

Combined Endoscopic Hemostasis in Upper Gastrointestinal Bleeding Caused by a Minimal Dieulafoy Lesion of the Duodenal Bulb: A Case Report and a Literature Review

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ABSTRACT

Background: Dieulafoy's lesion, an uncommon cause of upper nonvariceal bleeding, is a sub-mucosal vessel that erodes the near normal appearing mucosa without primary ulceration or erosion. The lesion occurs predominantly in the stomach, but it is also reported in extragastric sites.

Case and review of the literature: We present the case of a 69 years old patient, who presented in the emergency department with massive upper gastrointestinal bleeding caused by a duodenal Dieulafoy's lesion. Risk factors included: chronic renal failure on hemodialysis and low-dose Aspirin intake. CARE (CAse REports) guidelines were followed, and CARE-writer online application was used. We also performed a systematic review of available data literature, following PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines. An extensive literature search was performed using the following keywords: Dieulafoy lesion, duodenal bulb, case report, series. We searched databases such as PubMed, Embase, Google Scholar and Cochrane, as well as references of studies of screened articles to extract data about relevant articles.

Results: The review outlines current understanding of the epidemiology, risk factors and clinical importance of Dieulafoy's lesion as well as the currently available approaches to diagnosis and management.

Conclusions: We would also like to underline the importance of urgent endoscopy in diagnosis and treatment, delayed endoscopy being probably responsible for the "iceberg effect" on the current available data.

Keywords: Dieulafoy lesion, hemorrhage, hemoclip, injection therapy

BACKGROUND

Dieulafoy lesion has recently been described as "the little known sleeping giant of gastrointestinal bleeds" (1), which we find perfectly matching our presented case.

The lesion was first described by Gallard in 1884 (2). Later on, Paul

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Georges Dieulafoy was the first pathologist and surgeon who described a series of patients who presented with fatal massive acute gastrointestinal bleeding, due to a minimal superficial erosion of a sub-mucosal arteriole, described as "exulceratio simplex" or later "Dieulafoy lesion" (3,4). The essential typical characteristic is the fact that the nearby mucosa is in almost or perfect health, the lesion being quite different from a basic gastric or duodenal ulcer (5). First cases were described in the stomach (6-10), but later literature described localization almost everywhere along the gastrointestinal tract from the esophagus (10-13), duodenum and small bowel (14-24), colon and rectum (25,26), as well as the trachea (27) or bronchus (28-30). Besides "exulceratio simplex", other descriptions included: "caliber persistent artery", "gastric aneurysm", "gastric arterio-sclerosis", "submucosal arteriolar malformation" and "cirroid aneurysm" (1,2,31).

Etiology remains unknown, but no causality has been established between Dieulafoy lesion and other risk factors such as use of non-steroidal anti-inflammatory drugs, alcohol, smoking, previous ulcer peptic disease or *Helicobacter Pylori* infection (10,32,33).

Dieulafoy lesion accounts for about 1% of all upper gastrointestinal bleedings, varying between 0.5-14% (3,34,35). However, it is possible that an "iceberg effect" as a lack of correct diagnosis and underrecognizing is responsible, rather than a true rarity of the lesion (34,35). Intermittent bleeding on normal appearing mucosa covering the submucosal arteriole and especially delayed endoscopy could make it almost impossible to diagnose the lesion as it may not be visible once the bleeding has stopped for the moment (3,35).

REVIEW OF THE LITERATURE

CARE (CAse REports) guidelines were followed, and CARE-writer on-line application was used.

We also performed a systematic review of available data literature, following PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines.

An extensive literature search was performed using the following keywords: Dieulafoy lesion, duodenal bulb, case report, series. We searched databases such as PubMed, Embase, Google Scholar and Cochrane, as well as references of studies of screened articles to extract data about relevant articles.

CASE REPORT

A 69 years old woman presented to our emergency department for massive hematemesis and 3 days of black tarry stools, followed by generalized body weakness. Medical history included chronic renal failure, the patient is scheduled for hemodialysis 3 times per week. She is also known with chronic anemia (last hemoglobin value being 11g/dl, in the context of chronic renal failure), high blood pressure under treatment. Chronic medication also included Aspirin for maintaining the patency of the vascular fistula used for hemodialysis. She denied recent other non-steroidal anti-inflammatory drugs (NSAID) use.

