

Dieulafoy's Lesion: Pathology, Diagnosis and Treatment

Sunthorn Treesaranu wattana, MD
Choosak Khemtai, MD*

Department of Surgery, *Division of Emergency, St. Mary Hospital, Nakhon Ratchasima, Thailand 30000

Abstract

Background: Dieulafoy's lesion is uncommon cause of acute gastrointestinal bleeding which is potentially life threatening if unrecognized. It may be overlooked during endoscopy or even laparotomy. Understanding of this pathology will improve the diagnostic accuracy and selection of effective hemostatic procedure.

Methods: Data were reviewed from published literature searching Medline database and reference lists of relevant major articles. Figures were collected from authors experience.

Results: About 341 cases of Dieulafoy's lesion of gastrointestinal tract have been reported in English literature up to year 2001. In the early reports most of them were gastric lesion and surgery was the mainstay for treatment and diagnosis with high mortality. After the advent of flexible endoscope, much increase of reported cases included extragastric Dieulafoy's lesions. Currently, therapeutic endoscopy is the treatment of choice while surgery is indicated when endoscopy fails to arrest the bleeding or is inaccessible or unavailable.

Conclusion: Dieulafoy's lesion is underdiagnosed rather than a rare disease. Endoscopy is the essential diagnostic procedure and therapeutic endoscopy is safe and effective for permanent hemostasis. Surgical treatment is required in about 5 per cent of cases.

Among the rare causes of gastrointestinal bleeding (GIB) Dieulafoy's lesion is an interesting pathology because it can cause massively intermittent bleeding that may be potentially lethal if not recognized.¹ Gallard was first to report two fatal cases of this lesion in 1884 as "Miliary aneurysm". A French surgeon, George Dieulafoy, has been credited for his work that described and fully characterized of lesion in 1897. He called the superficial gastric mucosal lesion "Exulceratio simplex". It had different names in subsequent literature such as Gastric artery aneurysm, Cirroid aneurysm, Microaneurysms, Serpiginous aneurysm, Gastric artery arteriosclerosis, Peptic ulcer of peculiar location, Submucosal arterial malformation, Sclerotic submucosal gastric artery, Distinctive arteriovenous malformation, Ulcus ventriculi, Solitary simple erosion, Caliber persistent artery. The term Dieulafoy was introduced in English literature since 1966s and was generally accepted to name this lesion as Dieulafoy arterial malformation, Dieulafoy arteriovenous

malformation, Dieulafoy gastric erosion, Dieulafoy's ulcer, Dieulafoy's disease, Dieulafoy's lesion or Dieulafoy like lesion.¹⁻⁹ More than 300 cases of Dieulafoy's lesion of gastrointestinal (GI) tract have been reported, stomach is the most common location especially at the lesser curvature within 6 cm from esophagogastric junction.¹⁻⁹ Extragastric lesions have also been reported in esophagus,¹⁰⁻¹⁵ duodenum,¹⁶⁻²³ jejunum,^{24,25} ileum,^{26,27} caecum,²⁸ colon,²⁹⁻³² rectum,³³⁻⁴⁸ and anus.^{49,50} Extremely rare lesion outside GI tract could be found in lip⁵¹ and bronchus.⁵²

PATHOLOGY AND PATHOGENESIS

Dieulafoy's lesion in any location has the same pathology (Figure 1). Characteristic lesion consists of two components. (1) A large tortuous submucosal artery usually 1-3 mm in diameter, and (2) Minute mucosal defect usually 2-5 mm in diameter and solitary. When exposed artery ruptures acute GIB will

