

## Efficacy of a somatostatin analogue in a case of obscure gastrointestinal bleeding

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### Abstract

Gastrointestinal bleeding can have many reasons and therapy becomes tricky when the diagnostic workout is not conclusive. We describe the case of an 89 y.o. woman with severe anemia and gastrointestinal bleeding of an unknown origin after conventional imaging and endoscopic procedures, thus averting endoscopic, angiographic or surgical approach. This condition required 39 blood transfusions in 2 months. Subcutaneous Octreotide, reducing gastrointestinal mucosal perfusion, achieved hemodynamic stability, improved blood cell count, and ended the blood transfusions. The use of somatostatin analogues can be considered in refractory patients with digestive bleedings of an unknown origin not susceptible of first line therapy.

**Keywords:** Obscure gastrointestinal bleeding; Octreotide; Anemia; Blood transfusion; Somatostatin.

### Introduction

Obscure Gastrointestinal (GI) bleeding, defined as bleeding of an unknown origin after evaluation with standard bidirectional endoscopy, represents around 5% of all GI hemorrhages. It is defined as “overt” if bleeding is detectable (hematemesis, melena, hematochezia) or as “occult” when presenting signs are occult blood in stools and/or iron-deficiency anemia [1]. GI vascular malformations are responsible for 30-40% of all obscure hemorrhages, especially in the elderly. Other common causes are non-steroidal anti-inflammatory drug-induced ulcers, cancer and inflammatory lesions. These conditions usually induce chronic self-limiting bleeding in 50% of cases, requiring iron supplementation in 20%, with only 3% needing blood transfusions [2]. If significant anemia or brisk bleeding occurs, localization and targeted treatment of the bleeding source are mandatory. Video Capsule Endoscopy (VCE), Computed Tomographic Enterography (CTE), Technetium <sup>99m</sup>-labeled (<sup>99m</sup>Tc) Red Blood Cell (RBC) scintigraphy (plus angiography if hemo-

dynamic instability) represent workup's gold standard, followed by deep (balloon-assisted) enteroscopy. High mortality usually limits surgical approach in these patients. Technical (small lesions, intermittent bleeding) or clinical (age and comorbidities) reasons can hinder diagnosis and treatment, these cases also have high re-bleeding risk. Moreover, age, valvular disease, chronic renal disease worsen the prognosis of these patients. Current guidelines suggest the use of somatostatin for refractory patients with an identified source of bleeding, but there is not any consensus concerning the management of obscure GI bleedings.

## Case Report

E.P., an 89 y. o. woman living in a nursing home, was admitted to the internal medicine department for growing prostration and recently diagnosed with severe anemia. The patient did not recall obvious bleeding, melena, hematuria, recent trauma, invasive procedures and did not start new drugs interfering with blood coagulation. Past medical history reports paroxysmal atrial fibrillation, severe aortic stenosis, complicated hypertension, peripheral arterial disease, and diverticulosis. She was taking lansoprazole, losartan, furosemide and aspirin. At admission she was pale, with 88 bpm, 16 breathing acts/min, blood pressure of 120/80 mm/Hg, and melena at rectal examination. The most significant laboratory tests are reported in Table 1. Normal neuron-specific enolase and cromogranina A plasma levels ruled out neuroendocrine neoplasm.

Bidirectional GI endoscopy was not diagnostic, CTE showed intramucosal ectasia in the jejunum. <sup>99m</sup>Tc-RBC scintigraphy documented active jejunal bleeding (Figure 1). VCE confirmed the bleeding but did not identify neither the precise site (roughly located in left upper quadrant) nor the culprit lesion(s).

Even during an episode of brisk overt bleeding, angio-TC and arteriography did not recognize the source of active bleeding, therefore deterring embolization.

Empirical therapy, started at admission, encompassed intravenous proton-pump inhibitors (i.v. PPIs), tranexamic acid, vitamin B12, and folates, while aspirin was suspended. On average, the patient received one transfusion of red cell concentrates every other day, without effects on hemoglobin levels (mean level 7,1 g/dL after 35 units, see Figure 2).

