

Two cases of Wegener's granulomatosis with pancreatic pseudocyst treated by endoscopic ultrasonography (EUS)-guided drainage

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Wegener's granulomatosis is a systemic vasculitis with prominent involvement of the respiratory tract and kidney. There are 10 patients with Wegener's granulomatosis in the literature who were documented as acute pancreatitis. We present two cases with Wegener's granulomatosis presenting with acute pancreatitis and pancreatic pseudocyst. Endosonography-guided drainage of the pancreatic pseudocyst led to rapid clinical improvement. Pancreatic pseudocyst in Wegener's granulomatosis is not reported in the literature, and these are the first cases of Wegener's granulomatosis to be managed by endosonography-guided cyst drainage. The safety of endosonography-guided pancreatic pseudocyst drainage and the clinical features of the previous Wegener's granulomatosis cases with acute pancreatitis are discussed.

Key words: Pancreatitis, Wegener's granulomatosis, endoscopic ultrasonography

Endoskopik ultrasound ile tanı alan 2 adet Wegener granülomatozlu pankreatik psödokist vakası

Wegener granülomatozu sistemik bir vaskülit eşidi olup respiratuar sistem ve böbrek tutulumu belirgindir. Literatüde 10 adet pankreatit tanısı alan Wegener granülomatozlu vaka mevcuttur. Yazımızda 2 adet akut pankreatitle birlikte psödokist geliştiren vakayı bildiriyoruz. Pankreatik psödokistlerin endoskopik ultrasonografi ile drenajı çabuk klinik iyileşme sağlamaktadır. Pankreatik psödokist Wegener granülomatozu hastalarında sık olarak bildirilmemiş olup mevcut vakalar ilk örneklerdir. Bu yöntemin güvenilirliği yazımızda tartışılmıştır

Anahtar kelimeler: Pankreatit, Wegener granülomatozu, endoskopik ultrasonografi

INTRODUCTION

Pancreatic pseudocysts (PPs) belong to a large and heterogeneous group of cystic pancreatic lesions and represent a complication of acute or chronic pancreatitis. Because of improvement in their sensitivity and more widespread availability of diagnostic imaging techniques, the incidence of PPs seems to be steadily increasing. The development of new interventional options for the diagnosis and treatment of PPs allows for different approaches to the disease (1).

The ideal approach for puncture of PPs combines endoscopy with real-time endosonography (EUS) by using an interventional echoendoscope. Several investigators have described the use of EUS longitudinal scanners for guidance in transmural punctures and drainage procedures. By using this technique, the puncture of cysts under direct endosonographic control is possible, even when there is no bulging of the gastric or duodenal wall and also in patients with portal hypertension. This improves

the safety of the PP puncture and increases the number of patients amenable for endoscopic transmural drainage. Further, EUS-guided drainage reduces the risk of complications, e.g., bleeding, by using color Doppler to access vessels between the gastrointestinal (GI) wall and the cyst (2).

Wegener's granulomatosis (WG) is a vasculitis of unknown origin characterized by prominent involvement of the upper and lower respiratory tract and kidney. The histological pattern consists of the triad of giant cell granuloma, necrosis and vasculitis involving capillaries and small- and middle-sized arteries. WG can virtually affect any organ and tissue; it rarely involves the GI tract (3).

There are 10 cases of pancreatitis with WG in the literature. On the other hand, we could not find a case with PP treated with endoscopic drainage among the previous cases. Therefore, we describe herein two cases of WG with PPs. Pancreatitis could have occurred as a result of vasculitis in our case. We also think immunosuppression was a factor of the PP complication. We performed endoscopic drainage and observed a decrease in the cyst size with clinical improvement in both patients.

CASE REPORTS

CASE 1

A 37-year-old male was admitted to Gazi University Department of Gastroenterology in January 2007 with abdominal discomfort and nausea. He had been diagnosed as WG with lung and kidney involvement since June 2006. He was on cyclophosphamide and steroid treatment. He also had a massive upper GI bleeding episode in June 2006. He had a history of pancreatitis one month ago. After the acute pancreatitis, a PP appeared on the pancreas.

His temperature was 37.0°C, pulse 66 beats/min, and blood pressure 100/70 mmHg. The physical examination revealed a midline scar with epigastric pain.