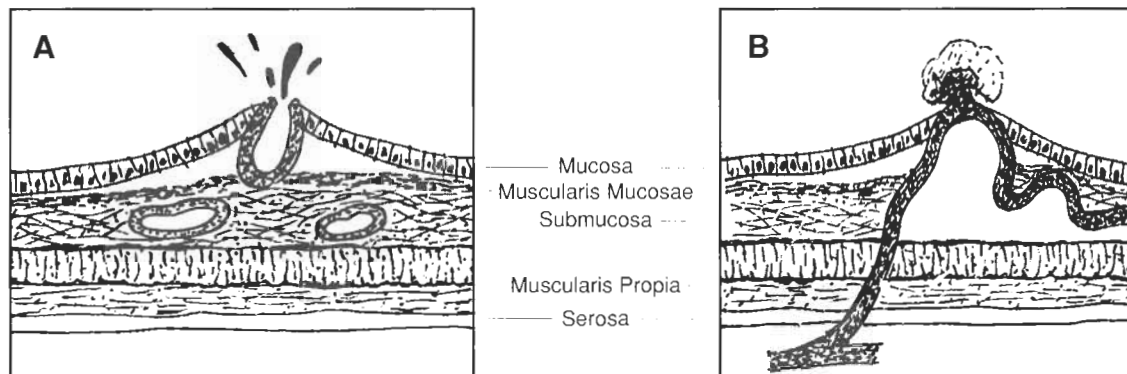


Fig. 1 Graphic illustration of pathologic artery in Dieulafoy's lesion. Bulging of lesion into the lumen of GI tract with arterial spurting (A), and sentinel clot or adherent clot (B).

suddenly occur.^{1,9} Miko and Thomazy⁵³ studied 24 pathologic specimens compared with normal control specimens revealed that the diameter of pathologic arteries was 1.8 ± 0.39 mm, whereas normal submucosal arteries was 1.02 ± 0.17 mm and normal arteries at level of muscularis mucosae was 0.10 ± 0.01 mm. These findings showed that pathologic arteries were significantly larger than normal arteries at level of muscularis mucosae rather than submucosal level. Barlow⁵⁴ in 1951 studying the artery and vein in normal stomach found that when artery penetrates the muscular wall into submucosa, simultaneous reduction in caliber from successive branching to form submucosal plexus occurs and then penetrates muscularis mucosae to become capillaries of the mucosa. In lesser curvature of stomach the submucosal arteries take origin directly from right and left gastric arterial chain then traverse in oblique manner to reach the mucosa without formation of submucosal plexus. Voth⁵⁵ in 1962 coined the term "Caliber persistent artery" to describe the pathologic arteries of Dieulafoy's lesion that taking a tortuous course in sub-mucosa for a variable distance without reduction in caliber and giving no branch. Fockens⁵⁶ detecting the length of submucosal artery in Dieulafoy's lesion by endoscopic ultrasonography revealed it running a course of 2-4 cm in submucosa; but he did not study this artery in normal subject. Most authors found that this abnormal large artery had normal structure of vascular wall; no histologic evidence of aneurysm, arteriosclerosis or vasculitis and generally agreed that this condition is congenital in origin rather than acquired.

The development of mucosal defect and pathogenesis of bleeding is still unclear and may be multifactorial. Juler⁵⁷ in 1984 studied nine specimens

of gastric Dieulafoy's lesions and found subintimal fibrosis of pathologic artery with dysplastic change and fibrin thrombosis in necrotic arterial wall. He postulated that chronic gastritis predisposed to vascular dysplasia leading to thrombosis and necrosis of vascular wall and eventually ruptured through overlying mucosa. This inside-out phenomenon can not explain the extragastric lesion in which lesion is not exposed to acid-pepsin digestion. Aforementioned study by Miko and Thomazy⁵³ found that the pathologic artery attached to the mucosa by virtue of Wanke's musculoelastic mantle instead of loose connective tissue. Linkage of mucosa to large artery prone to mechanical trauma and tissue ischemia from repeated strong pulsation leading to mucosal ulceration.⁵⁸

This musculoelastic mantle also prevents mucosal movement during peristalsis which produce peristaltic shear stress thereby vulnerable mucosal spot is created. The pathologic artery forces muscularis mucosae and mucosa upward; macroscopically the lesion is bulging into the lumen of GI tract with predilection to mechanical trauma.^{57,58} Because of this lesion occurring in old age group, degenerative change causes weakening of perivascular supporting tissue may be the precipitating factor as suggested by some authors.

