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Endoscopic treatment of primary aorto-enteric fistulas: A case report and review of literature

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Abstract

BACKGROUND

Primary aorto-enteric fistula (PAEF) is a rare condition, traditionally treated in the acute, bleeding phase with open surgery or endovascular repair. However, these approaches have high morbidity and mortality, indicating a need for new methods. With advances in endoscopic techniques and equipment, haemoclipping of fistulas has now become feasible. Therefore, we present a systematic review of the English literature and a rare case of a PAEF successfully treated by endoscopic haemoclipping.

CASE SUMMARY

A 74-year-old man with an abdominal aortic aneurysm presented with symptoms of haemorrhagic shock and bloody stools. An oesophago-gastro-duodenoscopy was performed with haemoclipping of a suspected PAEF in the third part of the duodenum. Afterward, a computed tomography-angiography showed a contrast filled protrusion from the abdominal aortic aneurysm. Based on the clinical presentation and the combined endoscopic and radiographic findings, we argue that this is a case of a PAEF.

CONCLUSION

Endoscopic therapy appears capable of achieving haemodynamic stabilisation in patients with bleeding PAEF, serving as a bridge to final therapy.

Key Words: Endoscopy; Gastrointestinal haemorrhage; Surgical clip; Intestinal fistula, Vascular fistula; Systematic review; Case report

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Core Tip: Primary aorto-enteric fistula is a rare condition with high mortality. The current acute phase treatment is surgical or endovascular and is followed by high morbidity and mortality. The aim of this systematic review and case report was to put forward endoscopic haemoclipping as a new treatment option in the acute bleeding phase of an aorto-enteric fistula and, in a systematic manner, to search the literature for any evidence behind this therapy, including other reported cases.

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INTRODUCTION

A primary aorto-enteric fistula (PAEF) is a communication between the native aorta and the enteric system without prior surgery on the aorta[1]. Traditionally, treatment of a PAEF with acute bleeding includes open emergency surgical repair with *in situ* reconstruction or an extra-anatomic bypass of the aorta combined with repair of the bowel lesion. Over the last decades, endovascular aortic stenting has been introduced as a minimally invasive treatment option for abdominal aneurysms[2-4]. Closure of enterovascular fistulas from the vascular side is associated with better early survival than open surgery. A review of literature by Saers *et al*[5] reported an overall 30-d mortality rate for patients with PAEF of 44% and a mortality of 34% for patients who have had surgical treatment. By comparison, they found a 30-d mortality of 14% in a small group of patients who had endovascular repair. However, most of the benefit of lower mortality rates for patients treated with endovascular aortic stent was lost during long-term follow-up due to recurrent infection or recurrent AEF[6,7].

An aorto-duodenal fistula often presents itself with upper gastrointestinal bleeding and circulatory shock, which are symptoms identical to those of the much more common bleeding duodenal or gastric ulcers. Oesophago-gastro-duodenoscopy (OGD) is recommended as the first diagnostic choice in patients with signs of upper gastrointestinal haemorrhage[8,9]. OGD is, in most cases, successful in achieving haemostasis in patients with bleeding ulcers, and dual therapy with injection of epinephrine, electrocoagulation, or haemoclipping of the bleeding site or vessel is the state of art technique[10]. Sometimes, however, the bleeding is not caused by an ulcer but by a Dieulafoy lesion, a Cameron lesion, or bleeding from varicose veins among other reasons. Endoscopic treatment is also effective in achieving haemostasis and preventing rebleeding in these cases[11]. With advances in endoscopic techniques and equipment, large clips for the closure of vascular-enteric fistulas have come forward[12]. Per the literature and in our institution, such clips are successfully used for endoscopic closure of full-thickness gastrointestinal wall defects as well as interenteric or enterocutaneous fistulas[13,14]. Thus, clipping of fistulas has now become feasible, and the clipping of aorta-duodenal fistulas might be the next step forward.

The aim of this systematic review and case report was to put forward endoscopic haemoclipping as a new treatment option in the acute bleeding phase of an AEF and in a systematic manner to search the literature for any evidence behind this therapy, including other reported cases.