During admission, an episode of a fever of an unknown origin (38°C) with chills was effectively treated with Piperacillin-Tazobactam 4,5 gr TID (blood cultures grew *Leclercia Adecarboxylata*) and a superficial thrombosis originated from a midline venous catheter in the right arm was successfully treated with local medication. Anticoagulation therapy was not considered, due to active bleeding.

The lack of a precise diagnosis (and indications for surgical treatment) left medical approach as the only option for an active and severe small bowel bleeding. The therapy was then implemented with Octreotide (starting dose 0.05 mg s.c. BID and then 0.1 mg s.c. TID for 18 days). After around 10 days of administration, the bleeding ended, hemoglobin rose well over 7 gr/dL and blood transfusion ended.

The time course of hemoglobin values and the number of blood transfusions are reported in Figure 2.

The only side effect was occasional mild nausea not requiring specific treatment. Blood glucose and liver enzymes remained normal throughout the whole admission, and no acute or chronic adverse reactions to blood transfusion have been noticed. At discharge, after 78 days, hemoglobin level was 9.0 g/dL and prescription was of subcutaneous Long-Acting Release (LAR) octreotide 20 mg/monthly for about 6 months and regular hemoglobin checks [4]. At 1 month from discharge the patient is still in good clinical conditions, with the hemoglobin level at 9.8 g/dL.

**Table 1:** Laboratory tests at admission discharge and follow up after 1 month from discharge.

	Admission	Discharge	Follow up
Hb (gr/dL)	4.5	7,9	9.8
Erythrocytes (x10 <sup>6</sup> /μL)	1.34	2.55	3.06
Ht (%)	14.7	25	31.4
MCV (ft)	106	98	102
MCH (pg)	33.6	30	32
Platelets (x10 <sup>3</sup> /μL)	308	333	344
INR	1.08	1.03	
aPTT (sec)		27.4	
Bilirubin total (mg/dL)	0.35	0.78	

## Discussion

In gastroenterology, somatostatin analogues use is limited to the treatment of refractory gastroesophageal variceal bleeding following portal hypertension. They reduce hydrochloric acid and pepsin output in the stomach, reduce splanchnic blood flow, increase vascular resistance and improves platelet agreeability [2,3], thus being potentially useful in untreatable small bowel bleeding. Our patient presented overt active GI bleeding (likely an angiodysplasia in small bowel) but without a definite diagnosis and indication for surgical or endoscopic treatment. Despite the hemodynamic stability, low hemoglobin values and persistent melena required frequent blood transfusions and strict clinical observation. Octreotide interrupted the bleeding, improved the clinical conditions and made possible to discharge the patient. Octreotide duration and dosage were chosen based on the largest retrospective study with longer follow up [4].

Usually, these patients undergo further investigations, blood transfusions and related complications, (transfusion-transmitted infections, overload of volume and iron, hospital-acquired infections) than patients with treatable GI bleeding [4]. It results in longer hospitalization and higher healthcare costs without a real improvement of the long-term outcome.

Despite several studies demonstrating the efficacy of octreotide in the management of difficult-to-treat GI bleeding, guidelines are unclear. To date, it is prescribed as an off-label drug for these conditions and currently there is not a “standard” treatment protocol because of the small number of patients enrolled, with wide differences in dosages and durations of therapy, short-term follow-up and different end-points

adopted to evaluate the efficacy of treatment [2].

Octreotide can be considered as an alternative therapeutic strategy because of its manageability, efficacy and modest adverse effects and because it may reduce risks and costs related to blood transfusions and prolonged hospitalization.

The diagnosis of intestinal angiodysplasia has been enhanced through the implementation of new radiological diagnostic techniques, and currently, optimal therapy involves endoscopy with argon plasma coagulation. However, this procedure is limited and challenging to apply in frail patients and in settings with limited resources (i.e., requiring high expertise and availability of anesthesiological support). In such cases, the use of octreotide as a second-line therapy may be beneficial due to its widespread availability and high safety profile.

## Declarations

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All authors contributed equally to manuscript creation and G.B. is the guarantor of the Study.

**Conflict of interest:** None declared.

Patient consent was obtained for publication of the case details.

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