

The clinical feature and outcome of groove pancreatitis in a cohort: A single center experience with review of the literature

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ABSTRACT

BACKGROUND: Groove pancreatitis (GP) is a rare form of chronic pancreatitis that is less common and is now gaining awareness with multimodal imaging modalities. Our aim is to analyze the mid-long term outcomes of patients diagnosed with GP with different treatment approaches.

METHODS: A computerized search from electronic patient record database between May 2013 and June 2019 with the keywords “groove”, “paraduodenal” was applied. The clinical, radiological and pathological data of 25 patients diagnosed with GP were obtained.

RESULTS: In the GP patient group, the median age was 55 (25–87) and 80% was male. Alcohol and tobacco abuse was 40% among GP patients. The most common symptoms were upper abdominal pain (84%) and nausea-vomiting (40%), respectively. Gastric outlet obstruction was observed in 4 (16%) patients. CT and EUS imaging were performed to majority of cases (96% and 92 %, respectively). EUS-FNA was done in 14 of 25 (56%) patients. It was reported as atypia, adenocarcinoma and benign in 2 (8%), 2 (8%) and 10 (40%) patients, respectively. EUS-FNA was helpful to diagnose two pancreatic head adenoCA whose preliminary radiological evaluation was GP. The mean follow-up period was 29 (3–71) months. Conservative approach was the predominantly preferred treatment (%56). Apart from conservative approach, treatment strategies included biliary stenting, sphincterotomy, wirsung stenting via ERCP, cholecystectomy etc. Considering all treatment modalities, symptoms improved in 12 (48%) patients and progressed with recurrent pancreatitis attacks in 7 (28%) patients.

CONCLUSION: Because GP is a less well-known form of pancreatitis, it presents several challenges for clinicians in diagnosis and treatment. This form, which can mimic pancreatic malignancy in particular, must be differentiated from carcinoma. EUS(±FNA) is a useful diagnostic tool complementary to imaging. Although the conservative approach remains the first choice in most patients, the clinician should consider invasive endoscopic procedures and surgical options in special cases when necessary.

Keywords: Groove; pancreatitis; paraduodenal.

INTRODUCTION

First described in the 1970s, groove pancreatitis (GP) is a segmental form of chronic pancreatitis characterized by fibrotic

scarring of the pancreaticoduodenal groove, an anatomic region bordered by the head of the pancreas, duodenum and the common bile duct.^[1] Cystic dystrophy of heterotopic pancreas, paraduodenal pancreatitis, pancreatic hamartoma

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of the duodenum, paraduodenal wall cyst, and myoadenomatosis are all terms grouped together, from a pathological viewpoint, as varying definitions of GP.^[2] GP develops on the background of heterotopic pancreas in duodenal wall. This heterotopic tissue may develop ischemic inflammation under alcohol and smoking stimulation. Such pancreatitis may result with intramural duodenal cysts and eventually becomes an inflammatory tumor in the periampullary region responsible for chronic obstructive pancreatitis.^[2,3] The other proposed pathophysiologies include aberrant drainage through the duct of Santorini,^[3,4] pancreas divisum^[5] and hyperplasia of Brunner's glands.^[6,7] Groove carcinoma (GC) is known to originate from the pancreatoduodenal groove area.^[8] There are increasing number of pancreatic cancers arising from the groove termed GC.^[9] Computed tomography (CT), magnetic resonance cholangiopancreatography (MRCP), endoscopic ultrasonography (EUS) and EUS-Fine Needle Aspiration (EUS-FNA) are the techniques used for the diagnosis and differential diagnosis. The aim of this study was to evaluate the clinical course of 25 patients with this relatively rare condition as well as review the relevant literature.

MATERIALS AND METHODS

This is a single center study encompassing the period between May 2013–June 2019. It was approved by the Local Ethics Committee of our institution (protocol no. 2019-22/419). In order to find the eligible patients, a computerized search from electronic patient record database of general surgery clinic, gastroenterology clinic and radiology departments with the keywords “groove”, “paraduodenal” was applied. 28 patients were filtered from the database but three of 28 patients were excluded from the study due to the final diagnosis was gastric cancer. As a result, a total of 25 GP patients were retrospectively analyzed on the basis of pathological findings following EUS, EUS-FNA and a combination of radiologic images. Baseline demographic features, laboratory test results, CT, MRI, EUS and EUS-FNA findings were documented. The current status of the patients was documented by contacting the phone numbers registered in the hospital data system. Common bile duct (CBD) dilation was defined as ≥ 7 mm and main pancreatic duct dilation was defined as ≥ 3 mm in diameter at CT or MR imaging. Patients with benign cytology GP were scheduled to a follow-up program with medical treatment.