Normal appearance of surrounding mucosa may be infiltrated by inflammatory cell as was described as miliary abscess in the past.^{53,57,60} Chapman and Lapi⁵⁹ suggested that intensity of inflammatory cell infiltration depended on the time of bleeding episode and the time that the lesion was removed for pathologic examination. Mucosal defect confined only to submucosa without penetration through muscularis propria. It must be kept in mind that more than one

lesion can be found in the same location as reported by Dieulafoy,⁶⁰ Norton,⁹ Asaki,⁶¹ and Yang.⁶² Eidus⁶³ reported a case of two lesions in vivo specimen where two mucosal defects occurred in the area which convoluted artery was in very close proximity to overlying mucosa.

CLINICAL PRESENTATION

Acute gastrointestinal bleeding is the main clinical presentation of Dieulafoy's lesion which accounts for 0.3-9 per cent²⁻⁹ of all GIB cases depending on the criteria of selection. Rare cases may present with symptom of anemia from chronic GIB such as fatigue, dizziness, presyncope. Fallows⁶⁴ reported a case of jejunal intussusception in which Dieulafoy's lesion was the leading point. Hematemesis, melena and hematochezia were the presenting symptoms. Hematemesis with melena are present in 51-68 per cent of gastric or duodenal lesion.⁶⁻⁸ Melena and/or hematochezia are present in all lesions below ligament of Treitz.²⁴⁻³² Massive rectal bleeding is present in all cases of rectal and anal lesion.³³⁻⁵⁰ Hemodynamic instability is found in 53-79 per cent at initial evaluation;^{6-9,61}

defined as hypotension (systolic BP < 100), tachycardia (HR > 100) or orthostatic change (systolic BP drop > 20 mmHg after changing of position). Recurrent episode of bleeding after failure of initial endoscopic diagnosis varies from few hours to many months⁷⁻⁹ but usually within 2-4 days.⁶⁹⁻⁷¹ Gough⁷² reported a case of five episodes of upper GIB before definite diagnosis and treatment were achieved. Blood transfusion is required to maintain hemodynamic status in most of cases with the average of 6 units.⁷⁻⁹ One case of Vetto⁷³ received 80 units of blood transfusion before segmental resection of jejunal lesion was performed. Summary of pathogenesis and clinical presentation is shown in Diagram 1.

Age incidence ranges from 20 months-93 years,^{1,73} median age is 72 years, and male is more frequently affected than female. Significant comorbidities are present in 45-90 per cent⁷⁻⁹; these are ischemic heart disease, hypertension, diabetes, chronic renal failure, cerebral stroke, chronic obstructive pulmonary disease, cirrhosis of liver, cancer of esophagus and stomach. History of GIB or peptic ulcer disease or previous peptic ulcer surgery is found in 11-53 per cent; taking NSAIDs, warfarin or aspirin 32-51 per cent, alcoholic

