DOI: 10.26717/BJSTR.2017.01.000229
Diana Penha. Biomed J Sci & Tech Res

BIOMEDICAL Journal of Scientific & Technical Research

ISSN: 2574-1241

Case Report Open Access

When Angiography Makes a Difference - Polyarteritis Nodosa- A Rare Cause of Mid- Gastrointestinal Bleeding

Diana Penha[1*], Erique Guedes Pinto[2], Belarmino Gonçalves[3], David Orta[4] and Ana Costa[5]

[1]*Department of Liverpool Heart and Chest NHS Foundation Hospital, UK*

[2]*Department of Aintree University Hospital NHS Foundation Trust, UK*

[3]*Department of Interventional Radiology service - Instituto Português de Oncologia do Porto FG, Interventional Radiologist, Angiography Section Chief, Portugal*

[4]*Department of Gastroenterology service - Hospital Prof. Dr. Fernando Fonseca, Portugal*

[5]*Departmentof Radiology service - Hospital Prof. Dr. Fernando Fonseca, Portugal*

Received: July 17, 2017; **Published:** July 31, 2017

***Corresponding author:** Diana Penha, Department of Liverpool Heart and Chest NHS Foundation Hospital, Radiology Consultant, Liverpool, UK, Email: dianapenha@gmail.com

Abstract

We present a case of overt and recurrent mid-gastrointestinal bleeding with hemodynamic repercussion and severe limitation to the patients' quality of life, followed in our department for the last 6 years. The final diagnosis of isolated gastrointestinal involvement of Polyarteritis Nodosa was only reached after multiple hospital admissions, imaging and gastroenterological examinations. A subtle finding of micro aneurysms in the mesenteric circulation opened the way to effective treatment when endoscopic treatment had failed to prevent recurrences.

Abbreviations: MGIB: Mid Gastro Intestinal Bleeding; IBD: Inflammatory Bowel Disease; GI: Gastro Intestinal; CTA: CT Angiography; Hb: Haemoglobin; VDRL: Venereal Disease Research Laboratory; TPHA: Treponema Pallidum Hemagglutination Assay; ANA: Antinuclear Antibodies; ETV: Entecavir; ACR: American College of Rheumatology

Introduction

Mid gastrointestinal bleeding (MGIB) is uncommon but represents the majority of cases of recurrent GI bleeding without an obvious source, even after endoscopic and imaging evaluation [1]. Overt MGIB manifestations depend on the rate of bleeding and when associated with hemodynamic instability may present with haematemesis, melaena and/or haematochezia. Five to ten percent of patients with GI bleeding will not have an identifiable source of bleeding after initial endoscopic and imaging evaluation [2]. The advent of push-and-pull enteroscopy, intraoperative enteroscopy and wireless video capsule enteroscopy has shed light on cases which previously could only be diagnosed as occult GI bleeding, allowing for the identification of a bleeding source in the small bowel in up to 75 percent of these patients [3]. MGIB may be caused by multiples aetiologies such as inflammatory bowel disease (IBD), angiodysplasia, Dieulafoy lesions, Henoch-Schöenlein purpura to name but a small subset (Table 1). Their relative frequencies in MGIB are not well established but appear to be age-dependent [4]. We present an elusive case of recurrent GI bleeding with severe hemodynamic repercussion where imaging proved essential to elicit a rare diagnosis when all other investigations had failed.

Table 1: Possible aetiologies for mid gastrointestinal bleeding (MGIB).

Common causes	Rare causes
Inflammatory bowel disease (under 40 years of age)	Henoch-Schoenlein purpura
Angiodysplasia (over 40 years of age)	Portal hypertensive enteropathy / small bowel varices
Dieulafoy lesions	Amyloidosis
Neoplasms	Blue rubber bleb nevus syndrome
NSAID users (over 40 years of age)	Osler-Weber-Rendu syndrome
Meckel's diverticulum (under 40 years of age)	Pseudoxanthoma elasticum Kaposi sarcoma
Polyposis syndromes (e.g. Lynch) (under 40 years of age)	Plummer-Vison syndrome Ehler-Danlos syndrome

Case Report

We report the case of a 58-year-old male patient of black race with recurrent overt gastro- intestinal (GI) bleeding since 2010. The patient has a previous medical history of ischemic heart disease (medicated with acetylsalicylic acid and clopidogrel), essential hypertension (medicated with perindopril and amlodipine), chronic hepatitis B infection without evidence of cirrhosis and latent syphilis (previous treatment). He also had a previous medial laparotomy for unconfirmed suspicion of gastrointestinal stromal tumour. There was no personal or family history of cancer. Since 2010, the patient had multiple hospital admissions with recurrent episodes of GI bleeding characterized by haematemesis, haematochezia and melaena, with hemodynamic repercussion and severely diminishing the patient's quality of life. During these hospital admissions, multiple and extensive endoscopic and imaging examinations were performed.