A systematic literature search was also performed in PubMed, Embase, and Cochrane Library for studies on GP published between January 1, 2005 and March 1, 2021. Search terms used were “groove pancreatitis,” “paraduodenal pancreatitis,” “cystic dystrophy of heterotopic pancreas,” “duodenal dystrophy,” “pancreatic hamartoma of the duodenum,” “paraduodenal wall cyst,” “myoadenomatosis,” and synonyms restricted to title, abstract, and keywords. Case reports were excluded. All original studies reporting on GP and all synonyms, with respect to diagnosis, treatment, and outcome were listed in Table 4.

The analysis was conducted with SPSS 23 (SPSS, Chicago, IL). Descriptive statistics were used to describe baseline characteristics and outcome variables.

RESULTS

When the baseline characteristics of 25 GP (shown in Table 1) were analyzed, patient sex was predominantly male (80%) and median age was 55. Alcohol and tobacco abuse was 40% among GP patients. The dominant presenting symptom was upper abdominal pain (84%) while nausea-vomiting symptom (40%), mostly, precede it (Table 2). Gastric outlet obstruction (GOO), which can be one of the surgical indications in patients with groove pancreatitis, was observed in 4 (16%) patients, while one of these patients died from prostate cancer complications in the 8th month after conservative follow-up. Duodenal stent was applied to a patient whose EUS-FNA result was reported as atypia and died due to lung squamous cell carcinoma complications. Another GOO symptomatic patient whose EUS-FNA reported as atypia, was followed closely and lived asymptotically in his 34-month follow-up without the need of any intervention after conservative management. Finally, the last patient who had GOO symptom was interpreted as GP according to the CT and MRI images (Fig. 1), with very high level of CA 19–9 underwent EUS-FNA and the final diagnosis was consistent with pancreatic head adenocarcinoma, the lesion was 2 cm in diameter and

Table 1. Patient characteristics

Patient characteristics	Median (min-max) or n (%)
Number of patients	25
Age-median (range)	55 (25–87)
Gender (male)	20 (80)
Comorbidities	
Hypertension	18 (72)
Diabetes	2 (8)
COPD	1 (4)
No comorbidities	4 (16)
Pancreatitis	
One attack	16 (64)
>1 attack	8 (32)
Addiction	
Alcohol and smoker	10 (40)
Only smoker	8 (32)
Co-existent cancer	
Prostat adeno CA	1 (4)
Pulmoner SCC	1 (4)
Renal cell carcinoma	1 (4)

COPD: Chronic obstructive pulmonary disease; CA: Carcinoma; SCC: Squamous cell carcinoma.

Table 2. Symptoms and laboratory values

	n (%)
Presenting symptoms	
Upper abdominal pain	21 (84)
Nausea-vomiting	10 (40)
Weight loss	6 (24)
Jaundice	4 (16)
Gastric outlet obstruction	4 (16)
Median (Min-Max)	
Laboratory values	
CRP (mg/L)	4.1 (0–317)
WBC ($\times 10^9/L$)	9630 (5100–19500)
Serum Amylase (U/L)	98 (33–1359)
Serum Lipase (U/L)	173 (24–2800)
Serum CEA (ng/ml)	2.03 (0–186)
Serum CA 19-9 (U/ml)	13 (0–21351)
Serum AST (U/L)	20 (9–1300)
Serum ALT (U/L)	20 (6–840)
Serum bilirubin (mg/dl)	0.73 (0.11–19)

CRP: C-reactive protein; CEA: Carcino Embryonic Antigen; CA 19-9 = Cancer antigen 19-9; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; WBC: White blood cell.

resectable with no vascular abutment/encasement. Pancreaticoduodenectomy was recommended to the patient but the patient refused surgery.