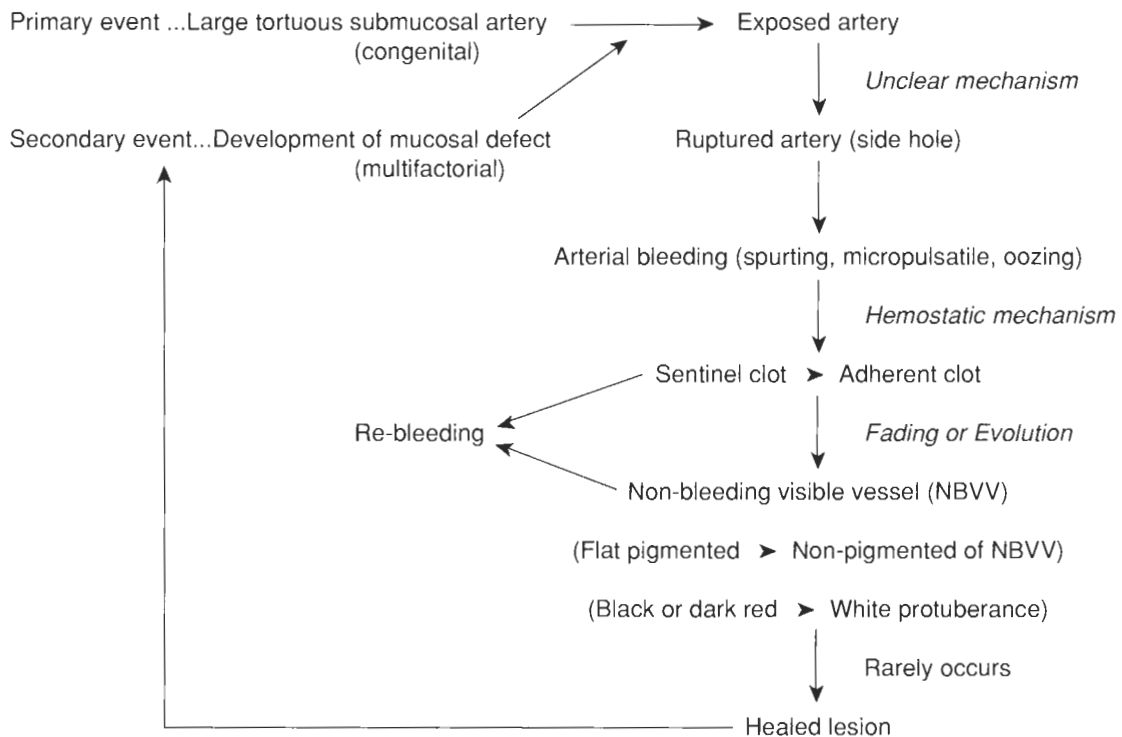


Diagram 1 Summary of the pathogenesis and clinical presentation of bleeding in Dieulafoy's lesion.

Table 1 Summary of gastrointestinal Dieulafoy's lesion*

Location	Number of cases	Percentage
Esophagus ¹⁰⁻¹⁹	12	3.5
Stomach ^{1,2,4,6,9}	>230	67.5
Duodenum ¹⁶⁻²³	33	9.7
Jejunum ^{24,25,64}	13	3.8
Ileum ^{26,27,117}	3	0.9
Caecum ^{28,66}	2	0.6
Colon ^{9,29-32,67,77,85}	18	5.2
Rectum ³³⁻⁴⁸	27	7.9
Anus ^{49,50}	3	0.9
Total (1884-2001)	>341	100

*Data collected from reports in literature up to year 2001.

abuse 21-30 per cent.^{7-9,61,65}

DIAGNOSIS

Table 1 summarizes gastrointestinal Dieulafoy's lesions collected from reports in literature up to year 2001. Histologic examination provides definitive diagnosis of Dieulafoy's lesion. Before endoscopic era, diagnosis could be made at urgent laparotomy or at autopsy which had tissue for histologic confirmation. Currently endoscopy is the best diagnostic procedure. Selective visceral angiography and scintigraphy are helpful for demonstration and localization if endoscopy is inaccessible or fails.^{16,24,25,71,74,75} Initial endoscopy can identify bleeding lesion in 66-92 per cent.^{6-9,65} Multiple endoscopies are often necessary. Some patients^{7,16,18} require four endoscopic attempts to delineate the bleeding lesion. In non-bleeding phase, this minute lesion can be easily overlooked. Fockens and Tytgat² advised insufflate air for full distention of stomach because the lesion may be hidden between two mucosal folds. In active bleeding phase all clots must be removed by large bore nasogastric tube irrigation prior to examination. If large blood clots obscure visualization, changing of patient's position can shift away of clots from inspected area or changing of endoscope to a new endoscope with 6 mm accessory channel for rapid removal of clots.⁷⁻⁹ Haematin and loose adherent clots must be irrigated with water or water pump for perfect visualization.⁷⁶ Emergency endoscopy within 2-4 hr after presentation or immediate after stabilizing hemodynamic status by basic resuscitation is the crucial point in visualization of

stigmata of recent hemorrhage.^{3,4,7,9,66}

In lower GIB, prior upper endoscopy should be done to rule out the possibility of upper GI tract lesion then emergency colonoscopy performed by rapid infusion of 3-4 liters of polyethylene glycol electrolyte solution administered via nasogastric tube within a period of 2 hours.^{9,66} Yamamoto⁷⁷ introduced the technique for better visualization by colonoscopy in flowing water for irrigation of active bleeding colonic lesion with continuous drainage through another overtube drain. Enteroscopy must be considered in case of blood seen in duodenum and terminal ileum in absence of lesion in stomach and colon. Push enteroscopy can visualize proximal jejunum within 40-60 cm from ligament of Treitz.^{7,9,66,78,79} It can be done with specific type of push enteroscope or pediatric colonoscope or standard adult colonoscope. Sonde enteroscopy can visualize all part of small bowel but it is time consuming and arduous for both of patient and endoscopist and is not suitable for acute situation and therapeutic intervention.⁸⁰ Intraoperative enteroscopy^{72,81,82} or laparoscopic assisted panenteroscopy^{83,84} is the alternative method for both diagnosis and treatment of bleeding lesion of small bowel. Patient who underwent Billroth II gastrectomy and developed Dieulafoy's lesion in jejunal loop can be detected by standard upper endoscopy.⁸⁵