Between 2010 and 2012, endoscopic examinations including upper GI endoscopy, push-and-pull enteroscopy and colonoscopy, were all interpreted as normal. Conventional and CT-angiography (CTA) only documented high-density intra-luminal content of the proximal jejunum, interpreted in the context of recent upper GI bleeding, but no evidence of active bleeding. Capsule enteroscopy suggested the presence of a possible sub-mucosal lesion at the level of the proximal jejunum. In 2013, both upper GI endoscopy and push-and-pull enteroscopy reported a likely Dieulafoy lesion in the proximal jejunum. The lesion was treated with 1:10,000 epinephrine, four haemostatic clips and the mucosa was tattooed. In 2013, the patient was admitted with a myocardial acute infarction for which he was submitted to percutaneous coronary angiography and stented, starting dual anti platelet therapy.

In early 2014, the patient was again admitted on three more separate occasions for episodes of haematochezia, with active bleeding being identified from a Dieulafoy lesion in a previously tattooed zone of the proximal jejunum. Two more haemostatic clips were used to treat the acute bleeding. In October of 2014, the patient was again admitted to our hospital for haematochezia with hemodynamic instability. Blood tests showed microcytic anemia with 5.9g/dL of hemoglobin (Hb). Upper GI endoscopy and colonography failed to identify relevant changes. Complete intra-operative enteroscopy was performed showing blood in the distal ileum but again no lesions. Biopsies performed at the time failed to document microscopic criteria of vasculitis.

During this hospital admission, mesenteric angiography revealed "tortuous parietal gastric arterial branches with reduced calibre and millimetric aneurysmatic focal dilatations with similar changes along the vasa recta of the marginal artery of the colon." (Figure 1). CTA performed after the angiography (Figure 2) confirmed active bleeding with evidence of intraluminal contrast medium (no contrast medium given per mouth) and focal dilatations of the mesenteric circulation. No changes were identified in the renal vessels. A retrospective review of the previous angiographies allowed for the identification of subtle calibre irregularities along the mesenteric vessels with topographic correlation with the aneurysmal dilatations seen in the later scan.

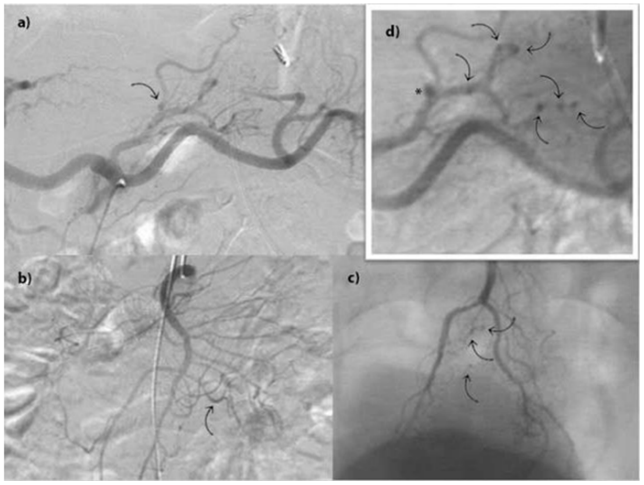

Figure 1: Selective arteriography of the a) coeliac trunk, b) superior mesenteric artery and c) inferior mesenteric artery from October, 2014. Multiple micro-aneurysms are seen (curved arrows). d) Close up of the left gastric artery showing numerous short dilated segments (curved arrows) corresponding to the micro-aneurysms, and a slightly larger aneurysm in the proximal left gastric artery.

