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CASE REPORT

Small bowel Dieulafoy lesions: An uncommon cause of obscure bleeding in cirrhosis

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Abstract

Dieulafoy lesions (DLs) are an uncommon cause of gastrointestinal bleeding, accounting for up to 2% of cases overall. They are largely under recognised and difficult to treat. Up to 95% occur in the stomach, and only case reports document their occurrence in the small bowel (SB). Little is known about their pathophysiology, although there have been associations made previously with chronic liver disease, thought to be due to the erosive effects of alcohol on the mucosa overlying the abnormally dilated vessels. We present a case series of 4 patients with a long duration of obscure gastrointestinal bleeding, who were diagnosed with small intestinal DLs and incidentally diagnosed with chronic liver disease. The histories describe the challenges in both diagnosis and treatment of small intestinal DLs. Our case series suggest a previously unreported link between chronic liver disease and SB DLs which may be due to anatomical vasculature changes or a shift in angiogenic factors as a consequence of portal hypertension or liver cirrhosis.

Key words: Obscure gastrointestinal bleeding; Dieulafoy lesions; Cirrhosis; Portal hypertension; Capsule endoscopy; Double balloon enteroscopy

Core tip: Patients with advanced liver disease are known to have a high rate of obscure gastrointestinal bleeding, the cause of which is often left undetected. Our case series suggests that there may be an increased risk of small intestinal Dieulafoy lesions (DLs) in patients with cirrhosis. Although the pathophysiology of DLs is unknown, our case series of jejunal lesions in patients with cirrhosis raises the question of a potential alteration in the vasculature secondary to portal hypertension, as either an anatomical abnormality or due to a shift in angiogenic factors in these patients.

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INTRODUCTION

Dieulafoy lesions (DLs) are an uncommon cause of gastrointestinal bleeding (GIB), accounting for up to 2%, and are largely under recognised and difficult to treat. Endoscopically they are characterised by the following diagnostic criteria: Active bleeding from a mucosal defect < 3 mm in size, an isolated protruding vessel with or without a minute mucosal defect, or an adherent clot with a narrow point of attachment to a tiny mucosal defect or occasionally normal appearing mucosa[1]. The majority, up to 95%, of DLs are found in the stomach, generally within 6 cm of the oesophagogastric junction, with over 60% on the lesser curvature of the stomach, however they also occur in the colon, duodenum, and rarely in the small bowel (SB). The presentation of bleeding is usually acute overt haemorrhage, and due to the intermittent nature of bleeding, rates of diagnosis at initial endoscopy can be as low as 70%[2]. Endoscopic treatment with argon plasma coagulation (APC), clipping, injection of adrenaline or banding is successful in up to 90% of cases, with angiographic embolization or surgical resection reserved for cases unresponsive to endoscopic therapy[3]. Although the initial response is very high, recurrence is common, and up to 10% of patients present with massive acute GIB, and despite advances in endoscopic treatment mortality rates are as high as 8%[4]. DLs in the SB are rare, however with the increasing availability of SB endoscopy, there have been a number of case series in recent years, understandably suggesting that SB lesions are more difficult to treat[5,6]. Several hypotheses have been put forward as to the cause of bleeding from these DLs, and although an association has been suggested between the use of non-steroidal anti-inflammatories (NSAIDs) and anticoagulants, no causal link or pathophysiological basis for their development has been established. Interestingly a number of small studies have identified an association between advanced liver disease and DLs, suggesting a similarity of these lesions to spider naevi, however the numbers in each study have been small[7-9]. We present a case series of 4 patients with SB DLs who were found incidentally to have advanced liver disease during their workup for obscure GIB. These patients presented consecutively to our institution over approximately a two year time period.

CASE REPORT

Case 1

PS: A 67-year-old female was referred for investigation of obscure overt GIB ongoing for 2 years. Her past history included rheumatic fever, with metallic aortic and mitral valve replacements, for which she was anticoagulated, and congestive cardiac failure. She had initially presented with recurrent episodes of melaena and underwent multiple upper and lower endoscopies and a CT mesenteric angiogram which failed to reveal the source of her bleeding. Cross sectional imaging revealed cirrhosis, without significant varices. A serological screen failed to show any cause of cirrhosis and it was presumed to be secondary to her cardiac failure. She was initially treated empirically with iron and red cell transfusions, however her requirements increased and she became dependent on fortnightly transfusions to maintain her haemoglobin above 8 g/dL. At this stage she was admitted electively and underwent SB capsule endoscopy (SBCE) which showed a large volume of fresh bleeding in the proximal jejunum, with melaena and transported clots throughout the SB. Double balloon enteroscopy (DBE) showed no active bleeding but an isolated protruding vessel in the proximal jejunum, consistent with a DL was detected, and APC and endoclips were applied. Following this she was treated with 20 mg of a long-acting intramuscular somatostatin analogue and she remained bleed free for 12 wk. Unfortunately she then suffered an acute haemorrhage, presenting with haemoglobin of 5 g/dL. She underwent repeat SBCE and DBE which again showed active bleeding from the DL in the proximal jejunum which was again treated with APC and endoclips which initially controlled the bleeding. However PS suffered a massive further haemorrhage, a bleeding source could not be identified by CT mesenteric angiography and despite undergoing an emergency jejunal resection; she died post operatively due to cardiac complications.