Literature search

This case report adheres to the SCARE criteria[15]. The systematic review follows the PRISMA guidelines[16]. The protocol was registered in Prospero (number CRD42019142202) before the literature search was commenced. Included were all original studies, including case reports describing symptomatic PAEFs treated with therapeutic endoscopy. A PAEF was defined as a fistula from the thoracic or abdominal aorta to the intestines, including the duodenum, ileum, jejunum, and all segments of the colon. Endoscopic treatment was defined as all therapeutic endoscopic procedures. Excluded were papers describing treatment of secondary fistulas, fistulas

from other branches of the aorta and other segments of the gastrointestinal tract, and papers not using endoscopy for treatment. The language was limited to English.

We performed an electronic literature search in PubMed, Embase, and The Cochrane Library for articles published between January 1999 and April 2020. The search was built as a “text word” search combining synonyms for “aortoenteric fistula” and “primary” and limited to English literature. The first author screened all titles and abstracts of the retrieved studies and performed full-text assessments to determine the inclusion. In any case of doubt, the second author assessed the study. Disagreements were resolved through discussion and consultation of the supervisor (BB).

Additional articles were found by screening reference lists of studies included after full-text assessment. To assess the risk of bias, the included studies were analysed according to the assessment tool provided by Murad *et al*[17]. **Figure 1** shows the PRISMA search strategy and the inclusion of studies. The data extracted were patient age, gender, anatomic location of the fistula, endoscopic finding, endoscopic treatment modality, subsequent treatment, follow-up length, and outcome. Because we did not expect to find any randomized clinical trials or high-quality cohort studies, we did not plan for any statistical analysis.

CASE PRESENTATION

Chief complaints

A 74-year-old man was admitted to our department with fresh bloody stools and melena during the evening.

History of present illness

Earlier on the same day, the patient was discharged after 4 d of admission due to gastrointestinal bleeding. During the earlier admission, an OGD to the second part of the duodenum revealed two small (8.0 mm) fibrin-covered ulcers in the duodenum with no sign of bleeding. Because this was the only pathological finding and considering the patient’s history, they were treated with dual therapy (injection of diluted epinephrine and electrocoagulation). Also, the patient received blood transfusions, intravenous fluid, and pantoprazole. During the following 4 d, the patient had minor episodes of dark stools but no fresh bleeding, and the haemoglobin levels increased.

History of past illness

The patient had several comorbidities including oropharynx cancer, chronic obstructive pulmonary disease, paroxysmal atrial fibrillation, and essential arterial hypertension. Also, the patient had an infrarenal abdominal aortic aneurysm with a diameter of 6.3 cm and a long neck of 2.2 cm in diameter, and an aneurysm on the right common iliac artery measuring 5.0 cm. The patient had regular check-ups for his aorta aneurysm at a vascular surgical department in another hospital.

Physical examination

At admission, the patient was pale but alert with a blood pressure of 95/70 mmHg and a heart rate of 68 beats per minute. On physical examination, auscultation of heart and lungs was normal, the abdomen was soft and without tenderness, but a pulsating filling could be felt to the left of the umbilicus. The rectal examination showed melena with fresh blood.

Laboratory examination

The plasma haemoglobin was 4.0 mmol/L.

FINAL DIAGNOSIS

The final diagnosis of the presented case is, in our opinion, PAEF, based on the combined endoscopic and CT-angiographic findings.

