Prognostic factors for recurrence of gastrointestinal bleeding due to Dieulafoy’s lesion

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Abstract

AIM: To analyze the effectiveness of the endoscopic therapy and to identify prognostic factors for recurrent bleeding.

METHODS: Retrospective study of patients with gastrointestinal bleeding secondary to Dieulafoy’s lesion (DL) from 2005 to 2011. We analyzed the demographic characteristics of the patients, risk factors for gastrointestinal bleeding, endoscopic findings, characteristics of the endoscopic treatment, and the recurrence of bleeding. We included cases in which endoscopy described a lesion compatible with Dieulafoy. We excluded patients who had potentially bleeding lesions such as angiodysplasia in other areas or had undergone other gastrointestinal endoscopic procedures.

RESULTS: Twenty-nine patients with DL were identified. Most of them were men with an average age of 71.5 years. Fifty-five percent of the patients received antiaggregatory or anticoagulant therapy. The most common location for DL was the stomach (51.7%). The main type of bleeding was oozing in 65.5% of cases. In 27.6% of cases, there was arterial (spurting) bleeding, and 6.9% of the patients presented with an adherent clot. A single endoscopic treatment was applied to nine patients (31%); eight of them with adrenaline and one with argon, while 69% of the patients received combined treatment. Six patients (20.7%) presented with recurrent bleeding at a median of 4 days after endoscopy (interquartile range = 97.75). Within these six patients, the new endoscopic treatment obtained a therapeutic success of 100%. The presence of arterial bleeding at endoscopy was associated with a higher recurrence rate for bleeding (50% vs 33.3% for other type of bleeding) \( P = 0.024, \text{ odds ratio (OR) } = 8.5, 95\% \text{ CI } = 1.13-63.87 \). The use of combined endoscopic treatment prevented the recurrence of bleeding (10% vs 44.4% of single treatment) \( P = 0.034, \text{ OR } = 0.14, 95\% \text{ CI } = 0.19-0.99 \).

CONCLUSION: Endoscopic treatment of DL is safe and effective. Adrenaline monotherapy and arterial (spurting) bleeding are associated with a high rate of bleeding recurrence.

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Key words: Dieulafoy’s lesion; Gastrointestinal bleeding; Hemorrhage; Recurrent bleeding; Endoscopic treatment

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INTRODUCTION

Dieulafoy’s lesion (DL) was first described in 1884 by Gallarden, and characterized in 1898 by the French surgeon George Dieulafoy, who described its characteristics in three patients and gave it its name. It is a rare but important cause of gastrointestinal bleeding. Up to 6% of the cases of nonvaricose bleeding in the upper gastrointestinal tract and 1%-2% of all gastrointestinal hemorrhages are caused by DL. In spite of this, its mortality rates are similar to those of other causes for gastrointestinal bleeding. This lesion is defined by the presence of an abnormally thick arteriole (1-3 mm in diameter, 10 times higher than the diameter of submucosal capillaries at that level) that maintains the caliber of the feeding vessel when it reaches the mucous membra. Histologically, it is characterized by subintimal fibrosis of the artery and a lack of inflammation at the edge of the mucosal defect, which sets it apart from peptic ulcers. The exact mechanism that triggers the bleeding is unknown. Some authors have speculated on the combined effect of atrophy and ischemia of the mucosa. It is believed that this thick vessel applies pressure to the mucosa and leads to a small erosion and rupture of the vessel towards the lumen. Clinically, it appears with intermittent and painless gastrointestinal bleeding. The most common location is the stomach, specifically the lesser curvature. In 80%-95% of these cases it is located within 6 cm of the gastroesophageal junction, because the arterial flow in this area emerges directly from the left gastric artery. Approximately one third of the lesions are located outside the stomach, most of them in the duodenum, followed by the colon. They have also been described in the esophagus, jejunum and ileum, rectum and anal canal. There have also been some cases in which the lesion was outside the gastrointestinal tract (bronchial tubes).