Case 2

MF: A 74-year-old lady was referred with intermittent melaena ongoing for 18 mo. She had a history of rheumatic fever, a mitral valve replacement, requiring anticoagulation, congestive cardiac failure and a SB resection in the 1990s for angiodysplasia. Similarly, MF had undergone multiple upper and lower endoscopies which had been unyielding and again, she was found to have features of cirrhosis and portal hypertension on cross sectional imaging, the cause of which was idiopathic. Prior to referral to our services she had received over 50 units of red cell transfusions. She underwent SBCE which showed active bleeding and a minute mucosal defect in her proximal jejunum consistent with a DL, with clots of likely transported blood seen more distally. Her DL was treated with APC *via* DBE on 4 occasions due to early re-bleeding, along with 20 mg of long-acting somatostatin analogue. MF developed cholecystitis secondary to choledocholithiasis, which was managed conservatively, requiring her to discontinue the somatostatin analogue. She has been bleed-free for the last 24 mo, with a most recent

haemoglobin level of 12.1 g/dL.

Case 3

MB: A 76-year-old lady was admitted electively for investigation of a 12-mo history of recurrent obscure overt bleeding in the form of melaena. She had a background of a mitral valve replacement requiring anticoagulation, chronic myeloid leukaemia, cirrhosis of unknown aetiology, and hypertension. MB had undergone embolization of a bleeding source in her proximal jejunum *via* mesenteric angiography prior to her referral to our services; however her melaena recurred within 4 mo of the procedure, and she was requiring weekly red cell transfusions. SBCE showed active bleeding in her proximal jejunum; however at DBE although fresh blood was seen in her proximal jejunum no active bleeding or mucosal abnormalities were seen. During her admission she suffered a number of large volume overt bleeds requiring multiple red cell transfusions, again DBE showed active bleeding in the proximal jejunum. However this was not detected by either CT mesenteric angiogram or a formal heparin-provoked angiogram. After prolonged consideration and discussion, MB underwent a laparoscopic resection of her proximal jejunum, with histology findings consistent with that of a DL. Her haemoglobin remained stable without any red cell transfusions for over 9 mo at which point she re-presented with melaena. On this occasion she was not found to have and SB bleeding, however a new DL was found in her gastric fundus.

Case 4

EN: A 75-year-old lady was referred to our institution for investigation of recurrent melaena. She had undergone multiple upper and lower endoscopies which had not revealed a source of bleeding. Her past medical history included congestive cardiac failure, atrial fibrillation for which she was anticoagulated, type 2 diabetes mellitus, hypertension and cirrhosis, again diagnosed incidentally by imaging during her workup for GIB. SBCE showed fresh blood in the proximal jejunum and she underwent a DBE where a small amount of fresh bleeding was noted in the first part of her duodenum, with the visualisation of a pinpoint vessel consistent with a DL. The area was injected with adrenaline and endoclips were applied with initial haemostasis. However due to the need for ongoing anticoagulation the lesion continued to ooze and a definitive treatment was sought. EN underwent a CT mesenteric angiogram which revealed an occluded coeliac artery with retrograde filling of the gastroduodenal artery from the superior mesenteric artery. Due to the anatomical abnormalities in her vasculature, embolization therapy was not possible and an ileohepatic artery bypass was planned. However, despite previously normal imaging, at laparotomy EN was found to have macro nodular cirrhosis with multiple small intra-abdominal varices. The proposed bypass was abandoned and multiple small DLs around D1 were ligated and/or clipped. EN recommenced anticoagulation shortly after her surgery and has not had any recurrent bleeding episodes in over 10 mo.

DISCUSSION

The above 4 cases outline the challenges in both diagnosis and treatment of SB DLs, and they also present a number of potentially new associations with SB DLs. Firstly regarding demographics, in keeping with the published literature, our patients were elderly with multiple comorbidities, however in contrast to the suggested male preponderance, our 4 patients with SB DLs were all female. In addition, all 4 patients had SB without coexistent lesions in the stomach, where 95% of DLs reportedly occur, although the third case was found to have a de novo gastric DL over 9 mo later. There was also no history of NSAID, or alcohol use, although all patients were anticoagulated, which has been proven to increase the risk of bleeding. Each of the cases highlights the difficulties in diagnosis of SB DLs and reiterates the importance of heightened vigilance in patients with obscure GIB. Despite active bleeding causing systemic compromise and large red cell transfusion requirements, none of the DLs were detected by mesenteric angiography, and were only diagnosed by mucosal visualisation with SB endoscopy, either *via* SBCE or DBE.

