

## Lecture no. 7

### ANGIODYSPLASIAS OF THE GASTROINTESTINAL TRACT

An angiodysplasia ranks among the rare and occult causes of intestinal hemorrhaging ultimately able to provoke massive bleeding. It is often problematic due to the disparity between the bleeding event, which can be serious, and the cause, since the lesion is generally minimal and difficult to diagnose. Works on the subject are replete with unresolved questions, starting with the very term itself, which includes different forms of even differing etiopathogenesis, but sharing the hemorrhaging symptoms. Even the pathologist's task is burdened by the difficulties arising in accurately and conclusively detecting the lesion.

Angiodysplasia remains for all practical purposes a clinical question, above all for its differential diagnosis, localization and treatment.

These issues are raised and discussed, drawing on the existing bibliography and the author's personal experience.

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An angiodysplasia is a vascular abnormality characterized by the generally focal dilation of submucosal veins and overlying mucosal capillaries. While numerous synonyms exist, such as vascular ectasia, angioectasia, etc., the term angiodysplasia (though not entirely correct) has become the standard moniker. Our understanding of angiodysplasia of the gastrointestinal (GI) tract is incomplete due to the infrequency with which the pathology is observed and its frequently minimal dimensions. The lesion is often no more than 5 mm in diameter and does not produce alterations visible to the naked eye. They are therefore difficult to detect even with instrumentation, let alone through physical examination and direct contact. Nevertheless angiodysplastic lesions can constitute the cause of hemorrhaging, at times massive, which for the above mentioned reasons places the condition among occult and/or rare causes.

In a 1993 review by Gregory Foutch<sup>1</sup>, angiodysplasia is the principal cause of hemorrhaging with an incidence varying between 1.2 and 8.0% in the upper GI and from 2.0 to 6.2% in the colon. Other surveys document that rare causes are responsible for 10% of all intestinal hemorrhaging, with angiodysplastic lesions making up 8 to 20% of these (thereby accounting for from 0.5 to 2.0% of all such events).

All segments of the GI tract may be affected (Table 1).

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Vascular disorders of the GI tract have yet to be fully defined and classified, and this shortcoming has only further prevented our full understanding of these lesions, angiodysplasia included.

While some Authors<sup>2</sup> are inclined to consider these lesions as congenital (a hypothesis borne out by the occurrence of pediatric cases), others<sup>3</sup> from a neoplastic standpoint, others<sup>4</sup> hold that angiodysplasia is an acquired vascular ectasia which arises from probable degenerative phenomena. This last conviction stems from the observation that a high number of cases, especially those localized in the colon, occur in the elderly.

One attempt at an anatomical-clinical-radiological classification was that by Moore<sup>5</sup>, who split the disorders into three types: the first acquired, the second having a congenital component (arterial-venous fistula), and the third bearing similarity to Rendu-Osler-Weber disease (hemorrhagic telangiectasia).

Most of our understanding comes from studies of angiodysplasia of the colon, the most frequently observed localization. In 1977 Boley and co-workers<sup>6</sup> formulated, using colonic localizations as a model, a pathogenetic explanation for their origin (acquired) whereby they arose from intermittent, partial obstruction of submucosal veins where they transverse the muscular layers of the colon. This contractile action, by exposing the veins to repeated episodes of pressure and obstruction, and without any force exerted on the arterial flow, gradually leads to the transient dilation of the submucosal veins. In elderly patients, be it for degenerative reasons or the deterioration of vascular tissues, venous dilation becomes permanent and eventually extends to the venules and arteriolar capillary units. Ultimately, with the progressive dilation of the capillary lumen, precapillary sphincters lose their competency and a stable arteriovenous communication forms (Table 2). The high prevalence of angiodysplastic lesions in the right colon is to be traced to the larger diameter and the greater intramural pressure that, according to the Laplace law, conditions wall tension. For these reasons such lesions, particularly those of the colon, should be viewed as acquired and should not be defined as angiodysplasia, but as vascular ectasia. Nevertheless, the occurrence of these lesions in younger subjects is evocative of a malformation or perhaps a dysfunction, even congenital, which calls into play the above-mentioned mechanisms. At any rate, the term vascular ectasia is too vague to describe these disorders; angiodysplasia, therefore, despite the shortcomings of its name (as discussed above), should be kept, since it's expressive and understood by all.

