

Angiodysplasia of Colon or GI Tract

Background

Phillips first described a vascular (blood vessel) abnormality that caused bleeding from the large bowel in a letter to the *London Medical Gazette* in 1839. During the 1920s, cancers were considered the major source of GI bleeding/hemorrhage. However, in the 1940s and 1950s, diverticular disease was recognized as an important source of bleeding. In 1951, Smith described active bleeding from a diverticulum visualized through a sigmoidoscope.

Galdabini first used the name angiodysplasia in 1974; however, confusion about the exact nature of these lesions resulted in a multitude of terms that included **AVM = arteriovenous malformation**, **hemangioma**, **telangiectasia**, and **vascular ectasia**. These terms have varying pathophysiologies, with a common presentation of GI bleeding and may be *used interchangeably* by many physicians.

Angiodysplasia is a **degenerative lesion of previously healthy blood vessels** found **most** commonly in the **right-side of colon**. 77% of angiodysplasias are located in the cecum and ascending colon, **15%** are located in the **jejunum and ileum (small intestine)**, and the remainder are distributed throughout the GI tract. These lesions typically are nonpalpable and **small** (<5 mm).

Angiodysplasia is the most common vascular abnormality of the GI tract. After diverticulosis, it is the second leading cause of lower GI bleeding in patients older than 60 years. Angiodysplasia may account for approximately 6% of cases of lower GI bleeding. It may be observed *incidentally* at colonoscopy in as many as 0.8% of patients older than 50 years. The prevalence for upper GI lesions is approximately 1-2%. Small bowel angiodysplasia may account for 30-40% of cases of GI bleeding of obscure origin.

Angiodysplasia may present as an isolated lesion or as multiple vascular lesions. Unlike congenital or neoplastic vascular lesions of the GI tract, this lesion is not associated with angiomatous lesions of the skin or other viscera.

Clinical presentation is usually characterized by maroon-colored stool, **melena** = black tarry stool, or **hematochezia** = bright red rectal bleeding. Bleeding is usually low grade but can be massive in approximately 15% of patients. In 20-25% of episodes, only tarry stools are passed. **Iron deficiency anemia** and stools that are intermittently positive for occult blood can be the only manifestations of angiodysplasia in 10-15% of patients. **Bleeding stops spontaneously in over 90%** of cases but is **often recurrent**.

Pathophysiology

The **exact mechanism** of development of angiodysplasia is **not known**. One prominent hypothesis accounts for the high prevalence of these lesions in the right colon and is based on the Laplace law. The Laplace law relates wall tension to luminal size and transmural pressure difference in a cylinder whereby the wall tension is equal to the pressure difference multiplied by the radius of the cylinder. In the case of the colon, wall tension refers to intramural tension, pressure difference is that between the bowel lumen and the peritoneal cavity, and cylinder radius is the radius of the right colon. Wall tension is highest in bowel segments with the greatest diameter, such as the right colon.

This theory suggests that repeated episodes of colonic distention are associated with transient increases in lumen pressure and size. This results in multiple episodes of increasing wall tension with obstruction of submucosal venous outflow, especially where these vessels pierce the smooth muscle layers of the colon. Over many years, this process causes gradual dilation of the submucosal veins and, eventually, dilation of the venules and arteriolar capillary units feeding them. Ultimately, the capillary rings dilate, the precapillary sphincters lose their competency, and a small arteriovenous communication forms. This accounts for the characteristic early-filling vein observed during mesenteric angiography. The developmental theory of angiodysplasia accounts for several clinical and pathologic features, including occurrence in older individuals, location in the cecum and proximal right colon, and prominent submucosal veins that dilate after traversing the muscularis propria.

Of note, the aforementioned pathophysiological mechanisms responsible for the development of cecal lesions are unlikely to apply to lesions in the upper GI tract, despite being morphologically identical.

Frequency The prevalence of angiodysplasia is **0.8% in healthy patients older than 50 years** who are undergoing screening colonoscopy. Patients with von Willebrand disease may have an increased incidence of gastrointestinal bleeding from colonic angiodysplasia.