At presentation, hemoglobin level was 7.1g/dl, the patient was hemodynamically unstable with blood pressure of 90/50 mmHg and a ventricular rate of 110 beats per minute. Pre-endoscopic Rockall score was 6 points. In the emergency department, the patient was stabilized. Proton pump inhibitors (PPI) were initiated according to current guidelines on upper gastrointestinal bleeding (36,37).

Due to episodes of hemodynamic instability and high-risk comorbidities (renal failure on hemodialysis), urgent upper endoscopy was performed, which revealed active massive upper gastrointestinal bleeding, being quite difficult to initially exactly identify the bleeding source. After intensive washing, we found a bulbar Dieulafoy lesion, with a practically normal surrounding surface mucosa but active continuous bleeding, as depicted in the images below. Endoscopic hemostasis was performed: first we injected 10 ml of diluted adrenalin solution 1:10.000, in an attempt to lower the bleeding rate and "clean" the bleeding site, as well as to help us identify the exact lesion and the possible localization of the submucosal artery, in order to intuitively guide us when placing the hemoclips. Bleeding persisted as relatively massive oozing after injection therapy. The first clip placement attempt failed. Afterwards, 3 hemoclips were successfully placed and the bleeding eventually stopped (*figs. 1-6*).

Following endoscopic treatment, Aspirin was stopped for the next 5 days, proton pump inhibitors were continuously administered at a rate of 8 mg/hour for the next 72 hours, and peritoneal dialysis was performed the second day after endoscopic hemostasis. Clinical evolution was favorable, the patient didn't rebleed and no major gastrointestinal events were encountered the following weeks. At 3 months follow-up, the patient did not rebleed.



Figure 1 - Identification of the bleeding minimal lesion under vigorous wash with saline.

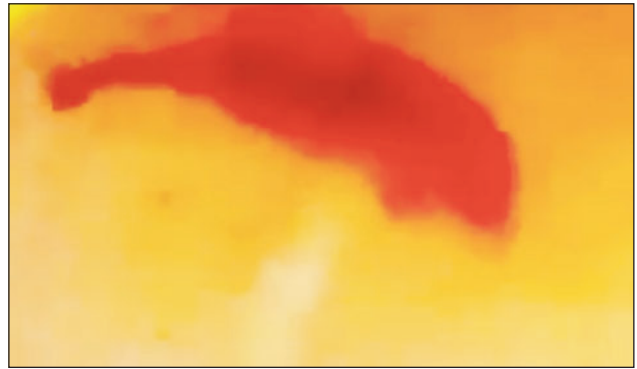


Figure 2 - Active bleeding Dieulafoy lesion.



Figure 3 - Injection with 10ml of 1:10.000 diluted adrenalin solution.

DISCUSSIONS

Localization

The most common encountered localization of gastrointestinal Dieulafoy lesion is within 6 cm of the gastro-esophageal junction, mostly on the lesser gastric curvature, possibly due to the particular anatomic vascularization of this region (3). A significant proportion of cases were found at intestinal anastomoses, predominantly Billroth II anastomosis after gastrectomy (29,31). Though multiple extra-gastric localization are possible, duodenal one was once considered to be rare, the first one being reported in 1988 (38). Almost ten years later, on a large series of 100 cases of Dieulafoy's lesion, Veldhuyzen found no duodenal localization (9). However, possibly due to increased awareness of the disease and development of endoscopic diagnosis and