CT and EUS imaging (Fig. 2) were performed in almost all of the cases (96% and 92%, respectively). When all the radi-

ologic tools and EUS investigations included, the dominant findings were edematous duodenal wall (EDW) in 92% and swollen head of pancreas (SHOP) in 80% (Table 3).

EUS-FNA was done in 14 of 25 (56%) patients. It was reported as atypia, adenocarcinoma and benign in 2 (8%), 2 (8%) and 10 (40%) patients, respectively. Management of the three patients (two with atypia and one with pancreas head adenocarcinoma) was mentioned above. The management of the remaining one with pancreas head adenocarcinoma (this patient was also interpreted as GP in the first work-up) underwent whipple procedure (pT3N0M0, The American Joint Committee on Cancer (AJCC) TNM staging) and he has local recurrence in post-surgery 63-month follow-up. Four of 10 patients with benign pathology treated conservatively while 4 patients had endoscopic biliary/wirsung stenting and 2 patients underwent laparoscopic cholecystectomy.

Symptomatic relief was obtained in 12 of 25 (48%) patients. Eight (32%) patients were treated with conservative approach, 2 (8%) patients received biliary stenting/sphincterotomy, one (4%) patient underwent laparoscopic cholecystectomy and one patient received both of the aforementioned treatments. Recurrent pancreatitis was encountered in 7 (28%) patients. Three patients (12%) were followed-up with conservative approach and 4 (16%) patients received biliary stenting/sphincterotomy one of whom had concomitant laparoscopic cholecystectomy. Conservative approach was abstinence of alcohol and tobacco, pancreatic rest and analgesics.

Two mortalities (8%) were related to the complications of accompanying malignancies (one patient had metastatic prostate adenocarcinoma, and the other one had metastatic squamous cell carcinoma).

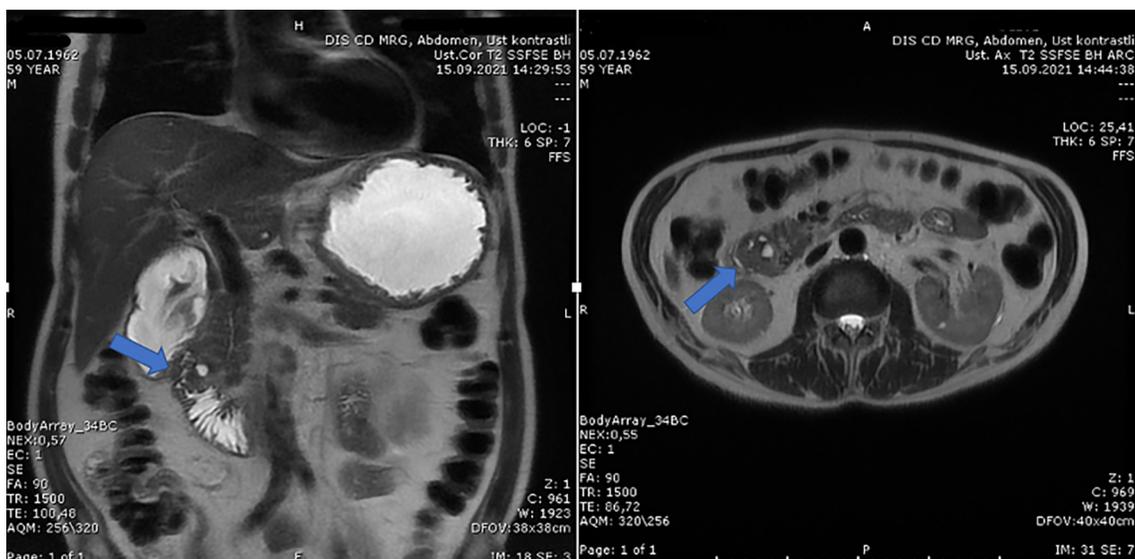


Figure 1. In the coronal and axial T2-weighted MR images, Soft tissue thickening with cystic openings (blue arrows) within the head of the pancreas and 2nd part of the duodenum localization was interpreted as GP, but noticeably high levels of CA 19-9 prompted a suspicion of malignancy and EUS –FNA revealed a pancreatic head carcinoma.

