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Case Study

Acute gastrointestinal bleeding from a chronic cause: a teaching case report

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Abstract

Gastrointestinal bleeding (GI bleed) is a common and potentially life-threatening reason for emergency room and intensive care unit admission. This article reports the case of an 83-year-old man with acute GI bleeding from an unusual cause. The clinical information is presented in a step-by-step and question-answer format for learning purposes. This paper is particularly aimed at an internal medicine readership.

Case presentation

In March 2011, an 83-year-old man developed paroxysmal atrial fibrillation and distal right leg ischaemia successfully treated with embolectomy. He had a remote medical history of hypersensitivity pneumonitis (from mushroom farming), coronary artery bypass grafting (CABG) surgery, chronic lymphocytic leukaemia (CLL), and Billroth type II gastrectomy for previous gastric ulcer bleeding.

His medication included a β-blocker, a statin, low-dose aspirin, an angiotensin II receptor blocker and a proton-pump inhibitor (PPI).

Lab results were normal except for slight thrombocytopenia (141'000 platelets/µL; normal range 150'000-450'000 platelets/µL) and lymphocytosis (21'675 cells/µL, normal range 1'200-3'600 cells/µL with smudge cells, monoclonal B-lymphocytes 17'700 cells/µL).

Echocardiography showed only left atrial dilatation and grade 2 mitral insufficiency, without inferior vena cava dilatation.

He lived independently and was in an excellent general condition, going on regular skiing holidays.

Question set 1

1. *Which risk factors for bleeding does this patient have?*
2. *Which anticoagulation strategy would you recommend?*

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Short answer set 1

1. *Which risk factors for bleeding does this patient have?*
   His older age (≥75 years), low-dose aspirin treatment and prior gastric ulcer bleeding with Billroth II gastrectomy.
2. *Which anticoagulation strategy would you recommend?*
   Continuation of his PPI and an upper GI endoscopy (with Helicobacter pylori eradication if required) prior to initiating an oral anticoagulant instead of low-dose aspirin.

Long answer

The new diagnosis of non-valvular atrial fibrillation with peripheral embolism is a clear indication for oral anticoagulation. The CHA_2DS_2-VASc score (**Table 1**) may be useful to determine which individuals would benefit from oral anticoagulation: this patient's age ≥75 years (two points), thromboembolism (two points) and history of vascular disease (total score 5) clearly put him in a high risk category for recurrent venous thromboembolic (VTE) complications (7.2% per year risk of VTE[1]).

This patient's risk of VTE should be weighed against the risk of bleeding, which is also elevated in this patient. Recommended strategies for the prevention of GI bleeding include PPIs and Helicobacter pylori eradication -if required- prior to starting oral anticoagulants.

Vitamin K-antagonists such as warfarin are first line anticoagulants; novel oral anticoagulants (NOACs) may also be appropriate in this patient because they have been associated with lower bleeding risks (but these were not yet available in 2011). Aspirin has only weak preventive effects against VTE and is not recommended for this purpose.

The prior history of CABG is a clear indication for low-dose aspirin. However, the combination of warfarin and aspirin increases the risk of bleeding and has not been shown to decrease the risk of cardiovascular events compared to warfarin alone.[2][3] Whether the combination of NOACs with aspirin or dual anti-platelet therapy is safe and effective requires further study.

	Condition	Points
C	Congestive heart failure (or Left ventricular systolic dysfunction)	1
H	Hypertension: blood pressure consistently above 140/90 mmHg (or treated hypertension on medication)	1
A2	Age ≥75 years	2
D	Diabetes Mellitus	1
S2	Prior Stroke or Transient ischemic attack or thromboembolism	2
V	Vascular disease (e.g. peripheral artery disease, myocardial infarction, aortic plaque)	1
A	Age 65–74 years	1
Sc	Sex category (i.e. female sex)	1

Table 1 | CHA_2DS_2-VASc score

Case continued (part 2)

Gastroscopy and biopsies showed an inflammatory pseudopolyp at the gastro-jejunal suture line of the previous Billroth surgery, and hyperaemic gastric mucosa with negative immunohistochemistry for *Helicobacter pylori*. Subsequently, a vitamin K-antagonist was added to prevent recurrent thromboembolic events. Despite the above-mentioned evidence-based recommendations, low-dose aspirin was continued after discussion with the patient and his cardiologist.

One week later, while INR was 2.5 (target 2.0 - 3.0 therapeutic range for vitamin K-antagonists), he was brought by ambulance to the emergency room because of blood vomiting (haematemesis) and passage of dark stool (melena). The patient denied drinking alcohol or taking non-steroid anti-inflammatory drugs.

Blood pressure was low (86/44 mmHg), pulse irregular 88/minute, temperature 36.5°C (orally) and oxygen saturation 97% while breathing room air. There were no clinical signs of cirrhosis.

Liver tests and ferritin serum concentrations were normal.

An emergency upper endoscopy showed massive blood and clots in the distal oesophagus and fundus without obvious ulcers.

