LETTERS TO THE EDITOR

Is needle biopsy of the liver necessary to diagnose HCC?

Editor,—Schotman and colleagues (Gut 1999;45:626–7) reported a patient with subcutaneous seeding of hepatocellular carcinoma (HCC) after percutaneous needle biopsy. We agree with their conclusion that percutaneous biopsy should be reserved for cases with highly suspicious radiological findings. However, we have some concerns and comments on the mentioned case.

Firstly, why did the authors perform tumour biopsy in a resectable HCC? Furthermore, why was a needle biopsy performed in these cases and correctly outlined the necessity for a critical evaluation of the role of needle biopsy in resectable HCC. 1,2

We agree with their conclusion, namely that if it is not possible to diagnose HCC by other means (namely increased a fetoprotein (AFP) concentrations, spiral computed tomography (CT), magnetic resonance imaging); in these cases a single pass with a large needle (18 gauge) may be preferable to multiple passes with smaller calibre needles; (ii) needle biopsies are not indicated to confirm HCC in patients suitable for liver transplantation; and (iii) the entire needle tract should be resected at surgery for the primary tumour. This has been important in other skin recurrences, namely those after laparoscopic cholecystectomy for undiagnosed gall bladder carcinoma. 1,2

However, we have some questions and comments concerning the reported case. Firstly, why did the authors perform tumour biopsy in a 30 year old woman with hepatitis B liver cirrhosis and raised serum AFP, showing a 2 cm diameter subcapsular nodule in segment V and two additional satellite lesions in the same segment? Adequate imaging procedures were already available four years ago. In fact, the patient had percutaneous liver biopsy together with an informative diagnostic procedure such as spiral CT. In addition, subcapsular liver lesions are known to give a high rate of both subcapsular recurrence and intraperitoneal subdiphragmatic seeding. 3 Therefore, in contrast with recurrence after laparoscopic surgery which mostly cluster around abdominal port tracts, 4 simple removal of the needle tract could not be sufficient to prevent the side effects of percutaneous liver biopsy. Secondly, why did they perform right heptectomy in a cirrhotic liver rather than segment V segmentectomy? The latter could be a similarly adequate procedure while preserving better residual liver function.

The authors should be congratulated for focusing once again on a very important question (to biopsy or not to biopsy liver nodules in suspected HCC in the present era of highly effective imaging) and for their collection of 15 cases, which is obviously an underestimation of what occurs in practice and is currently observed in many transplantation centres. However, their message for the reader should be clearer as there is an apparent contradiction between what they state and what they actually did.

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Reply

Editor,—We read with interest the letter of Cetta et al in which they discussed our case (Gut 1999;45:626–7) of subcutaneous seeding of a hepatocellular carcinoma (HCC) after percutaneous needle biopsy. Firstly, they state that a needle biopsy was not indicated in the case presented. It must be stated that the biopsy was performed elsewhere before the patient was admitted to our hospital. Secondly, they suggest that a smaller partial heptectomy might have been sufficient to treat the HCC in this 30 year old woman with hepatitis B liver cirrhosis. In the case presented there was no deterioration in liver function or improved functional reserve after resection. The postoperative course was uneventful.

In general, we agree with the opinion to limit resection as far as possible and presently we would perform a segmentectomy.

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Management of gastric fundal varices associated with a gastrorenal shunt

Editor,—We read with great interest the article by Jalan and colleagues (Gut 2000;46:578–81) on the clinical position of transjugular intrahepatic portosystemic shunt (TIPS). This procedure is a useful method of reducing portal pressure by creating a portosystemic shunt in the liver. They suggested that TIPS can be a successful treatment of bleeding gastric fundal varices (FV) unresponsive to pharmacological and endoscopic therapy. However, Sanyal et al determined the one year probability of bleeding as a function of all possible combinations of two endoscopic variables (variability size and the presence of red spots) for patients in Child’s class A, B, or C. According to their classification, FV with a one year probability of bleeding (16%) can be considered as high risk varices.

