LETTERS TO THE EDITOR

Small bowel haemorrhage due to cytomegalovirus vasculitis

Sir,—We read with interest the report by Sackier et al (Gut 1991; 32: 1419–20) where the authors postulate a pathogenic role for cytomegalovirus in the small bowel of a patient on immunosuppressive therapy. Cytomegalovirus has been described associated with bleeding and ulceration of the upper and lower gastrointestinal tract in renal transplant patients, although there has been no conclusive evidence that the virus is a pathogen in the gastrointestinal tract of these patients.1,2

We have recently completed a prospective study of renal transplant recipients, obtaining endoscopic biopsies of the gastroduodenal mucosa for the study of cytomegalovirus. Immunohistochemical analysis of the specimens (mouse anti cytomegalovirus monoclonal antibody, Dako Ltd, High Wycombe, Bucks) revealed evidence of virus in 16 of 33 patients (48%). The virus was detected in the duodenum in 13 patients and in the gastric mucosa of six patients, three patients having both sites involved, and was found to involve surface epithelium and vascular endothelium. The presence of cytomegalovirus was significantly associated with histological duodeni (p < 0.001, Fisher's exact test) and was not associated with histological gastritis or with peptic ulceration. There was no significant relationship between cytomegalovirus infection and upper gastrointestinal symptoms. A prospective study by Alexander et al in liver transplant recipients reported a similar prevalence to our own and an association with duodenitis but not with dyspeptic symptoms.3

We feel that it is difficult to be certain that cytomegalovirus is a pathogen, and the histological changes witnessed by Sackier and other authors may merely be a casual association, reflecting the high prevalence of the virus in immunosuppressed patients.4 The vasculitis witnessed in their patient may have been because of the underlying disease process, as gastrointestinal involvement in Wegener's granulomatosis, while not common, certainly can occur.5

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Reply

Sir,—It has been suggested by Teenan and Murray that the vasculitis witnessed in our patient may have been caused by the underlying disease process—that is, Wegener's granulomatosis, and that the presence of cytomegalovirus may have been a casual association, reflecting the high prevalence of the virus in immunosuppressed patients. The histological changes in the gut in our patient, however, were not compatible with Wegener's granulomatosis.

There have been numerous reports of cytomegalovirus causing bleeding and ulceration in the gastrointestinal tract.1,3 A recent report by Teixidor et al described 11 patients with AIDS and cytomegalovirus infection and/or enteritis.6 Seven of the 11 patients had significant lower gastrointestinal tract bleeding, five of whom died as a result of it. Mucosal ulceration was present in the involved intestine and occasionally resulted in full thickness perforation of the bowel wall. The length of involved intestine is variable. Isolated cytomegalovirus colitis is more likely to involve the entire colon, whereas small bowel involvement tends to affect shorter segments.7,8 It may have involved the entire gastrointestinal tract. Schwartz et al9 reported an infant with AIDS and cytomegalovirus infection which presented with massive life threatening lower intestinal haemorrhage. Arteriography was useful in localising a bleeding source before operation. The cytomegalovirus infection produced necrotising enterocolitis with deep ulcerations. Vasculitis was a prominent feature and has also been suggested as the basis for perforation.9

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7 Levine J, Sackier B, Miller HA, et al. Adenocarcinoma and Barrett's oesophagus

Sir,—I read with much interest the article by Miro et al regarding the sequential dysplastic changes in Barrett's oesophagus (Gut 1991; 32: 1441–6). I found the article helpful to improve the understanding of the pathogenesis of Barrett's adenocarcinoma. The authors, however, demonstrated that if dysplasia is not detected in Barrett's mucoa those individuals should be 'endoscopically screened' less often. This latter point requires a word of caution and needs to be confirmed against the potential risks of implementing such a policy.

First, the sampling error from a handful of mucosal biopsies, in a multifocal disease such as Barrett's mucoa, will be large and therefore biopsy (six or more) and adjunct uses of brush cytology should be recommended.1

Second, as stated in the article, the period of conversion from one type of metaplasia or dysplasia to a more premalignant variety is not yet fully established and therefore any time scale for subsequent repeat-endoscopy is at best empirical.