The initial laboratory investigations showed: hemoglobin: 8.6 g/dl (reference range: 11.7-16 g/dl), C-reactive protein: 34 mg/dl (0-6), sedimentation: 52 mm/hour, total bilirubin: 1.1 mg/dl, serum amylase: 463 IU/L (28-128 IU/L), urinary amylase: 232 IU/L, gamma glutamyl transpeptidase: 95 IU/L (normal: 0-38 IU/L), alkaline phosphatase 104 IU/L (30-120 IU/L), serum creatinine 1.7 mg/dl (normal: 0.81-1.44 mg/dl), and blood urea nitrogen: 20 mg/dl (17-43 mg/dl). Other electroly-

tes were in the normal range. c-ANCA showed a positive pattern with p-ANCA negativity. An upper GI series disclosed no definite abnormality, and a chest X-ray was normal.

An abdominal US performed upon his admission to the hospital revealed a 9x7 cm in diameter cystic lesion in the body of the pancreas. There was another cystic lesion in the head of the pancreas, 3x5 cm in diameter. Magnetic resonance imaging (MRI) of the abdomen was also performed, revealing two cystic lesions in the head and the body of the pancreas (head cyst, 48x40 mm; tail cyst: 83x79 mm).

The immunosuppressive treatment was stopped after the diagnosis of acute pancreatitis. Broad spectrum antibiotics (piperacillin and tazobactam) were started for the septic fever. Parenteral nutrition was also initiated.

Technique of EUS-guided PP drainage

EUS examination revealed a pancreatic cyst 10 cm in diameter (Figures 1, 2). We performed a one-step approach for PP drainage using a 3.8 mm working channel linear array echoendoscope (Pentax, Montvale, NJ, USA) and a cystotome (Wilson Cook, Winston-Salem, NC, USA). The optimal puncture site was determined using linear scanning function. Doppler ultrasound function is used to discriminate major vessels and collateral veins. After determination of the optimal site for puncture, the PP was punctured with cystotome using the knife tip of the inner catheter. Electrocautery (ERBE Generator, USA Inc., Marietta, GA, USA) was performed with needle knife settings (coagulation power 25-30 W and autocut to 80-100 W). The metal part of the inner catheter was then withdrawn, leaving the Teflon® catheter in the pancreatic cyst. A sample of cyst contents was then aspirated and submitted for biochemical, cytological and tumor markers analysis. A 0.035-inch guidewire was passed through the inner catheter into the cyst cavity. The guidewire position was confirmed using fluoroscopy. The outer 10 Fr sheath of the cystotome is equipped with a diathermy ring, which was advanced through the puncture site using electrocautery, thus enlarging the puncture site. The cystotome was then removed, leaving the guidewire in the cyst cavity. The puncture site was dilated using an 8 mm dilator balloon over-the-wire. A 10 Fr double pigtail stent was placed over-the-wire under endoscopic and fluoroscopic monitoring (Figure 3).

After EUS-guided PP drainage, the size of the cyst decreased significantly after one week and at 10 days, the PP had disappeared. There was also a decrease in the size of the smaller secondary cyst without drainage. There were no signs of septic complications including fever. Abdominal pain resolved. The patient was discharged with steroid treatment, which was restarted by the Rheumatology Department for the treatment of WG.

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CASE 2

A 54-year-old female was admitted to the emergency department in November 2008 with the complaint of abdominal discomfort and high fever. She had been diagnosed with WG and related end-stage chronic renal failure since early 2007. She was on a chronic hemodialysis program. The patient was under steroid treatment for WG. She was diagnosed as acute pancreatitis with high levels of serum and urine amylase levels and had high fe-

ver in the follow-up, which was probably related to the infected PP in the tail portion of the pancreas. Vancomycin and imipenem were started for septic picture; however, after 21 days of broad spectrum antibiotic treatment, the fever persisted.

At the first physical examination, she was a poorly nourished patient. Her temperature was 38.1°C, pulse 88 beats/min, and blood pressure 110/60 mmHg. Physical examination revealed rebound and tenderness in the epigastrium.



Figure 1. EUS (endosonographic) view of the first case with PP (pancreatic pseudocyst).



Figure 2. EUS drainage in the first case.