Selective mesenteric angiography is useful if multiple endoscopies fail to identify the lesion or in area which endoscopy is difficult to gain access as in post bulbar duodenal lesion, distal small bowel, ileum and right side colon. It demonstrates and locates the lesion only in bleeding phase. If no extravasation is seen in lumen of bowel, angiographic catheter should be temporarily left in situ, as to facilitate repeat examination to be performed immediately after sign and symptom of rebleeding are detected.^{71,72}

Currently diagnosis of Dieulafoy's lesion depends upon endoscopic visualization in most cases. Dy⁶⁶ introduced endoscopic criterion used to establish the diagnosis as the followings: (1) active arterial spurting or micropulsatile streaming from a minute mucosal defect or through normal surrounding mucosa; (2) visualization of a protruding vessel with or without active bleeding within a minute mucosal defect or through normal surrounding mucosa; (3) fresh densely adherent clot with a narrow point of attachment to a minute mucosal defect or to normal appearing

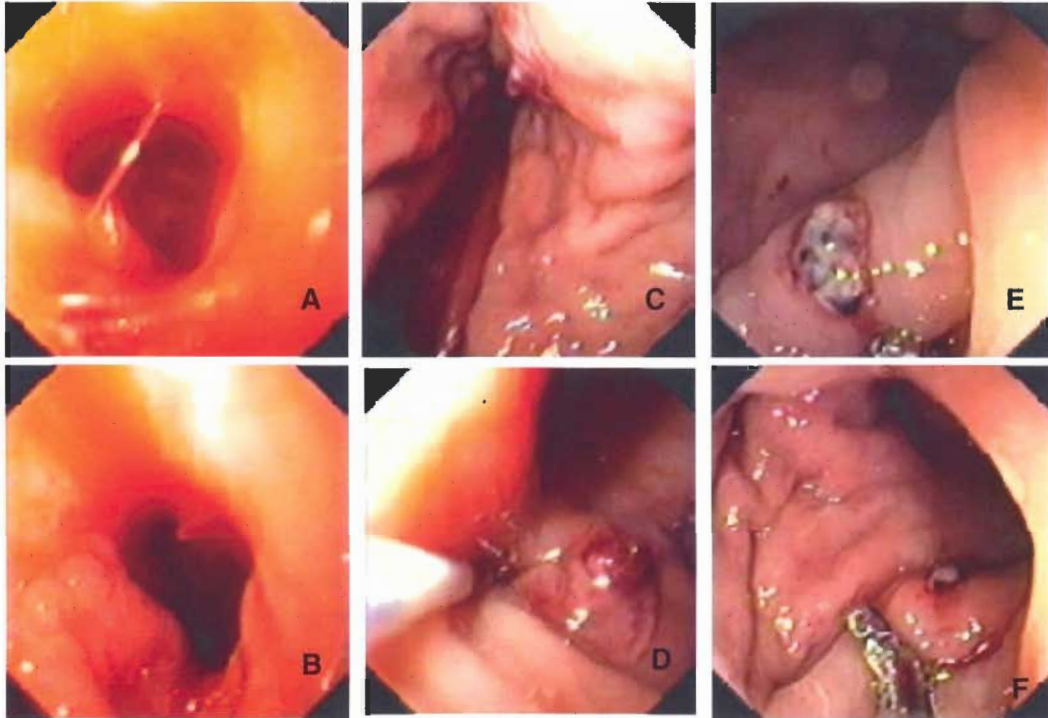


Fig. 2 Endoscopic visualization of stigmata of recent hemorrhage.

Duodenal lesion :

A = Active arterial spurting.

