

CASE REPORT

Lethal gastric hemorrhage from a caliber-persistent artery of the antrum - a branch of the right gastric artery

Gurzu S¹, Copotoiu C², Molnar C², Azamfirei L³, Jung I¹¹ Department of Pathology² Department of Surgery³ Department of Intensive Care

Faculty of Medicine, University of Medicine and Pharmacy of Tirgu-Mures, Tirgu-Mures, Romania

Abstract**Aim:** To present a rarely diagnosed case of gastric Dieulafoy lesion.**Description of case:** A 62-year-old male was hospitalized with hematemesis. Laparoscopic ligation of two gastric ulcers located in the antrum was performed but the upper gastrointestinal bleeding was not stopped. The patient was transferred to another surgical clinic and he underwent an emergency abdominal laparotomy with re-suture of gastric ulcers. Considering his general condition and another recurrent bleeding, he was transferred to our hospital and a total gastrectomy of necessity was performed. The patient died four days after surgery because of sepsis. At autopsy, we identified diffuse peritonitis, hypertrophic cardiomyopathy and chronic pancreatitis with expanded fibrotic areas. Histological examination of the surgical specimen showed oversized tortuous vessels in the gastric submucosal layer with expansion into mucosa. Some of the vessels presented acute and/or organized thrombi with recanalization, in the others, lipid-rich atherosclerotic plaques were observed. Based on these criteria, the 'caliber-persistent artery', also known as 'Dieulafoy's lesion', was diagnosed.**Conclusion:** Dieulafoy's lesion should be suspected in every case of gastrointestinal bleeding in both adults and children. Hippokratia 2014; 18 (2):172-176.**Keywords:** Vascular malformation, gastrointestinal hemorrhage, gastroepiploic artery**Corresponding author:** Gurzu Simona, Associate Professor, PhD, Department of Pathology, University of Medicine and Pharmacy, 38 Ghe Marinescu Street, Post code: 540139, City: Targu Mures, Romania, tel: +40745673550, fax: +40265210933, e-mail: simonagurzu@yahoo.com**Introduction**

The most frequent causes of upper gastrointestinal bleeding are acute and chronic peptic ulcers. Lesser causes include vascular malformations that account for approximately 5% of cases¹ and can lead to patient's death.

Several types of congenital vascular malformations of the gastrointestinal tract were described and the differential diagnosis is difficult to be done. Their low incidence is rather based on the incorrect diagnosis than the true rarity². The 'caliber-persistence' is also known as 'caliber-persistent artery', 'submucosal aneurysm', 'large submucosal arteries', 'submucosal arteriole malformation', 'vascular malformation', 'gastric arteriosclerosis' or, in the French literature, 'Dieulafoy's erosion or lesion'²⁻⁴. The Dieulafoy's lesion was first described by Gallard in 1884 as 'millier aneurysm of stomach' and later by Paul Georges Dieulafoy (1839-1911), a French Professor of Pathology in 1897 as 'exulceratio simplex'^{2,5}. Both first used the term 'caliber-persistence' in 1962 in German literature⁶, and Krasznai in 1968 in English literature⁷. Although they were first considered distinct lesions, a unifying approach was proposed in 1988⁸ and was accepted

by most of the authors. This lesion usually involves the gastrointestinal tract, the stomach being followed by duodenum, colon and then jejunum, ileum, esophagus, rectum and anal canal¹⁻⁸ but caliber-persistent-arteries of the bronchial tubes, lips, eyelid and sciatic areas were described^{1,2,9,10}.

In the gastrointestinal tract, Dieulafoy's lesion refers to the persistence of an abnormally large and tortuous primary arterial branch that extends in the submucosa without caliber loss protruding through a small mucosal defect^{1,2,4,9}. In the stomach, it usually involves the proximal part and the lesser curvature.