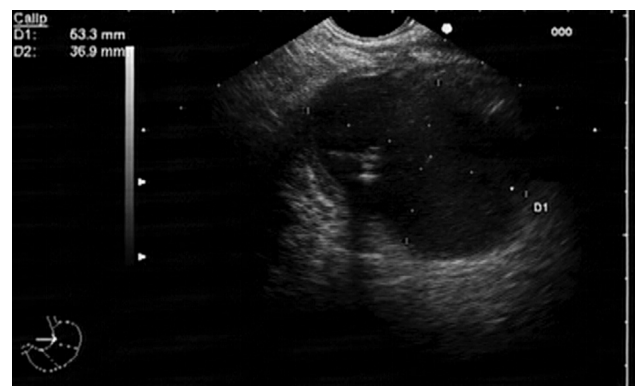


Figure 3. Pancreatic cyst with catheter.

Her hemoglobin value was 7.32 g/dl (reference range: 11.7-16 g/dl) and hematocrit 20.8%. Other complete blood counts were normal. C-reactive protein was 96 mg/dl (0-6). Sedimentation rate was 48 mm/hour. Creatinine and blood urea nitrogen were 2.41 (normal: 0.81-1.44 mg/dl) and 27 (17-43 mg/dl), respectively. Other electrolytes were in normal limits. Total bilirubin was 1.1 mg/dl. Fasting blood glucose was 101 mg/dl. Gamma glutamyl transpeptidase and alkaline phosphatase were 114 IU/L (normal: 0-38 IU/L) and 170 IU/L (30-120 IU/L), respectively. Serum amylase was 625 IU/L (28-128 IU/L). Serum lipase was 89 ng/dl. Serum albumin and total protein were 1.8 g/dl (3.5-5.2 g/dl) and 4.6 g/dl (6.6-8.3 g/dl), respectively. Serum α -fetoprotein, serum CA 19-9 and CEA were all within normal limits.

An abdominal computed tomography (CT) performed upon her admission to the prior hospital revealed a pseudocyst in the tail and body of the pancreas measuring 121x70x80 mm. There were also perigastric, peripancreatic and mesenteric multiple lymphadenopathies. We performed an endosonography, revealing a PP containing parenchymal debris. The size of the cyst was 12x10x9 cm and it was seen to bulge into the antral region of the stomach. We performed EUS-guided cystogastrostomy. After the catheter implantation, pus material was discharged from the cystic lesion. The sample of the aspirate revealed high amylase and lipase values (656 IU/L and 89 IU/L, respectively). CA 19-9 and CEA were in normal limits. The culture of the aspirate was unsuccessful, which may have been related to the simultaneous broad spectrum antibiotic therapy.

After one week, we observed a clinical and laboratory improvement and a reduction in the cyst size. The PP had completely disappeared after three weeks. We did not give a greater spectrum of immunosuppression to our two patients because of the new PP occurrence and the clinical improvement with drainage.

DISCUSSION

Pancreatic involvement in WG has been described rarely. It may present as a tumor-like lesion (4-6), acute pancreatitis (7-9) or exocrine pancreatic insufficiency (10). Very seldom, pancreatic involvement represented the initial manifestation of the disease (4,5,7). Two out of the three cases described showed a rapid progressive course (5,7); the

third was promptly treated with cyclophosphamide and corticosteroid therapy (4).

Data from 123 patients with pancreatic cystic lesions of unknown origin indicated that the combination of EUS with fine needle aspiration (FNA) allowed for the correct diagnosis in 97%, whereas EUS alone yielded only 73% correct diagnoses (11,12).

EUS was suggested as a technique that allows more accurate drainage of the cysts, with a lower risk of perforation and bleeding. With regard to hemorrhage, it should be emphasized that color Doppler and power Doppler assessment rules out the risk of vascular perforation during puncture, but the risk of hemorrhage from decompression of a vascular lesion of the cyst still remains (3). Giovannini *et al.* (13) performed EUS-guided drainages of a PP or a pancreatic abscess (PA) in 35 patients, with a mean cavity size of 7.8 cm. EUS-guided drainage was successful in 31 of 35 patients (88.5%); only 4 patients with PA underwent surgery. One recurrence of the 15 PPs and two relapses of the 18 PAs were observed, with a mean follow-up of 27 months (6-48 months). Sriram *et al.* (14) reported their experience on 8 patients with PP and portal hypertension. All patients were found to have successful resolution of the cyst at follow-up six weeks later. More recently, Kahaleh *et al.* (15) retrospectively compared the results of EUS-guided PP drainage versus endoscopic transmural treatment. A total of 99 consecutive patients underwent endoscopic PP management according to this predetermined treatment algorithm: patients with bulging lesions without obvious portal hypertension underwent endoscopic transmural drainage (n=53); all others underwent EUS-guided drainage (n=46). There were no significant differences between the two groups regarding short-term success (93% vs 94%) or long-term success (84% vs. 91%). No clear differences in efficacy or safety were observed between conventional and EUS-guided cystoenterostomy.

