CASE REPORT

DOI: http://dx.doi.org/10.15403/jgld-4798

Recombinant Tissue Plasminogen Activator: The New Concept for Dissolving Septae in Loculated Peri-pancreatic Fluid Collection prior to Endoscopic Drainage. A Case Report

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Received: 29.12.2022
Accepted: 16.03.2023

ABSTRACT

Peri-pancreatic fluid collections are late complications of acute pancreatitis. Loculated peri-pancreatic fluid collections, even rare, remain the „black sheep" in terms of drainage, due to difficulty to puncture all compartments, thus prohibiting proper drainage of all compartments. Recombined tissue plasminogen activator (r-tPA) has been advocated as treatment of the loculated collections, due to its ability to dissolve the fibrinous strands and thus facilitate proper drainage. We report the case of a 58 years-old male presenting with a painful loculated peri-pancreatic fluid collection secondary to acute pancreatitis. We performed Alteplase injection, followed by successful endosonographic drainage with lumen apposing metal stent of the collection after 48 hours. Our observation suggests that r-tPA could be a new strategy for loculated collections management, ensuring better drainage and limiting the indication for surgical treatment.

Key words: loculated – peri-pancreatic fluid collection – r-tPA – Alteplase – pancreatitis – case report.

Abbreviations: EUS: endosonography; LAMS: lumen apposing metal stent; MRI: magnetic resonance imaging; r-tPA: recombined tissue plasminogen activator; WOPN: walled off pancreatic necrosis.

INTRODUCTION

Endosonographic (EUS)-guided drainage is the most efficient nonsurgical alternative for draining post-pancreatitis fluid collections into the stomach or duodenum. There is limited data on EUS-guided drainage of loculated peri-pancreatic fluid collections.

In the early 2000s, studies documented the efficacy of instillations with fibrinolytics in loculated collections for proper drainage of pleural collection and ascites. There are few studies on instillation of fibrinolytics in post-pancreatitis loculated collections such as pseudocysts or walled off pancreatic necrosis (WOPN), mostly limited on streptokinase instillation [1]. Alteplase has a well-defined role in treating loculated collections, due to its potential in dissolving the fibrin strands, thus acting as a fibrinolitic.

We present the case of a 58-year-old male diagnosed with loculated peri-pancreatic fluid collection, consecutive to an episode of acute pancreatitis. We performed transcutaneous ultrasound-guided Alteplase injection in the collection, followed by successful EUS-guided drainage with a lumen apposing metal stent (LAMS) at 48 hours.

CASE REPORT

A 58-year-old male presented to our unit 4 months after an abdominal trauma in the epigastric area. The patient was nonsmoker and admitted regularly drinking alcohol; no other risk factors or family history of pancreatic diseases were identified. The patient mentioned progressive abdominal pain that started 2 months prior the presentation. On clinical examination he had normal weight (body mass index of 19.7 kg/m2) and pale skin, without visible jaundice. The blood work documented increased values of lipase (534 IU/dL; normal range: under 60 IU/dL), moderate anemia (hemoglobin 92 g/L; normal range: 132-166 g/L) and slightly elevated inflammatory markers (C reactive protein levels of 12.6 mg/L; normal range: under 8 mg/L). Abdominal ultrasound described an inhomogeneous peri-pancreatic cystic lesion of 98 over 140 mm

with multiple septa, but minimal debris. Upper gastrointestinal endoscopy described an extrinsec compression located in the posterior part of the gastric body. Endoscopic ultrasound and magnetic resonance imaging (MRI) confirmed a giant (>10 cm diameter), peri-pancreatic cystic lesion with hypoechoic content and multiple septations; no communication with main pancreatic duct, no visible vessels within the surrounding wall and no dilatation of the biliary tree or pancreatic duct were described. No discontinuation of the Wirsung duct was seen in the imaging examinations. The pancreatic parenchyma did not meet the criteria for chronic pancreatitis.