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Angiodysplasia is usually observed better by visual inspection than by histological analysis, as a consequence of the lesion's small size and the fact that the overlying mucosa always appears intact

with very few irregularities, even following hemorrhaging. In the colon, when viewed on endoscopy, it appears flat or slightly raised, bright red in color, 2 to 10 mm in diameter. The lesions may be round, stellate or fern-like in shape. Prominent vessels may be visible, and in some cases a halo of pale mucosa (area of relative ischemia) may surround the lesion. Multiple lesions are present in a high percentage (40-75%) of cases: more than two segments of the colon are affected in 17 to 60% of patients. This explains the frequent recurrence of hemorrhaging if these additional sites are not detected during treatment, which happens more often than not. In vivo the lesion may be visible on transillumination.

By contrast, the lesion is difficult to discern on specimens unless particular techniques are applied. A number of methods of vasculature injection and clearing have been devised to detect angiodysplastic areas<sup>7,8,6</sup>. We were able to show the lesion in a resected right colon through imaging of contrast medium injected into vessels (Figure 1). Using vasculature injection of silicon rubber, followed by refrigeration, dehydration and polymerization techniques, Mitsudo and co-workers<sup>9</sup> were able to obtain transparent specimens for dissecting microscope studies. These samples reveal ectasia with distortion of capillary connections and large, tortuous and dilated vessels communicating with submucosal vessels. Clearly different from normal in appearance, angiodysplastic lesions often take on a radiating shape, with forms resembling a “coral bed” (Figure 2). Other samples have shown how the dilation of submucosal vessels extends to the muscular layer where this is transversed. Still another method for histopathological analysis entails an intraluminal formalin fixation technique on the resected specimen: after fixation and detachment, the mucosa is thin enough to allow identification and excision of areas to study histologically<sup>10</sup>.

Histological features are characteristic: dilated, distorted, and thin-walled submucosal veins and venules. Vascular lacunas usually show endothelium and occasionally small elements of smooth muscle, with signs of arteriovenous communication (arteriovenous shunt; Figure 3).

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From a clinical standpoint the telltale symptom of angiodysplasia is bleeding: the patient generally presents with active hemorrhaging of varying entity.

**Serious hemorrhaging**, at times massive, requires immediate emergency care, including the stabilization of the source, which emergency angiography can provide when the blood loss does not exceed 0.5 ml/m<sup>2</sup>. In addition, angiography can also actually demonstrate the angiodysplasia. Caution is nonetheless recommended in emergency settings, in view of possible concomitant disorders (e.g., diverticula of the colon). As with all hemorrhaging emergencies, it is best to attempt resolution with non-surgical means; if surgery is resorted to, it is advisable to have an endoscope on

hand since localization in the case of angiodysplasia can become problematic. Indeed, the risk exists of performing insufficient, or altogether wrong, treatment.

Patients with **previous and/or current history of low grade or chronic (anemia) bleeding** have normally already undergone a long series of diagnostic tests that are either inconclusive or have revealed a different disease as the hemorrhagic source (generally diverticula of the colon).

**The third case** regards those patients who have already been subject to surgical intervention, which normally means:

- one or more laparotomic explorations;
- colon resection for diverticula;
- colon resection for angiodysplasia;
- other operations (Meckle, gastric resection, hemorrhoidectomy, polypectomy, etc.).

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From a diagnostic standpoint, the features distinguishing angiodysplasia, including some those cited in the cases above, are:

- ascertained past and operated angiodysplasia;
- past repeating episodes of bleeding for unknown causes (with or without surgical treatment);
- 55 years of age and older;
- renal failure<sup>11,12,13</sup>;
- Von Willebrand disease (factor VII and Von Willebrand factor deficiencies)<sup>14</sup>;
- aortic stenosis<sup>6,14,15,16</sup>;
- liver cirrhosis;
- lung diseases<sup>17,1</sup>.

The last five of these are associations that, with a frequency depending on the reporting author, accompany intestinal hemorrhaging from angiodysplastic with the first three being, in the view of many, pathogenetically meaningful.

