

Clinical Topics

Diagnosis and management of obscure gastrointestinal bleeding

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British Medical Journal, 1978, 2, 751-754

Summary and conclusions

Twelve consecutive patients presenting with unexplained recurrent gastrointestinal bleeding were investigated by selective visceral angiography. A cause for the bleeding was shown in all 12 cases, and in eight the lesion responsible was diagnosed radiologically as an area of angiodysplasia. Abnormal areas were pinpointed by fluoroscopy and examination of the resected bowel with a dissecting microscope after injecting the vessels with barium. Histologically these areas had various microvascular abnormalities.

Angiodysplasia is a useful descriptive radiological term, but does not seem to represent a single pathological entity.

Introduction

Acute or chronic occult gastrointestinal bleeding still presents difficult problems of investigation and management. Standard investigations entail excluding systemic or haematological disorders, inquiring about drug ingestion, a search for parasites, barium studies, and full endoscopic examination.¹⁻³ If the results of these studies prove negative the patient probably has one or more small vascular abnormalities somewhere in the gastrointestinal tract. These may be manifestations of rare systemic disorders such as hereditary haemorrhagic telangiectasia or polyarteritis nodosa. More often, especially in the elderly, they are microvascular anomalies limited to the intestinal tract and found most frequently in the right side of the colon. The term angiodysplasia has been applied to such lesions,⁴ but their pathology has been incompletely studied and their pathogenesis remains unknown. Rupture of these tiny malformations is probably the commonest cause of major bleeding from the lower gastrointestinal tract in the elderly,⁵ and resection of the affected portion of bowel usually cures the bleeding.

Small vascular lesions in the intestine can only rarely be localised by traditional methods of investigation.³ Intubation of

the bowel, the use of radiochromium-labelled red cells, and string tests are cumbersome and inefficient, and inspecting the bowel at laparotomy is usually unrewarding. New endoscopic techniques may occasionally show a vascular malformation,⁶ but in studying 12 patients over the past two years we have found angiography as introduced by Baum *et al*⁷ to be the most effective diagnostic method.⁸ Furthermore, using the specialised techniques described below we have studied the histology of vascular lesions of the intestine in detail.

Patients and methods

We studied 12 consecutive patients (five men, seven women) referred to the gastrointestinal unit, Hammersmith Hospital, for investigation of gastrointestinal bleeding from an unknown site (table). Eight had undergone repeated investigations over periods ranging from three months to 20 years. The other four presented with acute life-threatening gastrointestinal haemorrhage from an unidentified site.

RADIOLOGY

Angiography was undertaken under local analgesia with standard techniques. In most patients we performed selective angiograms of all three principal visceral vessels, filming sequences continuing up to 20 seconds after the contrast injection. If the radiological interpretation was in doubt arteriography was repeated after intravenous hyoscine (Buscopan) to arrest peristaltic activity. In three cases a catheter was left in the superior mesenteric artery to permit further angiography in the operating theatre. Segments of intestine removed at operation were gently irrigated with saline, then inflated with air. The vessels were injected with a barium-gelatin mixture under fluoroscopic control, the site of any vascular lesion was marked, and the bowel was fixed in 10% formalin solution.

PATHOLOGY

After fixation for 24 hours the bowel was opened and the mucosa examined. Macroscopic lesions were noted and samples taken for histological examination. Any sites of contrast leakage were inspected for underlying lesions. The mucosa was then studied with a dissecting microscope and any minute vascular abnormalities were photographed and samples taken for histological and electron-microscopical examination. Such lesions were easily visualised when filled with the white contrast medium (fig 1). Tissues were studied by routine histological methods including special stains for elastin and collagen.

