Vascular malformation of the jejunum associated with nodal non-Hodgkin's malignant lymphoma

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ABSTRACT

We report a case of multiple minute angioectasia of the jejunum presenting with fatal gastrointestinal bleeding. Repeated endoscopies, mesenteric angiography and scintigraphy failed to locate the bleeding site. Multiple minute angioectasia was suspected on intraoperative enteroscopy; however, surgical resection failed to permanently control gastrointestinal haemorrhage. The final histology report confirmed the presence of multiple minute angioectasia of the jejunum. In this case study, we review current diagnostic and therapeutic modalities, and discuss the association between gastrointestinal angioectasia and malignant lymphoma.

Keywords: angiodysplasia, angioectasia, gastrointestinal haemorrhage, lymphoma

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INTRODUCTION

Bleeding vascular malformation of the jejunum is a diagnostic challenge. The jejunum is not easily accessible for endoscopy, and the minute size of the malformation can make it quite difficult to detect. The vascular malformation may develop spontaneously or may be related to some disease. No association between vascular malformation and lymphoma has been found in the literature. We report the first observation of multiple minute vascular malformations of the jejunum in a patient with malignant lymphoma. The conundrum of diagnosis and treatment is discussed in this report.

CASE REPORT

A 55-year-old African woman was admitted with complaints of weakness and passage of black stools for five months. She had melaena and her haemoglobin was 7.3 g/dl. Two upper gastrointestinal (GI) endoscopies and colonoscopy with ileal intubation failed to reveal the source of bleeding. Laparotomy was performed due to profuse bleeding. It showed blood in the jejunum

at a distance of 30 cm from the ligament of Treitz and three jejunal diverticula at a distance of 5 cm from the ligament of Treitz, with a trace of fresh blood on intra-operative upper endoscopy. The jejunal diverticula were thought to be the source of bleeding, and they were thus resected. Histological examination confirmed diverticular disease of the jejunum with mucosal oedema and haemorrhage in the submucosa; however, the source of bleeding was unclear. On further exploration, nodular lesions were detected in the ileum and resected, which were histologically confirmed as schistosomal egg granuloma. Mesenteric lymphadenopathy revealed diffuse lymphocystic malignant lymphoma. A test for human immunodeficiency virus was negative. The patient recovered uneventfully without any signs of gastrointestinal bleeding (GIB) and was discharged with an appointment for oncology treatment.

In two weeks, the patient was re-admitted with severe GIB. Upper GI endoscopy with 20 cm of jejunal examination did not reveal the source of bleeding. After stabilisation and repeated episodes of bleeding, the patient was operated on. The second laparotomy revealed blood in the small intestine at a distance of 45 cm from the ligament of Treitz. Intraoperative enteroscopy showed three tiny ruptures of the mucosa with stigmata of bleeding, out of which one site was profusely bleeding; all the three sites were resected (Fig. 1). The patient bled again on postoperative Day 5. Multifocal vascular malformations were suggested. The patient was treated conservatively, with intermittent success. She was later transferred for angiography and scintigraphy. Capsule endoscopy and balloon enteroscopy were not available at our institution. During the two admissions (within five months), 64 units of red packed cells, 18 units of fresh frozen plasma and one unit of platelets were required to stabilise the patient. No vascular abnormalities or bleeding were found on angiography. Scintigraphy revealed increased tracer activity in the descending colon, which was not confirmed on repeated colonoscopy. The patient was scheduled to start treatment for malignant lymphoma, but she died before the initiation of chemotherapy. The final histology report

