

## Successful conservative treatment of enterocutaneous fistula with cyanoacrylate surgical sealant: case report

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**SUMMARY: Successful conservative treatment of enterocutaneous fistula with cyanoacrylate surgical sealant: case report.**

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*Aim. Enterocutaneous (EC) fistula is an abnormal communication between the gastrointestinal tract and the skin. The majority of EC fistulas result from surgery. Only 15-25% of EC fistulas are spontaneous and they often result from underlying diseases such as Crohn's disease, radiation and chemotherapy.*

*Case report. A 62-year old woman who, in 2012, underwent Pylorus-preserving cephalic pancreaticoduodenectomy (PPPD sec. Traverso-Longmire), due to an advanced pancreatic ductal adenocarcinoma (pT3N1M1). After surgery, the patient underwent chemotherapy with folfirinnox regimen. In December 2016, as a result of the appearance*

*of metastatic liver lesions and perianastomotic recurrence, the patient underwent second line treatment with Gemcitabine and pab-paclitaxel. After five months from the beginning of this new second line therapy she presented an EC fistula. The fistula of the patient was successfully treated with total parenteral nutrition and with percutaneous injection of cyanoacrylic sealant.*

*Results. The result suggests the advisability of percutaneous injection of sealant devices, such as cyanoacrylate glue; in order to successfully control stable Enterocutaneous fistulas with acceptable morbidity and mortality especially in particular situations, such as, with low output EC fistulas without signs of complications or on patients considered not suitable for surgery, a conservative approach could ensure the control of the fistula.*

*Conclusion. This approach is easy and safe, viable and useful for future trials on the efficacy in conservative treatment of EC fistula.*

KEY WORDS: Enterocutaneous fistulas - Cyanoacrylate sealant - Minimally invasive - Spontaneous closure.

### Introduction

Enterocutaneous fistula is an abnormal connection between the small or large bowel and the skin which leads to external drainage of intestinal content. Post-operative fistulas occur frequently in standard abdominal surgery practice and only 15-25% arises spontaneously (1). These often result from an underlying disease such as Crohn's disease, malignancy, radio or chemotherapy, diverticular disease, vascular failure and ischemia of the mesentery (2, 3). EC fistulas are associated with significant morbidity and mortality because the fistula often leads to nutritional deficits, septic complications and con-

comitant diseases that may appear as a result of prolonged hospital stay. Sepsis is the leading cause of death in most cases. Increased mortality has been shown to be associated with high initial fistula output (4, 5). The presence of complications and the presence of patient comorbidity are factors increasing the risk of death. The management of enterocutaneous fistula should initially consist of its identification, followed by correction of fluid and electrolyte imbalance, aggressive treatment of sepsis and control of fistula output. Another very important aspect to take into account, in order to choose between surgery and conservative treatment is the clear definition of the anatomy of enterocutaneous fistula (6). The exact anatomy of an EC fistula is usually defined by a combination of clinical observation, biochemical analysis of fistula effluent and radiological investigation, of which contrast studies, such as computed tomography and magnetic resonance imaging are the most commonly employed (5). The most common risk factors associated with non-healing fistulas are foreign body radiation, inflammation, infection, inflammatory bowel disease, epithelization of the fistula tract, neoplasm and distal obstruction. The pre-

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sence of any of these components in EC fistula represents an indication to surgery (7).

However, the goal is always to close the fistula with minimal morbidity and mortality. Many retrospective studies reported experiences from around the world. These studies emphasize a high associated mortality and give some insight into factors that predict fistulas closure, both spontaneous and operative, and death. There is an ongoing discussion on which is the better route of nutrition, and a related debate on whether periods of “bowel rest are beneficial or detrimental in patient with fistula”. The practice of total parental nutrition (TPN) for EC fistulas is widely adopted. The primary role of nutritional support is the prevention of malnutrition (8-10).

This paper presents the conservative treatment of a consolidation using cyanoacrylate glue (Glubran 2<sup>®</sup>, GEM Italy). This glue performs an adhesive hemostatic and sealing action on the tissues and creates an antiseptic barrier against the most common pathogenic agents. Glubran 2<sup>®</sup> is already used in surgical and endoscopic procedures to guarantee high bonding strength between biological tissues, and when applied on anastomoses it provides a higher resistance to intraluminal pressures (11).