As TIPS seems to be ineffective for FV associated with a gastrorenal shunt, 1,2 blockers or nitrates (which are widely used to treat high risk oesophageal varices) may also be ineffective for primary prophylaxis of bleeding from FV. Accordingly, prophylactic B-RTO may be justifiable due to its simplicity and safety. Because the gastrorenal shunt tends to be occluded after B-RTO, 3 however, the long term effect of this procedure on portal haemodynamics needs to be evaluated.

Although a prospective randomised study comparing B-RTO with TIPS is to be performed, the prevention of bleeding or rebleeding from FV is still needed, we hope that B-RTO will become a frontline treatment for high risk FV associated with a gastrorenal shunt in the near future.

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The data in the literature do not support the notion that portal hypertension has been suggested by Matsumoto et al. Although data on the use of B-RTO for the treatment of fundal varices are exciting, we look forward to randomised controlled clinical trials comparing TIPSS with B-RTO.

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Letters, Notes, Correction

The science, economics, and effectiveness of combination therapy for hepatitis C

EDITOR,—No one affected by hepatitis C virus (HCV) will question Professor Dushenko’s insistence on the importance of effective therapy for HCV and the funding to meet them (Gut 2000;47:159–61). With research and clinical evidence pointing to a prevalence of HCV infection far in excess of human immunodeficiency virus (HIV), the issue has now become urgent. Patients and clinicians alike will await the forthcoming NICE appraisal in the hope it recommends in favour of allocating sufficient resources to cover treatment costs for those most in need and best able to benefit.

However, while a positive response will be welcome it will also uncover issues that have still to be fully addressed. These centre on who will should be selected for treatment and the effects of the treatment itself.

Regarding the first issue there remains a debate around who will benefit most from treatment. The morbidity and impacts of HCV infection vary in terms of genotyping, age, duration of viraemia, extent of liver damage, and other complicating factors, such as continued drug and alcohol abuse. While there may be some validity to such categorisations, they are not at all absolute and can denigrate patients. Nevertheless, and leaving such considerations aside, if HCV infection is as widespread as some clinicians anticipate, it would be unrealistic to believe that effective treatment will be available to treat everyone. This means that some form of treatment selection will need to be adopted. Should this occur, the question remains as to how clinicians will make choices and what criteria they will use. Furthermore, will protocols be in place to govern these criteria to ensure they are standardised nationwide?

Although Dushenko et al cite the potential priority given by the NHS to combination therapy as the salient issue, this needs to be addressed in conjunction with the equally important matter of who should receive this treatment. In other words, patients are offered standard combination therapy, combination therapy with pegylated interferon (PEG IFN), or PEG IFN alone in some ways secondary to the issue of who is actually going to be given treatment. Will it be based on disease progression or expected response to treatment, or both?

Before considering this further, a factor that needs to be implicated in discussions around HCV, but which clinicians tend to underestimate, is patient tolerance and possible lingering effects of the drugs. Although there seems to be a fairly clear cut case in favour of the greater efficiency of combination treatment, it is harder for patients to tolerate than monotherapy with IFN, particularly when taken over 48 weeks. During this time, it has been stated that the 20% (approximately) of patients who discontinue therapy before 48 weeks usually do so because of “insomnia, depression, irritability, or anaemia”. This would seem to suggest that those with less risk of progressive disease, and therefore less motivation to seek a cure, are more resistant to therapeutic intervention.

Notwithstanding the obvious factor of the greater and more urgent need of treatment for patients with progressive disease following HCV infection, perhaps this trend in mild HCV sufferers might offer some insight as to how patients sometimes choose for themselves to be involved with alternative therapies. A recent nationwide trial offered to patients with mild HCV failed to recruit anywhere near its target numbers. This would suggest that those with less risk of progressive disease, and therefore less motivation to seek a cure, are more resistant to therapeutic intervention.