The diagnostic procedure of choice is endoscopy, which is effective in > 90% of patients. The endoscopic diagnosis may be difficult, especially during the first episode, due to the size of the lesion and the intermittent nature of the hemorrhage. For this reason, up to 6% of patients require three or more endoscopies in order to reach a diagnosis. Endoscopic ultrasound has been highlighted as a useful technological resource that can support the diagnosis of this condition, because it can locate the submucosal vessel with great accuracy.

Traditionally, the treatment of DL was surgical. However, with the development of endoscopic hemostasis techniques, the need for surgery has been reduced, and the mortality rates have decreased from 80% to 8.6%.[23] Therefore, the current treatment of choice in accessible lesions is endoscopy, with a success rate of > 90% and low rates of recurrence and complications. The endoscopic hemostasis procedures are classified into three groups: (1) thermal: electrocoagulation, heater probe and argon plasma coagulation; (2) local injection of substances, such as adrenaline or sclerosing solutions; and (3) mechanical: hemostatic clips and bands.

All these procedures achieve high rates of primary hemostasis, with low rates of recurrence (generally < 10%).[27-33] However, in the clinical field, the choice of a procedure depends on the experience and the decision of the endoscopist.

The objectives of our study were to assess the effectiveness of endoscopic treatment of DL, and to identify potential prognostic factors for recurrence of bleeding in patients with this kind of lesion.

MATERIALS AND METHODS

Patients

This was a retrospective study of patients who were admitted to the University Hospital of Salamanca with a diagnosis of gastrointestinal bleeding caused by DL between 2005 and 2011. We collected data regarding clinical presentation of the disease, diagnosis, and effectiveness of medical and endoscopic treatment of gastrointestinal bleeding caused by DL. We included cases in which endoscopy described a lesion compatible with Dieulafoy. We excluded patients who had potentially bleeding lesions such as angiodyplasia in other areas or had undergone other gastrointestinal endoscopic procedures.

Descriptive analysis

In the descriptive analysis of the sample, we used percentages for the qualitative variables and measures of central tendency (mean and/or median when there was a large asymmetry or dispersion) and of dispersion (SD) for the quantitative variables.

Statistical analysis

We used the SPSS Version 15.0 (Chicago, IL, United States) for the analysis. The dichotomous variables were analyzed with the χ² test on contingency tables in order to compare the distribution of categorical variables, and we calculated the odds ratios (ORs) and 95% CIs. The analysis of variance test was used in the analysis of continuous and categorical variables. The multivariate analysis was done using binary logistic regression. Statistical significance was established at P < 0.05.

RESULTS

Out of the 2582 patients admitted in the endoscopy unit with upper gastrointestinal bleeding, we identified 29 with DL (1.12%). In this group, 21 (72.4%) patients were

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men with an average age of 71.5 ± 14.5 years. Their personal records showed arterial hypertension (62.1%), ischemic heart disease (27.6%), valvular heart disease (20.7%), and chronic liver disease (3.4%). Sixteen patients (55.2%) were receiving antiaggregatory or anticoagulant therapy, and five (17.2%) a combination of both therapies.

Among the patients treated with antiaggregatory agents, five (55.5%) were being treated with acetylsalicylic acid (ASA), and the remainder with clopidogrel. Among the anticoagulant patients, 11 (91.6%) were being treated with acenocoumarol, and one patient was being treated with low molecular weight heparin. No patient was receiving triple therapy (ASA/clopidogrel/acenocoumarol). Only three (10.3%) of the patients were being treated with a proton-pump inhibitor (PPI) before the bleeding episode.

*Figure 1* Dieulafoy’s lesion located on the esophagus with arterial (spurting) bleeding.

Symptoms of clinical instability were present in 10 (34.5%) patients (systolic arterial pressure < 100 mmHg and/or heart rate > 100 beats/min) and the average hemoglobin levels before gastroscopy were 8.6 ± 2.48 mg/dL.