B = Non-pigment protuberance of non-bleeding visible vessel (NBVV).

Gastric lesion :

C = Pigmented protuberance of NBVV in tangential view.

D = Pigmented protuberance of NBVV or sentinel clot in surface view seen by retroflexion of endoscope.

Rectal lesion :

E = Whitish mounds on a large adherent clot indicative of the aged clot.

F = Dark red adherent clot was seen after irrigation.

mucosa. Endoscopic finding of stigmata of recent hemorrhage are arterial spurting or micropulsatile streaming or continuous oozing were seen 57-77 per cent in reported of emergency endoscopy. Protuberance vessel or non-bleeding visible vessel (NBVV) and adherent clots were found in the remaining case^{7-9,65} (Figure 2). Coincidental endoscopic findings of comorbidity such as isolated varices, peptic ulcer, Mallory - Weiss tear, diverticular disease and tumor may be misinterpreted as the cause of bleeding.

TREATMENT

Surgery is the mainstay for treatment of Dieulafoy's lesion in the early report. Goldman¹ in 1963 reviewed literature of 24 cases of gastric Dieulafoy's lesion, the mortality rate was high (79%) because of preoperative diagnosis could not be obtained and minute lesion was easily overlooked during urgent

laparotomy. If blind gastrectomy was performed, the lesion may not be included in the resected specimen. Recurrent hemorrhage and reexploration often ended in a fatal outcome. After the advent of visceral angiography and endoscopy in 1963, preoperative localization enables surgeon to perform early operation to arrest the bleeding lesion.⁶⁸⁻⁷² Veldhuyzen⁵ reviewed 101 cases of gastric Dieulafoy's lesion in 1986, the mortality was 23 percent. In 1982 Wordeholf⁶⁶ reported a first successful case of endoscopic injection sclerotherapy, followed by another six cases by Hoffmann,⁸⁷ Bakka⁵⁸ and Boron.⁷⁰ Pointer⁸⁸ reported a large series of 22 cases in 1988 with 18 cases were successfully treated by injection sclerotherapy and bipolar electrocoagulation. Thereafter, many large series of preliminary endoscopic treatment had been subsequently reported by Asaki,⁶¹ Lin,³ Stark,⁷ Baettig,⁸ Dy⁶⁶, Parra-Blanco⁶⁵ and Norton⁹ achieving high successful rate of permanent hemostasis with the

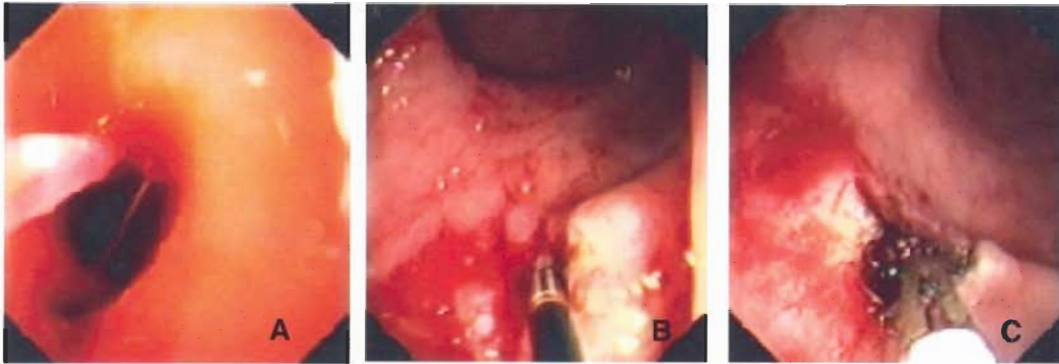


Fig. 3 Method of endoscopic treatment.

- A = Perilesion injection sclerotherapy .
 B = Application of monopolar electrocoagulation probe.
 C = Application of heater probe.

overall mortality rate around 10 per cent. It is now widely accepted that therapeutic endoscopy is the treatment of choice. Surgery and selective arterial embolization are the alternative after unsuccessful endoscopic attempts. Selective arterial embolization reported by Durham,⁸⁹ Helliwell,⁹⁰ Sherman,⁹¹ Pollack⁹² had the success rate of less than 50 per cent. This may be due to extensive collateral circulation in gastroduodenal area. Systemic vasopressin infusion reported by Barbier,⁶⁷ Mortensen,⁷⁴ Gadenstatter⁸⁵ was ineffective unlike its successful use in diverticular disease.