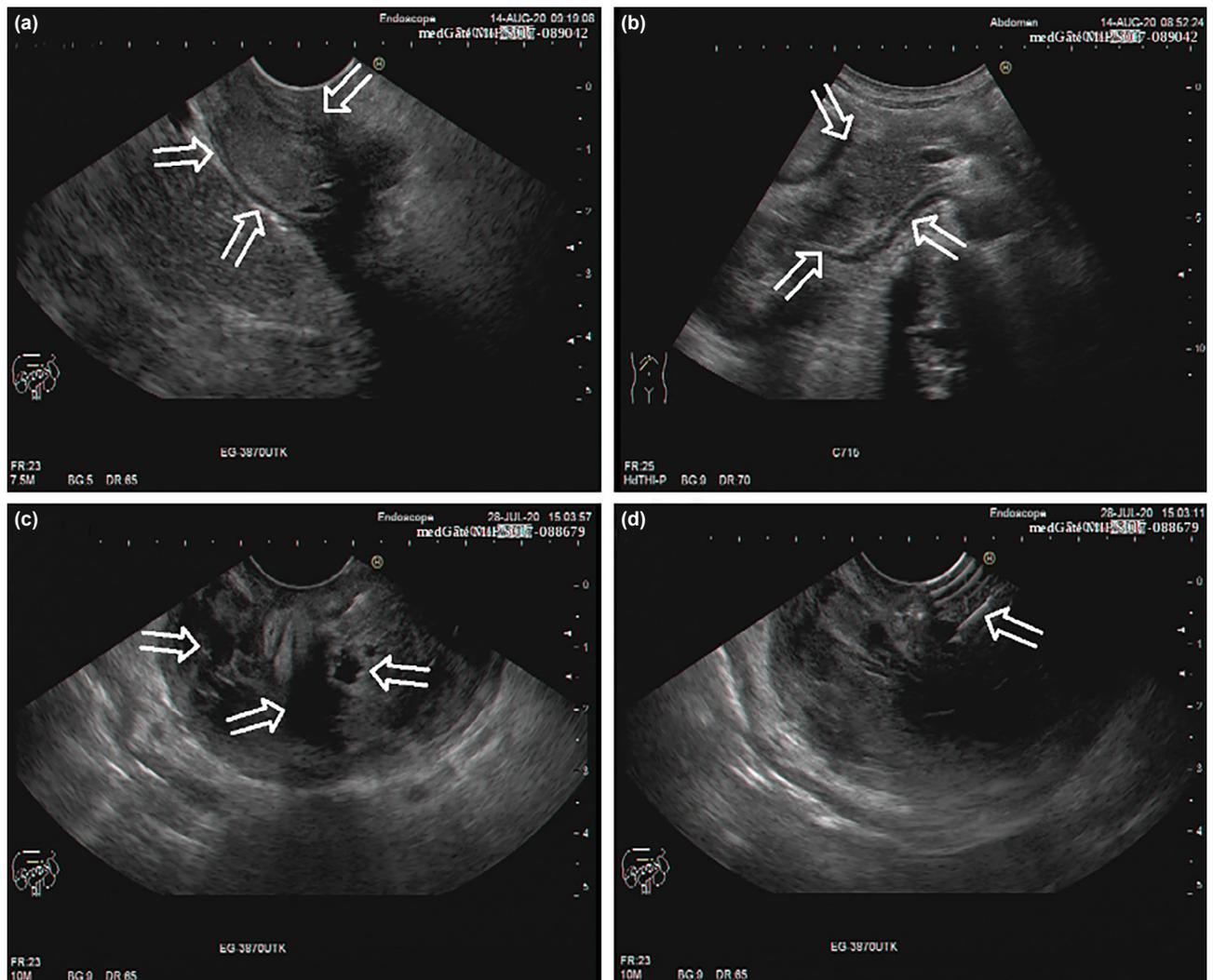


Figure 2. EUS pictures of a sixty years-old gentleman presented with abdominal pain, nausea and vomiting (a-d). The arrows indicating; a. Significantly thickened duodenal wall in groove area (b). Pancreatic Head appears completely normal. (c) Cystic areas of various sizes in the thickened wall-characteristic finding of groove pancreatitis (d). Aspirated fluid from intramural cyst revealed Amylase 51625 U/L, Glukoz: 70 mg/dl, Total kolestrol: 75 mg/dl, CEA: 229 ng/ml, CA 19.9:65541 U/ml.