Results

RADIOLOGY

In all 12 patients the actual or presumed site of bleeding was localised radiologically (table). In four patients (cases 8, 9, 10, 11) active bleeding was shown during the study by contrast medium

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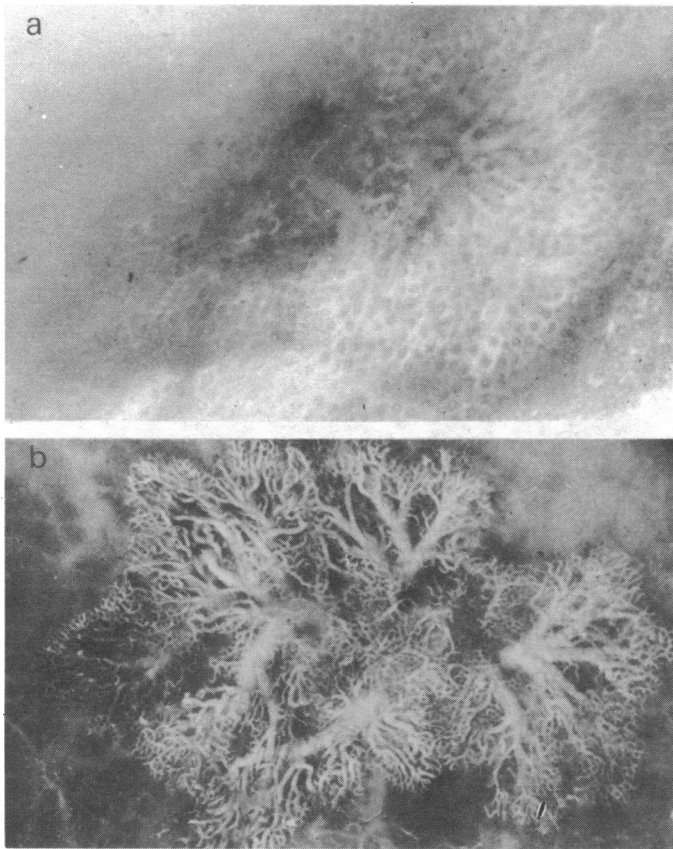


FIG 1—Case 2. Dissecting microscope view of barium-injected vessels in bowel mucosa showing normal bowel (a) and mucosal telangiectasis (b).

leaking into the lumen of the bowel. In the remaining patients tiny vascular abnormalities were apparent. These consisted of one or more of the following features: (1) An unusually conspicuous early-filling tuft of small arteries (fig 2); (2) persistent local vascular filling showing as tiny "lakes" of contrast medium that remained opacified until late into the venous phase (figs 3(a), 4(a)); and (3) a prominent draining vein that often opacified earlier than other veins (figs 3(b), 4(b)). The most constant and easily detectable of these signs was (3), which in our experience seems to be the angiographic "hallmark" of a small vascular abnormality in the gastrointestinal tract.

MANAGEMENT

Intestinal resection was performed in 11 subjects; the patient with a rectal lesion was treated with cryosurgery. Two patients died with leaks from their intestinal anastomoses: one (case 3) had severe atheroma and the other (case 8) polyarteritis nodosa. Of the 10

survivors, three had further episodes of bleeding: in one (case 1) the resection was incomplete, and after a second intestinal resection there was no further bleeding. In another patient (case 5) an episode of haematemesis occurred one year later, and at operation a single, punctate bleeding point in the stomach was oversewn. There was no evidence of ulceration and no tissue was taken for histological examination, but the vascular lesion responsible may have been similar to the six areas of angiodysplasia found previously in his resected caecum. In the third (case 10) recurrent rectal bleeding was again treated by cryoprobe. A fourth patient (case 2) was found to be anaemic one year after operation (haemoglobin 9.2 g/dl), but he responded to treatment with oral iron and there was no definite evidence of further gastrointestinal bleeding.

PATHOLOGY

Vascular lesions were identified in all 11 specimens studied. In four the abnormality was part of a systemic disorder: two patients had polyarteritis nodosa, one a tiny gastrointestinal lymphoma, and one ulceration of the mucosa associated with uraemia. As these are well-recognised causes of gastrointestinal bleeding we do not discuss their pathological features further. The remaining seven patients had local microvascular anomalies in the bowel wall. In three cases there