Mortality/Morbidity

Bleeding from angiodysplasia **usually is self-limited**, but it can be chronic, recurrent, or even acute and life threatening. About 90% of bleeding angiodysplasias spontaneously cease bleeding. Death is related to the severity of bleeding, hemodynamic instability, age, and the presence of comorbid medical conditions.

Age Most patients found to have angiodysplasia are older than 60 years; of these patients, most are older than 70 years. However, case reports exist of occurrence in young people. It occurs with equal frequency in men and women and all races

CLINICAL

History

Many patients with angiodysplasia lack symptoms. Others present with **GI bleeding or its consequences**.

- The incidence of active GI bleed in patients with angiodysplasia is less than 10%. However, because these lesions may be located throughout the GI tract and because the rate of bleeding may be variable, presentation ranges from bloody vomiting or rectal bleeding to occult iron deficiency **anemia**. Bleeding is **usually chronic or recurrent** and, in most cases, low grade and **painless** because of the venous source.
- GI bleeding from **small bowel** lesions has occurred in as many as 22% of patients. In 50% of patients with **gastric/stomach and duodenal** angiodysplasia have multiple lesions / EGD with colon lesions associated in 20%. Lesions in the colon are more frequently multiple than single.
- Bloody vomit frequently is observed in patients with angiodysplasia of the upper GI tract. Presentation with low grade chronic bleeding is typical and may have had bleeding from days to years.
- Bleeding from **colon** lesions most often is chronic and low grade, but as many as **15%** of patients present with **acute massive** hemorrhage. Patients may present with rectal bleeding (0-60%), melena (passing black tarry bloody stool) (0-26%), occult blood positive stool (4-47%), or iron deficiency anemia (0-51%).
- **Spontaneous cessation** of bleeding (90%) is the rule for lesions located in any part of the GI tract.

Causes

The exact cause is **unknown**, but theories include the following:

- **Degenerative changes** of small blood vessels associated **with aging** (most widely accepted theory)
- Long-term local low-oxygenation of the microcirculation from heart, vascular, or lung disease
- Angiodysplasia has been reported to be associated with aortic stenosis. Heyde first reported this association in 1958, describing Heyde syndrome as the combination of calcific aortic stenosis and GI bleeding due to angiodysplasia of the colon.¹ Subsequent critiques of the literature by Imperiale and Ransohoff found a lack of conclusive evidence to support the association of aortic stenosis, angiodysplasia, and GI bleeding.⁵ However, case reports describe cessation of bleeding after aortic valve replacement in severe aortic stenosis or after correction of heart failure in hypertrophic subaortic stenosis.
- Bleeding angiodysplasias of upper GI tract found often in patients with **chronic renal failure** requiring **dialysis**; however, is not a consistent finding. Patients with chronic renal failure are more likely to have coagulopathies that are related to platelet defects and abnormal function and structure of **von Willebrand factor**.

WORKUP

Lab Studies

- **CBC** count: 10% of patients present with anemia.
- **Serum iron** level: Iron deficiency is found in 10% of patients with bleeding angiodysplasia.
- **Stool for occult blood**: Up to 15% with bleeding angiodysplasia are intermittently positive for occult blood.

Imaging Studies

- **Selective mesenteric angiography** is a useful diagnostic technique, especially in patients with massive bleeding in whom a colonoscopic diagnosis is difficult.

The sensitivity of angiography ranges from 58-86%. Detection of bleeding depends on the rate of bleeding (as low as 0.5 mL/min), technique, and timing of angiography in relation to period of bleeding.

- **Nuclear scans lack the specificity of an angiogram** in differentiating the nature of bleeding lesions, despite the fact that they are noninvasive and relatively easy to perform. Nuclear scans have proven more useful as an **adjunct to angiography** by localizing and **confirming the presence of bleeding**, minimizing the number of angiograms that do not yield meaningful diagnostic information, and allowing rapid selection of the artery to be injected by angiography. Confirm positive findings from a radionuclide study by colonoscopy or angiography if surgical resection is contemplated.

Procedures

- **Endoscopy** is the **most common** method of **diagnosing** angiodysplasia in both the upper and lower GI tract.
- Upper endoscopy is used to establish a diagnosis of gastric and duodenal angiodysplasia. Celiac artery and superior mesenteric artery **arteriograms** frequently fail to demonstrate these lesions. Angiography can

demonstrate lesions in the more distal small intestine, a region less accessible to endoscopic evaluation. Other methods of visually evaluating the small bowel are **double-balloon enteroscopy** and **capsule enteroscopy** are currently used in clinical practice.