The diagnosis of angiodysplasia is always difficult. It may be suspected on the grounds of findings mentioned above, the ultimate certainty and recognition of the localization(s) often demands repeated examinations. It should first be reiterated that the anatomic-pathologic features described above, especially the dimensions and the absence of modifications to the mucosal surface, prevent conventional radiological tests with contrast media. The same examinations can, however, be used for a differential diagnosis and for the detection of possible associated lesions<sup>18,19</sup>. As already mentioned, even direct observation on laparotomy (or laparoscopy) may not yield results. Angiography and endoscopy are the instruments of choice for diagnostic purposes: the former, even in emergency cases as already stated, the second (again, in emergency) for the proximal GI tract.

Overall, although the two tests are complementary, endoscopy is consistently more effective for the esophagus-stomach-duodenum tract and, in specialized settings, also for the ileum (endoscopic capsule<sup>20,21,22</sup>), but becomes less sensitive in the colon (especially the right) where angiodysplasia more commonly arises. Transendoscopic Doppler ultrasonography is thought by some authors<sup>23</sup> to be equally effective for detection and treatment planning. The most characteristic angiographic features are reported in Table 3 and are illustrated in Figures 5 - 8. Angiographic false positives may be due to polyps, Crohn's disease or malignant neoplasia. Endoscopic false positives may derive from artifacts of instrument caused trauma or of suction; false negatives, on the other hand, may be seen in highly anemic subjects (lack of or attenuation of the distinctive bright red color of the angiodysplastic lesion), or according to some authors as a result of anesthetics or analgesics. At present, reliable results with CT scan or MRI are not available<sup>24</sup>. During a hemorrhagic episode, especially in pediatric patients, radionuclide techniques may be employed (labeled red blood cells).

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The natural history of these lesions is still incompletely understood due to a lack of prospective studies. Three retrospective reports are available that take into account the follow-up of surgically and non-surgically treated patients. Tedesco<sup>25</sup> reported 15 cases with bleeding; five of these did not receive therapy, only one (20%) had re-bleeding after 10 months of follow-up, thereby suggesting that at short-term recurrence is infrequent. Hutcheon and co-workers<sup>26</sup> followed 15 subjects who had experienced hemorrhaging, ten of whom were treated medically: they were able to show that with time bleeding diminished or disappeared altogether. Richter e Coll.<sup>27</sup> studied a series of 101 patients with angiodysplasia of the colon: 15 who had never hemorrhaged were followed for 68 months (mean 23) and none of these had an episode of bleeding during this period.

This implies that when the angiodysplasia is detected incidentally bleeding is not always the rule and that treatment is not needed. Thirty-one patients from this series who had experienced bleeding were treated only by transfusions: 26% of patients had bleeding at one year, and 46% at 3 years. This suggests that the risk of recurrent bleeding increases as time passes (nearly 50% of already bleeding patients had recurrent episodes within 36 months); data from longer follow-up periods are not available. This study therefore seems to indicate that the high incidence of recurrent bleeding in these cases over time warrants therapeutic intervention.

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These data allow us to conclude that the incidentally found asymptomatic angiodysplasia does not require treatment. At the same time, it is clear that the patient must be aware of and be able to handle the situation in the event hemorrhaging occurs. When hemorrhaging is profuse, conventional therapies (transfusions, somatostatin, etc.) are able to arrest bleeding if the source is an

angiodysplasia (which tend to stop bleeding spontaneously); the only pitfall is that most often this is impossible to know this in advance.

**Should the bleeding not stop**, and if it is proximal (hematemesis-melena), an attempt at endoscopic hemostasis may be indicated. Alternatively, an angiography may be performed, which further allows localization of the source and/or characteristic imaging of the angiodysplasia and the site. The selective injection of vasoconstrictors and/or embolization are measures which may halt the hemorrhaging. For both endoscopic hemostasis and angiography, the rule of thumb under elective (and not emergency) conditions is for subsequent surgical therapy (high percentage of even early bleeding).

**If hemorrhaging cannot be stopped**, emergency intervention, during which localization of the bleeding lesion can be difficult, is required. Indications may be dictated by the blood level in the intestinal lumen, by transillumination analysis and by perioperative endoscopy. **The literature is replete with examples of useless intervention in such cases.**

Medical therapy<sup>28</sup> has at times been the treatment of choice. A number of studies have reported the successful stoppage of bleeding using estrogen-based and estrogen-progesterone hormone therapies<sup>29,30,31</sup>. These approaches are controversial and do not enjoy consensus. Even octreotide has been shown to be effective<sup>32,33,34</sup>, though temporarily, against bleeding from GI angiodysplasia.

