Nonspecific small bowel ulceration

W.E.G. Thomas and R.C.N. Williamson

University Department of Surgery, Bristol Royal Infirmary, Bristol BS2 8HW, UK.

Summary: Six patients (4 male, 2 female) developed nonspecific small bowel ulceration between the ages of 4 months and 76 y. Five had gastrointestinal haemorrhage, usually chronic and resulting in iron deficiency anaemia. Four had features of subacute intestinal obstruction; there were no perforations. A small bowel enema was the most useful single investigation for delineating the lesions, and surgical excision was curative in all but one case. No aetiological causes could be implicated, other than in one patient taking a daily tablet of Navidrex-K.

Introduction

Since nonspecific ulceration of the small bowel is rare (Boydston *et al.*, 1981), the diagnosis is commonly overlooked and seldom established before operation (Strodel *et al.*, 1981). First described by Baillie in 1795, 'simple' ulcers of the small bowel were reviewed by Combes in 1897. The lesion was defined by Grasman (1925) as 'sharp-bordered, solitary ulceration with no surrounding inflammation, of unknown cause, indefinite pathogenesis, and an acute or chronic course'. Sporadic case reports have not added a great deal to our understanding of these curious ulcers (Boydston *et al.*, 1981; Watson, 1963; Morgenstern *et al.*, 1965; Alexander & Schwartz, 1966; Billig & Jordan, 1965; Brown & Pemberton, 1936; Evert *et al.*, 1948; Morlock *et al.*, 1956), although enteric-coated potassium tablets have now been identified as one specific cause in certain cases (Morgenstern *et al.*, 1965; Campbell & Knapp, 1966; Dayer *et al.*, 1977).

To draw attention to a potential cause of protracted morbidity, we report 6 patients with nonspecific enteric ulceration. Five were eventually cured by resection but one represents a continuing problem.

Patients and results

Age and sex

During the last 5 y 6 patients with nonspecific ulceration of the small intestine have been treated or remain under treatment in Bristol. There were 4 males and 2

females. The age of onset of symptoms ranged from 4 months to 76 y.

Presentation

Five of the 6 patients presented with evidence of gastrointestinal bleeding (Table I). Haemorrhage was occult in 3 cases, resulting in persistent iron-deficiency anaemia. Two patients had melaena, and in one of these a subsequent and profuse haematochezia led to emergency operation. Four patients complained of mild obstructive symptoms, with intermittent crampy abdominal pain and occasional distension. Only one patient vomited, but another 2 had noticed some degree of weight loss.

Apart from one patient (no.4) who had been receiving 1 Navidrex-K tablet*/d for 3 y, none of these patients had taken enteric-coated potassium. Oral iron was the only other therapy received by any patient. There were no abnormal physical findings apart from anaemia. The only associated clinical conditions were an old healed duodenal ulcer (patient 2) and a successfully resected coarctation of the aorta (patient 3).

Investigation

In 2 patients with solitary ileal ulcer emergency presentation led to a fairly rapid diagnosis. Patient 5 had a brisk bleed per rectum, and angiography identified a bleeding site. Patient 4 had clinical and

Correspondence: Professor R.C.N. Williamson, M.A., M.D., M.Chir., F.R.C.S.
Accepted: 7 February 1985

*Navidrex-K tablets (Ciba) have an outer coat of sugar containing 0.25 mg cyclopentiazide and an inner slow-release wax core containing potassium chloride 600 mg (8.06 mEq).

Table I Symptoms, investigations and treatment of patients with nonspecific enteric ulceration

Patient no.	Age (y)	Length of history (y)	Presenting symptoms		Biliary X-rays	Radiology				Endoscopy			Laparotomy findings	Resection	Follow-up
			Obstructive	Bleeding		Ba meal	Ba FT	SB enema	Ba enema	Angiography	^{99m} Tc scan	Upper GI	Lower GI		
1	25	M	5		+	+	+	+	+	+	+	+	+	Local enterectomy	Well at 11 y
2	44	M	10		+	+	+	+	+	+	+	+	+	Local enterectomy	Well at 3 y
3	20	M	2		+	+	+	+	+	+	+	+	+	Local enterectomy	Well at 3 y
4	66	M	(1 wk)		+	+	+	+	+	+	+	+	+	Local enterectomy	Well at 1 y
5	76	F	0.5		+	+	+	+	+	+	+	+	+	Right hemicolectomy	Well at 4 y
6	33	F	33		+	+	+	+	+	+	+	+	+	Right hemicolectomy 2 enterectomies	Still needs regular transfusion

GI: gastrointestinal; FT: follow through; SB: small bowel.