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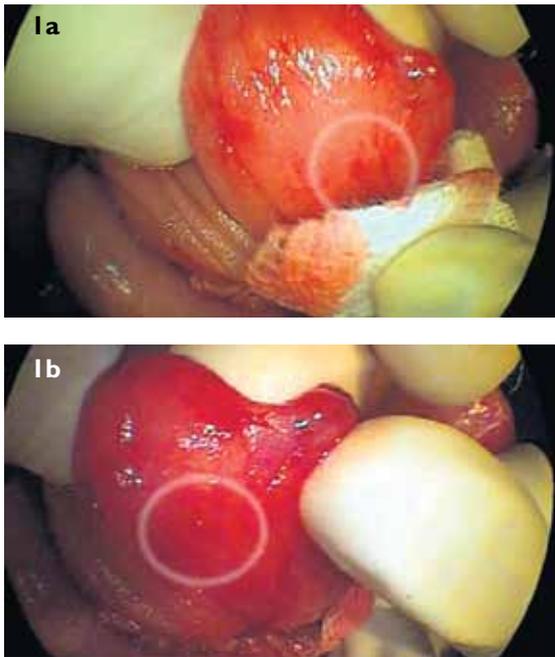Fax: (27) 0 15 297 7554
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Fig. 1 (a & b) Enteroscopy images show tiny (2 mm) profusely bleeding mucosal ruptures (circle).

Fig. 2 Photomicrograph shows the submucosa of the small intestine with an increased number of thin-walled vascular channels. (Avidin-Biotin complex immunostaining with CD 34, × 100).

showed the presence of multiple thin-walled dilated vascular channels in the submucosa without evidence of vasculitis (Fig. 2). These were frequently deficient of a muscle coat. The presence of multiple minute vascular ectasia of the jejunum was concluded.

DISCUSSION

In the literature, the nomenclature of vascular lesions of the GI tract is confusing. In order to avoid any misunderstanding, we define the terms used in this article. Vascular malformation is a general term that includes all badly formed vessels due to different causes. Vascular is a Latin word, and the Greek equivalent is *angeion*. In our opinion, angiodysplasia (*dys* = bad; *plasis* = molded) is the Greek synonym of vascular malformation. Angioectasia (AE) is a distinct clinical and pathologic entity, which is microscopically characterised by dilated, distorted, thin-walled venules, capillaries and arterioles that are lined by endothelium, with few smooth muscles and no inflammation or fibrosis.[1] The term 'angiodysplasia' is sometimes used in the literature instead of 'angioectasia'.[2,3]

In 30%–40% of the cases, AE is the cause of haemorrhage from the small intestine. The pathogenesis of AE is not well understood. Its incidence increases with age and is more common after the age of 60 years. An association with end-stage renal disease, Von Willebrand's disease and aortic stenosis is reported. The reason for its prevalence is poorly explained and remains controversial. AE of the small intestine can be a feature of

hereditary haemorrhagic teleangiectasia and progressive systemic sclerosis (CREST variant).[1-3] None of these diseases was found in our case. Instead, a diagnosis of nodal malignant lymphoma was confirmed.

A few cases of jejunal lymphoma presenting as GIB have been reported in the literature. Occasionally, lymphomas arising from mucosa-associated lymphoid tissue may be located in the jejunum and may present with occult or overt GIB.[4] NK/T-cell, Burkitt's and large B-cell lymphomas presenting with lower GIB have been found in the jejunum, although it is a very unusual location.[5-7] B-cell lymphoma of the jejunum as a complication of post-transplant lymphoproliferative disease manifesting as a life-threatening GIB was also reported.[8] All these lesions appear as superficial erosive or nodular lesions with ulcerations. These lesions are easily detected during endoscopy and can be felt in the bowel wall during laparotomy. Only a single case of AE of the whole intestine in a patient with recurrent non-gastrointestinal Hodgkin's lymphoma has been reported.[9] The authors associated the bleeding AE of the whole intestine with high-dose chemotherapy and haematopoietic stem cell transplantation.[9]

The association of AE of the GI tract with nodal malignant lymphoma has not been reported anywhere else in the literature. The presentation of multiple minute jejunal AE as recurrent massive GI bleeding despite multiple surgical resections of bleeding lesions in this patient might suggest an association with her systemic condition. However, the association with nodal (non-GI) malignant lymphoma is difficult to explain and may be casual. Vascular lesions of the small intestine should be suspected when gastroduodenoscopy and colonoscopy fail to identify the possible cause of gastrointestinal bleeding. The next step should be visualisation of the small bowel. Traditional barium studies are rarely utilised owing to their low diagnostic yield, particularly in detecting AE of the small bowel. New imaging techniques, such

as computed tomography enterography and magnetic resonance enterography, may play an increasing role in evaluating Crohn's disease and small-bowel neoplasm, but they may have limited scope in diagnosing VE or neoplasms less than 15 mm in diameter.[10]

