease who are in remission.

D Padilla, T Cubo, R Pardo, J M Molina, J Hernández

Department of Surgery, Complejo Hospitalario, 13005 Ciudad Real, Spain

Correspondence to: Dr D Padilla; maymona@terra.es

References

Adoptive transfer of genetic susceptibility to Crohn’s disease

We read with interest the stimulating case report on fulminant Crohn’s colitis following allogenic bone marrow transplantation 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 −845 is the only SNP of the HLA-DRB1 gene 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 do not describe in detail which particular genetic polymorphism 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 the best 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 adhesion of bacteria to the intestinal mucosa, which might particularly be facilitated in the presence of mutated NOQ2 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 biotherapeutic treatment (for overview see Folwaczny and colleagues).4 Thus a complementary explanation for the described phenomenon might be the persistent immunomodulatory therapy the donor had received.

C Folwaczny, J Glas, T Mussack, H P Türök
Klinikum Innenstadt, Ludwig-Maximilians University, Munich, Germany

Correspondence to: Dr C Folwaczny; Christian.Folwaczny@medizin.uni-muenchen.de

References

Self Assessment Colour Review of Hepatobiology Medicine


Roger Chapman and Henry Bodenheimer have produced a useful addition to the libraries of gastroenterologists with an interest in liver disease. Hepatobiology 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 content of the questions will test experts. Hepatobiology 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. However, 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 disease 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 subspeciality and the shortening of training programmes reducing the opportunities for trainees to “learn by osmosis” in a 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 been better. Hepatobiology 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 Hepatobiology 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 reasonably current overview 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, serodiagnstics, genetics, imaging developments, and...
eighty years. The book is an excellent guide for anyone requiring a comprehensive overview of the condition, and is a valuable resource for both healthcare professionals and patients.

The book is divided into several chapters, each focusing on a different aspect of irritable bowel syndrome. The chapters cover topics such as diagnosis, treatment options, and managing the condition in different settings. The authors provide a balanced and pragmatic view of the condition and its management, making it easy for readers to understand the complex nature of irritable bowel syndrome.

In summary, 'Fast Facts: Irritable Bowel Syndrome' is an informative and practical guide to the condition. It is an excellent resource for anyone looking to gain a deeper understanding of irritable bowel syndrome and its management. Whether you are a healthcare professional or a patient looking for information about the condition, this book is a must-read.