Previous associations between cirrhosis and DLs have been thought to be due to the erosive effect of alcohol on the mucosa overlying the dilated DL vessel; however alcohol was not a factor in any of our 4 patients. As mentioned in the introduction, comparisons have been made between the appearances of DLs and spider naevi, a known feature of chronic liver disease, with the suggestion that DLs are gastrointestinal forms of spider naevi; however the pathophysiology for the development of spider naevi is also unknown. Cirrhosis can increase the risk of GIB, mainly due to portal hypertension, leading to portal gastropathy and intraluminal varices; however in our case series all patients had undergone multiple endoscopies, out ruling varices as a cause of bleeding. Patients with advanced liver disease are known to have a high rate of obscure GIB, the cause of which is often left undetected, however; our case series suggests that there may be an increased risk of DLs in patients with cirrhosis. In general the most common cause of obscure GIB is SB angiodysplasias, which have a similar clinical presentation to DL; however there were no characteristic endoscopic features of angiodysplasias in the vascular lesions in any of these 4 patients. We have recently identified an association between the abnormalities in the Angiopoietin pathway along with other angiogenic factors, with the presence of SB angiodysplasias[10]. Our finding of jejunal DLs in patients with cirrhosis raises the question of a potential alteration in the vasculature secondary to portal hypertension, as either an anatomical abnormality, as was described in case 4, or potentially due to a shift in angiogenic factors in these patients. As referenced in the case series by Akhras *et al*[9], the examination of biopsies

from DLs is likely to yield more information about their pathophysiology. Finally, 3 of our 4 patients were treated both medically with long-acting somatostatin analogues and endoscopically, due to a combination of their long history of bleeding and its significant burden on their quality of life, and their need for long-term anticoagulation. Somatostatin analogues are known to reduce GIB due to a combination of effects, including reducing the splanchnic and portal pressure and *via* an anti-angiogenic effect on vascular endothelial growth factor. This makes it difficult to determine which treatment modality was effective in controlling further bleeding episodes but the seemingly successful use of somatostatin analogues in these patients would support both a "vascular pressure system" and an "angiogenic disarray" hypothesis in the pathogenesis of SB DLs. Further work in the field of portal hypertension and angiogenic factors in the pathophysiology of SB DLs and other vascular lesions including angiodysplasias will be interesting and could lead to more targeted treatment options in cases of refractory bleeding.

COMMENTS

Case characteristics

All cases had a long history of significant gastrointestinal bleeding from small intestinal Dieulafoy lesions (DLs) and were found to have cirrhosis and portal hypertension, suggesting a potential association between the two conditions.

Clinical diagnosis

Small intestinal DLs were diagnosed by a combination of capsule endoscopy and double balloon enteroscopy in all patients, with a diagnosis of cirrhosis initially suggested by radiological imaging and confirmed by clinical examination ± laboratory features of cirrhosis.

Differential diagnosis

There are a number of other vascular lesions which can affect the small intestine and share similar endoscopic features with DLs including: Angiodysplasias, telangiectasias, arteriovenous malformations, mucosal ulceration and trauma.

Laboratory diagnosis

All patients presented with iron deficiency anaemia, in addition features of cirrhosis including thrombocytopaenia and a low serum albumin were found in 2 patients.

Imaging diagnosis

Small intestinal DLs were diagnosed endoscopically by characteristic visual appearances, using either capsule endoscopy or double balloon enteroscopy.

Pathological findings

When examined histologically, DLs are found to consist of abnormally large calibre sub-mucosal end arteries which lie close to the surface of the mucosa, making them delicate and prone to rupture and bleeding.

Treatment

Treatments included endoscopic; a combination of injection of adrenaline, application of endoclips, and/or thermal coagulation, *via* angiographic embolization, or ultimately *via* surgical resection of the segment of affected bowel, or ligation of the vessels feeding the DLs.

Related reports

Small intestinal DLs are reported only rarely in the literature and are thought to be difficult to treat. An association between patients with advanced liver disease and DLs outside the small intestine has also been made in a few other case reports, although the pathophysiology linking the two conditions is still unknown.

Term explanation

DLs are uncommon causes of gastrointestinal bleeding characterised by tiny defects in the gastrointestinal mucosa.

Experiences and lessons

This case series highlights the difficulties in the diagnosis of DLs and the need for heightened vigilance and repeated investigation in patients with obscure gastrointestinal bleeding, particularly in patients with cirrhosis. It also highlights the difficulties and poor outcomes following treatment, which addresses the need for further research in the area to identify the pathophysiology of DLs and develop targeted therapies.

Peer-review

The paper is a useful addition to the literature concerning this difficult to treat lesion.

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