In our paper, we present an undiagnosed Dieulafoy's lesion of the antrum in a 62-year old male which produces a lethal gastric hemorrhage. Considering the rarity of this lesion, (fewer than 140 papers published to date), we present the clinical and histopathological criteria used for its diagnosis, the particular pathogenesis of this case, and the therapeutic possibilities based on a review of the relevant literature.

Case presentation

A 62-year-old, previously healthy male, was presented with fulminant hematemesis and melena. No alcohol abuse, tobacco use or consumption of aspirin or non-steroidal anti-inflammatory drugs was declared. His serology demonstrated a severe anemia (hemoglobin 8 g/dl, hematocrit 22.8%).

An emergency esophagogastroduodenoscopy evidenced two bleeding protruded lesions with ulcerations, each of them 5-mm-sized, in the antrum and lesser curvature. Laparoscopic ligation of the 'kissed-ulcers' was performed but the bleeding recurred. One day later, the patient was transferred to the second surgical department. Emergency laparotomy and re-suture of the ulcers, below the gastric serosa were performed and was followed by three units of blood transfusion.

Because of syncope caused by severe re-bleeding, the patient was transferred to our hospital. Considering his general status, the extremely low-hemoglobin level (5.44 g/dl), and the massive hematemesis, we decided to perform a total gastrectomy and esophago-jejunal anastomosis. On exploration during surgery, we observed a pseudotumoral hardening of the pancreas with large fibrotic areas in the mesentery and the lesser omentum; iatrogenic injury of spleen also occurred intraoperatively. Splenectomy and pancreatic biopsy was performed. The patient was later managed in the Intensive Care Unit. His hemoglobin and hematocrit values reverted to normal ranges but he died within four days with an acute diffuse peritonitis and septic shock.

Macroscopic examination of the surgical specimen revealed two protruded and ulcerated lesions located in the antrum and lesser curvature, 5-mm-sized each of them, that were previously sutured in the laparoscopic surgery. Several fibrino-purulent membranes were observed on the serosa (peritonitis). On the cut section, corresponding to the two ulcerated lesions, blood-filled spaces protruding into the gastric wall from their base were identified. A hematoma was also observed in the deep layers of the gastric wall (Figure 1).

Histopathologic examination showed focal mucosal erosions lined by several vascular structures. Oversized vascular spaces and clusters of irregular vessels were observed in the muscularis mucosae and submucosa. These spaces, having a rich anastomosis of varying sized vessels, were closely linked to the mucosa. One of the largest submucosal vessels involved the mucosa, causing abnormal closure to the gastric lumen facilitating vascular rupture. Being tortuous and presenting recent mixed or red thrombi, some vessels presented aneurysm-like dilatations. Several large vessels with organized thrombi with recanalization were identified in the deep submucosal layer near to the muscularis propria (Figures 1, 2). In the high power view, Hematoxylin-Eosine, Van Gieson and Masson trichrome stains showed that most of these vessels were arteries and/or arterialized veins. Some of them had an indeterminate nature (vein versus artery). Focally, they presented large sprouting branches that connected the submucosal vessels with the mucosal

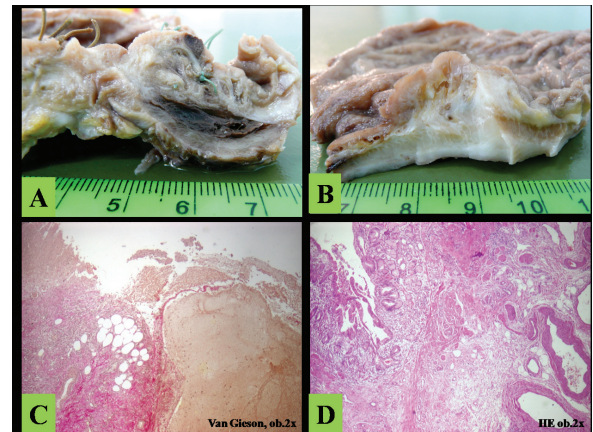


Figure 1: In case of gastric caliber-persistence, macroscopic examination reveals protruded lesions with large vascular spaces (A, B); mucosa is ulcerated and large hematoma is observed into the gastric wall (A). Microscopically, the vascular erosion can be seen (C), and the submucosal layer contains abnormally dilated arteries (D).