Although the literature details many endoscopically treated cases<sup>1,35,36,21,23,37</sup>, a thorough assessment of data is hindered by the different techniques adopted, the limits of the cohorts examined and the short follow-up periods considered. The accepted source of reliable - perhaps not definitive - results remains the proximal GI. As far as the ileum and the right colon are concerned, the methods described above are still insufficient and not without risk (perforation). Another limit is that of the frequent multiple-site localization of lesions, above all in the colon: the difficulty of accurate identification entails the risk of partial therapy.

Surgery is by resection, and this by itself represents a risk due to other unrecognized sites. Still another problem, especially when angiodysplasia has not been detected on angiography and when diverticula are present (in elderly patients), is to attribute bleeding to these lesions and to carry out a resection, for example of the left colon, thereby overlooking the hemorrhagic source in the right: this is sadly still a risk, even if transillumination can detect such lesions. In such cases (diverticula of the left and suspected angiodysplasia of the right), Golligher<sup>4</sup> recommends total colectomy with ileo-rectal anastomosis. In any case, it is always wise to go heavy with the treatment of such lesions: in the colon, therefore, we could perform an ample right hemi-colectomy with a limited segment of the last ileal loop (another possible localization of angiodysplasia). The same holds true for the ascending colon and transverse colon, without hesitating to carry out a total colectomy in

cases of suspected multiple lesions. Surgeons may often be reluctant to adopt such a drastic approach; however, with Golligher we can say that demolition of this sort is always preferable to re-bleeding and additional operations. Things become simpler with the ileum, if a pre-operative diagnosis of the site has been made. In any case, the use of perioperative endoscopy is extremely useful for the identification of the segment (or segments) to resect<sup>38,39</sup>.

### **Figures and Legends**

Included below are:

- Figures and synoptic tables summarizing the text
- Radiological, histopathological and surgical documentation from the case series treated c/o the Surgical Clinic of the University of Genoa<sup>41</sup>.