Third, individuals with Barrett's mucoa may be more likely to develop in Barrett's carcinoma in immediately juxtaposed tissues—oesophageal squamous carcinoma—and possibly also gastric cardiac adenocarcinoma. Therefore, regardless of the presence or absence of dysplasia in the Barrett's mucoa, screening for premalignant lesions in these other areas should also be performed.

Fourth, by conventional screening techniques the three individuals found to have early adenocarcinoma in the present study either died postoperatively or were unsuitable for surgery. Therefore, the screening programme failed to make a desired impact on the incidence of oesophageal adenocarcinoma. This is partly because the markers of premalignant potential do not reflect any of the functional processes responsible for mitogenesis or oncogenesis. It should perhaps be emphasised therefore that the contemporary logic regarding who, how, and with what techniques to screen are highly unsatisfactory at present. In this regard we have shown that the expression of transforming growth factor alpha and epidermal growth factor receptors are significantly raised in dysplastic and malignant mucosa.1 In addition, we have also shown that flow cytometric analysis of the expression of transforming growth factor alpha and epidermal growth factor receptors can be a useful adjunct in the diagnosis and assessment of the prognosis of Barrett's mucoa.10

Finally, before clinicians exclude potentially well motivated patients from a screening programme perhaps we should first exclude those who have proven poor compliance at clinic visits and/or those who are more likely to develop complications from a diagnosis of Barrett's disease or subsequent surgery (those with respiratory diseases or ischaemic heart disease, etc).

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Omeprazole versus ranitidine in the treatment of resistant duodenal ulcer

Sir,—Bardhan et al have clearly demonstrated the effect of omeprazole in the therapy of refractory peptic ulcer (Gut 1991; 32: 435–8). It is well known that about 5–10% of peptic ulcers do not heal when treated with 
H2 antagonists and are considered to be refractory. The optimal management of these patients is not yet established. Published data are contradictory about the efficacy of omeprazole therapy in patients with peptic ulcer that are resistant to the 
H2 receptor antagonist treatment.

It is important, therefore, to take into consideration all experiences which could help us to find the best treatment. We have conducted a controlled randomised study to assess the effect of omeprazole 40 mg daily compared with ranitidine continued at the same dose in patients with duodenal ulcers that were refractory to the previous ranitidine treatment. Forty five outpatients were treated during this study. Patients were randomised to either a duodenal ulcer of at least 5 mm diameter which did not heal after six weeks’ treatment with 300 mg ranitidine were admitted to the trial. Endoscopy, performed at the beginning of the trial, showed active duodenal ulcer in all cases. Patients were randomly allocated to two groups—23 ranitidine therapy was continued in the same dose (150 mg twice a day) and in 22 omeprazole 40 mg was given at bedtime. All patients received antacid relief. No other anti-ulcer treatment was allowed.

The two groups were not significantly different as to age, duration of ulcer disease, smoking habits and alcohol consumption. Control endoscopy was performed after 4 weeks’ treatment. Omeprazole was significantly better than continued ranitidine therapy in healing rates of duodenal ulcers at the four week control endoscopy (healing rates: omeprazole group 19 (86%) patients; ranitidine 11 (50%) patients; \( \chi^2 \) test: 7.811; p<0.01). Omeprazole also gave better symptom relief than ranitidine. No side effects were reported and all patients completed the study.

Patients with unhealed ulcers received omeprazole (40 mg at bedtime) for a further four weeks. At the end of this period endoscopy was repeated and showed healed ulcer in all through the omeprazole group and in nine of 12 patients from the ranitidine group.

Our results indicate that omeprazole is more effective in patients with duodenal ulcer that fail to heal with ranitidine treatment. Our findings contrast with those of Bardhan et al although in our study the previously unsuccessful H2-receptor antagonist therapy was conducted with the same drug, and at the same dose in all cases and only patients with duodenal ulcer were included to the study.

Our results, obtained from strictly defined subset of patients with duodenal ulcer, confirm that omeprazole has a significant beneficial effect in the management of resistant duodenal ulcers.