- The **endoscopic appearance** of gastric/stomach lesions typically has been described as discrete, flat, or slightly raised (2-10 mm) and **bright red** in color. These lesions have **fernlike** margins or stellate configurations. Proximal small intestinal lesions are the size of a **pinpoint**, with a similar gross appearance.
- Either angiography or colonoscopy may be used to detect colonic lesions. Colonoscopy is the principal method in the evaluation of GI bleeding, diagnosis of these lesions often results from colonoscopic exam.
- Comparative studies using selective angiography and colonoscopy indicate that the sensitivity of colonoscopy exceeds 80% when the lesions are located in the area examined by colonoscopy. Most angiodysplastic lesions are located in the right colon, so the entire colon must be examined. Angiography has the advantage of detecting additional angiodysplastic lesions not depicted by colonoscopy. Angiography and colonoscopy can play important **complementary** roles.
- Skibba et al first described the **colonoscopic appearance** of angiodysplasia in 1976.⁹ Angiodysplasia often is described as discrete and small, with scalloped or frondlike edges and a visible draining vein. They can be flat or slightly raised and can be hidden within mucosal folds. Although angiodysplasia may be detected anywhere in the colon, a strong **propensity exists for the right colon**. The endoscopic appearance of angiodysplasia can be **confused with** the ectasias associated with systemic diseases, such as **hereditary hemorrhagic telangiectasia (HHT)**, **Turner syndrome**, and the **CREST** syndrome (calcinosis, Raynaud phenomenon, esophageal hypomotility, sclerodactyly, and telangiectasia). The lack of systemic manifestations distinguishes angiodysplasia from these syndromes.
- In addition, the endoscopic appearance of angiodysplasia may be difficult to **discern from spider angiomas due to cirrhosis, radiation injury, ulcerative colitis, Crohn's disease, ischemic colitis, and suction artifacts**. Evaluation of a patient who may have angiodysplasia requires that the colonoscope be inserted carefully, with minimal use of suction, and that the mucosa be examined more carefully as the instrument is advanced than during withdrawal. Obtaining biopsy of suspicious lesions may be necessary if classic features are not present.
- Because blood pressure and volume influence the colonoscopic appearance of vascular lesions, angiodysplasia may not be evident in patients who have **bled recently**. Accurate evaluation of the colon may not be possible until **effective fluid resuscitation and blood transfusions**.
- **Intraoperative enteroscopy** can help in localization of distal small bowel lesions. In addition, an angiographic catheter can be placed before surgery into the appropriate feeding vessel supplying the angiodysplastic lesion. The surgeon then can identify the catheter during surgery and explore and resect the appropriate small bowel segment.

TREATMENT

Medical Care Medically manage each patient in accordance with the severity of bleeding, hemodynamic stability, and recurrence of symptoms. A **conservative** approach to patients who are hemodynamically stable is recommended because most bleeding angiodysplasias will cease spontaneously. Treatment usually is *not advocated for asymptomatic* patients when angiodysplasias are *found incidentally*.

When intervention is warranted, institute steps to control bleeding. Endoscopic techniques have been employed most frequently.

Gastric and duodenal angiodysplastic lesions have been managed **most commonly with endoscopic obliteration** techniques. **Rebleeding** after these techniques has been attributed to other areas of bleeding angiodysplasia rather than failure of obliteration. These techniques include monopolar electrocautery, heater probe, sclerotherapy, band ligation, and argon and neodymium:yttrium-aluminum-garnet (Nd:YAG) lasers.

