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# Review on gastrointestinal angiodysplasia throughout the gastrointestinal tract

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A B S T R A C T

Gastrointestinal angiodysplasia are rare but clinically important vascular aberrations found within the gastrointestinal mucosa and submucosa. Their clinical impact varies from being an asymptomatic incidental finding, to causing life threatening bleeding. In this review we critically appraise the key findings from the current literature on the pathology, clinical presentation and management of these lesions.



## Introduction

Gastrointestinal (GI) Angiodysplastic (AD) lesions are pathological communications between dilated mucosal capillaries and submucosal veins. Interchangeably known as angioectasias, vascular ectasias or arterio-venous malformations, these lesions account for the majority of diagnosed vascular lesions of the GI tract [1]. These aberrant vessels were first described as a clinical entity and a potential cause of GI blood loss in 1839. During the 1960–70s, in the advent of fibreoptic endoscopy GIADs became increasing recognised and described in the literature, with the term angiodysplasia coined in 1974 [2]. In modern endoscopic practice these lesions are detected with increasing frequency in both those with symptoms and as an incidental finding. In this review we will examine the presentation and natural history of GIAD and the evidence for the available management strategies.

## Clinical presentation

GIADs can occur throughout the entire GI tract and are located within the submucosal and mucosal layers, with no dermatological or organ involvement. GIADs are often asymptomatic and as such their true prevalence is unknown. These are usually incidental findings upon endoscopic examination of the GI tract for the investigation of unrelated symptoms. In One series of patients undergoing screening colonoscopy a prevalence of incidental, asymptomatic GIAD of 0.8% was demonstrated. [1]. GIAD occur at an equal incidence amongst genders. There is however, an increased propensity with advancing age, with two thirds of cases occurring in patients over 70 years old [3]. Earlier presentations tend to occur in association with comorbidities such as cardiac disease, chronic renal failure or hereditary syndromes.

Symptomatic GIADs present with the clinical features of GI bleeding, this can range from occult iron deficiency anaemia to overt blood loss. Bleeding may take the form of haematemesis, maleana or haematochezia, depending on the location of the responsible lesion. Where GI bleeding is investigated GIADs will be found to be the cause in 2.6% of cases [4]. The likelihood increases where initial bi-directional endoscopy fails to diagnose the cause, with one series diagnosing GIADs as the underlying cause of bleeding in 40% of patients undergoing subsequent visceral angiography [5]. This diagnostic challenge is likely to be attributable to the fact that GIADs tend to bleed intermittently and once stopped their diminutive size may cause their bleeding potential to be underestimated. There is a 2% mortality associated with bleeding where GIAD is the underlying cause [6].

## Pathogenesis

The pathogenesis of angiodysplastic lesions is poorly understood, with several proposed theories. Whilst the development of these lesions is likely to be multifactorial, the potential underlying mechanisms can be broadly classified as below.

### Mild chronic venous obstruction

In a surgical series of patients undergoing colectomy for colorectal cancer it was noted that several resected specimens had

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mucosal AD. However, clinically imperceptible submucosal lesions were more prevalent [7]. It is therefore hypothesised that GIAD are degenerative lesions formed where a chronic obstructive effect at the submucosal level exerts pressure on the submucosal vessels causing dilatation. Only a proportion of these vascular units will dilate to the extent that pre-capillary sphincters become incompetent creating arterio-venous communications with a resultant mucosal lesion [7,8]. This may be an influential factor in location and distribution of GIAD, which have a predilection for the right colon and gastric antrum. Due to increased wall tension and muscular density in these locations there may be a propensity to local venous obstruction.

### Chronic mucosal ischaemia

The vascular nature of GIAD could intuitively be explained by vascular proliferation in response to mucosal hypoxia [7]. This theory is supported by increased levels of the angiogenic factor Vascular Endothelial Growth Factor (VEGF) found in patients with colonic GIADs [9,10]. This reinforced further by the observation that medications with anti-angiogenic properties are effective in reducing GIAD related bleeding [10]. This theory however fails to explain the distribution of GIADs in the GI tract or why there does not appear to be an increased incidence in those with conditions that cause hypoxia, such as coronary artery disease or peripheral vascular disease.

### Related to co-existing comorbidities

There has been an attempt to understand the pathological process that lead to GIAD formation by observing relationships with co-existent disease. Although some of these apparent associations may be due to confounding factors given the correlation between the prevalence of GIAD and age. One such controversial link is that between GIAD and aortic stenosis, also known as Heyde syndrome [11]. It has been postulated that suboptimal cardiac function may increase mucosal hypoxia. This relationship has not been observed with any other form of valvular heart disease or with ischaemic heart disease. Current opinion is that the passage of blood through a defective aortic valve causes the destruction of high molecular weight multimers of von Willebrand factor, leading to an acquired form of von Willebrand disease and a consequent bleeding tendency [12–15].