Endoscopic Treatment

Many kinds of endoscopic modality had been reported with high successful permanent hemostasis. However, there have been no comparative study results to indicate the most effective and appropriate modality. Endoscopic treatment can be summarized in three methods (Figure 3).

1. Injection therapy. Many kinds of sclerosing agent can be used such as epinephrine or adrenalin, polidocanol, absolute alcohol,⁶¹ sodium tetradecyl sulfate,⁷⁰ hypertonic glucose,³ histoacryl^{93,94} and combination of hypertonic sodium chloride plus epinephrine (HSE solution).^{4,34} Epinephrine and polidocanol are more favorable. Two to four perilesion injection with or without intralesion injection were used by most authors and more than one agent were used for each lesion by some endoscopists. The goal for injection therapy is obliteration of pathologic artery. Epinephrine causes mild focal mucosal damage and mild tissue inflammation without tissue necrosis

or vascular thrombosis. Other sclerosing agents cause mucosa, submucosal and muscular necrosis and vascular thrombosis with occasional serositis.^{95,96} Initial hemostasis attributed to volume tamponade and longterm hemostasis affected from vascular thrombosis. Excessive volume injection causes extensive tissue necrosis⁹⁷⁻⁹⁹ and perforation.^{9,100,101} Epinephrine and polidocanol should not be used in excess of 10 ml and ethanol 2 ml.

2. Thermal therapy. All thermal modalities generate heat, at 60 °C heat produces protein coagulation and contraction of treated area. Heating with firm pressure on vessel causes coaptation.⁷⁶ Thermal modalities used in Dieulafoy's lesion include the followings.

2.1 Monopolar or Multipolar electrocoagulation (MPEC or BICAP)

2.2 Thermocoagulation (Heater probe)

2.3 Laser photocoagulation (Nd : YAG Laser).

Heater probe and BICAP are more favorable by most authors. They provide the same effectiveness and application. Depth of tissue destruction is less than 3-4 mm.¹⁰² Heat probe application initially made at perilesion and then directly to vessel is recommended if bleeding vessel is larger than 1 mm.¹⁰³ Few reports of laser photocoagulation by Nd : YAG using non-contact mode showed successful control of bleeding but has not received popular attention due to its cumbersome nature and expensiveness.^{7,9,66} Monopolar electrocoagulation is less favorable because it causes deeper tissue destruction and adherence to coagulated tissue requiring frequent cleaning of the probe and high recurrent bleeding rate.^{9,3,58,101} Despite

the advent of liquid monopolar electrocoagulation or electrohydrothermal probe, they had no advantage over multipolar electrocoagulation or BICAP.¹⁰⁴ However, dry monopolar electrocoagulation is available in most hospitals and can provide good hemostatic effect if bleeding vessel is less than 0.5 mm.¹⁰² Many endoscopists prefer prior epinephrine injection to thermal coagulation with heater probe or MPEC (BICAP). Prior epinephrine injection is useful to slow or stop bleeding before thermal therapy application or clot guillotine.^{7,9} It also prevents excessive tissue destruction and transmural necrosis by thermal therapy. Removal of adherent clot can be done only when endoscopic therapy and surgical back up is readily available.¹⁰⁵

3. Mechanical therapy. For hemoclip application and band ligation, theoretically they come closely to surgical ligation. Parra - Blanco⁶⁵ reported largest series of 18 cases of hemoclippping with permanent hemostasis achieved in 95 per cent. Few cases series of band ligation were reported.^{4,9,14,106,107}

After endoscopic therapy the lesion should be under endoscopic observation for 5 minutes to make sure of no further bleeding. Then the patient is closely observed for rebleeding in at least another 72 hours by monitoring of vital sign, hematocrit and nasogastric intubation. Rebleeding, occurred in 9-22 per cent of large series, were usually within 1-4 days.^{6,8,9,61,65,88} Immediate endoscopy and repeat intervention were carried out for rebleeding by most authors. Some authors had tried repeated endoscopic bleeding control for more than once before sending patient to surgery. Successive endoscopies reveal tissue necrosis which heal within 4 weeks after endoscopic treatment and left a tender scar at 6 weeks.⁸⁸ About 5 per cent of Dieulafoy's lesions require surgical treatment.^{6,8,9,61,65}