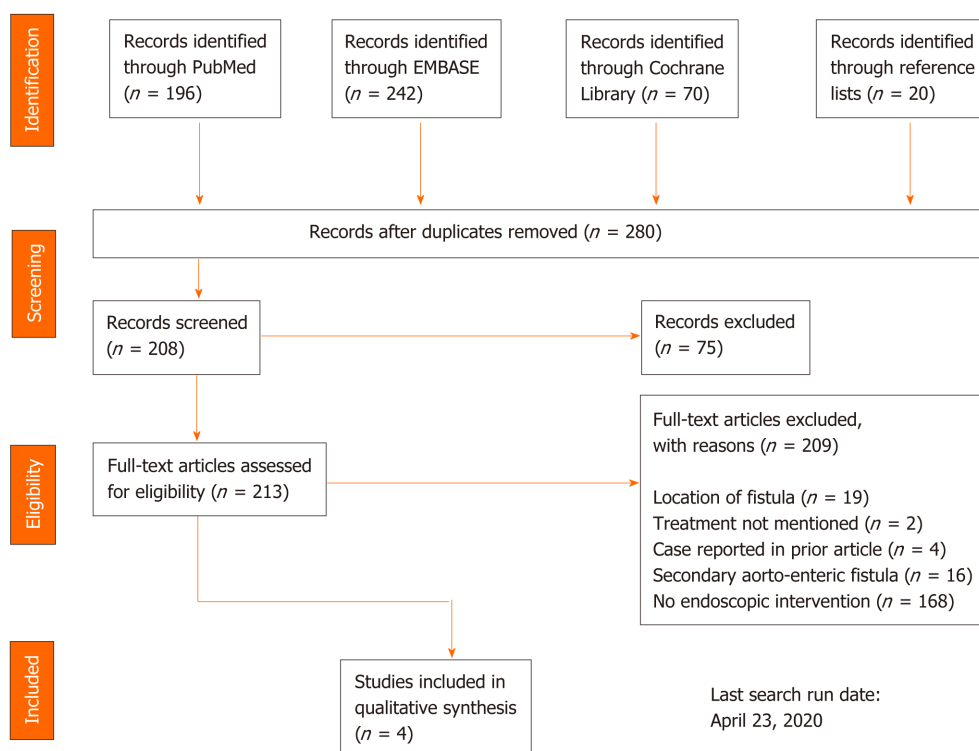


Figure 1 The PRISMA search strategy.

TREATMENT

The patient was readmitted with the abovementioned symptoms. An emergency OGD was performed, and the nonbleeding small ulcers in the duodenum were visualized without signs of bleeding. However, this time the endoscope was advanced further, and an erosion of the mucosa in the third part of the duodenum (measuring 5.0 mm) with a blood clot and a visible pulsating aorta underneath was found (Figure 2A). A PAEF was suspected, and haemostasis was achieved with three haemoclips placed deep in the wall of the gut, covering the fistula (Figure 2B). Following this procedure, no subsequent haemorrhage was identified. To support the hypothesis of an aorto-duodenal fistula, contrast-enhanced computed tomography (CT) with arterial and venous phase was performed the following day. The CT showed a contrast-filled protrusion from the abdominal aortic aneurysm towards the haemoclips adjacent to the aneurysm sack, separated by a mural thrombus (Figure 3). For possible vascular intervention, we contacted two vascular surgical departments. However, based on the patient's cancer disease and the CT-angiography, they did not find vascular therapy indicated and did not find it proven that a PAEF caused the bleeding. To our knowledge, the endoscopic pictures were not included in the decision-making.

OUTCOME AND FOLLOW-UP

The patient was discharged in his habitual condition after 10 d, without any signs of infection or rebleeding. Fourteen months later, the patient succumbed due to respiratory problems and terminal cancer without any incidences of gastrointestinal bleeding. The death was expected, and an autopsy was not sought.

DISCUSSION

The English literature identified only four case reports[18-21] fulfilling the inclusion criteria (Table 1). The anatomical location of the PAEF varied, and the endoscopic findings included pigmented protuberances, lesions/erosions, and oozing bleeding[22, 23]. In two of the cases, the treatment was dual, as recommended for bleeding ulcers

Table 1 Cases of primary aorto-enteric fistula

	Tsai <i>et al</i>[18]	Lee <i>et al</i>[19]	Kim <i>et al</i>[20]	Mok <i>et al</i>[21]	Present case
Age in year, Sex	69, male	86, female	63, male	67, male	74, male
Anatomic location	Third part of duodenum	Sigmoid colon	Second part of duodenum	Oesophago-jejunal anastomosis	Third part of duodenum
Cause of PAEF	Aortic aneurysm	Aortic aneurysm	Aortic aneurysm	Infectious thoracic pseudo-aneurysm; oesophago-jejunal anastomotic leak	Aortic aneurysm
Endoscopic finding	Vessel-like bleeding with blood clot adhesion	Nodular lesion with central dimpling (small, depressed area)	Active bleeding	Oozing blood and blood clot	Mucosal erosion/nodular lesion with central depression and blood clot; Pulsating aorta underneath
Endoscopic treatment	Epinephrine and haemoclips	Electro-coagulation and haemoclips	Haemoclips alone	Fibrin sealant	Haemoclips alone
Endoscopic outcome	Successful haemostasis	Initial haemostasis, rebleeding	Successful haemostasis	Successful closure of fistula	Successful haemostasis
Following treatment	Open surgical repair of the aneurysm and bowel	Angiographic embolization	Endovascular stent repair with angiographic embolization and open surgical repair of the bowel	Endovascular stent repair with drainage of aneurysm sac (performed before endoscopic treatment)	None
Outcome	Alive at 24 mo follow-up	Died during the angiographic procedure	Alive at 12 mo follow-up	Alive at 14 mo follow-up	Died 14 mo after endoscopy

PAEF: Primary aorto-enteric fistula.