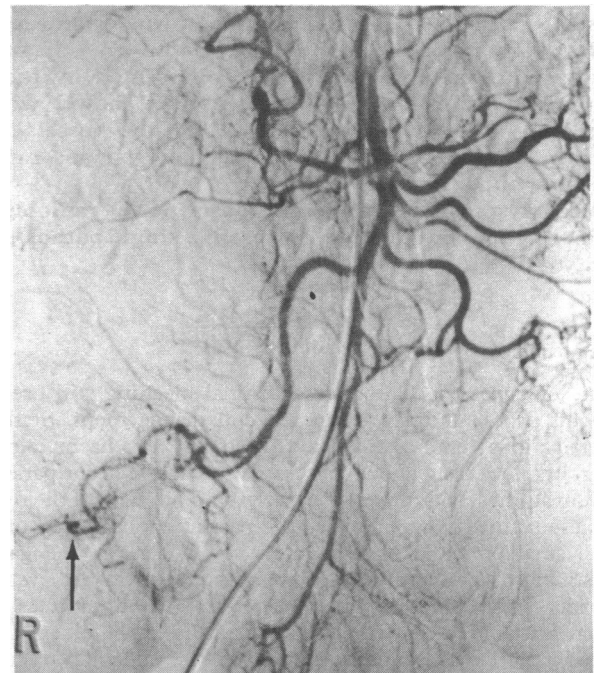


FIG 2—Case 2. Superior mesenteric arteriogram. Arterial phase shows early filling, tortuous arteries indicating area of angiodysplasia in caecum (arrowed).

TABLE 1—Clinical details of 12 patients with obscure gastrointestinal bleeding

Case No	Age	Sex	Length of history (years)	Previous treatment	Associated disorders	Site of bleeding	Final diagnosis
1	68	F	4	Two laparotomies; 10 transfusions	Duodenal and jejunal diverticulosis	Jejunum	Angiodysplasia
2	61	M	9	One transfusion; parenteral iron	Gall stones	Caecum	Angiodysplasia
3	63	M	3/12	Transfusion	Aortic graft	Caecum	Angiodysplasia
4	54	F	≥20	Transfusion; iron	Skin nodules (venous malformation)	Caecum	Angiodysplasia
5	72	M	6	Two transfusions; parenteral iron	Gastritis	Caecum	Angiodysplasia
6	20	F	3/12	Transfusion; laparotomy	Pelvic surgery	Rectum	Possible arteriovenous malformation (radiology only)
7	40	M	12	Two laparotomies; possibly transfusions	None	Caecum	Arteriovenous malformation
8*	49	M	2/12	Massive transfusion; laparotomy	Thrombotic thrombocytopenic purpura	Jejunum	Microvascular occlusion
9*	45	F			Polyarteritis nodosa	Ileum	Polyarteritis
10*	53	F	2/12	Transfusion	Resistant coeliac disease	Ileum	Lymphoma
11*	47	F			Uraemia	Left colon	Uraemic ulcer
12	63	F	15	Transfusions	None	Caecum	Angiodysplasia

*Presented with acute gastrointestinal haemorrhage.

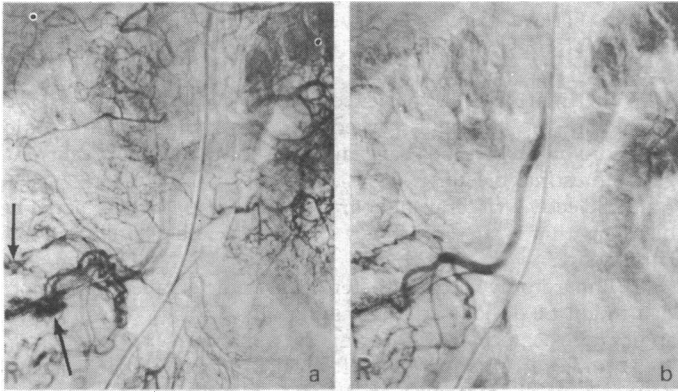


FIG 3—Case 2. Superior mesenteric arteriogram. Capillary phase (a) shows abnormal vascular lakes (arrowed). In the venous phase (b) an early filling prominent vein is shown draining the abnormal area.