The patient was seen by a multidisciplinary team, bringing also focus on the nutritional status. Bearing in mind that the patient would further benefit from drainage and after having explained the risks and benefits of the procedure to the patient, we performed a transabdominal ultrasound guided alteplase injection in the collection 48 hours' prior the interventional procedure (EUS guided drainage with LAMS). At first after reaching the cyst, we suctioned dark brown fluid, highly suggestive for pancreatic pseudocyst, with negative string sign (not suggestive for mucinous fluid), with no hematic content. We then injected 50 mg of Alteplase diluted in 0.9% sodium chloride under ultrasound guidance into the loculated collection, without changes in the coagulation tests or other adverse reactions (Fig. 1). Broad spectrum antibiotic treatment was initiated at this point and continued for 5 days (3 days after EUS-guided drainage), according to the American Society for Gastrointestinal Endoscopy stating that antibiotics should be maintained 3 to 5 days after EUS-guided drainage of cystic lesions [2]. The fluid analyses showed high lipase levels and low mucin, with negative cultures. Endosonographic examination 2 days after the injection of the Alteplase revealed that the septa were dissolved within the peri-pancreatic lesion measuring 9/10 cm (Fig. 2). Additional data obtained from EUS were minimal ascitic fluid, multiple peri-pancreatic lymph nodes (suggestive for inflammatory origin). The next step performed was EUS-guided transmural drainage using 15mm diameter LAMS (HOTAXIOS, Boston Scientific, USA) using a linear probe (GF-UCT180, Olympus, Europe) performed by an experienced endosonographist (having performed over 1,000 EUS). The procedure was successful with efficient drainage of dark brown fluid in the stomach (Fig. 3). At one week the follow-up endoscopy showed the stent in position, being able to enter the cavity. No necrotic

Fig. 1. Ultrasound image presenting a giant loculated peri-pancreatic fluid collection measuring 14/10 cm during Alteplase injection.

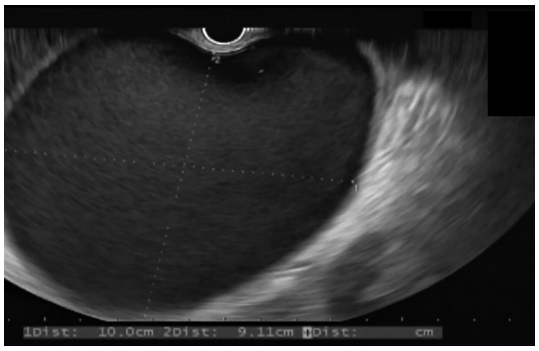

Fig. 2. Endosonography view of a cystic peri-pancreatic lesion measuring 9/10 cm with hypoechoic content, with no fibrin septations (48 hours after Alteplase injection).

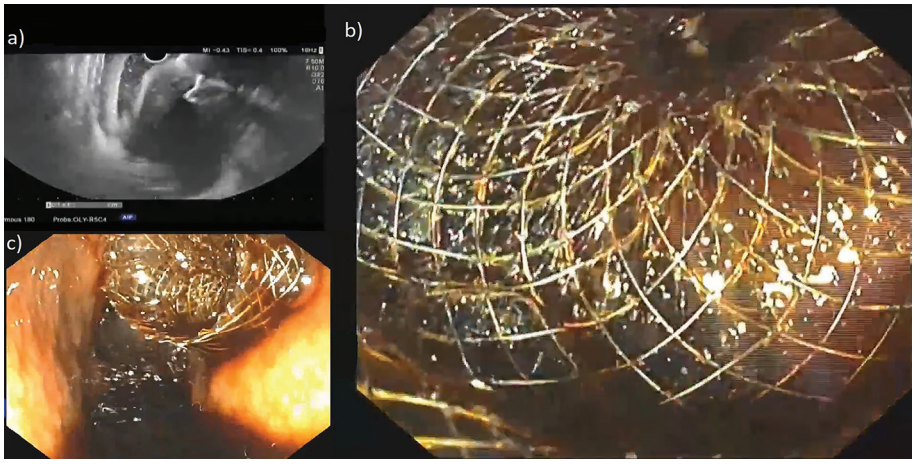

Fig. 3. a) Endosonography image showing opened flange of self-expandable metal stent inside the collection (Hotaxios); b) Endoscopic view of intragastric flange of lumen apposing metal stent at deploy; c) Endoscopic view of intragastric lumen apposing metal stent after deploy showing exteriorization of dark brown fluid suggestive for pancreatic pseudocyst.

areas were detected. At 4 weeks the stent was removed after complete resolution of the collection at computer tomography evaluation, without any further complications. The patient undergone close follow-up.

DISCUSSION

We described the use of r-tPA in loculated peri-pancreatic fluid collection prior to EUS-guided drainage. By dissolving the fibrinous bridges, r-tPA fluidified the content of the peripancreatic collection allowing a rapid resolution of the collection once it was drained.

Acute pancreatitis has become one of the most frequent causes of hospitalization in gastroenterology departments worldwide. Even though mortality has decreased to 5%, severe and difficult to treat complications warrant special interventions [3]. Peri-pancreatic fluid collections include pancreatic pseudocysts and WOPN. Pseudocysts are extrapancreatic cavities filled with fluid, presenting a thick fibrin or granulation tissue wall, occurring in 10-20% of cases of acute pancreatitis and in a third of patients with chronic pancreatitis. Endoscopic treatment for symptomatic, complicated or fast-growing pseudocyst and for WOPN is nowadays the first line therapy, with success rated of 80-90% [4].