[8]: Diluted epinephrine injection and haemoclipping[18]; and respective electrocoagulation and haemoclipping[19]. In the third case, haemoclipping alone was used as a bridge to surgery[20]. A fourth case described fibrin sealant placed through the endoscope combined with percutaneous endovascular aneurysm repair[21]. In all four cases initial endoscopic haemostasis was achieved. In one case, endoscopic haemostasis was only achieved for a couple of hours whereafter massive rebleeding occurred[19]. Two cases described successful endoscopic haemostasis until final surgery was performed[18,20]. In the fourth case, the combined treatment successfully closed the fistula[20].

More than 50% of PAEF are situated in the duodenum because of its close anatomical relation to the aorta. Other locations include the oesophagus, stomach, ileum, jejunum, and colon[5,24]. One review found an incidence of PAEF as the cause of gastrointestinal haemorrhage in 0.18% of cases[25]. Another study, asking 180 surgeons if they have ever treated a patient with a PAEF during their career, suggested the incidence to be greater[26]. The classic clinical presentation includes abdominal pain, signs of upper gastrointestinal bleeding, and an abdominal pulsating mass.

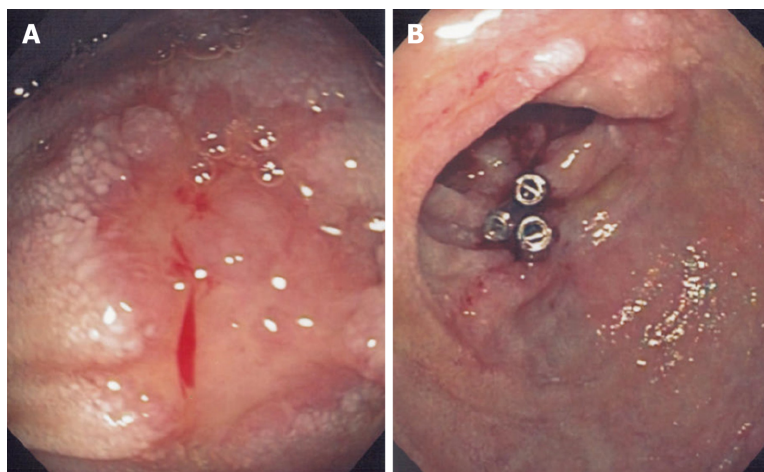


Figure 2 Endoscopic findings. A: The mucosal erosion with a blood clot; B: The erosion closed with three haemoclips.



Figure 3 Computed tomography-angiography reconstruction showing the protrusion from the aortic aneurysm towards the haemoclips in the duodenum (arrow).

Before the diagnosis, patients often have a “herald bleeding” that may cause exsanguination and death. However, only 6%-28% of the cases present all three symptoms. Thus, the majority of the patients present as “atypical”[5,24,27,28]. An AEF is therefore important to consider in patients with gastrointestinal haemorrhages and an aortic aneurysm.

A contrast-enhanced CT scan is regarded as the best diagnostic tool for the detection of AEF[28-31]. However, in a patient without a history of vascular surgery presenting with upper gastrointestinal bleeding, an AEF is not the first diagnosis that comes to mind. Hughes *et al*[31] investigated the signs found on CT scans. They showed that CT scans have an overall specificity of 100%, but the sensitivity was only 50%. The presence of ectopic bowel gas or extravasation of contrast into the bowel lumen increased the sensitivity to 100%. The finding of a branch from the aortic wall had a sensitivity of 80% and specificity of 75%. These numbers are in agreement with the findings of others[5,24,31,32]. Thus, in the diagnosis of an AEF, a positive CT result is useful but a negative CT finding does not yield reliable information. Because ulcers are common, OGD is the gold standard for the diagnosis and treatment of upper gastrointestinal bleeding. An OGD identified the AEF or showed other abnormalities in only 25%-50% of confirmed AEF cases, likely due to a typical OGD often omitting the examination of the third part of the duodenum[5,33]. In four of the cases described in this study, active bleeding was seen at the sight of the fistula during OGD[18,20,21].