Because of high success rate in therapeutic endoscopy, most reports obtained no tissue for histologic confirmation. Endoscopic ultrasonography with Doppler examination is a novel procedure to confirm the diagnosis by demonstration of vascular lesion and also guiding for intralesion injection sclerotherapy. Absence of arterial signal after endoscopic treatment is the indicator of therapeutic efficacy.^{56,108-111}

Surgical Treatment

Indications for surgical treatment are (1) Failure of therapeutic endoscopy, (2) Torrential bleeding

obscure visualization and preclude therapeutic modality, and (3) Therapeutic endoscopy is not available. Preoperative localization by endoscopy or angiography is the crucial point for surgical outcome and prognosis. Operative procedure should be a wide oversew ligation, wide wedge resection or segmental resection. Suture ligation may be inadequate because the pathologic artery run a tortuous course in the submucosa for as long as 2-4 cm.⁵⁶ Report of recurrent bleeding following surgery is rare.⁶² Theoretically wide wedge resection is the appropriate surgical treatment because of adequate pathologic artery removal with histologic confirmation. Conventional surgery or laparoscopic surgery with endoscopic guided can reduce operative time and prior gastrotomy is unnecessary.¹¹²⁻¹¹⁴ Segmental resection usually performed in lesion of jejunum and right colon. In case with preoperative angiographic study, angiographic catheter should be left in-situ for guiding surgeon to perform limited resection.^{24,72,72}

In acute upper GIB without preoperative localization, long anterior gastrotomy for adequate exploration of whole gastric mucosa is essential. Clots must be removed. If no bleeding lesion found, all mucosa surface is gently brush with dry gauze. Small adherent clot is teased away and brisk arterial bleeding can then be identified.^{16,68} Searching for duodenal lesion is done in the same manner through duodenotomy. It is very difficult to detect bleeding lesion of jejunum in emergency situation. Vetto⁷² reported intraoperative enteroscopy by using colonoscope in detection of jejunal Dieulafoy's lesion after angiographic catheter guide left in-situ and another one case by segmental irrigation after insertion of Anderson tube through multiple enterotomy. Barbier,¹⁵ Fox²⁶ and Matuchansky²⁵ can find this lesion by carefully palpation in the suspected area. Intraoperative endoscopy with peroral enteroscope or through enterotomy or laparoscopic assisted panenteroscope may be use for treatment of Dieulafoy's lesion of small bowels.^{83,84,115}

SUMMARY

Dieulafoy's lesion is unrecognized and underdiagnosed rather than a rare lesion. Diagnosis is mainly made on endoscopic visualization. Emergency endoscopy within 24 hr or immediately after correction of hemodynamic status is essential for successful initial

- diagnostic endoscopy. If initial endoscopy fails, repeated endoscopies is mandatory with meticulous searching for this minute lesion. Although endoscopic treatment of Dieulafoy's lesion utilizes the same principle as in treatment of bleeding peptic ulcer, but it is important to note that (1) All type of stigmata of recent hemorrhage must be treated because conservative treatment is associated with high recurrent bleeding rate and mortality due to the pathologic artery of Dieulafoy's lesion is larger than bleeding artery of peptic ulcer^{11,6}; (2) The absence of inflammation or scar formation of Dieulafoy's lesion is prone to necrosis or perforation from injection sclerotherapy or thermal therapy especially in the thin wall gut segment eg. duodenum, small bowel and colon. In contradiction, normal mucosa of Dieulafoy's ulcer makes mechanical therapy by hemoclipping or band ligation technically easier and yields successful treatment more than in peptic ulcer.
- Endoscopic treatment of Dieulafoy's disease is safe and effective with low related mortality and morbidity. Surgical treatment is indicated in about 5 per cent of cases. Understanding of pathology and natural history despite unclear pathogenesis contributes to increase accuracy of diagnostic endoscopy and selection of the effective and appropriate endoscopic or surgical treatment for this uncommon entity.
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