ones (Figure 2). These vessels had either a thick fibrotic wall or a large amount of foamy macrophages that were stored in their intima and medial layer leading to the formation of lipid-rich atherosclerotic plaques and luminal stenosis (Figure 2). The muscularis propria and subserosa also presented large tortuous arteries, hemorrhagic areas and a moderate inflammatory infiltrate composed by neutrophils, lymphocytes and few plasma cells. The inflammatory infiltrate was also observed on the serosal surface (peritonitis). Histological examination of the pieces that, macroscopically, showed pseudotumoral hardening of

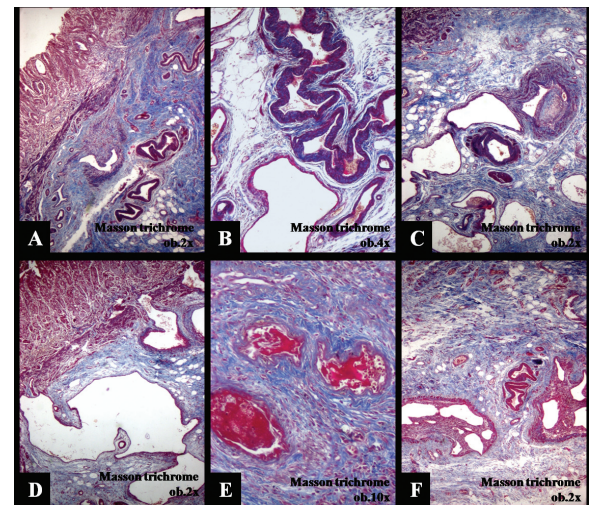


Figure 2: Histopathological findings of gastric caliber-persistence or Dieulafoy's lesion. Oversized vascular submucosal clusters containing tortuous vessels can be seen within the submucosal layer (A-D). Some of these large persistent vessels from the submucosa protrudes in the muscularis mucosae and communicates to the mucosa (D). Thick wall arteries (A, B), some of them with intramural foamy macrophages (C) are admixed with vessels with indeterminate origin (C, D). Some of vessels contain recent thrombi (E) but recanalized thrombi are also present (F).

the pancreas revealed a chronic pancreatitis with large fibrotic areas.

Based on the macro- and microscopical features, the final diagnosis was 'caliber-persistent artery' or 'Dieulafoy's lesion' in the stomach. The patient died owing to sepsis (peritonitis and bronchopneumonia). Hypertrophic cardiomyopathy, the patient's heart having 850 grams, and chronic pancreatitis were the associated lesions.

Discussion

'Caliber-persistent artery' or 'Dieulafoy's lesion' usually occurs in white males within the 5th decade of their life into the stomach^{2,4}, as in this case, but it can also be diagnosed in children, the youngest one being an eight-week-old infant^{2,11,12}. The proximal stomach is involved in about 90% of the cases and the antrum being affected in fewer than 10% of the cases^{5,13}. Although the pathogenesis of this lesion is not elucidated, most of the authors agree that this is a vascular malformation. This hypothesis is also sustained by its occurrence in children^{2,12}. It usually involves branches of the left gastric artery, which arises from the celiac trunk and supplies to the lower esophagus, esophagogastric junction and the first 6-10 cm of the proximal stomach, respectively of the lesser curvature. The antrum and its corresponding part of the lesser curvature are irrigated from branches of the right gastric artery, which arises directly from the hepatic artery passing through the lesser omentum to the lesser curvature. However, vascular anastomosis occurs among the left and right gastric artery, along the lesser curvature. Based on the antral location of the two ulcerated lesions, in our case, we suppose that the background of a variant branch of the right gastric artery was involved. Knowing the anatomy of the stomach is mandatory to identify the Dieulafoy's lesion and endoscopically perform sclerotherapy of the affected artery.