Figure 1 Small bowel enema (patient 2): two frames delineate a jejunal stricture (arrowed).

radiological evidence of subacute small bowel obstruction, and a small-bowel enema localized a stricture adjacent to the site of ileal ulceration. In the other cases diagnosis was elusive, and investigation was much more protracted (Table I). Repeated barium studies, colonoscopy and gastroduodenoscopy were undertaken.

Small bowel enema and selective visceral angiography were the most productive examinations. In 4 patients a small bowel enema correctly identified a stricture in the ileum (Figure 1), in one case (patient 6) on more than one occasion. Superior mesenteric arteriography demonstrated a bleeding point in the region of the ileocolic vessels in 2 patients (5 and 6), but was negative in another 2 patients. A string test proved valuable in roughly localizing the site of haemorrhage to the ileum in one patient (no. 3). An intravenous injection of fluorescein was given after oral passage of a length of string. The string was then retrieved, and the position of the fluorescence was observed.

Treatment

In each patient local resection of the affected segment of small bowel was undertaken with end-to-end anastomosis. In 2 patients with disease in the terminal ileum, resection included the caecum and ascending

colon. Excision of the ulcer-bearing segment appears to have been curative in all but one case. In the exception (patient 6) the history has been extraordinary. Intermittent melaena from infancy led to right hemicolectomy at the age of 9 y. In adult life this patient required two further resections of small bowel. Renewed ulceration causing anaemia was then treated by Argon laser photocoagulation with no effect. Repeated attempts to control the bleeding with cimetidine, carbenoxolone, De-Nol and zinc sulphate have been equally unsuccessful. The patient currently requires blood transfusion every second month to maintain a normal haemoglobin level.

Pathology

In all but 2 cases the ulcers were multiple (Figure 2). They were usually linear and circumferential (Figure 3), leading to stenosis of the bowel lumen and thus explaining the obstructive symptoms. Histologically the ulcers were characterized by a circumscribed zone of granulation tissue, which was associated with local hyperplasia of the muscularis mucosae and patchy pyloric metaplasia in the mucosa close to the ulcers (Figure 4). Low-grade chronic inflammation of the submucosa and deeper layers of the bowel was present, but granulomas, oedema and lymphiectasia (as seen in Crohn's disease) were lacking. Some ulcers had re-epithelialized, but retained the focal muscular hyperplasia beneath them. Vascular changes were all attributable to secondary effects of the ulcers.

Discussion

Nonspecific small bowel ulceration is certainly very uncommon, though its precise incidence is difficult to

Figure 2 Multiple nonspecific ileal ulcers (patient 3). Arrows point to the areas of ulceration, which have produced a central pseudo-diverticulum.

Figure 3 Healing of a typical nonspecific ileal ulcer (patient 2) has produced a linear, circumferential scar.

quantify. The condition itself may not be a distinct entity but merely embrace residual 'idiopathic' cases of enteric ulceration after other definitive aetiological types have been excluded. Thus a recent report describes two fatal cases of (multiple) simple ulceration in patients with severe heart disease, in whom intestinal ischaemia was thought to be involved (Glynn *et al.*, 1984), whereas our patients were generally younger and had a less acute presentation.

In any case of small bowel ulceration it is important to look for evidence of infection, including tuberculosis, histoplasmosis, aspergillosis, typhoid, syphilis and cytomegalovirus. Vascular, traumatic, nutritional and hormonal causes should also be excluded. Crohn's disease and lymphoma have characteristic histological patterns, but malignant histocytosis (Isaacson &

Figure 4 Nonspecific ulcer of the small bowel. Central granulation tissue overlies extensive proliferation of the muscularis mucosae (long arrow). There is a focus of pyloric metaplasia (short arrow) beside the ulcer. H. & E. $\times 30$.