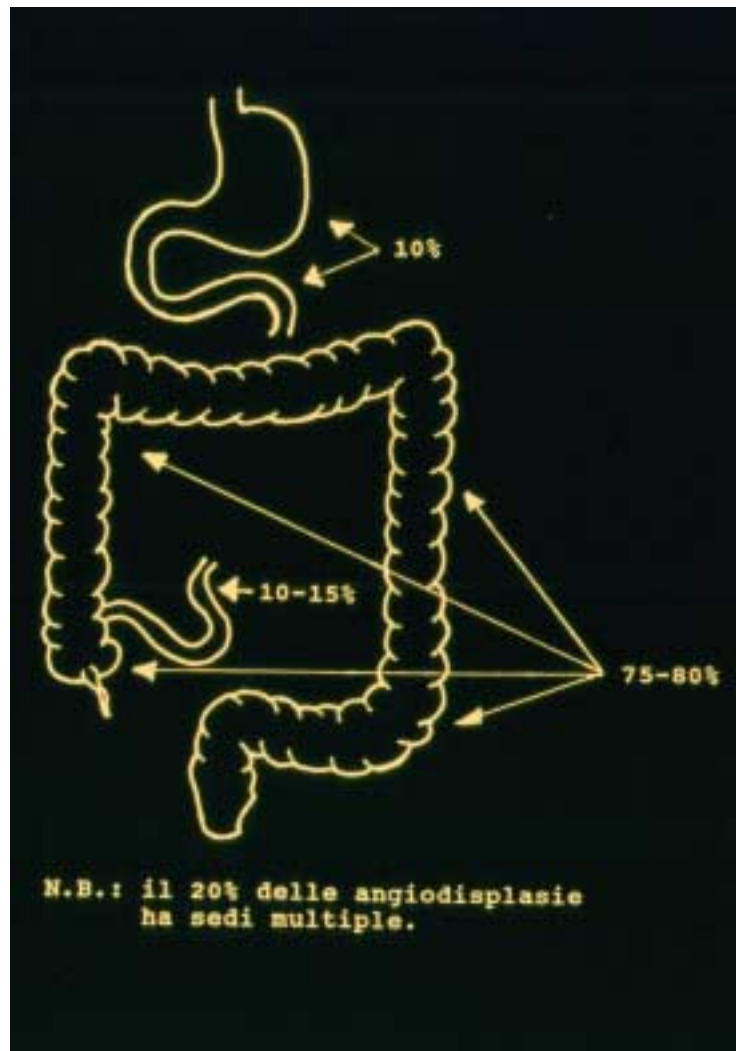


Table 1

## Angiodysplasias

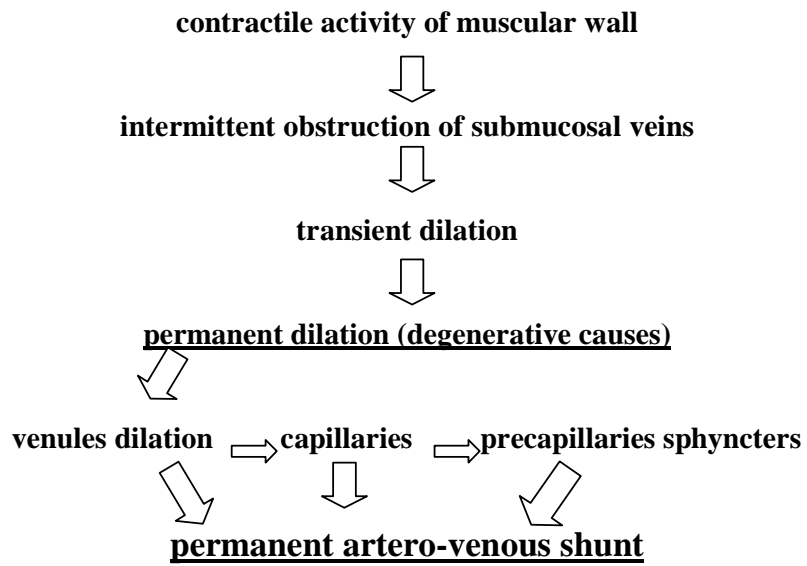


Table 2



Fig. 1



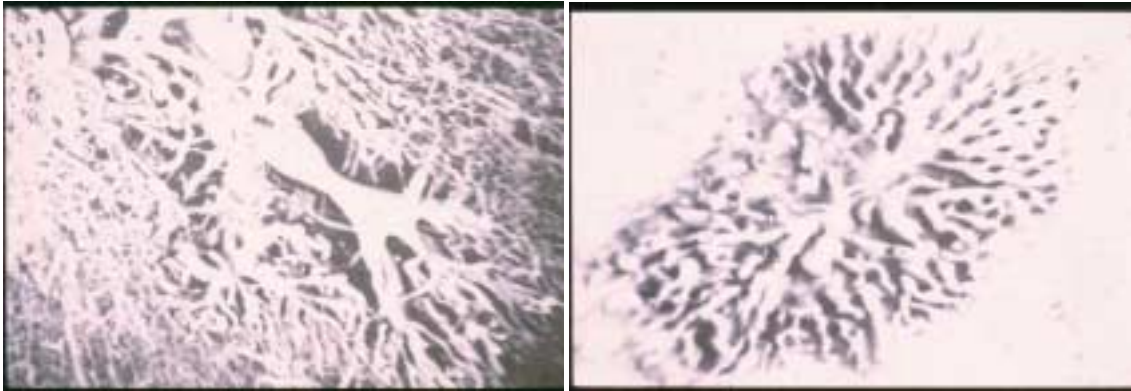


Fig. 2

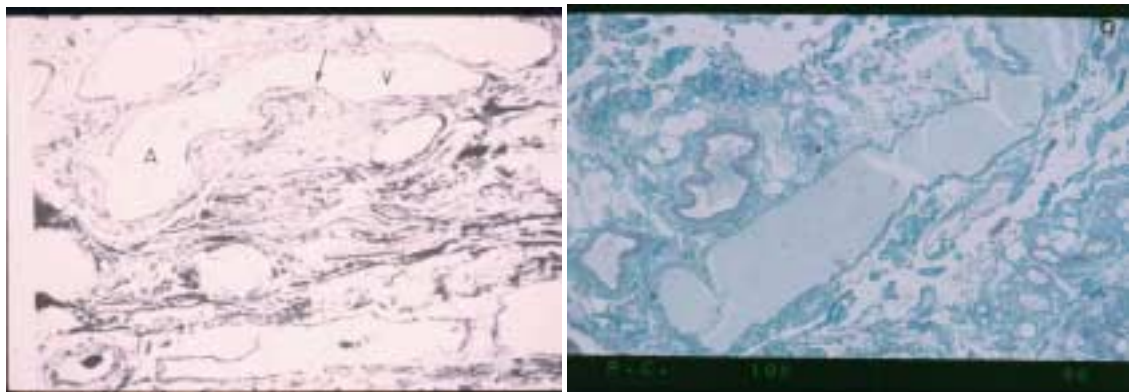


Fig. 3

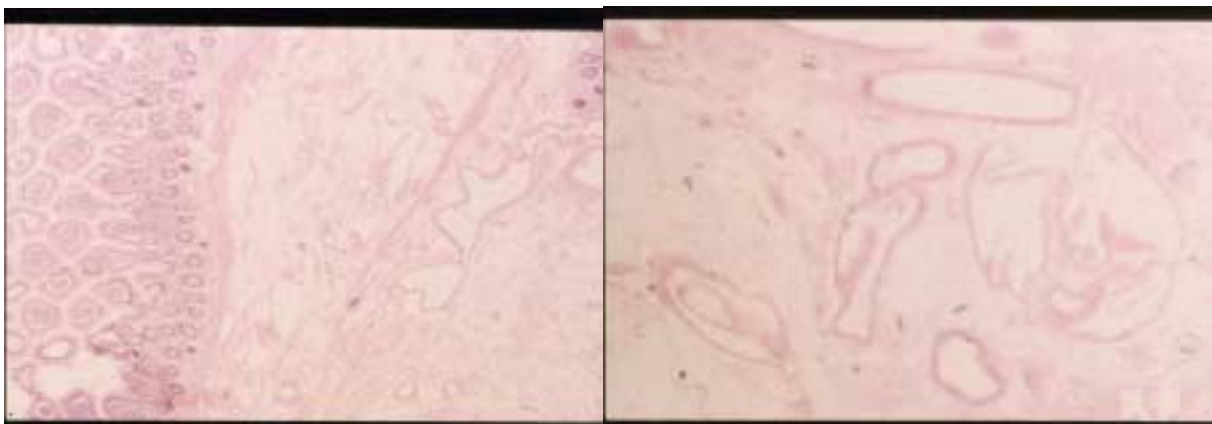


Fig. 4

### Angiodysplasias

- Tangle of little arterial vessels with early refilling
- Tuft-like heap of the contrast medium in capillary phase
- Early opacification of venous network with possible sign of “double binary”
- Pattern of the intestinal wall on bleeding