DISCUSSION

GP is a less known form of pancreatitis and often poses a diagnostic and therapeutic challenge for the clinicians. Its prevalence is between 2.7 to 24.5% in resected specimens that is operated for chronic pancreatitis and mostly affecting male patients during the 5th decade.^[10] Risk factors include heavy smoking and alcohol abuse.^[11] It is also associated with chronic pancreatitis in two-thirds of GP patients.^[12] GC, which originates from groove area that resides between the head of the pancreas, duodenum, and common bile duct, is separated from pancreatic adenocarcinoma by means of tumor localization.^[13] GP must be discarded from closely mimicking diseases like groove carcinoma, duodenal carcinoma and pancreas head carcinoma. The discrimination between GP and GC is essential because it significantly affects the management and the prognosis of the patients, however it may not always be possible to differentiate. Unfortunately, in

our study we do not have a diagnosed GC patient to make a comparison between GP and GC patients. There were two malignities which were diagnosed as pancreatic head adeno carcinoma but not groove carcinoma. But It should be especially noted that both of these patients were misdiagnosed as groove pancreatitis initially and the final pathological review by EUS-FNA provided the final diagnosis. There are some cohort and small case series including GP patients and some of them^[8,12,14-17] comparing with GC patients in the literature (Table 4). One of the largest series which was conducted by Jun et al.^[8] compared the baseline characteristics laboratory findings, CT findings and EUS-FNA results of 36 GC patients and 44 GP patients. According to the study, the diagnosis was more likely to be GC if laboratory findings were consistent with elevated levels of ALP, AST, ALT, total bilirubin, CRP, and CA19-9. EUS-FNA should be considered in patients with elevated CA19-9 levels and mass-like lesions on CT. Intramural or paraduodenal cystic areas, thickening of the medial duode-

Table 3. Imaging modalities and treatment strategies

	n (%)
Imaging modality	
CT	24 (96)
EUS	23 (92)
MRI	18 (72)
EUS-FNA	14 (56)
ERCP	8 (32)
Findings	
Edematous duodenal wall	23 (92)
Swollen head of pancreas	20 (80)
Wirsung dilation	12 (48)
Cystic dilation duodenal wall	8 (32)
Bile duct dilation	5 (20)
Gastric outlet obstruction	4 (16)
Head of pancreas mass	3 (12)
EUS-FNA	
Benign cytology	10 (40)
Atypia	2 (8)
Adenocarcinoma	2 (8)
Management	
Conservative	14 (56)
Biliary stenting	6 (24)
Wirsung stenting	4 (16)
Sphincterotomy	3 (12)
CHolecystectomy	3 (12)
Whipple procedure	1 (4)
Duodenal stenting	1 (4)
Follow-up status	
Follow-up period, months (median, range)	(29, 3–71)
Symptom relief	12 (48)
Recurrent pancreatitis	7 (28)
Death	2 (8)

CT: Computed tomography; MRCP: Magnetic resonance cholangiopancreatogram; EUS-(FNA): Endoscopic ultrasound-(Fine needle aspiration); ERCP: Endoscopic retrograde cholangiopancreatography.

num wall with cystic changes are all together highly suggestive for GP in MDCT images. In contrast, there may be a separate hypoenhancing solid lesion in the head of the pancreas that invades the second part of the duodenum and extends into the pancreaticoduodenal groove area in a PDAC patient image. In some patients, however, it may be impossible to distinguish a discrete pancreatic mass from the soft tissue infiltrating the pancreatic groove. In such cases, EUS biopsy is helpful to confirm the diagnosis.^[18] In accordance with this study, the importance of EUS-FNA was shown in two of our pancreatic head adenocarcinoma cases and most of our patients had EUS (92%) and EUS-FNA (56%), if needed.