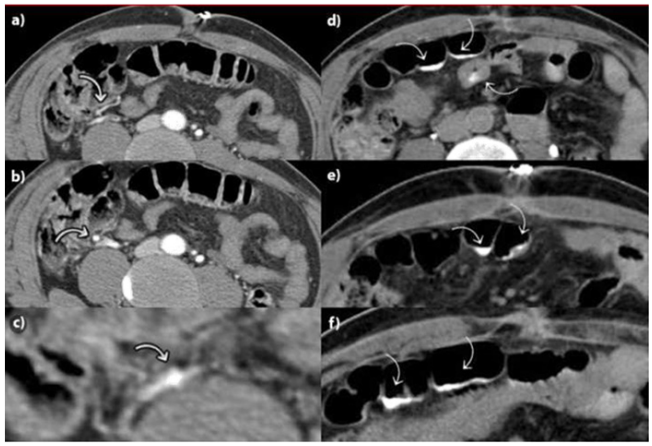

Figure 2: CTA performed immediately after the conventional angiography confirms the presence of short arterial segment dilatations. a) The ileocolic artery can be seen (thick arrow) immediately anterior to the ileocolic vein. b) At the level immediately below, the ileocolic artery shows a 5mm focal dilatation (thick arrow). c) Close-up of the ileocolic artery in MPR through the micro-aneurysm (thick arrow). d - f) Intra-luminal contrast medium (thin arrows) confirms active bleeding of low output, which was not identified during angiography.

Additional analytical evaluation performed at this time revealed anaemia with 8 g/dL of Hb, elevated C reactive protein (CRP of 1.2 mg/dL) and sedimentation rate (32 mm/h). Review of infection markers revealed viral load for HBV of 8625 copies, positive screening tests for syphilis (Venereal disease research laboratory test [VDRL]; titre of 1:4 and Treponema pallidum hemagglutination assay test [TPHA]; titre of 1:5120) and a positive Strongyloides stercoralis antigen test (result of 1.25). Auto-immune screening

revealed positive antinuclear antibodies (ANAs) (1:160, midbody). The differential diagnosis at this point in time included Polyarteritis Nodosa (PAN), Strongyloidiasis and Syphilis, all of which could explain micro-aneurysms in the mesenteric circulation. Further investigations included skin biopsy, electromyography and biopsies by upper GI endoscopy and colonoscopy, which were all normal. A lumbar puncture also excluded neurosyphilis. Renal artery Doppler scan and CTA of the brain did not show further vascular changes. Treatment was started with Entecavir (ETV) for HBV infection, penicillin for late latent syphilis and Ivermectin for Strongyloides infection.

In January of 2015, the patient was again admitted for a new episode of haematochezia with haemodynamic instability, progressing to hypovolemic shock.

During the hospital admission, the second episode of haemodynamic instability allowed for imaging and gastroenterological studies to be performed in the acute phase (within 12 hours of the start of symptoms). However, CTA and conventional angiography failed again to report significant changes and complete intra-operative enteroscopy identified blood in the colon but failed to identify any lesion. Clinical haematochezia was only evident after 21 hours of the start of haemodynamic instability. Therapy was started for PAN with methylprednisolone and cyclophosphamide, clopidogrel was suspended (conversion to single antiplatelet therapy) and blood pressure control was optimized.

In February of 2015, one week after starting therapy with cyclophosphamide a new episode of haematochezia with haemodynamic instability occurred with 6 g/dL of Hb with an active bleeding site at the proximal jejunum was confirmed by 99m-Tc scintigraphy. Exploratory laparotomy identified blood in the proximal jejunum with at least three bleeding points in a 25cm segment, about 20cm distal to the angle of Treitz. A segmental small bowel resection was performed and the histological report documented "focus of haemorrhage in the submucosa and predominantly muscular is propria, associated with inflammatory polymorph nuclear infiltrate of the wall of the arterioles." which is a diagnostic criterion for PAN. In July of 2015, the patient was again admitted for an episode of melaena. Enteroscopy performed in the Emergency department identified a Dieulafoy-like lesion near the surgical anastomosis site by the tattooed mucosa, 30cm from the Treitz angle. Blood clots and low output active bleeding were identified and treated with three haemostatic clips. Presently, 15 months after the presumptive diagnosis of PAN, the patient continues therapy with prednisolone, having completed seven cycles of cyclophosphamide. The last hospital admission for GI bleeding was in July of 2015, eleven months ago. (Table 2) (Figure 3) summarise the bleeding events and gastroenterological and imaging evaluations from 2010 to 2016.

Table 2: Summary of events.