Question set 2

3. *What would be the appropriate next steps in the management of this patient?*
4. *What single tests or examination would be the most useful step to determine the cause of this patients bleeding?*

Short answer set 2

3. *What would be the appropriate next steps in the management of this patient?*
   Placement of 1-2 large-bore intravenous lines, volume resuscitation with crystalloids, transfusion of red blood cells and platelets, correction of INR, i.v. administration of PPIs, and admission to the intensive care unit.
4. *What single tests or examination would be most useful to determine the cause of this patients bleeding?*
   Repeat endoscopy after resuscitation.

Long answers

Management of serious GI bleeding involves placement of 1-2 large-bore i.v. lines, volume resuscitation with crystalloids and red blood cell transfusions, correction of INR, and admission to the intensive care unit.

INR can be corrected quickly with fresh frozen plasma or coagulation factor concentrate; the latter is more expensive but may have advantages when administration of large volumes of i.v. fluid is not desired. Vitamin K should also be given to antagonize the effect of warfarin in the coming days, but this does not reverse the effect of vitamin K antagonists immediately.

PPIs are usually started empirically and continued until the source of bleeding is identified.

Red blood cell transfusions are usually given to maintain haemoglobin > 7 g/dL, but in this patient with prior history of CABG, a threshold of 8 g/dL may be considered.[4]

The platelet count in this patient was only very mildly lowered, which in itself is not expected to pose an increased risk of bleeding. However his low-dose aspirin treatment impairs platelet function, which can be corrected with platelet transfusions.

The clinical presentation with haematemesis is suggestive of a bleeding source proximal to the ligament of Treitz. Emergency upper endoscopy may be false-negative e.g. because the patient is hypotensive and bleeding stops, or because the bleeding source is obscured by massive blood; prokinetics could have been given before emergency endoscopy to enhance visualization. Patients without haematemesis may be investigated by colonoscopy or transvenous angiography for identification and source control of acute GI bleeding.

Case continued (part 3)

The patient was given crystalloids for volume resuscitation and admitted to the intensive care unit for red blood cell transfusion, immediate correction of coagulation with transfusion of platelets and fresh frozen plasma, and PPIs. His aspirin and vitamin K antagonist were discontinued and vitamin K was administered prophylactically to maintain reversal of his oral anticoagulant.

Repeat endoscopy the next day revealed oozing from fundal and oesophageal varices. The oesophageal varices were treated with ligation, and the patient became haemodynamically stable and required no more transfusions. A somatostatin drip and prophylactic ceftriaxone were administered.

Hepatitis B and C virus serology, antinuclear-, anti-smooth muscle- and anti-mitochondrial antibodies, α1-antitrypsin and ceruloplasmin were normal. Ultrasonography and computed tomography of the abdomen and magnetic resonance cholangiopancreatography showed emboligenic right kidney infarction but a normal liver, spleen (11 cm long), pancreas and portal veins.

Question set 3

1. What would be the most appropriate next investigation to determine the cause of this patient's oesophageal varices?

Short answer set 3

1. *What would be the most appropriate next investigation to determine the cause of this patient's oesophageal varices?*
   A transjugular liver biopsy and measurement of the portosystemic venous pressure gradient.

Long answer

Oesophageal varices are almost always due to cirrhosis. In this case however, biochemical and imaging findings do not indicate cirrhosis, suggesting non-cirrhotic portal hypertension. A liver biopsy can definitively exclude cirrhosis. When performed via the transjugular route, the portosystemic venous pressure gradient can be measured during the same session to confirm portal hypertension and whether or not it results from presinusoidal, sinusoidal or a post-sinusoidal cause.[5]

Case continued (part 4)

On transjugular catheterization, the hepatic venous pressure gradient was 17 mmHg (normal values <6 mmHg), and biopsy showed engorged sinusoids and signs of portal hypertension with normal parenchyma. Propranolol and enoxaparin were initiated. On two annual follow-up endoscopies, grade I varices were noted which required no further ligations.

Discussion

Variceal bleeding should be considered in the differential diagnosis of otherwise unexplained acute upper gastrointestinal bleeding, even in the absence of clinical or biochemical signs of cirrhosis. Insufflation can obscure moderate varices at initial or previous endoscopies, as can hypotension during haemorrhagic shock.

Portal hypertension is assessed by the hepatic venous pressure gradient (HVPG). An HVPG of 1 to 5 mmHg is normal. Portal hypertension is defined as HVPG ≥ 6 mmHg, but this usually only becomes clinically significant ≥ 10 mmHg when varices start developing. From 12 mmHg HVPG, ascites may develop and there appears to be a risk of variceal bleeding, while from 16 mmHg a risk of hepatic decompensation and mortality has been noted.[5] Other non-invasive measurements may qualitatively suggest portal hypertension e.g. portal vein duplex and ultrasound assessment of portal vein diameter, although formal quantification relies on invasive HVPG measurement.