The most common location for DL was the stomach (51.7%), followed by duodenum (31%) and esophagus (13.8%). In one patient, the lesion was located on the colon. The main type of bleeding was oozing, in 65.5% of the cases. In 27.6% of the cases there was arterial (spurting) bleeding (Figure 1), and 6.9% of the patients presented with an adherent clot. A single endoscopic treatment was applied to nine patients (31%); eight of them with adrenaline and one with argon, while 69% of the patients received combined treatment (several different combinations with clip, adrenaline, sclerosing therapy and argon). Hemostatic bands were not used in any of the cases. All medical treatments were initiated before endoscopy; 16 patients (55.2%) received continuous intravenous perfusion of PPI with an average dose of 156.92 ± 62.1 mg/24 h for an average period of 3 ± 1.82 d, and 13 (44.8%) patients received treatment with oral PPI, with an average dose of 57.5 ± 34.93 mg/24 h. Most of the patients (n = 26) required red blood cell transfusion, with a median value of 2 U concentrate per patient (interquartile range (IQR) = 2).

Bleeding reappeared in six patients (20.7%), at a median 4 d after endoscopy (IQR = 97.75). In this group of patients, the second endoscopic treatment achieved a therapeutic success rate of 100%. The recurrence of bleeding was not associated with age, sex, personal record, previous medical treatment (including antiaggregants and/or anticoagulants), the seriousness of the hemorrhage or its location, or the medical treatment used (Table 1). However, the presence of arterial (spurting) bleeding at endoscopy was associated with a higher rate of bleeding recurrence (50% vs 33.3% for other types of bleeding) (P = 0.024, OR = 8.5, 95% CI = 1.13-63.87). Multivariate analysis adjusted for age, sex, type of anticoagulant, type of anticoagulation and single or combined endoscopic treatment, confirmed the association (P = 0.039). The use of combined endoscopic treatment prevented recurrence of bleeding (10% vs 44.4% with monotherapy) (P = 0.034, OR = 0.14, 95% CI = 0.19-0.99), and multivariate analysis confirmed this association (P = 0.049). Two patients died; one due to postoperative septic shock and the other to complications of previous heart disease.

### DISCUSSION

In our hospital, the prevalence of gastrointestinal bleeding due to DL was 1.12%. This percentage was similar to that in other studies\[23,31,34\]. The demographic characteristics of our patients were similar to those in other studies; we found a higher prevalence of the condition in men, compared to women, with a ratio of 3:1, and an average age of 71.5 years. DL usually affects patients with associated comorbidity\[28\], such as cardiovascular disease, arterial hypertension or renal failure. Some authors have proposed that these conditions alter the normal process of angiogenesis and trigger the formation of aberrant ves-

### Table 1 Prognostic factors analyzed in cases of bleeding recurrence caused by Dieulafoy’s lesion n (%)

| Factor                        | Bleeding recurrence | No bleeding recurrence | P value |
|-------------------------------|---------------------|------------------------|---------|
| Male patients                 | 4 (66.7)            | 17 (73.9)              | 0.54    |
| Arterial hypertension         | 5 (83.3)            | 13 (56.5)              | 0.23    |
| Ischemic heart disease        | 3 (33.3)            | 6 (20.1)               | 0.54    |
| Valvular heart disease        | 1 (16.7)            | 5 (21.7)               | 0.63    |
| Renal failure                 | 1 (16.7)            | -                      | -       |
| Anticoagulant or antiaggregant| 3 (50)              | 13 (56.5)              | 0.56    |
| Antiaggregant                 | 6 (100)             | 7 (30.4)               | 0.62    |
| Anticoagulant                 | 1 (16.7)            | 11 (47.8)              | 0.18    |
| Location in the stomach       | 3 (50)              | 12 (52.2)              | 0.63    |
| Mean systolic arterial pressure (mmHg) | 107.3               | 112                    | 0.62    |
| Mean heart rate (beats/min)   | 83                  | 85.7                   | 0.77    |
| Urea (mg/dL)                  | 76.8                | 84.3                   | 0.66    |
| Hemoglobin (mg/dL)            | 8.76                | 8.75                   | 0.98    |
| Need of transfusion           | 6 (100)             | 20 (87)                | 0.48    |
| PPI perfusion                 | 2 (33.3)            | 11 (47.8)              | 0.43    |
| Arterial bleeding type        | 4 (66.7)            | 4 (19)                 | 0.02    |
| Combined endoscopic treatment | 2 (33.3)            | 18 (78.3)              | 0.03    |