Wright, 1978) can cause rather nonspecific appearances. When enteric ulceration is associated with malabsorption, it is important to exclude coeliac disease as well as lymphoma (Isaacson & Wright, 1978; Baer *et al.*, 1980; Robertson *et al.*, 1983). No patient in this series presented with malabsorption.

The cause of nonspecific ulcer remains unknown. During the 1960s enteric-coated potassium was implicated (Morgenstern *et al.*, 1965; Campbell & Knapp, 1966), and its administration was shown to reproduce such lesions in the dog (Boley *et al.*, 1965). However, in a review of 395 patients from around the world, less than half were taking enteric-coated potassium (Lawrason *et al.*, 1965), and in a recent review from the Mayo Clinic only 10% were receiving such medication (Boydston *et al.*, 1981). In the present series, none of the patients had received enteric-coated potassium at any time, apart from the one man taking Navidrex-K.

There appears to be a changing pattern in the clinical presentation of nonspecific ulcers. The earlier reports described a high incidence of perforation (Watson, 1963; Evert *et al.*, 1948), whereas more recent studies record a high incidence of intestinal obstruction (Boydston *et al.*, 1981). In the present series perforation did not occur, and obstruction (in 4 of 6) was never complete. The commonest presenting feature was gastrointestinal haemorrhage, either acute or chronic, but resulting in anaemia. Anaemia was a rare feature in the early reports of this condition (Morgenstern *et al.*, 1965; Billig & Jordan, 1965; Morlock *et al.*, 1956; Lawrason *et al.*, 1965). Later studies suggest that patients with bleeding tend to be younger than those with obstruction (Boydston *et al.*, 1981; Grosfeld *et al.*, 1970).

References

- ALEXANDER, H.C. & SCHWARTZ, G.F. (1966). Non-specific jejunal ulceration: in search of an aetiology. *Gastroenterology*, **50**, 224.
- BAER, A.M., BAYLESS, T.M. & YARDLEY, J.H. (1980). Intestinal ulceration and malabsorption syndromes. *Gastroenterology*, **79**, 754.
- BAILLIE, M. (1795). *The morbid anatomy of some of the most important parts of the human body*. 1st American Ed. Albany, Barber and Southwick, 1795. Cited by Guest, J.L. Jr (1963).
- BILLIG, D.M. & JORDAN, G.L. (1965). Non-specific ulcers of the small intestine. *American Journal of Surgery*, **110**, 745.
- BOLEY, S.J., SCHULTZ, L., KRIEGER, H., SCHWARTZ, S., ELGUEZABAL, A. & ALLEN, A.C. (1965). Experimental evaluation of thiazides and potassium as a cause of small bowel ulcer. *Journal of the American Medical Association*, **192**, 763.
- BOYDSTUN, J.S. JR, GAFFEY, T.A. & BARTHOLOMEW, L.G. (1981). Clinicopathologic study of non-specific ulcers of the small intestine. *Digestive Diseases and Sciences*, **26**, 911.
- BROWN, P.W. & PEMBERTON, J. DE J. (1936). Solitary ulcer of the ileum and ulcer of Meckel's diverticulum. *Annals of Internal Medicine*, **9**, 1684.
- CAMPBELL, J.R. & KNAPP, R.W. (1966). Small bowel ulceration associated with thiazide and potassium therapy: review of 13 cases. *Annals of Surgery*, **163**, 291.
- COMBES, C. (1897). *Des ulcères simples de l'intestin*. Thèse de doct., Faculté de Médecine et de Pharmacie de Toulouse, 1897. Cited by Grasman, M. (1925).
- DAYER, P., CECHE, P. & COURVOISIER, B. (1977). Chlorure de potassium et ulcères non spécifiques de l'intestin grêle. *Schweizerische Medizinische Wochenschrift*, **107**, 379.
- EVERT, J.A., BLACK, B.M. & DOCKERTY, M.B. (1948). Primary non-specific ulcers of the small intestine. *Surgery*, **23**, 185.
- GLYNN, M.J., PENDOWER, J., SHOUSA, S. & PARKINS, R.A. (1984). Recurrent bleeding from idiopathic ulceration of