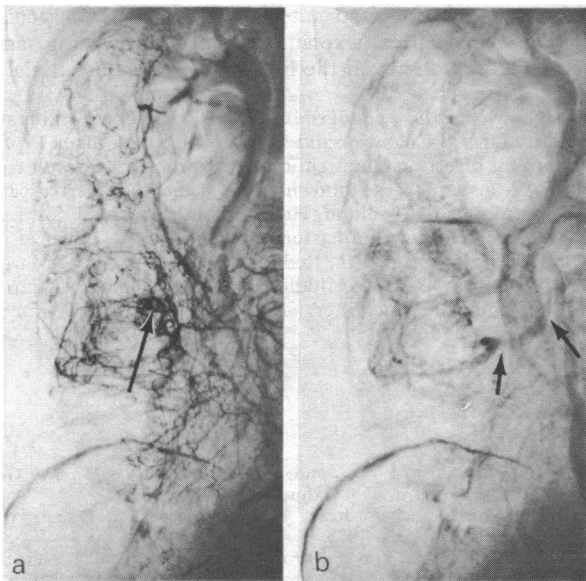


FIG 4—Case 7. Super-selective ileocolic arteriogram. Late arterial phase (a) shows tortuous vessels and abnormal vascular lakes in the caecum (arrowed). Later film (b) shows abnormally conspicuous draining vein (arrowed).

were capillary abnormalities producing multiple spider-like telangiectases in the superficial mucosa, which in places were denuded of epithelium (figs 1, 5(a)). In two further cases the abnormality was probably venous, with dilated thin-walled veins in the superficial submucosa. The remaining two cases showed abnormalities in both small arteries and veins, which may be classified as arteriovenous malformations.

In some patients the vascular abnormalities were surrounded by moderate fibrosis that might have been caused by recurrent ulceration and healing, and in none was there any evidence of appreciable inflammation. All the lesions we found corresponded to the sites of angiographic abnormalities.

Case histories

Case 4

A woman aged 54 had been intermittently anaemic for 40 years. She underwent repeated investigations for gastrointestinal bleeding and was referred to Hammersmith Hospital in 1976. Physically she was normal apart from a few small nodules on both palms, and biopsy of one of these showed an arteriovenous malformation. Visceral angiography showed a single tiny vascular malformation in the caecum with a prominent draining vein. The intestine was macroscopically normal at laparotomy; a right hemicolectomy was performed, and she was in good health a year later (haemoglobin 13.4 g/dl). A minute vascular anomaly was found in the superficial submucosa of the caecum and shown to consist of a collection of

partially occluded veins. The lumina of these veins were reduced by regular circumferential distribution of dense collagen in the media (fig 5(b)). The cause of the venous sclerosis was uncertain but might have been due to the organisation of luminal thrombi. There was also moderate fibrosis in the surrounding submucosa, which, together with the vascular mural fibrosis, would have impaired vascular contractility, thereby contributing to continued bleeding after damage. Venous angiodysplasia was diagnosed. This case illustrates how serious, recurrent bleeding may originate from a single, minute vascular malformation.

Case 5

A man aged 66 had a 10-year history of anaemia treated with iron. He was referred to Hammersmith Hospital in February 1976 with history of increasing dyspnoea, angina, and lassitude. Investigations elsewhere had shown