PPI: Proton-pump inhibitor.
sels with a constant caliber that increase the incidence of DL. In our study, most of the patients presented with comorbidity; mainly hypertension (62.1%) and ischemic heart disease (27.6%). Similarly, some researchers have proposed a causal relation with the use of nonsteroidal anti-inflammatory drugs and aspirin, and they argue that the erosive gastritis and the subsequent necrosis of the vascular wall induced by these drugs may lead to rupture of the submucosal vessels, although there is little evidence in the literature that supports this relationship.

In our study, although a high percentage of the patients received antiaggregant therapy, only three patients (10%) received some additional PPI.

Gastrointestinal bleeding caused by DL can be serious. In our study, 10 patients (34.5%) presented with symptoms of hemodynamic instability, and 27 (93.1%) showed active bleeding at the moment of endoscopic exploration. Two patients died; one due to postoperative complications (septic shock) and the other to complications of previous heart disease.

Most of the studies have shown that the most common location of DL is the stomach. In our series this was also the most common location, followed by the duodenum and the esophagus, plus one case in which the lesion was in the colon and two cases in which it was located on the gastric anastomosis caused by gastrectomy.

The first endoscopy was diagnostic in 93% of cases. Early exploration seems to increase sensitivity due to the intermittent nature of bleeding caused by DL but we did not study this factor.

The success rate of endoscopic treatment in our study was high, similar to that reported in other studies. Primary hemostasis was achieved in 89% of the cases (n = 26).

The endoscopic methods used were: injection (adrenaline, aethoxysklerol), thermal techniques (argon), and mechanical techniques (clip). In most of the cases, combined endoscopic treatment was applied (69%), and the technique was chosen according to the criteria of the endoscopist. The most commonly used technique was a combination of adrenaline injection and a sclerosing agent. Recurrent bleeding was found in six cases (20.7%), compared with other studies that have described rates of 9%-40%.

The recurrence of bleeding was associated with monotherapy with adrenaline and endoscopic findings of arterial (spurting) bleeding. Although there is no consensus on the endoscopic treatment of choice, several studies have compared the effectiveness of different techniques. Adrenaline injection is the most commonly used method due to its availability, low cost and safety. Some studies have shown a higher effectiveness of mechanical methods compared with injection techniques. In recent years, several studies have proven that the hemoclip and endoscopic ligation improve the rates of primary hemostasis and reduce the need for subsequent endoscopy. Theoretically, the mechanical hemostasis leads to a smaller lesion of the surrounding tissue than thermal therapy or injection techniques, which suggests that these procedures could be a first-line approach for the management of DL.

Another study has shown better results for thermocoagulation vs injection of a single substance. A recent study has concluded that combined therapy with hemoclip and aethoxysklerol injection is the most effective, while other studies have shown that sclerosis with adrenaline was associated with a higher risk of bleeding recurrence. Similar to endoscopic treatment of bleeding due to peptic ulcer, a lower rate of bleeding recurrence has been described with the use of combined endoscopic treatment compared with monotherapy, as could be seen in our study.

With regard to the limitations of our study, we must first mention the small size of the sample, and the retrospective design. The low number of prospective studies may be due to the low incidence of DL.

In conclusion, endoscopic treatment of DL is effective. Treatment with adrenaline monotherapy, and arterial (spurting) bleeding, are associated with a higher rate of bleeding recurrence. For this reason, combined treatment is recommended.

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