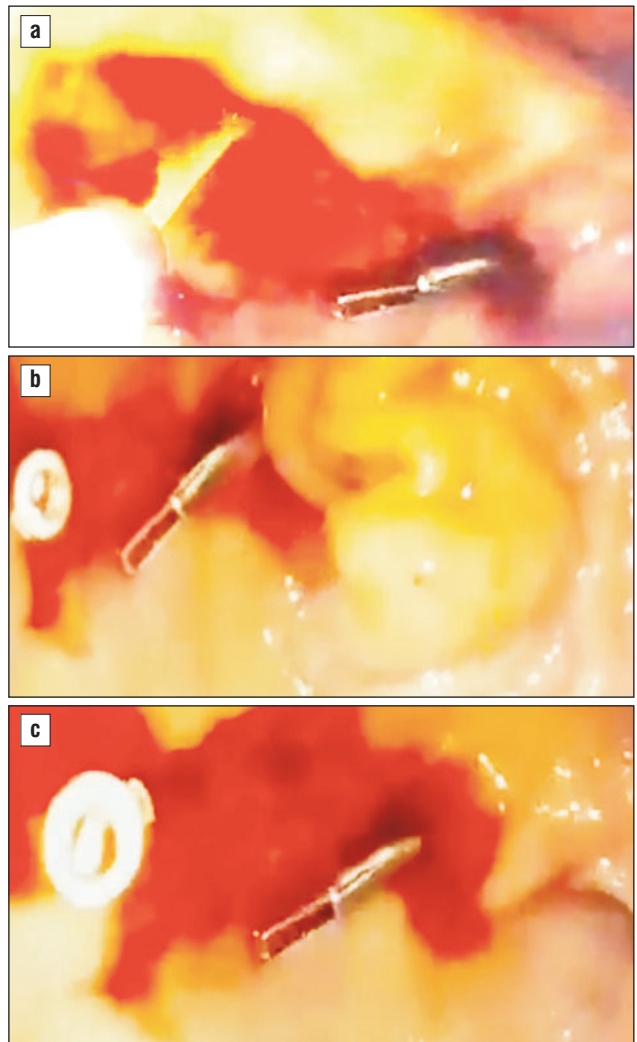


Figure 4 a,b,c - Placement of first hemoclip, one hemoclip failed before.

hemostasis, several recent studies (10-26) have reported more extra-gastric localization cases: in the light of new data, the duodenal lesion has become the most frequently non-gastric lesion, followed by the colon

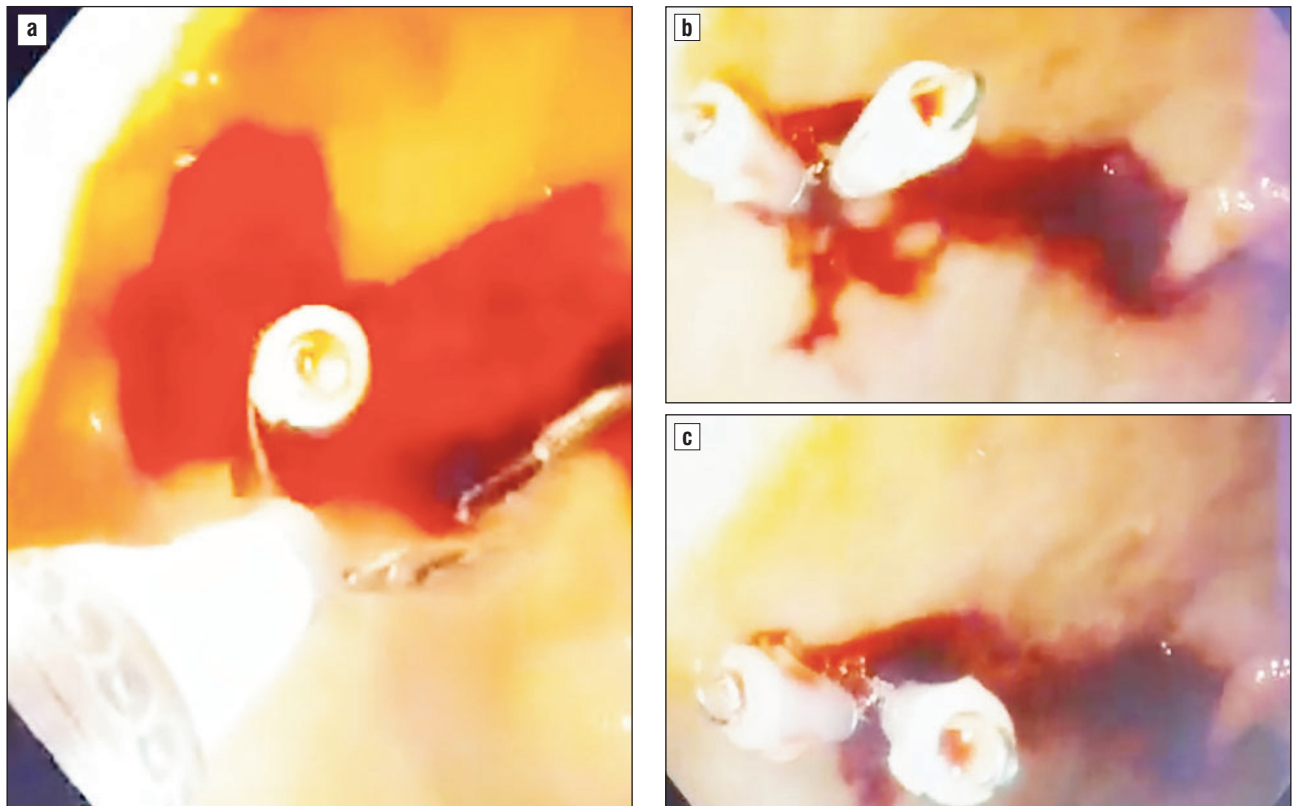


Figure 5 a,b,c,d - Placement of second hemoclip.

