High Dose Oestrogen in Life Threatening Obscure Gastrointestinal Bleeding

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ABSTRACT

Obscure gastrointestinal bleeding is defined as recurrent or persistent gastrointestinal bleeding in the setting of normal upper and lower endoscopies. There are reported use of numerous pharmacological agents to halt the bleeding, including oestrogen. We report a case of middle age gentleman with multiple comorbidities, presented with life threatening gastrointestinal bleeding. He underwent bidirectional endoscopies and mesenteric angiogram, but failed to localise the bleeding. Red blood cell scintigraphy showed numerous bleeding points in small and large bowels. A 5-day oral high dose oestrogen was prescribed in view of difficulty to manage the bleeding, in which the hemostasis was ultimately achieved.

***Keywords*:** *Angiodysplasia, hormonal therapy, oestrogen, obscure gastrointestinal bleeding.*

INTRODUCTION

Obscure gastrointestinal bleeding (OGIB) is defined as recurrent or persistent gastrointestinal bleeding in the setting of normal upper and lower endoscopies. It can manifest as overt bleeding with visible passage of blood or occult bleeding which manifest as iron deficiency anaemia or positive faecal occult blood test.[1] It usually arises from small bowel with varying nature, ranging from angiodysplasia, Dieulafoy lesion to Meckel's diverticulum. Despite the advancement of small bowel endoscopy and video capsule endoscopy, 25% of patients may still have unidentifiable source of bleeding.[1] Besides, despite identification of source of bleeding, some of these patients may not be amenable for therapeutic endoscopic or surgical intervention due to severe comorbidities. In this group of patients, medical therapy may be considered to ameliorate the bleeding.

CASE ILLUSTRATION

A 63-year-old gentleman presented to us with a 3 days history of haematemesis and melaena. He was on double antiplatelet agents from recent myocardial infarction and coronary angioplasty. Other comorbidities included end stage renal failure, hypertension, dyslipidemia, and non-cirrhotic chronic hepatitis C. On examination, vital signs were unremarkable and per rectal examination revealed stale melaena. Laboratory investigations showed haemoglobin of 7.4 g/dL and platelet of 220 x 10^9/L, with normal coagulation profile.

Antiplatelet agents were withheld, and he was started on intravenous bolus esomeprazole 80mg followed by 8mg/hour infusion. Two units red blood cells were transfused. Oesophagogastroduodenoscopy (OGD) showed Forrest 2c ulcer at prepyloric region, however no varices and active bleeding was seen. On

the next day, he still passing out melaena. Repeated OGD was unremarkable. Subsequent computed tomography of mesenteric angiogram (CTA) failed to show any evidence of arterial bleeding. Colonoscopy was performed and showed oedematous ileocaecal valve with right sided diverticulosis, without active bleeding. Intubation into the terminal ileum was failed due to the oedema. Video capsule endoscopy was deemed not feasible due to concern of trapped capsule.

He was managed conservatively with blood transfusion until the day 7 of admission, when he developed another melaena with hypovolemic shock, requiring fluid/blood resuscitation and vasopressor. After initial stabilization, CTA was repeated but reported as unremarkable. Thus, he underwent a Tc-^{99m}-red blood cell scan which eventually showed multiple bleeding sites arising from the distal duodenum, proximal jejunum and colonic hepatic flexure. Deep push enteroscopy was performed on the same occasion, but only showed pooling of blood, with no source of active bleeding. Surgical opinion was sought but he was deemed unsuitable for any surgical intervention due to poor functional cardiac status.

In view of ongoing bleeding episode, he was started on high dose oral conjugated oestrogen 12.5 mg daily for 5 days after counselled on possible thrombotic risk with no further antiplatelet therapy. After the initiation of oestrogen, he had no more bleeding episode, and haemoglobin remained stable with no further blood transfusion requirement. He was discharged well with haemoglobin of 10.5 g/dL. Up to 150 days after initiation of oestrogen, no further bleeding episode or thrombotic event was noted.

DISCUSSION

Hormonal therapy was initially explored by Harrison in 1982 after observing few case series of epistasis improvement in patients with HHT during pregnancy and puerperium.[2] The mechanism of action of hormonal therapy is not well understood. Oestrogen and progesterone receptors have been detected in telangiectatic lesions in patients with hereditary haemorrhagic telangiectasia (HHT), and the hormone-receptor binding improved endothelial integrity in patients with HHT. In animal model, oestrogen was found to improve the vascular stasis within the mesenteric microcirculation and decreased mucosal blood flow. In patients on hemodialysis, oestrogens shorten bleeding time by the reduction of endothelial prostacyclin production.[3]

Hormonal therapy has been reported in several case reports and controlled/uncontrolled studies of gastrointestinal angiodysplasias or OGIB.[4-6] The results, however, were conflicting. In a study of 43 patients with OGIB who were treated with hormonal therapy, rebleeding was effectively stopped in 38 patients (follow-up of a mean time of 535 days).[7] However, two controlled studies on angiodysplasia bleeding did not demonstrate any benefit. Both studies had small number of sample and with lower dose of oestrogen used. This discrepancy suggest that dosing of oestrogen may play a role.[8,9]

Overall, the effectiveness of hormonal therapy remains unclear, except for the treatment of HHT, von Willebrand disease, chronic kidney failure and gastric antral vascular ectasia.[10] Its utilization in OGIB should be of last therapeutic resort. The treatment with oestrogen is not without risk, which includes thrombosis, gynecomastia, breast tenderness, fluid retention, heart failure, and vaginal bleeding in females.[7] In our patient, he had achieved hemostasis despite having multiple bleeding sites after 5 days of high dose conjugated oestrogen. Spontaneous resolution of the bleeding could be argued due to the cessation of antiplatelet. However, in this gentleman, he still experienced OGIB despite the antiplatelet therapy being stopped for more than 9 days.

CONCLUSION

Despite lack of convincing clinical data, we believe that hormonal therapy especially oestrogen at higher dose, remains one of the pharmacological therapy options in patient with difficult to manage OGIB.

CONFLICT OF INTEREST

Authors declare there is no conflict of interest.

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