Date	Event
28-10-2010	CTA AP: Normal
16-11-2010	CTA AP: Normal
25-2-2012	Hospital admission for haematochezia
25-2-2012	CTA AP: Normal
21-3-2012	Hospital admission for haematochezia
21-3-2012	Emergency upper endoscopy: Normal
29-3-2012	Angiography: Normal
18 to 21-2-2013	Hospital admission for new episode of haematochezia and haematemesis
18-2-2013	Enteroscopy with paediatric colonoscope: Vascular lesion in the proximal jejunum with active bleeding of low output, treated with three haemostatic clips and the mucosa was tattooed
25-7 to 2-8-2013	Hospital admission for new episode of haematochezia
25-7-2013	Upper endoscopy: Normal Enteroscopy: Dieulafoy lesion in the proximal jejunum treated with 1:10,000 and four haemostatic clips
15 to 24-6-2014	Hospital admission for new episode of haematochezia with haemodynamic instability
15-6-2014	Upper endoscopy and push and pull enteroscopy: Normal
18-6-2014	Colonoscopy: Normal Wireless videocapsule enteroscopy: Normal
6 to 16-9-2014	Hospital admission for new episode of haematochezia with haemodynamic instability

6-9-2014	Push and pull enteroscopy: Dieulafoy-like lesion near tattooed mucosa without evidence of active bleeding. Treatement with two haemostatic clips.
22-10 to 19-11-2014	Hospital admission for new episode of haematochezia with haemodynamic instability
22-10-2014	Enteroscopy: Normal
27-10-2014	New episode of melaena
28-10-2014	CTA AP and Angiography: "tortuous parietal gastric arterial branches with diminished caliber and milimetric aneurysmatic focal dilatations with similar changes along the vasa recta of the marginal artery of the colon" Presumptive diagnosis of PAN
30-10-2014	Upper endoscopy, enteroscopy and colonoscopy with biopsies: Normal
4-11-2014	Start of therapy for HBV with Entecavir
13-11-2014	Start of therapy for PAN with Prednisolone
14-11-2014	Start of therapy for late latent Syphilis with Penicillin Start of therapy for Strongyloidiasis with Ivermectin
2 to 8-1-2015	Hospital admission for new episode of haematochezia with haemodynamic instability
18-1 to 11-2-2015	Hospital admission for new episode of haematochezia with progression to hypovolemic shock (Hb- 4.8 g/dL)
10-2-2015	Start therapy for PAN with cyclofosfamide
28-1-2015	New episode of haemodynamic instability while an inpatient Angiography: Normal

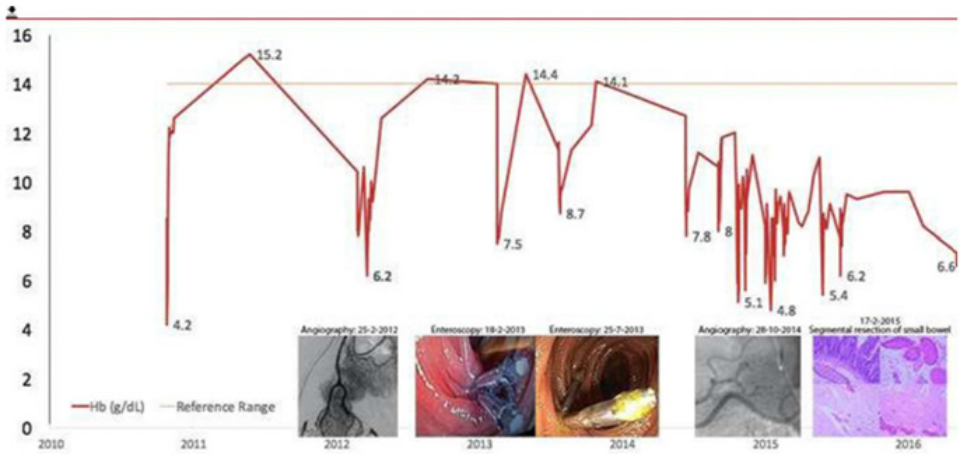

Figure 3: Chart showing the correlation between Hb levels over time and specific evaluations, namely the enteroscopies which identified a Dieulafoy-like lesion, the angiography study that identified and micro-aneurysmatic dilatations and the histological H&E images identifying inflammatory polymorph nuclear infiltrate of the wall of the arterioles.