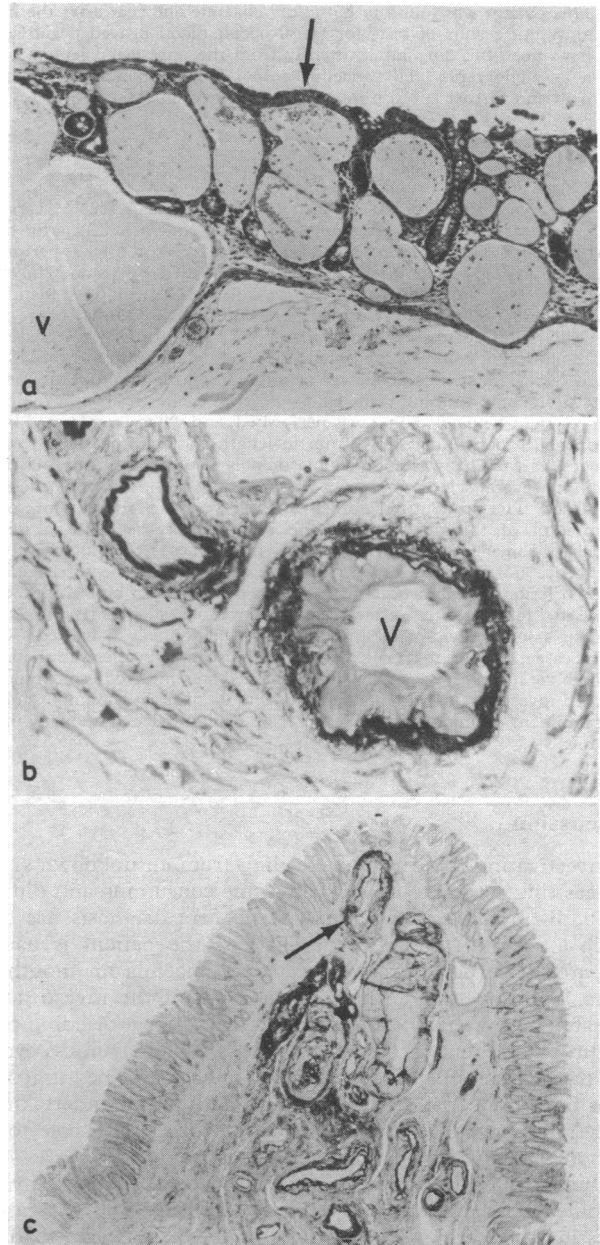


FIG 5—Case 2. Histological section (a) showing mucosal telangiectasis with dilated capillaries and a submucosal vein (v) entering the mucosa. The epithelium over some of the dilated capillaries is very thin (arrowed), suggesting that surface damage might easily lead to bleeding.

Case 4. Histological section (b) showing superficial submucosal vein (v) with collagenous sclerosis of the media and narrowed lumen.

Case 7. Histological section (c) showing small arteriovenous malformation at ileocaecal junction. One arterial vessel (arrowed) enters the mucosa.

occult blood in the faeces, but barium studies had indicated no cause for the gastrointestinal bleeding. Investigations at Hammersmith Hospital showed a haemoglobin concentration of 9.5 g/dl; occult blood was repeatedly found in the faeces; and ^{51}Cr studies showed blood loss of up to 17 mg/day (mean 8 ml/day). Repeat barium studies showed nothing abnormal, but visceral angiography indicated an area of angiodysplasia in the caecum with a large draining vein (figs 2, 3). A similar small jejunal lesion was also present. At laparotomy no macroscopic abnormality was seen, and a right hemicolectomy was performed on the strength of the angiographic findings.

Examination of the resected specimen showed several vascular telangiectatic lesions filled with barium in the mucosal surface of the caecum and ascending colon. Inspection under the dissection microscope showed distended vessels with feathery terminal ramifications (fig 1) surrounded by intramucosal haemorrhage. The presence of mucosal telangiectases was confirmed histologically. The many distended capillaries containing contrast medium communicated with large submucosal veins (fig 5(a)). Electron microscopy confirmed that the vessels were capillaries lined by only a single layer of endothelium. Capillary angiodysplasia was diagnosed.

This case shows the value of a full angiographic study in obscure gastrointestinal bleeding when conventional studies have failed to detect a bleeding site. This patient was found to be mildly anaemic one year after the hemicolectomy but results of tests for faecal occult blood proved negative. He may have been bleeding intermittently from the unresected jejunal lesion shown at angiography. His anaemia responded completely to oral iron treatment and further surgical interference seemed unwarranted.

Case 7

A 47-year-old West Indian had had recurrent melaena for 12 years. He had had repeated hospital admissions in London and in St Lucia for blood transfusion and parenteral treatment for anaemia. Laparotomy was performed twice and on the second occasion was accompanied by colonoscopy and enteroscopy (via a duodenotomy). No vascular lesion could be identified. Visceral angiography was performed. The films of the arterial phase were technically good but the examination stopped before the venous phase and no vascular lesion could be identified. Visceral angiography was repeated at Hammersmith Hospital and showed an angiodysplastic lesion in the caecum with a prominent draining vein (fig 4) and two smaller lesions in the distal ileum. A right hemicolectomy was performed, and when the resected bowel was opened a polypoid lesion 6 mm in length was seen on the lip of the ileocaecal valve. This was not a neoplastic polyp but a mass of fibrous tissue containing several sclerosed arteries and veins (fig 5(c)), some of which had recanalised. The pronounced fibrosis of these vessels probably represented organisation of thrombi. One of the sclerosed arteries with a minute recanalised lumen extended into the superficial mucosa covering the fibrous excrescence and was thought to be the site of the recent haemorrhage. The polypoid lesion on the ileocaecal valve was concluded to be a thrombosed, organised, and partially recanalised arteriovenous malformation. Angiodysplasia associated with arteriovenous malformation was diagnosed.