Table 3 - Angiographic signs of angiodysplasia

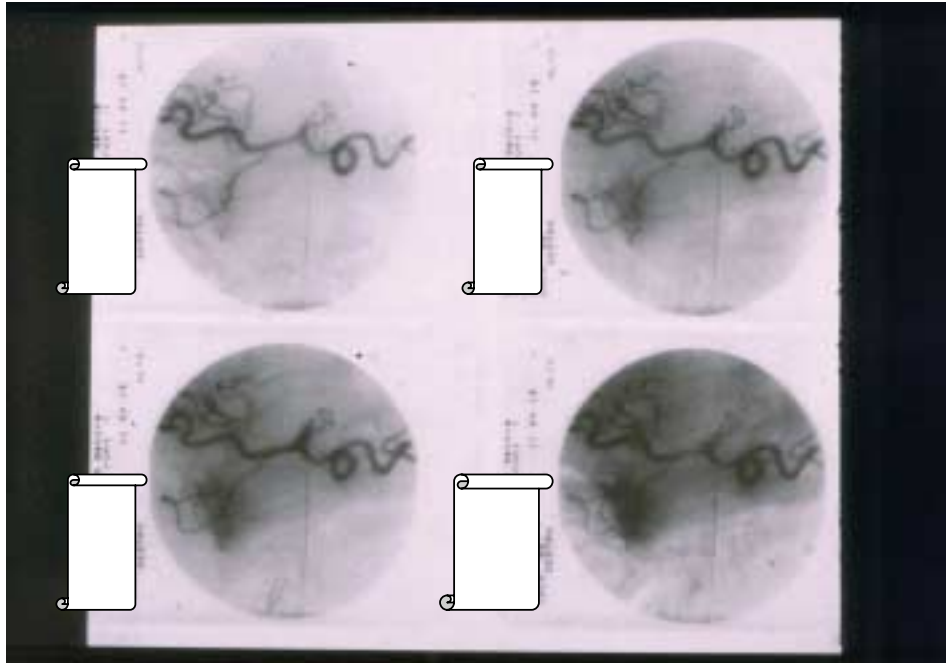


Fig. 5 - Duodenal angiodysplasia with active hemorrhaging



Fig. 6 - Duodenal angiodysplasia with active hemorrhaging

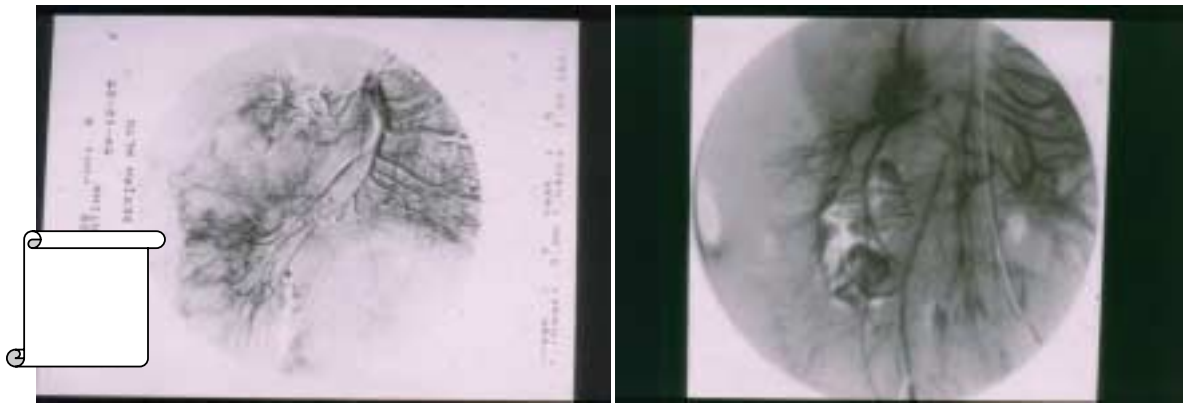


Fig. 7 - Angiodysplasia of the right colon

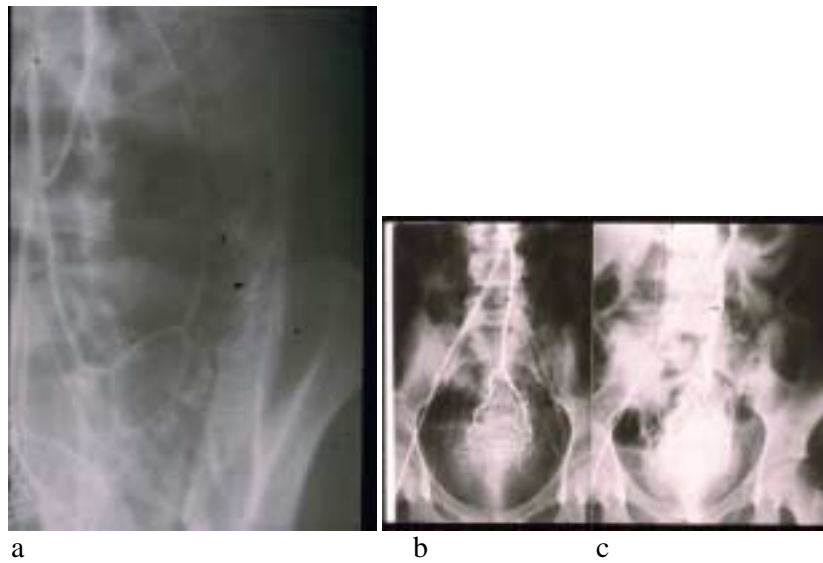


Fig. 8 - a) Localization in the left colon  
 b) rectal angiodysplasia: arterial rate  
 c) immediate venous return (double track sign)



Fig. 9 - Exceptionally evident angiodysplasia of the colon

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