

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 recipients, although there has been no conclusive evidence that the virus is a pathogen in the gastrointestinal tract of these patients.^{1–3}

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 duodenitis ($p=0.001$, 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.⁴

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.⁵ 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.⁶

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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*⁴ described 11 patients with AIDS and cytomegalovirus colitis and/or enteritis. 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. Occasional cases, however, have involved the entire gastrointestinal tract. Schwartz *et al*⁵ 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.

The mechanisms by which cytomegalovirus produces tissue damage are not known. Vasculitis has been reported in some cases and suggested as the basis for necrosis and ulceration.^{2,6–8} Muscle cell destruction has also been suggested as the basis for perforation.⁹

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Adenocarcinoma and Barrett's oesophagus

SIR,—I read with much interest the article by Miros *et al* regarding the sequential dysplastic changes in Barrett's oesophagus (*Gut* 1991; 32: 1441–6). I found the article helped to improve the understanding of the pathogenesis of Barrett's adenocarcinoma. The authors, however, implied that if dysplasia is not detected in Barrett's mucosa those individuals should be 'endoscopically screened' less often. This latter point requires a word of caution and needs to be weighed 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 mucosa, will be large and therefore more biopsies (six or more) and adjunctive use 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 re-endoscopy is at best empirical.

Third, individuals with Barrett's mucosa may also be more likely to develop carcinomas in immediately juxtaposed tissues — oesophageal squamous carcinoma² and possibly also gastric cardiac adenocarcinoma.³ Therefore, regardless of the presence or absence of dysplasia in the Barrett's mucosa, 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.⁴ 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 mucosa.⁵

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 the endoscopy or subsequent surgery (those with respiratory diseases or ischaemic heart disease, *et al*).

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