There is a more convincing association between GIAD and chronic renal failure (CRF), with AD responsible for an up to a third of GI bleeding events in this population [16,17]. However, it is unclear whether there is an increased likelihood of developing AD or merely an increased chance of becoming symptomatic from ADs due to bleeding diathesis. It is known the presence of bleeding GIAD correlates with the severity of CRF and the need for dialysis [16], where the use of anticoagulants, thrombocytopaenia and uraemic platelet dysfunction are likely to be more common [18,19].

## Diagnosis

Direct endoscopic visualisation has become the gold standard modality for diagnosis [20]. GIADs have a characteristic cherry red spot appearance composed of tortuous thin walled vessels emanating from a feeding vessel, often with a pale 'halo' of surrounding mucosa (Fig. 1). GIADS are typically between 2 and 5 mm in size and no larger than 10 mm. Biopsy is not required to confirm the diagnosis, where histological examination is performed this reveals endothelium lined thin walled vessels. ADs are rarely a solitary finding, with more than one lesion noted in 60% of patients [21]. Synchronous lesions can be found in a different location within the GI tract in one fifth of patients [22]. Diagnostic approach, clinical suspicion, technical expertise and patient factors may influence the number lesions identified at endoscopy.

The diagnosis of GIAD is achieved with relative ease in the upper and lower GI tract by means of gastroscopy and colonoscopy respectively. Where upper GI bleeding is investigated GIADs are found to be responsible in 4% of cases [21]. The colon is the most common location for GIADs, accounting for 80% of all lesions [3,8,23]. There appears to be a predilection for the right colon with over 60% located in the caecum [1]. This observation may however be influenced by genetic factors, with a Japanese series demonstrating the descending colon to have the greatest likelihood of ADs [24].

Gastric Antral Vascular Ectasia (GAVE) is a related vascular condition whereby multiple ectatic lesions, often in longitudinal streaks, occupy the gastric antrum. These characteristic endoscopic appearances have led to the descriptive term of 'watermelon stomach'. Erosive gastritis and portal hypertensive gastropathy may have similar features but can be differentiated by histology if required. This condition accounts for 4% of upper GI bleeds. The underlying causes and associations vary form that of GIAD, however due to the similar therapeutic approaches used this condition is often considered as a similar entity in some clinical studies.

The small bowel is the location of 10–15% of all GIADs. Previously investigation of small bowel has been challenging owing to its long and tortuous course. This has largely been overcome upon the introduction of small bowel capsule endoscopy that enables non-invasive inspection. There is high level of agreement in the diagnosis of GIAD where capsule and balloon enteroscopy are compared, although false negatives are more likely to occur with capsule endoscopy [25]. Further investigation should be therefore be considered in the event of a negative capsule where the clinical suspicion is high. Where bidirectional endoscopy has failed to reveal the cause of GI bleeding small bowel AD will be found to be the cause in 40% of patients. Evidence suggests those who have evidence of UGI AD are more likely to have concurrent jejunal GIAD [26]. Capsule endoscopy has no therapeutic potential and so where endoscopic therapy is indicated push, spiral or balloon assisted enteroscopy is required.

Radiographic techniques may be useful for localising the site of GI bleeding in the acute setting. CT angiography, MRI and Radio nucleotide scanning are all potential options, however only Digital Subtraction Angiography (DSA) can achieve vascular interventions such as coiling. Visceral angiography suggests a diagnosis of GIAD where vascular tufts are observed during the arterial phase of the study, early opacification draining veins and delayed emptying tortuous lesion in the venous phase are seen [27]. These radiographic features may be mimicked by other pathologies, in particular inflammatory bowel disease. With this in mind a GIAD identified at angiography can only be attributed as a cause of blood loss if this can be seen to be actively bleeding.

## Management

The management of GIADs remains controversial. Although acute bleeding will spontaneously stop in as many as 90% of cases, lesions tend to be multiple, with a high probability of recurrent bleeding. As such it can be difficult to accurately assess the efficacy of any particular treatment modality. In clinical practice the treatment approach is decided on an individual basis. In general where there are no symptoms patients are treated conservatively with correction of anaemia. In those with an ongoing transfusion requirement endoscopic thermal therapy is currently the treatment of choice, with the use of pharmacological therapies where this is not appropriate. In the event of overt or severe blood loss the first