Sometimes, this lesion can be associated with other malformations, such as the loss of interstitial cells of Cajal¹². Associated-diabetes mellitus, arterial hypertension, ischemic heart disease, neurological diseases, liver, and respiratory or renal failure were also reported^{2,4}, but these significant comorbidities can be rather due to its occurrence in elderly people. Senger et al (2012) suggested that male predominance (M:F=2:1) can be because of hormonal dysfunctions at the submucosal arteriole arcade that occurs as result of lack of estrogenic protection². Senile atrophy of the tissues and aberrant angiogenesis associated with vascular ectasia were also postulated⁹. The associated lesions could trigger the arterial rupture but arterial pulsation may also disrupt the mucosa being exposed to gastric chemical content². In the present case, hypertrophic cardiomyopathy, pseudotumoral pancreatitis, lipid-rich atherosclerotic plaques and recanalization of some organized thrombi in the deep submucosal layer were associated. The organized thrombi that reflect a recurrent angioectatic thrombosis and atherosclerotic plaques could increase pressure in the submucosal persistent artery and favorize the rupture of its branches. To

our best knowledge, no other cases showing these associations have been reported to date.

The clinical diagnosis of gastric Dieulafoy's lesion can be established by performing a superior mesenteric angiogram, especially in patients with recurrent or fulminant hematemesis. In most of the reported cases, the lesion was undiagnosed and the mortality rate was over 60%^{1,3,6,8} although some of the recent reports have shown a decreasing rate to 8%².

Based on the literature data^{1-8,11-14} and the clinicopathological aspects of this case, some specific features can be established for the diagnosis of Dieulafoy's lesion of the gastrointestinal tract. It is a round mucosal defect, seen at endoscopy as a flat, ulcerated or protruded lesion lined by a vascular structure and centered by an artery protruding from its base⁵. Sometimes, both endoscopy and exploratory laparotomy can be negative owing the excess of blood² - the diagnosis being done either at angiography or under a microscope. Microscopically, the diameter of the submucosal artery is quite large, almost 10 times the normal diameter, and this artery penetrates into the muscularis mucosae and mucosa through the persistent Wanke's musculoelastic mantle without caliber loss^{1,3,8}. The arterial wall either can have a normal structure⁸, and fibrotic⁴ or can present atherosclerotic changes, as in our case. The accompanied vein can either be arterialized and dilated or can have normal diameter, with or without perforation^{4,8}. The clinico-pathological features are synthesized in Table 1^{1-8,11-14}.

Differential diagnosis of gastric caliber-persistent artery includes a range of lesions such as the true submucosal aneurysm or 'cirroid aneurysm' that involves the venous channels, angioectasia/angiodysplasia characterized by venous and capillary ectasias and an early angiographic venous filling (venous phase), arteriovenous malformations that represent direct connection between large feeding arteries and draining veins lacking the capillary beds, and hemangiolymphangiomas that consist of proliferation of capillary-type and lymphatic-type vessels^{4,9,15}. Other lesions taken into account are as follows: chronic peptic ulcer, portal hypertensive gastropathy, esophageal varices, Mallory-Weiss tears, tumors, gastric antral vascular ectasia ('watermelon stomach'), hemobilia, inflammatory diseases, telangiectasia, and aortoenteric fistulae^{7,10-13}. Incorrect diagnosis as chronic peptic ulcer can lead to vessels' ligation, as in this case, that can contribute to increasing likelihood of re-bleeding.

Other lesions taken into account in the differential diagnosis are the autoimmune diseases, such as the antiphospholipid syndrome that can produce gangrene of the stomach¹⁶. It can be primary or secondary to other autoimmune diseases and is characterized by intramural arterial and venous thrombosis, independently, by their caliber¹⁶.