Regarding the second issue, whether patients are offered effective monotherapy or combination therapy, considerable resources are being devoted to ensure that HCV patients an indicator of how best to prioritise treatment should such selection prove necessary.

1 Figures released by the Communicable Disease Report of 26 May 2000 (Vol 10, No 21) cite 41 174 cases of HIV infection in the UK—that is, less than 0.07% of the population. UK data from the PHLS AIDS and STD Division, Scottish Centre for Infection and Environmental Health, Institute of Child Health, London and Oxford Haemophilia Centre—on behalf of UK Haemophilia Centre Directors Organisation. HCV infection is currently anticipated to be around 10 times higher, an estimate that would seem to be underscored by the recent study carried out at St Mary’s Hospital (Ward C, Tudor-Williams G, Cotzas T, et al. Prevalence of hepatitis C virus (HCV) infection in women attending an inner London obstetric department: uptake and acceptability of routine antenatal testing. Gut 2000;47:277–80), which reported a prevalence of HCV infection in 0.8% of women who took part. In the 0.6% who were viraneous, in the US HCV infection is reported to be possibly four times higher than HIV with 3.5 million affected and 30 000 new cases each year (Turkington C. Hepatitis C: the silent killer. Chicago: Contemporary Books, 1998:xvii).

Screening for genetic haemochromatosis in blood samples with raised alanine aminotransferase

EDITOR,—Bhavnani et al (Gut 2000;46:707–10) claim to have identified 12 patients

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homozygous for C282Y or with compound heterozygosity at a cost of only £117 per patient identified. This astonishingly low total of £1400 allowed them to:

- Select out of 35 065 blood samples 4.2% (1490) with an elevated alanine amino-transferase.
- Undertake measurement of 1490 serum iron, transferrins, and ferritin concentrations.
- Give information on haemochromatosis and offer genetic screening to the 56 patients found to have a transferrin saturation >60%, and to re-contact those not responding.
- Obtain informed consent from the 33 patients who did respond, and undertake genetic testing for HFE mutations.
- Offer appropriate management to the 12 patients with C282Y homozygocity or compound heterozygocity.

We have some difficulty in accepting that all this can be achieved for only £1400, and would be intrigued to know how the authors arrived at their costing.

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Reply

Editor,—Our preliminary study set out to examine the clinical usefulness of screening a targeted population for genetic haemochromatosis. The costing given in our paper was as stated, based solely on laboratory costs, a summary of which is given below. Costs of the clinician, nursing, and clerical time were not included in the paper, and are detailed below.

Laboratory costs:

- Screening for blood samples with elevated ALT incurred no additional costs as these samples were processed routinely as part of the normal hospital and GP biochemistry request.
- The marginal costs for the measurement of 1490 serum iron and transferrins, £1085; 33 serum ferritins, £51; and genetic testing: £264 (total £1400).
- Although serum ferritins were performed on all 1490 specimens as part of the study, we found only 6% had raised ferritin levels.

Thus we advocated “In those patients found to have a raised ALT, the cost of screening with iron saturation and follow up when appropriate with ferritin and gene testing would be £1400.”

Other costs:

We were awarded a research grant of £5000 from the Health Authority, and the rest of the money was used for employing a medical laboratory assistant, (8 h/week) who picked out the relevant specimens and batched them for future testing. Information on haemochromatosis, plus offering genetic screening to the 56 patients found to have a transferrin saturation >60% and recontacting the non-responders was done by means of a standard letter to the clinicians who had requested the original liver function tests. Consent for genetic testing was obtained by these clinicians. Management of the 12 patients (homozygotes and compound heterozygotes) was undertaken (with no extra funding) by one of the authors (MB) as part of the routine Clinical Haematology service.

Since then, the Health Authority has awarded us continued revenue for this targeted screening, and included in these monies are the clinical, the clerical, and nursing costs incurred in providing this service as a routine for patients in our District.