In other cases, where OGD was the diagnostic tool, the AEF was described as a submucosal tumour-like lesion and being “pulsating” [23,34]. Sometimes oozing bleeding, the presence of a blood clot or the sense of pulsation may be the only thing that differentiate the descriptions given of the AEF from a description of other enteric fistulas [35].

No study on the diagnostic specificity and sensitivity for the endoscopic detection of PAEF exists. In our opinion, the negative CT finding in the case presented here does not necessarily rule out an AEF, especially following endoscopic haemostasis. On the contrary, the CT-angiography with three-dimensional reconstruction showed a contrast-filled branch from the abdominal aorta aneurysm in close relation to the duodenum, a finding with a specificity of 75% according to the literature [31]. In our opinion, the endoscopic and the CT findings together strengthen the diagnosis.

In all the cases described in the literature, final surgery (endovascular or open) followed the endoscopic treatment, and the endoscopically achieved haemostasis successfully formed a bridge to surgery. The patient presented herein was the only patient who did not have surgery after endoscopic haemostasis was achieved. The reason for this was due to the patient’s multiple comorbidities, including incurable cancer, a limited life expectancy, and a high risk of postoperative adverse outcomes. However, the haemoclipping was immediately lifesaving and was an effective long-term treatment.

Haemoclips can remain *in situ* for a long period, but we found no literature describing the life span or the mean *in situ* time for a haemoclip. Olmez *et al* [36] described a haemoclip *in situ* for more than 2 years. In our experience, a well-placed haemoclip for haemostasis after polypectomy is often found *in situ* at the adenoma control endoscopy after 6-12 mo, but no studies were found to support this. However, the clip functions as a ligation, and the nature of the fistula determines whether a ligation is sufficient to close it. Open vessels are closed by ligation, as are fistulas following anastomotic leakage of the gut. It is unknown whether a PAEF can be closed by simple ligation (clipping).

When a PAEF is clipped, the clip may function as a marker for the fistula site before final therapy. A clip can mark a lesion in the gastrointestinal tract [37] and increases the success rate of angiographic embolization of bleeding arteries in ulcers [38]. Based on our knowledge of the more common secondary AEFs, we know that infection is a common problem when the fistula is closed from the vascular side only. In a trial comparing closure of secondary AEFs using a vascular stent to open surgical repair, Kakkos *et al* [6] found that vascular stent repair can achieve immediate haemostasis and has a better short-term outcome. However, an infection of the stent and sepsis often follow the procedure, losing most of the benefit during long-term follow-up. The open communication to the bacteria-filled enteric side likely causes the infection. Therefore, closure of the enteric lesion by open surgery is recommended to follow vascular stenting [6,39].

The option of two minimally invasive procedures combined have not been investigated. It may be possible to clip (or stent in the oesophagus) the fistula from the enteric side followed by stenting from the vascular side. A successful case of secondary AEF initially closed from the vascular side immediately followed by endoscopic closure from the enteric side has been reported [40].

The small number of endoscopically treated PAEFs described in the literature limits this study. This small number increases the difficulty of creating clinical recommendations. However, bleeding from an AEF is a life-threatening condition, and every effort to stop the loss of blood as soon as possible is desirable. By creating a bridge to surgery and achieving haemostasis, critical time is bought for the patient. This time may mean that the experienced surgeon is present or that the patient can be transferred to another facility for optimal care. Thus, any modality creating immediate haemostasis for these patients represents a therapeutic improvement. It is unknown whether endoscopic treatment such as haemoclipping or epinephrine injection can aggravate ongoing bleeding from an AEF.

CONCLUSION

Endoscopy is the first-choice modality for the diagnosis and treatment of upper gastrointestinal bleeding including a PAEF, which is a rare finding. Endoscopic therapy including haemoclipping can establish lifesaving, immediate haemostasis from a bleeding PAEF, thus stabilizing the patient without hampering subsequent endovascular therapy or surgery. Endoscopic therapy might be useful as a bridge to

surgery.

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