Discussion

By definition, a Dieulafoy lesion is a single tortuous artery in the submucosa and is a potential aetiology for MGIB. We present the argument that, in the present case, the lesion is a manifestation of PAN (an aneurysmal dilatation of a submucosal artery) and as such, the 'tip of the iceberg' of the underlying disease. Treating only the lesion with haemostatic clips and not the underlying cause (i.e. inflammation of the arterial wall) did not stop disease progression or bleeding recurrence. PAN is a rare spectrum of diseases characterized by a systemic necrotizing vasculitis affecting medium-sized muscular arteries [5], with an estimated prevalence rate between 2 and 33 per million [6]. The kidneys, skin, joints, muscles, nerves and GI tract may be involved, while sparring of the lung is noticeable. In this case of recurrent and overt MGIB, multiple gastroenterological and imaging evaluations had failed to conclusively identify the source of bleeding or, when a Dieulafoy-like lesion was identified and treated, failed to significantly affect the course of the disease. This led to an increase in the number and severity of bleeding events accompanied by haemodynamic instability and even hypovolemic shock.

A new diagnostic pathway was opened when micro-aneurysmatic dilatations were diagnosed. The patient presented

Strongyloidiasis, late latent syphilis and chronic HBV infection, which is associated with PAN [7], and all three of these diseases could explain the micro-aneurysmal dilatations in the mesenteric and splanchnic arteries. Empirical treatment was initiated for all these diseases and eventually, the histological report from the segmental resection of proximal jejunum confirmed PAN (isolated GI manifestation). In PAN, inflammatory cells infiltrate along the arterial wall predisposes to narrowing, thrombosis and aneurysm formation. These changes can be identified on angiographic evaluations although they may be subtle and easily overlooked, as happened on all but one of the angiographies. An inter-hospital MDT consensus was needed to confirm the presence of micro aneurysms in all angiographies and to establish a presumptive diagnosis of PAN by fulfilling the minimum of three out of ten of the American College of Rheumatology (ACR) 1990 criteria. These criteria were: diffuse myalgias and weakness of muscles; the presence of hepatitis B surface antigen and arteriogram showing aneurysms or occlusions of the visceral arteries, not due to arteriosclerosis, fibro muscular dysplasia or other non-inflammatory causes. Later, the histological changes further added another ACR criterion for the diagnosis. Treatment with steroids and cyclophosphamide has not prevented recurrence of MGIB although it has clearly reverted the accelerated rate of deterioration that the patient was experiencing.

Conclusion

Assessments of the whole GI tract is now possible with endoscopic techniques such as upper endoscopy, colonoscopy, and push and pull enteroscopy, intraoperative enteroscopy and wireless video capsule enterography but imaging evaluation still provides an essential tool to assess vascular causes of MGID. In the presented case report subtle changes on angiography provided the diagnostic clues for the elusive final diagnosis and effective treatment.

References

1. Pasha SF, Leighton JA, Das A, Harrison ME, Sharma VK, et al. (2008) Double-balloon enteroscopy and capsule endoscopy have comparable diagnostic yield in small-bowel disease: a meta- analysis. Clin Gastroenterol Hepatol 6(6): 671-676.
2. Gerson LB, Fidler JL, Cave DR, Leighton JA (2015) ACG Clinical Guideline: Diagnosis and Management of Small Bowel Bleeding. Am J Gastroenterol 110(9): 1265-1287.
3. Pennazio M, Arrigoni A, Risio M, Spandre M, Rossini FP (1995) Clinical evaluation of push-type enteroscopy. Endoscopy 27(2):164-170.
4. Raju GS, Gerson L, Das A, Lewis B (2007) American Gastroenterological Association (AGA) Institute medical position statement on obscure gastrointestinal bleeding. Gastroenterology 133(5): 1694-1696.
5. Sato O, Cohn DL (2003) Polyarteritis and microscopic polyangiitis. In: Rheumatology, Klippel JH, Dieppe PA (eds) Mosby St Louis.
6. Mahr A, Guillevin L, Poissonnet M, Aymé S (2004) Prevalences of polyarteritis nodosa, microscopic polyangiitis, Wegener's granulomatosis, and Churg-Strauss syndrome in a French urban multiethnic population in 2000: a capture-recapture estimate. Arthritis Rheum 51(1): 92-99.
7. Guillevin L, Mahr A, Callard P, Godmer P, Leray E, et al. (2005) Hepatitis B virus-associated polyarteritis nodosa: clinical characteristics, outcome, and impact of treatment in 115 patients. Medicine (Baltimore) 84(5): 313-322.