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NOTES

American College of Gastroenterology 2001 International GI Training Grants Programme

The ACG International GI Training (IGT) Grant Programme provides funding for clinical or clinical research training in gastroenterology and hepatology so that an individual can acquire or develop new cognitive knowledge or a technical skill. This newly acquired knowledge or skill would then be used to improve patient care in the applicant’s geographic area. Physicians outside of the United States and Canada are eligible to apply. At least one fellowship within a maximum of $10 000 per IGT fellowship will be awarded during 2001, for a training period of not less than six months. Awards will be made by a special committee of the ACG and will be based upon the applicant’s credentials, the merit of the proposed training by the selected host training centre and the potential for enhancing the field of gastroenterology in the applicant’s home country. Application forms can be obtained from the ACG administrative office: 40000B South 31st Street, Arlington, Virginia 22206-1656. Tel: +1 703 820 7400; fax: +1 703 931 4520; website: www.acg.org. Deadline for submission of application is 1 April 2001.

Redefining Priorities in Gastroenterology

This congress will be held on 11–14 April 2001 in Monte Carlo, Italy. It will be chaired by Professor Massimo Crespi (Rome, Italy) and Professor Eamon Quigley (Cork, Ireland). Further information: Maddalena Massaro, Project Leader, AISC-AIM Group, Via A Ristori 38, 00187 Rome, Italy. Tel: +39 06 80968; fax: +39 06 80968229; email: gastro2001@aisc.it.

3rd European Federation of Autonomic Societies (EFAS)

The third European Federation of Autonomic Societies (EFAS) meeting in conjunction with the annual meeting of the sections “Autonomic nervous system” of the German Neurological Society, “Diabetes and Nervous System” of the German Neurological Society, and “Autonomic Nervous System” at the University of Erlangen-Nuremberg, Germany, will be held in Erlangen, Germany on 26–28 April 2001. Further information: Professor Dr M J Hla, Department of Neurology, University or Erlangen-Nuremberg, Schwabachanlage 6, D-91054 Erlangen, Germany. Tel: +49 0131 8534444; fax: +49 0131 8534328; website: www.neurologie.med.uni-erlangen.de/oeffentliche_Veranstaltungen.htm

Falk Workshop

The workshop entitled Update in Inflammatory Bowel Diseases will be held in Ljubljana, Slovenia, on 5 May 2001. Further information: Prof Dr S Markovic, University Medical Center Ljubljana, Division of Internal Medicine, Jalpeva 2, 1525 Ljubljana, Slovenia. Tel: +386 (1) 231 6925; fax: +386 (1) 433 4190; email: sasa.markovic@kclj.si

EPGS Endosonography Live in Amsterdam

This European Postgraduate Gastro-Surgical School congress will take place on 31 May and 1 June 2001 in Amsterdam, the Netherlands. Further information: Mrs Helma Stockmann/ Mrs Joyce Goedkoop, European Postgraduate Gastro-Surgical School, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands. Tel: +31 20 566 3926; fax: +31 20 566 5659; email: WJ.Stockmann@amc.uva.nl; website: www.epgs.nl.

33rd European Pancreatic Club

The meeting will take place on 13–16 June 2001 in Toulouse, France. A training course will be organised on 13 June on “Genomics and post genomics: developments in biomedical sciences”. Further information: Dr Nicole Vaysse, Inserm U531, CHU Rangueil, 31403 Toulouse, France. Tel: +33 (0)5 61 32 24 02; fax: +33 (0)5 61 32 24 03; email: nicole.vaysse@ranguel.inserm.fr; website: www.epg-congres.org.

Gastroenterology and Endotherapy: XIXth European Workshop

This course, to introduce the experienced gastroenterologist to the growing field of therapeutic endoscopy, will be held on 18–20 June 2001 in Brussels, Belgium. Further information: Mrs Nancy Beaufreux, Gastroenterology Department, Erasme Hospital, Route de Lennik 808, B-1070 Brussels. Tel: +32 02 555 49 00; fax: +32 02 555 49 01; email: beaufreux@ulb.ac.be

CORRECTION