(10%), jejunum (2%) and esophagus (2%) (31). Though extremely rare, even gall-bladder Dieulafoy lesion has been reported as a cause for haemobilia (39). Extra-digestive localization is rare but has also been reported in the literature in cases of tracheal or bronchial Dieulafoy's lesion (27-30).

Diagnosis

Clinical presentation consists of painless recurrent

intermittent hematemesis or melena/hematochezia and hemodynamic instability ranging from general weakness to syncope or hemorrhagic shock (7,8).

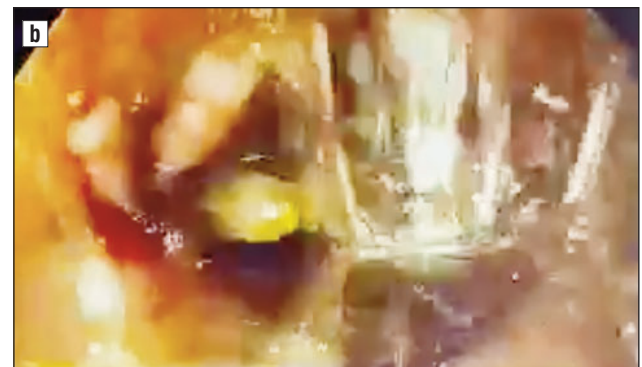
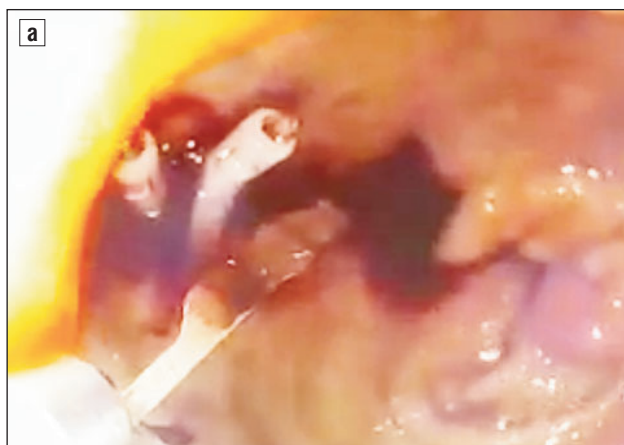


Figure 6 a,b - Placement of third hemoclip.

Clinical presentation may depend on the duration of the bleeding, general condition and comorbidities of the patient, localization and size of the bleeding vessel (2,14,17).

In the past preendoscopic era, the diagnosis was rarely made before surgery or post-mortem examination (3,5,6). With increasing endoscopic experience, as well as increased successful endoscopic hemostasis, diagnosis is now based more on endoscopic criteria rather than histopathological ones (35,40,41).

The hemodynamic status is also important for deciding on diagnosis modalities, most of the patients are initially evaluated by upper endoscopy or colonoscopy, especially in non-tertiary gastroenterological centers (32,42).

Even though index endoscopy may be effective for diagnosis for up to 70% of the patients, several endoscopies may be necessary, especially when bleeding has initially stopped (24,31). About 6% of the patients may require more than 3 endoscopies to establish the correct diagnosis (6). Risk factors for missing the lesion include: excessive blood, clots and sometimes (as in our case) very subtle lesions on normal appearing mucosa, the intermittent nature of hemorrhages (24,31,34).

Several endoscopic criteria have been proposed for Dieulafoy lesions:

- active or pulsing arterial bleeding from a minimal defect of the mucosa with normal surrounding mucosa;
- endoscopic visualization of a vessel that protrudes, with or without active bleeding, through a minimal defect of the mucosa or through surrounding normal mucosa;
- fresh clotting, adhering at a narrow point of attachment to a minimal defect of the mucosa or to mucosa of normal appearance (31).

