

## Successful Treatment of Massive Refractory Gastrointestinal Bleeding Caused by Angiodysplasia with Estrogen-Progesterone Therapy

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### Abstract

We report a case of a 64-year-old male who was admitted with massive gastrointestinal tract (GIT) bleeding secondary to angiodysplasia. Surgery (subtotal colectomy and end ileostomy) failed to control the bleeding. Bleeding continued despite blood products, octreotide and Factor seven administration. He was treated with topical oestrogen patch after which bleeding abated and no further blood products were required. We aim to highlight the rarely utilized role of oestrogen in the control of bleeding due to angiodysplasia.

**Keywords:** *GIT Bleeding; Oestrogen Patch; Angiodysplasia*

### Introduction

Upper gastrointestinal tract (GIT) bleeding is a medical emergency that can result in severe morbidity and mortality. It can present with hematemesis, melena or hematochezia. Angiodysplasia is the commonest vascular anomaly of the GIT [1]. It can be inherited or acquired. Endoscopy is the main tool for diagnosis [2] but it was non-diagnostic in our patient. Angiodysplasia is traditionally treated by Endoscopic Argon plasma coagulation (APC) [3]. It is an uncommon cause of occult and overt upper GIT bleeding [2].

### Case History

A 64 year old gentleman presented to the emergency department with a three day history of recurrent episodes of hematemesis, melena, abdominal pain and fatigue. He complained of central abdominal pain that was dull, severe and worsened by movement. He was a smoker with a twelve-pack year history. He had a background history of peripheral arterial disease, chronic obstructive airway disease, asbestosis and dyslipidaemia. He had a good functional status prior to admission.

### Physical examination

On presentation, he was conscious, alert and oriented to time place and person. He was pale with a BP of 110/60 mmHg, sinus tachycardia (120 bpm) and was afebrile. Oxygen saturation (SpO<sub>2</sub>) was 96% with supplemental oxygen. Respiratory rate was 18 breath/minute. Cardiovascular exam was normal. He had occasional bilateral sonorous rhonchi with equal air entry on chest auscultation. He had a tender abdomen, with no guarding or rigidity and no organomegaly or ascites.

### Laboratory examination

HB 6.8 g/dl with a platelet count of 126,000 and a reticulocyte count of 65%. Coagulation profile was normal. Blood film was consistent with anaemia.

C-reactive protein, Urea and electrolytes, liver and renal function tests were within normal limits. There were no new changes in his CXR.

### Hospital course

The patient was admitted to the intensive care unit. An oesophago-gastroduodenoscopy (OGD) showed gastritis and two non bleeding small duodenal ulcers. He was treated with proton pump inhibitor (PPI) infusion and empiric triple therapy (metronidazole, clarithromycin and amoxicillin). CT thorax, abdomen and pelvis (TAP) showed mural thickening of proximal jejunum. Following a further drop in Hb, OGD and colonoscopy was repeated. The duodenal ulcer was treated with endoclot and adrenaline injection. The patient continued to have persistent hematochezia with evidence of hypovolaemic shock despite massive blood and fluid resuscitation. He received a total of 41 units of RBCs, 26 units of Octaplex, 11 grams of fibrinogen and 1g Tranexamic acid TDS. A third OGD failed to reveal a source of bleeding. The patient was unstable requiring vasopressors and requiring ongoing resuscitation to maintain a MAP of 65 mmhg. Patient was transferred to our hospital for further care. Repeated CT angiogram failed to show a source of bleeding. The patient underwent a repeat colonoscopy, exploratory laparotomy, subtotal colectomy and end ileostomy. Intra-operatively, the patient had 3 units of RCC to maintain HB target above 7 g/dl.

Despite having a subtotal colectomy, he continued to have GIT bleeding postoperatively which manifested as hematemesis, melaena, hematochezia and bleeding via the stoma. He remained on IPPV. Factor VII, Octreotide, DDAVP (Desmopressin), prothrombin complex concentrate and PPI infusion were administered to stem the bleeding without success. Despite normal inflammatory markers and normal colonoscopy, 1000mg of methylprednisolone was administered in the case of occult inflammatory bowel disease. Consideration for repeat laparotomy was given but considered futile by the surgical team. In a last effort, a 17-beta estradiol 0.625 mg patch was applied to his abdomen. Over the following 24 hours, the bleeding abated and he did not require further blood transfusion. Subsequent histology of the colon demonstrated angiodysplasia.