Table 4. GP patient series: Studies with 5 or more patients

Study (year)	Country	Sample size, n (GC:GP)	Mean age, years (range)	Surgical treatment	Endoscopic treatment	MDCT, n	EUS, n (GC:GP)	FNA, n (GC:GP)	MRI	FU (Median, IQR) (mo)
Aimoto et al. (2006)	Japan	5 (5:0)	62 (47–73)	5	0	5	–	–	4	NA
Rebours et al. (2006)	France	105 (75:30)	46 (24–75)*	29	16	105	105	0	0	15 (0–243)
Jouannaud et al. (2006)	France	23 (0:23)	45 (30–66)*	14	2	22	22	0	NA	47 (12–108)
Rahman et al. (2007)	UK	11 (2:9)	48 (35–61)*	11	0	9	10	0	6	52 (1–39)
Casetti et al. (2009)	Italy	58 (0:58)	44.7 (36.8–51.8)*	58	0	49	30	0	28	96 (60–130)
Arvanitakis et al. (2014)	Belgium	51 (36:15)	49 (37–70)*	9	39	13	32	NA	51	54 (6–156)
Oza et al. (2015)	USA	13 (7:6)	51.9±10.5	9	0	13	9	2	0	12 (7–16)
Lekkerkerker et al. (2016)	Netherlands	38 (10:28)	53:GP, 57:GC	8	6	38	4 (2:2)	4 (2:2)	NA	45 (7–127)
Aguilera et al. (2018)	USA	8 (0:8)	51.9	8	0	8	8	4	7	18.15 (7.25–33.8)
Jun et al. (2018)	Korea	80 (36:44)	59.7±10.7:GC, 50.8±9.6:GP	26	–	80	34 (13:21)	23 (10:13)	NA	NA
Ooka et al. (2020)	USA	48 (0:48)	53.2 (32.4–89.7)	17	0	45	0	0	3	NA
Tarvainen et al. (2020)	Finland	38 (33:5)	55 (42–62)*	9	14	33	17	5	20	NA

*Median age (min-max). GC: Groove carcinoma; GP: Groove pancreatitis; EUS: endoscopic ultrasonography; FNA: Fine Needle Aspiration; MRI: Magnetic resonance imaging; MDCT: Multidetector computed tomography; FU: Follow-up; IQR: Interquartile Range.

Stenosis of the minor papilla which is believed to be related with santorinicele (cystic dilation of the accessory duct) leads to intraductal pressure increase and disruption of the duct resulting with recurrent pancreatitis attacks.^[19,20] However, Muraki et al.^[21] concluded in their study that, because the pancreas had an alternative drainage system to the main duct system, the dysfunction of the accessory system alone could not be solely responsible for the occurrence of GP as far as pancreas divisum is not present. Dysfunction of the wirsung canal might also be a factor responsible for the pancreatitis of the groove area. In our patient group, laparoscopic cholecystectomy was performed in 3 of our patients, and two of them benefited, but one patient had recurrent pancreatitis attacks despite the addition of endoscopic sphincterotomy.

There is a strong association between GP and both alcohol and tobacco abuse. Chronic ethanol abuse may be responsible for changes of volume and viscosity of pancreatic fluid that leads to potential luminal obstruction of the pancreatic ducts.^[22] One of the largest reported series by Rebours et al.^[16] examined 105 patients; the chronic alcohol abuse ratio was as high as 86%. According to our study this ratio was 40% among GP patients. Smoking is a less-recognized risk factor regarding etiopathogenesis of GP.

Endoscopic treatment, such as stricture dilation and pancreatic ductal or cyst drainage, are important nonsurgical approaches with good results. In a study conducted by Arvanitakis et al.^[12] involving 51 patients, these interventions, together with medical treatment, had a high rate of clinical success (nearly 80%) with low adverse effects. Surgery is a reasonable choice if symptoms do not improve, complications occur or malignancy cannot be ruled out. The preferred technique usually is pancreaticoduodenectomy.^[23] Surgery has been shown to improve the quality of life regarding pain cessation whatever the procedure was used. Unlike the existing literature, in our study group; endoscopic procedures were the main or complementary treatment modality in 9 of 25 patients. In the majority, relief of symptoms was obtained by conservative measures, only (32%). Also none of the GP patients required surgery regarding GOO. Rebours et al.,^[16] also, revealed in their report that GP symptoms can be severe but two-thirds of cases can be managed without surgery in line with our work. They also pointed out that GP may occur in nonalcoholic patients.