Capsule endoscopy (CE) is a non-invasive, well-tolerated and relatively safe option for examination of the small intestine. However, CE has well-documented limitations of incomplete small-bowel transit and poor luminal view quality. Incomplete visualisation of the small bowel mucosa occurs in 15%–26% of the cases due to inadequate luminal distention, rapid transit through the duodenum and jejunum, a limited and unidirectional view, inability to stop at or wash any area of interest, a relatively slow video-image capture rate and limited battery life. Due to its non-invasiveness and satisfactory diagnostic yield, CE is recommended as the first-line investigation for small-bowel bleeding.[10-12]

The diagnostic and therapeutic value of push enteroscopy (PE) is limited, as only 50–120 cm of the proximal bowel can be examined. With the advent of double-balloon enteroscopy (DBE) in 2001, it has become feasible to simultaneously visualise the entire small bowel, sample lesions and perform therapeutics. DBE has favourably replaced PE. Recently, single-balloon enteroscopy (SBE) was introduced; the technique seems to be slightly easier to perform but still needs evaluation. The diagnostic value of DBE and CE has been shown to be similar. DBE complements CE by increasing the diagnostic yield, offering sampling and endoscopic therapy.[10,13,14] Introduced in 2008, spiral endoscopy proved to be three times faster than DBE in examining the small intestine, although more comparative studies are required.

It should be noted that sedation, especially using meperidine, may cause AE to disappear. It has been reported that using naloxone could cause AE to appear in 2.7% and increase in size in 5.4% of cases. Similarly, significant anaemia, hypotension, dehydration, and even the use of cold water lavage to cleanse the luminal surface, may cause AE to disappear.[1,2] Radionucleotide imaging reveals the location of bleeding with a sensitivity and specificity of 93%–95%, providing a bleeding rate of 0.3 mL/min at the time of investigation. However, in practice, the sensitivity can drop by up to 79% and the specificity by up to 30%. It is non-invasive, does not require special preparations for the patient and detects both arterial and venous bleeding sites, although the localisation of bleeding source is often not precise. A provocation test with heparin may increase the diagnostic yield.[15]

Angiography may elucidate the angiographic signs of AE and the site of bleeding when the bleeding volume is at least 0.5 mL/min and when the bleeding may be controlled angiographically.[1] Laparotomy or laparoscopy should be considered for small bowel tumours or vascular lesions that are not amenable to endoscopic or angiographic treatment. When endoscopic or angiographic treatment fails or is not available and GIB is uncontrolled, laparotomy may be an option. Intraoperative enteroscopy may identify non-palpable lesions and all visible lesions should be resected. The negative laparotomy rate in a published series was 17% and the re-bleeding rate of resected vascular small bowel lesions was 39%.[16]

Bleeding AE of the small bowel may be controlled endoscopically or angiographically in most patients. When these modalities are not feasible, surgical resection is indicated. Different pharmacological modalities have been suggested but their efficacy is still not confirmed. Hormonal treatment with oestrogen and progestagen was considered to prevent re-bleeding from GI AE. The results obtained were, however, conflicting.[2] Octreotide was reported to reduce bleeding from intestinal AE and varices. Successful long-term use of octreotide long-active release once a month was reported in a few cases.[2,17] In another published series, thalidomide, an anti-inflammatory drug with potent inhibition of angiogenesis, has been reported to stop the bleeding of intestinal AE within two weeks in all patients.[18]

In conclusion, AE of the small bowel is difficult to diagnose, and is frequently multifocal and minute. It can present with life-threatening GIB, which may be difficult to control and may be fatal despite multiple surgical resections. Currently, endoscopic therapy of small-bowel AE is more beneficial, if it is feasible. Pharmacological modalities are promising, but their efficacy is still not confirmed. The association of AE with malignant lymphoma is suggested. However, there are still many unanswered questions on the pathogenesis and treatment of AE of the small bowel.

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