This case illustrates the inconvenience and discomfort suffered by a patient in whom the site of recurrent bleeding remained unidentified despite repeated standard investigations and angiography, and emphasises the importance of the prominent draining vein as a marker of a small vascular anomaly in the intestine.

Discussion

Investigating the cause of bleeding from an unknown site in the gastrointestinal tract is usually time consuming and difficult for both physician and patient. If no firm diagnosis has been made after the standard investigations the patient is usually prepared to struggle on with recurrent anaemia for months or years. Subsequently he has one or more of the investigations repeated and often laparotomy. The search for a bleeding point by direct examination of the intestine is usually fruitless even if the patient has bled shortly before operation. The surgeon is then faced with the choice of doing nothing or undertaking a resection (normally a partial gastrectomy or a partial colectomy) without having identified the site of the lesion.

During the past 12 years selective visceral angiography has become increasingly important in diagnosing obscure gastrointestinal bleeding.⁷⁻⁹ Since most of the lesions are small the angiograms must be of high quality, and the radiologist must recognise subtle disturbances in the vascular pattern. Since the pathological lesions we found were too small to be seen angiographically the radiological features were probably due principally to local disturbances in blood flow. As the causes of all these lesions showing similar clinical and radiological features are unknown we have referred to them collectively as "angiodysplasia."⁴ Our findings suggest, however, that while this term may be useful clinically and radiologically it should

not be taken to denote a single pathological entity: in the tissues that we examined the underlying pathological lesions affected arteries, capillaries, or veins, or combinations of these vessels.

In the light of our experience during the past two years, we now adopt the following procedure when standard endoscopic and radiological methods have failed to show a cause for recurrent gastrointestinal bleeding.

(1) Selective visceral angiography. If the patient is actively bleeding this is an emergency procedure and is followed by laparotomy.

(2) Laparotomy with a catheter left in the artery feeding a lesion that might be difficult to locate surgically. In such cases further angiography is performed during the operation.

(3) Radio-opaque markers left on the intestine if there is any doubt about the removing of all affected intestine.

(4) Injection of the arteries of the resected intestine with barium-gelatin to help the histologist to locate the lesions. This procedure is most important, since the vascular lesions are invisible in non-injected specimens.

This combined procedure has enabled us to find one or more vascular lesions in the gastrointestinal tract of 12 consecutively studied patients with unexplained recurrent bleeding, and to make new observations on the histology of angiodysplasia.

We acknowledge the work of the clinicians who helped in this study, particularly Dr V S Chadwick and Mr J Spencer, and thank Professor C C Booth for directing our attention to the problem of occult colonic bleeding. We also thank the following physicians who referred patients to the gastrointestinal unit at Hammersmith Hospital for further study: Dr G B Hollings (Kingston upon Thames); Dr E C B Keat (Brighton); Dr J P H Davies (Redhill); Dr J B Cocking (Margate); Dr T D Kellock (Central Middlesex); Dr J H Angel (Watford); Dr J D Whiteside (Chichester); Dr J Rhodes (Cardiff); Dr N F Coghil (West Middlesex).

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(Accepted 28 April 1978)

WORDS It has long been recognised that the immoderate enjoyment of alcohol is counterbalanced by disagreeable sequelae. To the Greeks, Bacchus embodied the sociable, jolly, even wildly hilarious frame of mind induced by wine-drinking, while his tutor, the fat drunken Silenus, seems to have shown the unwanted effects. Various methods have been tried of enjoying alcohol without getting drunk. Prior ingestion of milk or other fatty substance delays its exit from the stomach. The intention is to yield a modest plateau rather than a peak effect. Fructose increases its rate of catabolism. Caffeine, traditionally taken as black coffee for rapid absorption, is a cerebral stimulant and may yield a hoped-for pharmacological antagonism. The problem is not new. The ancient Greeks, who seem to have explored every aspect of human behaviour, had a far simpler way of dealing with it—provided one had the equipment. Drunkenness could be prevented by drinking from a cup made of purple quartz. They called it AMETHYST, from *a-*, not *+methystos*, inebriated (*methy*, wine).