Endoscopic ultrasound-guided drainage greatly reduced the number of postprocedural complications such as hemorrhage and perforation. Drainage is indicated in patients with symptomatic collections (abdominal pain, weight loss, jaundice, vascular stenosis, gastric outlet obstruction), collections over 5 cm that do not regress within 6 weeks or complicated pseudocysts (infected, ruptured, fistulized or bleeding). EUS-guided drainage is indicated in WOPN offering the possibility to perform minimally invasive necrosectomies during endoscopic reevaluation. ESGE recommends drainage of pancreatic pseudocysts using double-pigtail 7-10Fr plastic stents or LAMS, whilst when draining WOPN LAMS are preferred [5]. The superiority of EUS-guided drainage over conventional endoscopic drainage has been documented in two large randomized controlled trials indicating that EUS-guided drainage was more efficient and had less complications [6]. Since the content of our collection was homogenous multiple plastic stents were a viable and efficient method of drainage. However, we opted for a LAMS for a more rapid evacuation of the content and shorter duration of the drainage procedure albeit the higher cost of the LAMS compared to the plastic stents. Multiple randomized controlled trials show that early removal of LAMS is important in order to reduced risk of adverse reactions such as bleeding [7]. Extensive septations can indicate cystic neoplasia, though contrast enhanced EUS or MRI are required to clarify this differential diagnosis [4]. Although puncturing a post-pancreatic fluid collection bearded the risks of secondary infection, cellulitis, sepsis and fistula, it was important in our case, since Alteplase needed time to act within the collection [8]. In our case, to minimize the infectious risks, we opted for large spectrum antibiotic treatment.

Alteplase is a biosynthetic representative of r-tPA and works as thrombolytic agent. While Alteplase is mainly used in acute ischemic stroke, acute myocardial infarction, acute massive pulmonary embolism and blocked catheters, some studies report on its role in dissolving fibrin within loculated collections (ascites, pleural collections). The fibrinolytic agent disrupts loculations by breaking the fibrin septs and facilitates proper drainage of the collection [8]. Studies are scarce, focusing mostly on pleural collections with the use of urokinase or streptokinase and show even more efficient pleural drainage of the collections after intrapleural instillation of r-tPA. Surgimoto et al. [8] documented the resolution of loculated pleural collections in 75% of the patients after tPA instillation and drainage. Moreover, Froudarakis et al [9] showed that the use of r-tPA is effective in dissolving fibrin septa in loculated pleural collections. Van Veen et al [10] showed that the use of r-tPA in polymicrobial peritonitis in mice was effective in reducing the inflammation and cleaving the fibrin deposits. A Cohrane database review of 7 studies including 761 participants found that intrapleural fibrinolysis brought benefits (less need for surgery without increasing the rate of adverse events, shorter hospital stay, lower hospital costs) in the evolution of patients with pleural empyema or parapneumonic effusions [11]. The use of fibrinolytic agents in post-pancreatitis collections is scarcely documented, though in our case we can observe the efficacy of dissolving the fibrin septa after Alteplase injection. Even though Bhargava et al. [12] describe the efficacy of streptokinase instillation by percutaneous catheter in decreasing the need for necrosectomy, the study had a low power. When choosing the type of fibrinolytic agent, Alteplase presents benefits since it has less antigenic reactions compared to streptokinase and greater fibrin specificity compared to urokinase [13]. Studies on pleural collections show the efficacy of doses from 4 to 100 mg/day. In our case, we have used 5 0mg of Alteplase for fibrinolysis. One must bear in mind the possible complications associated with tPA administration such as: pain, hemorrhage, fever, anaphylaxis, abdominal discomfort [4].

CONCLUSIONS

Large multiloculated peri-pancreatic fluid collections are seldom encountered and only few data from the literature concern the management in these situations. In our patient we describe the injection of alteplase in a giant loculated peri-pancreatic fluid collection prior to EUS-guided drainage. Multicentric studies should further investigate the efficacy of tPA injection to dissolve septa in a multiloculated peripancreatic collection making drainage of loculated peri-pancreatic fluid collections more efficient.

Conflicts of interest: None to declare.

Author's contributions: C.V. and M.S.I. conceived the study. A.S. and R.T. analyses and interpreted the data. G.C and M.S.I searched the literature. C.V. drafted the manuscript. All the authors revised the manuscript and approved the final version.

Acknoledgements: We thank Vasile Sandru, Mihai Ciocîrlan, Oana Plotogea, Bogdan Florin Dumbravă and Adriana Carasel for their contribution.

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