There are several limitations of our study. First of all, this study was a retrospective one, and some data were missed in electronic records of the patients. Second, although our hospital is a high-volume hepatopancreato-biliary surgery center, owing to the paucity of groove pancreatitis patients, the number of patients involved in this retrospective study was relatively small to reach a definite conclusion so larger cohort, multicenter studies are needed to obtain more accurate results for this rare condition.

Conclusion

The diagnosis of GP remains difficult. Imaging may be helpful, but there is the potential to fail to distinguish GP from other more common causes of pancreatitis and even pancreatic malignancy. EUS(±FNA) is a useful diagnostic tool complementary imaging. Conservative management is the first-line option, and the natural course of GP is favorable in a majority of the patients. Invasive interventions are indicated for specific complications such as gastric or biliary outlet obstruction. Surgery is rarely needed for symptom control and must be reserved for unresponsive cases to other treatment strategies and suspicion of malignity.

Ethics Committee Approval: This study was approved by the Bezmialem Vakif University Non-interventional Clinical Research Ethics Committee (Date: 03.12.2019, Decision No: 22/419).

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ORJİNAL ÇALIŞMA - ÖZ

Groove pankreatitin klinik özellik ve sonuçlarına yönelik bir kohort: Literatür derlemesi ve tek merkez deneyimimiz

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AMAÇ: Groove (oluk) pankreatit (GP) kronik pankreatitin daha az karşılaşılan ve multimodal görüntüleme yöntemleriyle yeni yeni farkındalığı artmakta olan nadir bir formudur. Amacımız GP tanısı almış hastaların farklı tedavi yaklaşımlarıyla orta-uzun dönem sonuçlarını analiz etmektir.

GEREÇ VE YÖNTEM: Mayıs 2013–Haziran 2019 tarihleri arasında elektronik hasta kayıt veri tabanından “groove”, “paraduodenal” anahtar kelimeleri ile bilgisayar ortamında arama yapıldı. GP tanısı konulan 25 hastanın klinik, radyolojik ve patolojik verileri elde edildi.

BULGULAR: GP hasta grubunda median yaş 55 (25–87) ve %80 erkek cinsiyet hakimdi. Alkol ve sigara kullanımı %40 idi. En sık semptomlar sırasıyla üst karın ağrısı (%84) ve bulantı-kusma (%40) idi. Mide çıkış yolu obstrüksiyonu 4 (%16) hastada görüldü. BT ve EUS hastaların büyük bir çoğunluğunda uygulandı. (sırasıyla, %96 ve %92). 25 hastanın 14'üne EUS-FNA yapıldı. Patoloji sonuçları sırasıyla iki hastada atipi (%8), iki hastada adenoCA (%8) ve on hastada benign (%40) olarak geldi. EUS-FNA işlemi ilk radyolojik değerlendirmesi GP olarak yorumlanan iki pankreas başı malignitesinin nihayi tanısının konulmasında yardımcı oldu. Ortalama takip süresi 29 (3–71) aydı. Konservatif yaklaşım ağırlıklı olarak tercih edilen tedavi yöntemi (%56). Konservatif yöntemin dışında diğer tedavi stratejileri arasında, ERCP ile bilier stentleme, sfinkterotomi, wirsung stentleme, kolesistektomi vb. endoskopik/cerrahi girişimler yer aldı. Tüm tedavi modaliteleri göz önünde bulundurulduğunda, groove pankreatitli 12 (%48) hastada semptomlarda iyileşme görülürken, 7 (%28) hasta tekrarlayan pankreatit ataklarıyla seyretti.

TARTIŞMA: GP, pankreatitin daha az bilinen bir formu olmasından ötürü tanı ve tedavide klinisyenler için çeşitli zorlukları beraberinde taşır. Bilhassa pankreas malignitesini taklit edebilen bu form mutlaka karsinomdan ayırt edilmelidir. EUS(±FNA), radyolojik incelemeleri tamamlayan kullanışlı bir tanı aracıdır. Konservatif yaklaşım çoğu hastada hala ilk seçenek olarak yerini korumakla beraber, klinisyen gerekli özel durumlarda invaziv endoskopik işlemler ve cerrahi seçenekleri göz önünde bulundurmalıdır.

Anahtar sözcükler: Oluk; pankreatit; paraduodenal.

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