It is a measure of our ignorance of this disease that 3 patients suffered from occult bleeding and anaemia for 5 or more years before operation and were submitted to a battery of investigations. The most helpful tests were small bowel enema and arteriography, while a simple follow-through technique failed to delineate any of these lesions. Delayed diagnosis and operative correction are the rule for nonspecific enteric ulcer (Boydston *et al.*, 1981; Strodel *et al.*, 1981).

Ulceration was ileal in 4 patients and jejunal in 2. This distribution is in accord with other reviews (Boydston *et al.*, 1981; Evert *et al.*, 1948). Jejunal ulcers are said to have a higher incidence of perforation (Boydston *et al.*, 1981).

Treatment in every case was by local resection and primary anastomosis. Simple closure of a perforated ulcer has been advocated (Evert *et al.*, 1948), but recurrent bleeding and stricture would seem likely sequelae (Guest, 1963). Complete spontaneous healing seldom occurs (Evert *et al.*, 1948). Fortunately the disease appears to be self-limiting, as resection is generally curative. This is clearly not the case in our one patient with ongoing ulceration of undetermined cause, but it does hold true for the other 5 at a follow-up of 1–11 y.

Acknowledgements

We thank Mr L.R. Celestin, F.R.C.S., Mr H.J. Espiner, Ch.M., F.R.C.S., Mr W.K. Eltringham, Ch.M. F.R.C.S., and Dr R.F. Harvey, M.D., F.R.C.P. for permission to publish details of their cases. The histological appearances of enteric ulceration were kindly reviewed by Dr J.D. Davies, M.D., F.R.C.Path., Consultant Histopathologist at the Bristol Royal Infirmary.

- small bowel. *British Medical Journal*, **288**, 975.
- GRASMAN, M. (1925). Zur Frage des Ulcus Simplex des Dunndarmes. *Archiv für Klinische Chirurgie*, **136**, 449.
- GROSFELD, J.L., SCHILLER, M., WEINBERGER, M. & CLATWORTHY, H.W. (1970). Primary non-specific ileal ulcers in children. *American Journal of Diseases of Children*, **120**, 447.
- GUEST, J.L. JR. (1963). Nonspecific ulceration of the intestine. *International Abstracts of Surgery*, **117**, 409.
- ISAACSON, P. & WRIGHT, D.H. (1978). Malignant histiocytosis of the intestine: its relationship to malabsorption and ulcerative jejunitis. *Human Pathology*, **9**, 661.
- LAWRASON, F.D., ALPERT, E., MOHT, F.L., McMAHON, F.G. (1965). Ulcerative obstructive lesions of the small intestine. *Journal of the American Medical Association*, **191**, 641.
- MORGENSTERN, L., FREILICH, M. & PANISH, J.F. (1965). The circumferential small bowel ulcer: clinical aspects in 17 patients. *Journal of the American Medical Association*, **191**, 637.
- MORLOCK, C.G., GOEHRS, H.R. & DOCKERTY, M.B. (1956). Primary non-specific ulcers of the small intestine: clinicopathologic study of 18 cases with follow-up of 14 previously reported cases. *Gastroenterology*, **31**, 667.
- ROBERTSON, D.A.F., DIXON, M.F., SCOTT, B.B., SIMPSON, F.G. & LOSOWSKY, M.S. (1983). Small intestinal ulceration: diagnostic difficulties in relation to coeliac disease. *Gut*, **24**, 565.
- STRODEL, W.E., ECKHAUSER, F.E. & SIMMONS, J.L. (1981). Primary ulceration of the ileum. *Diseases of the Colon and Rectum*, **24**, 183.
- WATSON, M.R. (1963). Primary nonspecific ulceration of the small intestine. *Archives of Surgery*, **87**, 600.