## Case report

A 62-year old woman who, in 2012, underwent Pylorus preserving pancreaticoduodenectomy (PPPD) due to moderately differentiated pancreatic ductal adenocarcinoma with the infiltration of common bile duct, biliopancreatic ampulla and duodenum wall (pT3N1M1). The patient had a medical history of jaundice, about twenty days before the diagnosis of pancreatic cancer and surgery. No other morbidity in history. In June 2012, the patient underwent surgery with the presence of metastasis just in one of twenty isolated lymph nodes. After surgery, she was treated with adjuvant chemotherapy with folfirinnox regimen for two years until March 2014. From March 2014 to September 2016, chemotherapy was interrupted and a regular six-month follow-up with laboratory tests and imaging examinations was performed. During this period there was no evidence of persisting disease or recurrence. In November 2016, due to abdominal pain and sub-occlusive symptoms, the patient underwent abdominal computed tomography which revealed recurrence of disease in celiac axis, in the right abdominal aortic area and compression of the portal vein by local recurrence and thrombosis of the inferior vena cava. The CT also revealed three new liver metastasis. In December 2016, the patient started a second line chemotherapy treatment with gemcitabine and nabpaclitaxel. Since January, she repeatedly experienced fever, which caused the interruption of chemotherapy and

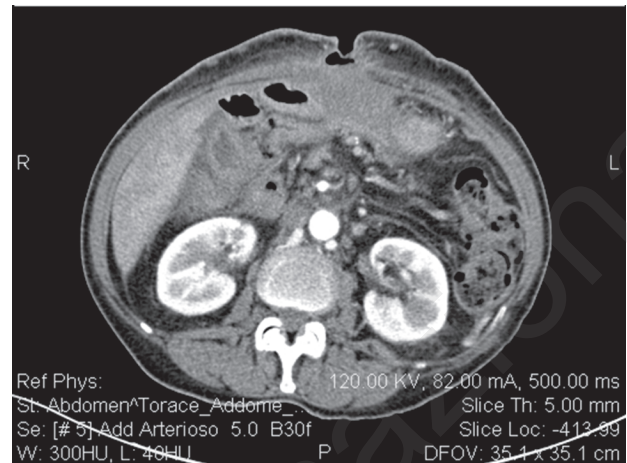


Figure 1 – CT scan: umbilical fluid collection.

started an antibiotic therapy. In April 2017, she presented a swelling in the umbilical region of the abdomen for which she underwent urgent abdominal ultrasound which revealed very severe distension of intestinal loops and thickening and hyperechogenicity of the subcutaneous adipose tissue with a connected sub-parietal intestinal loop. This situation was confirmed with CT scan (Figure 1). She underwent ultrasound guided percutaneous drainage of the umbilical fluid collection which revealed the presence of an *Escherichia coli* and *Enterococcus Faecalis*.

After this procedure, she started total parenteral nutrition (TPN) in order to improve fluid and electrolyte balance and assure adequate nutritional support, and she also started empirical broad spectrum antibiotic therapy. After a week on total parenteral nutrition, the average output of the fistula was less than 100 ml/die. The patient's general conditions were stable and there was no sign of sepsis or intraperitoneal contamination. It was therefore decided to treat the EC fistula with a percutaneous injection of cyanoacrylate glue. A 3 ml of Glubran 2<sup>®</sup> injection was performed with a flexible cannula passing through the outer fistula orifice to the internal lumen (Figure 2). On the day after the procedure the fistula stopped to drain. She continued TPN and antibiotic therapy for a few more days. After three days from the procedure, the patient started eating fluid aliments and no kind of material was produced from the orifice of the fistula.

## Results

The following CT scan with gastrointestinal contrast agent revealed the absence of fistula (Figure 3) and the patient started a 1350 Kcal semifluid diet with no enteric material deriving from the pre-existing outer fistula orifice. After 30 days an ultrasound control was performed.



Figure 2 - Cyanoacrylate percutaneous injection.

med and confirmed the absence of the subcutaneous fluid collection.