- Argon and Nd:YAG lasers are the most successful endoscopic oblitative techniques for upper tract lesions. **Argon beam coagulation/APC** is a no-touch electrocoagulation technique in which high-frequency alternating current is delivered to the tissue through ionized argon gas. A reduction in both the bleeding rate and transfusion requirement has been demonstrated for at least 12 months after laser therapy. Effectiveness appeared to be reduced in patients with more numerous lesions, those with coagulation disorders, and those who are older. Rebleeding commonly occurred over time.
- **Argon coagulation** appears the **best endoscopic option** at the moment to control bleeding in these patients with a low rate of adverse effects and complications and relatively lower costs.
- Fifty percent of patients with distal small bowel lesions and no other defined GI bleeding sites have benefited from enteroscopy and lesion obliteration. New endoscopic techniques to examine the small bowel, such as **double-balloon enteroscopy**, have been developed but are time demanding and operator dependent.
- Angiodysplasia of colonic origin has been managed by endoscopic obliteration. Heater probe and **multipolar electrocoagulation** probe have been more successful than monopolar electrocoagulation.

- Endoscopic laser photocoagulation has been successful in controlling bleeding from colonic angiodysplasia. However, **complications** occur in as many as 15% of patients, more common when the **Nd:YAG laser** is used in the right colon attributed to the deeper coagulation of the vascular abnormalities from laser sources, which incidentally has been responsible for more effective bleeding cessation. Patients with colonic angiodysplasia generally have a 60% chance of remaining free of bleeding at 24 months after laser obliteration.
- **Endoclips** have been used in anecdotal case reports for bleeding angiodysplasia of the cecum and right colon.
- Angiodysplasia that presents with acute bleeding can be controlled effectively with angiography, although it seldom is needed. **Angiography** is appropriate in severely ill patients who are not candidates for surgical intervention. In these patients, **transcatheter embolization** of selected mesenteric arteries has been quite effective. However, the rate of complications is still high and must be balanced against the risk of surgical resection.
- Selective infusion of **vasopressin** is less effective than embolization as a definitive therapy because of a high rebleeding rate. Despite the fact that intra-arterial vasopressin can achieve hemostasis for massive lower GI bleeding in 70-91% of patients, bleeding recurs after discontinuation of vasopressin in 22-71% of patients.
- Angiography plays a more important role in **preoperative** localization of small bowel lesions immediately before surgical resection because intraoperative palpation, endoscopy, and visual inspection through multiple enterotomies are of little value with angiodysplasia.

Surgical Care

Surgical resection is the definitive treatment.

- Partial or complete gastrectomy/stomach removal for management of stomach angiodysplasia was followed by bleeding in as many as 50% of patients. Rebleeding was attributed to other angiodysplastic lesions.
- **Right colon resection** for angiodysplasia is **second-line therapy after endoscopic ablation**, if repeated endoscopic coagulation has failed, if endoscopic therapies are not available, and for life-threatening bleeding.
- The **mortality rate** associated with **surgical** resection ranges from **10-50%**. This is based on the view that surgery carries a much higher risk in elderly patients who often have multiple coexisting medical problems, including coronary artery disease, coagulopathy, and renal and pulmonary dysfunction.
- Surgical resection is preferred for acute management of severe hemorrhage or for management of recurrent hemorrhage over a relatively short period accompanied by a large transfusion requirement..

Diet Withhold oral intake until diagnosis has been made and treatment has been initiated.

Medical treatment has been used in active and recurrent bleeding from colonic angiodysplasia with controversial results. **Hormonal** treatment with estrogen and progesterone has been evaluated by randomized trials but remains controversial and is probably not effective. Octreotide, both short and long acting, has been described effective in few case reports and case series only. Other agents, such as thalidomide, remain experimental. DDAVP has also been used in specific subsets of patients.

At the moment, **no medical therapy** has been **proven** to effectively treat bleeding from angiodysplasia, **however**, if possible one should **avoid aspirin** (as well as **Plavix**) and **NSAIDs** (anti-inflammatory arthritis medicines) which can trigger bleeding from these fragile angiodysplasia blood vessels. NSAIDs include: ibuprofen/Advil, Aleve/naproxen, Celebrex/celecoxib, Mobic/meloxicam, diclofenac, Relafen/nabumetone, Clinoril/sulindac, Toradol/Ketoprofen... and are in many OTC (over-the-counter) remedies for pain, headache, sinus, colds. **Avoid** Garlic, Ginseng, Gingko biloba, Vitamin E, Co-Q10, and Dong Quai, which increase risk of bleeding in patients on warfarin, aspirin or Plavix/clopidogrel.

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