### Discussion

We present a case of massive sustained upper GIT bleeding leading to hemorrhagic shock. The patient required massive transfusion of blood products in order to compensate for daily losses. Despite multiple diagnostic and therapeutic interventions, cause and source of the upper GIT bleeding was not identified. Despite a subtotal colectomy, ongoing transfusion, correction of clotting factor and octreotide, massive GIT bleeding continued until a 17-beta estradiol 0.625 mg patch was applied to his abdomen. Following oestrogen treatment, Hb remained within the range of 7.7 to 9.5 g/dl without the need for further blood transfusion. Throughout his entire hospital course, platelets number and coagulation profile were normal. His ICU course was complicated by respiratory sepsis, ICU myopathy and delirium. He required a tracheostomy after a failed trial of extubation but was liberated from mechanical ventilation after 3 weeks and returned to his baseline from a respiratory perspective. At 1 month post discharge from ICU he had not had any further bleeding and was discharged home.

The prevalence of angiodysplasia in the population is not known. More than half of patients with angiodysplasia have diverticulosis. The prevalence of angiodysplasia is increased in patients with end-stage renal disease, von Willebrand disease, aortic stenosis and in the presence of a Left ventricular assist device [2]. Which were not present in our patient.

Colonic angiodysplasia is more common in the right colon. The distribution of lesions is: Cecum 37%, ascending colon 17%, transverse colon 7%, descending colon 7%, sigmoid colon 18% and rectum 14%. Although the sensitivity of colonoscopy is more than 80% for the diagnosis of colonic angiodysplasia, it can be missed during endoscopy depending on operator skills, visibility and the size and location of the lesions, (e.g. if located behind mucosal folds) [4]. It may be misdiagnosed as an area of inflammation or trauma. Therefore, it is recommended to repeat the examinations in doubtful cases or with a suboptimal study [4]. CT or MRI is another tool used to diagnose angiodysplasia with a sensitivity 70% and specificity 100% [5]. Retrospective studies showed that haemorrhage is intermittent in most

cases with a recurrence rate up to 50% of patients within 3 years after the first episode of bleeding [6].

There are several endoscopic treatment options for bleeding angiodysplasia (Argon plasma coagulation, electrocoagulation, mechanical hemostasis). Surgical resection is definitive therapy for specific bleeding areas. The incidence of rebleeding in patients post right hemicolectomy for bleeding angiodysplasia is high. Rebleeding may be due to incomplete resection or occult lesions. More than 50% of patients have recurrent bleeding after surgery or endoscopic treatment. In these cases, medical treatment with hormonal therapy can be considered, including cessation of anticoagulants where appropriate, octreotide and in the case of refractory disease, oestrogen therapy.

### Hormonal therapy

Between 1990-2001, there were five studies evaluating the efficacy of oestrogen in the treatment of adult patients with GIT bleeding requiring transfusion and endoscopically confirmed sporadic angiodysplasia [7]. The commonest outcomes were a decrease in bleeding episodes and transfusion requirement. Evidence from three uncontrolled and retrospective studies suggested an advantage to hormonal therapy [8]. Several case reports suggested that oestrogen therapy is useful in the prevention of recurrent bleeding from gastrointestinal angiodysplasia [9]. A crossover study of 43 patients found a benefit in patients with bleeding from sporadic angiodysplasia [8]. Octreotide (given subcutaneously at a dose of 50 to 100 mcg BD) as a treatment of angiodysplasia has been evaluated in case reports. A response has been noted in some patients [10].

### Conclusion

Angiodysplasia may cause massive upper and lower GIT bleeding leading to hemorrhagic shock. Angiodysplasia can be difficult to diagnose either by colonoscopy or angiography. Oestrogen treatment was started in our patient as all other treatment modalities had failed. Despite negative randomized controlled trials comparing oestrogen therapy and placebo in patients with chronic bleeding from angiodysplasia, there may still be a role for its use in acute cases where all other treatment modalities have failed. Oestrogen therapy is a useful tool in the armamentarium for the management of refractory bleeding secondary to angiodysplasia. Patient can have excellent outcomes despite major prolonged severe bleeding with massive blood transfusion.

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### Competing Interests

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