Varadarajulu *et al.* (16) compared EUS and esophagogastroduodenoscopy (EGD) transmural drainage in a prospective randomized trial of PP patients. Thirty patients were randomized to undergo PP drainage by EUS (n=15) or EGD (n=15). Of the 15 patients randomized to EUS, drainage was not undertaken in one, because an alternative diagnosis of biliary cystadenoma was established. Although all the patients (n=14) randomized to EUS underwent successful drainage (100%), the procedu-

Table 1. Demographic, clinical and laboratory features of WG patients with acute pancreatitis in the literature (including our cases)

Patient (Ref)	Age (yrs)	Clinical presentation	Extra-pancreatic features	Treatment	F/U
Patient 1 (6)	68	Pseudotumor	Sinusitis, orchitis	Surgery, Cs+Cyc	R
Patient 2 (4)	62	Pseudotumor	Otitis, pulmonary nodules and cavitation	Biliary stent+ Cs+ Cyc	R
Patient 3 (5)	50	Pseudotumor	Polyneuritis, renal failure	Surgery, Cs+Cyc	R
Patient 4 (9)	57	AP (6 episodes)	Bilateral otitis media, nasal chondritis, pulmonary cavitation and nodules, renal failure	Cs+Cyc	R
Patient 5 (7)	65	AP (single episode)	Episcleritis, hemoptysis, arthralgia	No specific treatment given (diagnosis is post-mortem)	D
Patient 6 (8)	45	AP (single episode)	Pulmonary cavitation and nodules, bilateral parotis enlargement	Cs+Cyc	R
Patient 7 (10)	66	Pancreas insufficiency	Arthralgia, nasal and buccal ulcerations, renal failure	Cs+Cyc	R
Patient 8 (17)	48	AP + pancreatic mass	No extra-pancreatic involvement	Cs+Cyc	R
Patient 9 (18)	47	AP (2 episodes)	Rhinitis, eye involvement, mouth ulcers, arthralgia	Cs+Cyc	R
Patient 10 (19)	20	AP (2 episodes)	Multiorgan involvement (renal, lung, splenic vein thrombosis, skin, ischemic colitis)	Cs+Cyc, plasmapheresis	D
Patient 11 (Case 1)	37	AP (single episode)	Lung, kidney	EUS-guided PP drainage	R
Patient 12 (Case 2)	54	AP (single episode)	Lung, kidney	EUS-guided PP drainage	R

Cs: Corticosteroid. Cyc: Cyclosporine. AP: Acute pancreatitis. R: Remission. D: Died. F/U: Follow-up.

re was technically successful in only 5 of 15 patients (33%) randomized to EGD ($p < 0.001$). All 10 patients who failed drainage by EGD underwent successful drainage of the pseudocyst on a crossover to EUS. There was no significant difference in the rates of treatment success between EUS and EGD after stenting, either by intention-to-treat (ITT) analysis (100% vs. 87%; $p = 0.48$) or as-treated analysis (95.8% vs. 80%; $p = 0.32$). No significant difference was observed between EUS and EGD with regard to complications either by ITT (0% vs. 13%; $p = 0.48$) or as-treated analyses (4% vs. 20%; $p = 0.32$). Technical success was significantly greater with EUS than EGD, even after adjusting for luminal compression and sex (adjusted exact odds ratio 39.4; $p = 0.001$) [16].

Our two cases were under corticosteroid treat-

ment and the outcome was successful endoscopic drainage. WG is a vasculitis that can result in operative complications. Therefore, the most noninvasive technique will be the most suitable procedure in PP. There are few reports in the literature about WG presented with PP (Table 1).

In conclusion, we presented herein two cases of WG pancreatitis treated with successful EUS-guided endoscopic drainage. We described our drainage procedure in detail. Our aim in this regard was to show the effectiveness and confidence of the EUS-guided drainage. The endoscopic procedure resulted in a reduction in pseudocyst size and clinical improvement of the patients. These cases show that EUS-guided drainage of PP in WG is a safe method for treatment, with a short hospital stay.

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