In Dieulafoy's lesion the endoscopic hemostasis is the standard therapy achieved through mechanical rubber band ligation, thermocoagulation, laser photocoagulation, argon plasma coagulation, hemocliping, or chemi-

Table 1: Clinicopathologic features of the gastrointestinal caliber-persistence or Dieulafoy's lesion^{1-8,11-14}.

Parameter	Characteristics
Symptoms	<ul style="list-style-type: none"> - hematemesis (30%), sometimes preceded by recurrent 'minute vomits of blood' - melena (30%) or fresh anal bleeding - painless hematemesis+melena (20%) - hematochezia (5%) - iron-deficiency anemia (1%) - non-specific symptoms (9%): fever, fatigue, abdominal pain, vomiting, diarrhea, loss of consciousness, tachycardia, hypotensive, hemorrhagic shock - asymptomatic (5%)
Serology	<ul style="list-style-type: none"> - low level of hemoglobin (5-9 g/dl) - low hematocrit (22-25%)
Endoscopy	<ul style="list-style-type: none"> - ulcers or small red dots, polyps, dilated vessels - active arterial spurting from a minute, solitary and round mucosal defect - a fresh blood clot adherent to the mucosa - sometimes, negative findings
Panmesenteric angiography	<ul style="list-style-type: none"> - extravasation of the contrast medium into the gastrointestinal system, from an eroded artery (celiac trunk, left gastric artery, right gastric artery and gastroduodenal or mesenteric artery) - in the arterial phase: convoluted, enlarged and tortuous arteries - in the venous phase: late venous return, with accumulation of the contrast agent
Macroscopy	<ul style="list-style-type: none"> - small ulcers (2-5 mm), flat or protruded red masses - on cut section: within the wall, small or large blood-filled spaces
Microscopy	
<i>low power-view</i>	<ul style="list-style-type: none"> - large anastomotic vessels within the gastric/intestinal wall - hemorrhagic areas
<i>mucosa</i>	<ul style="list-style-type: none"> - aberrant indeterminate vessels, hemorrhages ± erosions, without inflammation
<i>m u s c u l a r i s</i>	<ul style="list-style-type: none"> - large vessels
<i>mucosae</i>	<ul style="list-style-type: none"> - the arteries are attached to the muscularis mucosae
<i>submucosa</i>	<ul style="list-style-type: none"> - large arteries with a diameter 10 times that of the normal arteries - the vessels have normal structure or present intimal thickening, subintimal sclerosis and medial muscular hypertrophy/fibroelastosis - acute thrombosis ± organized thrombi with/without recanalization - vessels abnormalities: vascular clusters, shunt vessels, feeder vessels, wall tufts, arterialized veins, aneurysm-like cavities, dissection-like lesions, atherosclerosis
<i>muscularis propria</i>	<ul style="list-style-type: none"> - normal structure or vascular clusters ± inflammatory infiltrate
<i>subserosa/serosa</i>	<ul style="list-style-type: none"> - normal structure or vascular clusters ± inflammatory infiltrate

cal vascular injection sclerotherapy using adrenaline/epinephrine, norepinephrine, ethanol, or polidocanol but combined therapy seems to offer the best results^{1,2,5,12,15}. In case of failure of endoscopic therapy, surgical thermo-coagulation or hemoclips application is used to control hemorrhage. The last therapeutic option is surgical resection - wedge resection, proximal/distal resection of the stomach, and total gastrectomy, respectively, depending on the involved artery.

Despite these well-defined diagnostic criteria and various available therapeutic approaches, Dieulafoy's lesion remains a life-threatening diagnostic challenge to the clinician that has important therapeutic and follow-up implications in both adults and children.

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Conflict of Interest

No conflicts of interest are declared.

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