When considering angiodysplasia (located in the small bowel and from an endoscopic point of view), some authors (43,44) have classified lesions into 6 groups. In this classification, Dieulafoy lesion may be considered a type 2a or b angiodysplasia. Angiodysplasias are classified into the following 6 groups: type 1a, punctuate erythema (<1 mm), with or without oozing; type 1b, patchy erythema (a few mm), with or without oozing; type 2a, punctuate lesions (< 1 mm), with pulsatile bleeding; type 2b, pulsatile red protrusion, without surrounding venous dilatation; type 3, pulsatile red protrusion, with surrounding venous dilatation; type 4, other lesions not classified into any of the above categories.

Several alternative diagnosis methods include enteroscopy, capsule endoscopy, angiography, red cell

scanning and surgical exploration, especially when the other methods fail (31,36,37,45). Barium studies were unsuccessful in the diagnosis of duodenal Dieulafoy's lesions (24).

Enteroscopy allows evaluation of the small intestine up to 150 cm from the pylorus, thus diagnosing 70-100% of patients with occult gastrointestinal bleeding. Push, single- or double-balloon enteroscopy can be used for both diagnosis and treatment (34). The decision as to whether the initial approach of enteroscopy is oral or anal is based on clinical presentation or the result of capsule endoscopy. Tattooing is sometimes used to mark the bleeding site but also to mark the deepest insertion point when the bleeding spot has not been localized. It was reported that at least 2 or more procedures may be necessary before diagnosis. Intraoperative enteroscopy from an enterotomy is also a diagnosis possibility, especially in distal lesions (31,34,46).

Capsule endoscopy is a valuable noninvasive tool but has the great disadvantage of not allowing endoscopic treatment. However, it is very useful in guiding therapeutic interventions in selected cases (47,48).

Angiography and red cell scanning can be used to pinpoint the location of jejunal/small intestine bleed (31,49). There is no specific radiological view of the lesion. Angiographic findings include extravasation of contrast from an eroded artery that may appear normal (50). If standard angiography fails, heparin may be used to help identify the bleeding site (31,52). However, existence of a tortuous and ectatic artery in angiography can provide important clues for the diagnosis (53). Technetium-99m labeled red blood cell scanning has the great advantage that the threshold for detecting extravasation into the gut is only 20% of that required by angiography (31,54,55).

Two studies have used technetium scintigraphy, but the method was unsuccessful to show the bleeding site (53,54). However, there are several case reports that show great utility of scintigraphy in diagnosis and management of these cases, especially when endoscopy fails and surgery is at high risk (12,31). According to new data, Tc99m RBCs may accurately localize the site of bleeding in 88–97% of patients, with positive findings resulting in a 5-fold greater likelihood that the patient will require surgery (31,55).

Pharmacologic, Endoscopic and Surgical Therapy, Rate of Rebleeding, Mortality, Need for Surgery

There is currently no consensus on the treatment of

Dieulafoy's lesions. Treatment depends on the presentation, lesion site and mostly on site available endoscopic and surgical expertise (36,37). Bleeding can be fatal and treatment was mostly surgical before 1990 (2,5,7,9,38). Nowadays, endoscopic therapy has replaced surgery (36,37). The need for surgery has decreased and so has mortality since progress in endoscopic diagnosis and hemostasis (5,10).

Proton pump inhibitors remain a valuable therapeutic tool and according to current guidelines (36,37), they should be initiated as intravenous bolus as soon as an upper gastrointestinal bleeding is suspected. Though the effect of pre-endoscopic therapy is nonsignificant on mortality, rebleeding, surgery or blood transfusion, it reduces the incidence of stigmata of recent hemorrhage. Most studies and case series and reports in the literature used intravenous proton pump inhibitors infusion after endoscopic hemostasis (3,4,6,17,24,35). There is little data to suggest the efficacy of proton pump inhibitors before or after endoscopy particularly in Dieulafoy lesion as compared to other non-variceal etiologies of upper gastrointestinal bleeding (31,36,37).

Available endoscopic methods include: injection therapy, heater probe, bipolar electrocoagulation, laser therapy, hemoclips and rubber band ligation, Hemospray (36,37).

Adrenaline injection is easy, low cost and safe, but as a single hemostatic method it is associated with a relatively high rebleeding rate. The advantages of adrenalin injection are represented by several facts: it provides temporary hemostasis, enhances visualization of the hemorrhagic site without the risk of tissue injury and perforation (36,37,56,57).

Contact thermocoagulation has the risk of trans-

mural injury and seems less effective than hemoclip placement (31,37,38,58). However, hemoclip placement may be difficult in the duodenum, sometimes acute duodenal angulation makes hemoclip placement impossible or very difficult. Hemoclip placement is effective especially if the surrounding mucosa is soft (8,34,59,60).