## Discussion

Enterocutaneous fistulas are common complications, deriving from abdominal surgery. Despite an advance in parasurgical care, nutritional support antibiotics and intensive care, these complications still represent a major cause for mortality. Sepsis, electrolyte disturbance and malnutrition are the three major causes for death in patients with EC fistulas.

There are several ways in which EC fistulas could be classified, such as their relationship to the output, to the etiology or to the source: a high output EC fistula is characterized by  $>500$  ml/24 hours, while a low output fistula produces  $<200$  ml/24 hours. Fistulas can also be classified as “complicated” and uncomplicated, where a complicated fistula is one which presents a septic complication or intra-abdominal infection or a fistula whose output causes electrolyte disturbance and severe malnutrition (5). When no adverse prognostic factors are present, often the best decision is to obtain the closure of the fistula through conservative strategies. Should there be septic complication or some adverse prognostic factors, such as, for example, the epithelization of the fistula tract, neoplasm and distal obstruction, surgery would be the most appropriate strategy.

All kinds of treatments need a preliminary study of the anatomy of the fistula and a multidisciplinary team

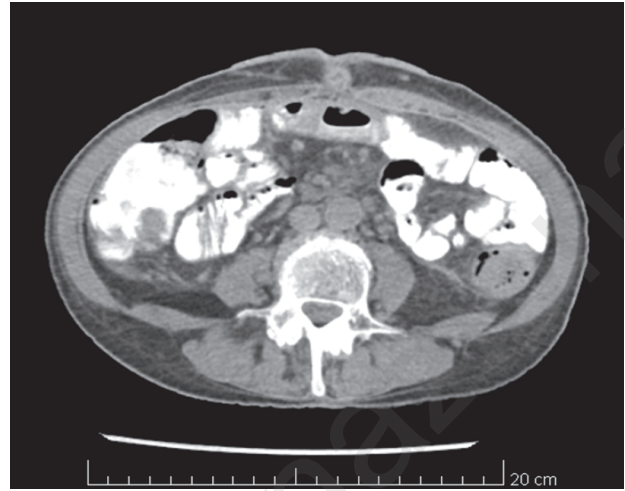


Figure 3 - CT scan: no evidence of enterocutaneous fistula after cyanoacrylate injection.

approach. Regardless of the option chosen, a correct management includes bowel rest with the use of total parenteral nutrition and an adequate nutritional input. There are often situations in which a conservative management is not enough and surgery is deemed to be dangerous. In such cases, a minimal invasive approach with percutaneous instillation of a sealant with high adhesive and haemostatic properties might be a safer solution and could ensure the closure of the fistula (4, 5, 12-15).

Glubran 2® is a cyanoacrylic glue with demonstrated high adhesive and haemostatic properties. As soon as the glue reaches living tissues, it starts to polymerize, generating a film with high tensile resistance (16). It was created to control the bleeding gastric varices. This synthetic glue has a triple action: sealing, haemostatic and bacteriostatic (10). Because of its chemical and physical features, this kind of glue may represent the ideal agent for percutaneous sealing of non healing EC fistulas (15).

## Conclusions

EC fistula is still a complex problem which can be optimally managed through a careful and interdisciplinary approach. Surgical treatment with resection should be carefully planned and should be used when conservative treatment fails. A low output fistula with no evidence of sepsis or localized infection should be treated with a conservative approach. In particular conditions, the conservative treatment does not ensure a definitive resolution of the fistula and patients cannot tolerate further extensive surgery because of comorbidity. Moreover, EC fistulas are among the main causes of prolonged hospitalization and delayed return to social activities. This case report aims to demonstrate that the percutaneous injection of cyanoacrylic glue is a flexible and

safe procedure that may be included in the treatment of non healing enteric fistulas.

In our case, cyanoacrylic glue immediately sealed the fistula thus preventing further leakage from the outer orifice.

Percutaneous injection of Glubran 2<sup>®</sup>, either imaging guided or not, has to be considered as an experimental

treatment. However, it is a flexible and safe procedure and may be helpful for the treatment of non healing EC fistulas, approached in a conservative way and which are not suitable for surgery. Furthermore, this technique could be effective in reducing the closure time of post-operative EC fistulas and reducing the number of re-operations.

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