Management of variceal bleeding

Haemodynamic resuscitation, correction of coagulation abnormalities, airway protection in case of active haematemesis, infection control (prophylactic quinolone or third-generation cephalosporin) and achieving haemostasis are the cornerstone of variceal bleeding management.[6]

The first step is to initiate pharmacological therapy to reduce portal venous pressure, usually terlipressin (a vasopressin analogue) or octreotide (a somatostatin analogue). As a group, these drugs reduce mortality, improve haemostasis and shortened duration of hospitalisation in patients with variceal bleeding but only terlipressin individually has demonstrated significant survival benefit.[7][8] Pharmacotherapy should be started early when variceal bleeding is suspected and should not be delayed until after endoscopic confirmation of the diagnosis of variceal bleeding. In our patient we used short-acting somatostatin in a continuous infusion due to availability in our hospital at that time.

Gastro-oesophageal endoscopy can confirm the diagnosis and allow haemostasis. Variceal ligation (banding of the varices) is the standard of care but sclerotherapy (injection of foam to occlude blood flow within the varices) is an alternative, which may be useful for gastric varices.[9][6] Balloon tamponade e.g. using the Sengstaken-Blakemore balloon can allow temporary or salvage bleeding control, but there are several possible complications and a high risk of rebleeding after balloon deflation.[6] Transjugular intrahepatic portosystemic shunt (TIPS) placement or surgery are effective second-line therapies after failure of endoscopic haemostasis, but surgery carries a far greater mortality risk.[10] Even if initial endoscopy successfully stops the variceal bleeding, early TIPS should be considered in patients at high risk of treatment failure.[11]

For further details, we refer to several recent international recommendations for the management of variceal bleeding.[6][12][13]

Noncirrhotic portal hypertension

Noncirrhotic portal hypertension can result from prehepatic, posthepatic (inferior vena cava obstruction or cardiac disease) or intrahepatic causes.[14] Hepatic causes can be further subdivided into presinusoidal, sinusoidal or postsinusoidal causes (**Table 2**).

	Conditions associated with non-cirrhotic portal hypertension
Prehepatic causes	Portal or splenic vein thrombosis
	Arteriovenous fistula
	Splenomegaly (due to increased portal blood flow)
Hepatic causes	Primary biliary cirrhosis
	Primary sclerosing cholangitis
	Chronic pancreatitis
	Hereditary haemorrhagic telangiectasia
	Schistosomiasis
	Congenital hepatic fibrosis
	Nodular regenerative hyperplasia
	Fibrosis of space of Disse
	Granulomatous or infiltrative liver diseases (Gaucher's disease, mucopolysaccharidosis, sarcoidosis, lymphoproliferative malignancies, amyloid deposition, ...)
	Toxicity (from arsenic, copper, vinyl chloride monomers, mineral oil, vitamin A, azathioprine, dacarbazine, methotrexate, amiodarone, ...)
	Viral hepatitis
	Fatty liver disease
	Veno-occlusive disease
	Budd-Chiari syndrome
Posthepatic causes	Inferior vena cava obstruction
	(Right-sided) heart failure
	Hepatic vein thrombosis

Table 2 | Conditions associated with non-cirrhotic portal hypertension

Proposed criteria for *idiopathic* noncirrhotic portal hypertension include the absence of the aforementioned conditions or other causes of chronic liver diseases, cirrhosis on biopsy, or portal or hepatic vein thrombosis.[14]

Variceal haemorrhage and ascites are the commonest presentations, and underlying disorders or the development of complications including ascites, bleeding or portal vein thrombosis may negatively affect survival.[15][16]

Chronic lymphocytic leukaemia (CLL) is not uncommon in elderly subjects and does not require specific therapy unless it causes symptoms e.g. from secondary cytopenia, B symptoms, splenomegaly or when there is a rapid increase in lymphocyte counts. CLL has been associated with idiopathic non-cirrhotic portal hypertension, ascites and hepatorenal syndrome although the incidence of portal hypertension in patients with CLL as well as any causal relationship or the benefit of haematological treatment remains uncertain.[14][17][18]

Different pathophysiological factors have been suggested including lymphocytic hepatosplenic infiltration (which was absent in this case), increased spleno-portal blood flow, thrombosis of terminal portal vein branches, reactive fibrosis, nodular regenerative hyperplasia or veno-occlusive disease.[14][17][18] Splenectomy may ameliorate portal hypertension in cases with increased splenic blood flow. Anticoagulation has been proposed by some and is recommended in cases of portal vein thrombosis or underlying thrombophilia, but may increase the risk of bleeding.

Our case report reminds physicians to consider the possibility of portal hypertension or its complications (including variceal bleeding, ascites or otherwise unexplained thrombocytopenia) in patients with suggestive symptoms even if they do not have cirrhosis, especially in the presence of potential causes of non-cirrhotic portal hypertension.

Final diagnosis

Variceal bleeding due to idiopathic non-cirrhotic portal hypertension, possibly associated with chronic lymphocytic leukemia.

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