Band ligation seems easier than hemoclip placement, as well as safer due to lower perforation risk compared with thermal methods. The risks of rebleeding and ulcer formation around the ligated mucosa are low (61,62).

Studies have shown that mechanical endoscopic methods such as hemoclip and rubber band ligation are more effective than injection and thermal therapy. It has also been shown that the use of 2 combined endoscopic techniques is superior to using a single endoscopic method (36,37,56).

Risk of rebleeding was high and surgical treatment was more indicated in the past, but numbers have definitely become much better in the last endoscopic years, as seen in the *table 1*. Duodenal localization does not appear to have a higher risk for rebleeding (63).

Another new endoscopic therapeutic tool are hemostatic powders, which seem quite attractive, as they are safe and technically much easier to apply than hemocliping and/or band ligation (65,66).

When endoscopic therapy fails, alternative treatments include angiography and eventually surgical treatment (31,50). Angiography followed by embolization is indicated in poor surgical candidates in whom endoscopy has failed or localization is difficult to reach. A major disadvantage of angioembolization is the risk of ischemia due to collaterals feeding the abnormal vessel. Re-bleeding can be explained by

Table 1 - Results of endoscopic hemostasis in different studies.

Study	No. of pts./ Year published	Endoscopic hemostasis technique	Successful hemostasis % of pts.
Ljubicic et al (64)	21/2006	hemoclip	90.5 %
Sone et al (42)	61/2005	hemoclip	100 %
Cheng et al (40)	29/2004	various	86.2 %
Park et al (60)	26/2003	hemoclip versus ligation	100 %
Nikolaidis et al (62)	23/2001	ligation	95.7 %
Schmulewitz and Baille (4)	40/2001	various (mostly injection+heater probe)	90 %
Chung et al (56)	24/2000	hemoclip / ligation versus injection	91.7 %
Cui et al (41)	107/2011	combination hemoclip sclerosis	96.7% 77.4% 71.7%

No. = number, Pts. = patients)

collateral circulation or non-complete embolization of the feeding artery.

Up to date, there is enough evidence in the literature to justify selective arterial embolization as a less invasive alternative therapeutic option. However, to the best of our knowledge, no study has established its role as the first initial treatment (50,51).

The rate for surgical necessity has decreased from 100% to 3% with increasing endoscopic and surgical expertise (57). The bleeding source can be sutured with a 3-point U stitch technique.

The normal surrounding mucosa makes it impossible to feel the lesion, so frequently pre- or intra-operative endoscopy is needed (31,57). Hemoclip placement can be useful for guiding the surgeon even if endoscopic hemostasis fails (6,60). Main indications for surgical treatment are: hemodynamic instability or failure of other methods (31,41).

Initially described as a necroptic study by Dieulafoy, nowadays early endoscopic treatment has decreased mortality rates by up to 8% (5,42). Mortality rates are mostly associated with comorbidities such as organ failure or sepsis (3,33). Previous studies with lower rates of endoscopic treatments show relatively higher mortality rates ranging between 23-35% (31,42).

CONCLUSIONS

We find our case very representative for the fact that mucosal lesion was minimal, adjacent mucosa was perfectly normal (no inflammation, exudate or ecchymosis) with a minimal Forrest IB hemorrhagic pinpoint. The case also underlines the importance of urgent endoscopy in selected cases, delay being strongly associated with the risk of impossibility to identify the Dieulafoy lesion localization once the bleeding has stopped.

The historical lesion is rare, subtle and possibly difficult to recognize (especially in delayed endoscopy) but it remains a potentially life-threatening condition mostly in patients with multiple comorbidities, such as our patient with chronic renal failure and hemodialysis. Urgent endoscopy remains a very useful diagnosis and life saving therapeutic tool, especially in patients with multiple comorbidities and high surgical risk. The specific treatment of choice should be individualized to each patients' clinical situation (hemodynamic stability, comorbidities) as well as technical expertise of the endoscopist and surgeon.

We think that delayed endoscopy in such cases could be responsible for the well-known "iceberg effect" but also the so called Baader-Meinhof

phenomenon (68), which refers to the cognitive bias when one has become aware of an entity through a new experience or learning and then begins to encounter and recognize it more frequently, even if it has been there all along.

Conflicts of Interest: none to declare.

Ethical Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013).

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