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A study on management in recurrent acute pancreatitis at a tertiary care hospital

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Abstract

Treatment of patients with RAP is aimed at the specific aetiology. In general, cholecystectomy is carried out in cases of microlithiasis along with clearance of common bile duct. Endoscopic sphincterotomy is advised if there is strong suspicion of SOD. Minor papilla sphincterotomy should be carried out in those with PD but with limited expectations. The study was conducted at Peerless Hospital & B.K. Roy Research Centre, Kolkata, a 300 bedded multi-speciality tertiary care Hospital. It was a prospective, observational study conducted during October 2014-August 2016. All patients with two or more distinct attacks of AP willing to give written informed consent irrespective of their age group without any evidence of CP were included in the study. In the present study EUS was performed on total 70 patients and found 11 to have CP out of 80 patients which was not detected by routine investigations. EUS and MRCP combined, diagnosed 14 patients to have GB & CBD Microliths/Sludge. EUS diagnosed more number of cases as compared to MRCP.

Keywords: recurrent acute pancreatitis, rap, cholecystectomy

Introduction

MRCP is an excellent non-invasive tool for assessment of ductal morphology. With the advances in pancreaticobiliary imaging and availability of EUS, ERCP is rarely used now-a-days for diagnostic due to its associated complications [1]. Over the years, EUS has replaced ERCP for diagnosing most of the aetiologies of RAP and chronic pancreatitis. EUS has been documented to have a sensitivity of 96% for diagnosing microliths and has a negative predictive value of 95.4% for diagnosing common bile duct stones. EUS is a well-established and less-invasive modality for CP diagnosis [2]. The higher imaging resolution provided by EUS enables detection of subtle pancreatic abnormalities, not only parenchymal but also ductal changes, that are undetectable using other modalities. The most useful role of EUS is to diagnose early CP in patients who have presented with RAP and do not show evidence of chronicity on other imaging modalities such as computed tomography (CT) scan or MRCP [3].

Treatment of patients with RAP is aimed at the specific aetiology. In general, cholecystectomy is carried out in cases of microlithiasis along with clearance of common bile duct. Endoscopic sphincterotomy is advised if there is strong suspicion of SOD. Minor papilla sphincterotomy should be carried out in those with PD but with limited expectations [4]. Regular follow-up of patients with RAP is necessary because most patients are likely to develop CP in due course and it is characterized by irreversible damage that engenders fibrosis and necrosis of pancreatic tissue, with the consequent loss of endocrine and exocrine function of the pancreas and engenders a high rate of morbidity and mortality over a 20-25-year period [5]. In view of this fact, current efforts emphasize the establishment of early diagnosis to commence intervention that can positively affect the natural course of the disease [6]. Hence the above study was initiated to study the management in RAP.

Methodology

The study was conducted at Peerless Hospital & B.K. Roy Research Centre, Kolkata, a 300 bedded multi-speciality tertiary care Hospital. It was a prospective, observational study conducted during October 2014-August 2016. All patients with two or more distinct attacks of AP willing to give written informed consent irrespective of their age group without any

evidence of CP were included in the study. All patients with a labelled CP by standard investigations like abdominal ultrasound (USG) and Computerized Tomography (CT) were excluded from the study.

The diagnosis of AP was made in the presence of suggestive clinical features, increased serum amylase and/or lipase (2 times the upper limit of normal) levels, and evidence of pancreatitis on USG and/or CT of the abdomen.¹¹ Pancreatitis was considered to be idiopathic when no definite cause for it could be detected, such as gallstones, alcoholism, hyperlipidemia, hypercalcemia, drugs known to cause acute pancreatitis, and viral infection after clinical evaluation and appropriate investigations.

A detailed history including the general details of the patients (age, gender, date of admission etc.) chief complaints and associated complaints with duration, past history including any chronic conditions, general examination and systemic examination especially abdominal examination was recorded in pre-structured proforma. Evaluation of a patient with RAP after the first episode of acute pancreatitis included a detailed history of alcohol intake, smoking, medication associated with AP, trauma, viral illness, exposure to toxins, and a family history of AP. Acute alcoholic pancreatitis was considered in this study if the alcohol consumption is more than 40 g per day for more than 5 years. Hypertriglyceridemia and hypercalcemia were considered as a cause of RAP if TG >1000 mg/dl and fasting serum calcium was elevated (normal range, 8.5–10.5 mg/dl)^[12].

Real-time transabdominal USG was performed in a fasting state using a 3.5-MHz curved probe in the supine and left lateral decubitus positions. The gallbladder, CBD, and pancreas were imaged with special attention. The diagnosis of gallstones was made if there were movable intraluminal echogenic foci casting acoustic shadows. The diagnosis of biliary sludge was made if there were low-amplitude echoes in the gallbladder without shadowing and that layered in the dependent part of the gallbladder.

Phase II investigations included Magnetic MRCP and EUS for diagnosis of etiologies of RAP like biliary (microliths, sludge), occult biliary tumours, congenital anomaly of the pancreas, and CP as a cause of recurrent episodes of pancreatitis. Microliths predominantly composed of cholesterol are defined as gallstones <3 mm in size and microlithiasis should not be confused with biliary sludge. Biliary sludge is composed of a suspension of crystals, mucin, glycoproteins, cellular debris and proteinaceous material. However, both microlithiasis and biliary sludge are used interchangeably in the context of idiopathic pancreatitis.

In the present study only phase I and phase II investigations were performed. Rosemont criteria was used for diagnosis of chronic pancreatitis using EUS.

The diagnosis of pancreas divisum was suggested by looking for following two signs on EUS: (1) absence of stack sign and presence of crossed duct sign (2) inability to follow the pancreatic duct from the major papilla to the pancreatic body. Autoimmune pancreatitis was diagnosed using Japanese criteria. There are 3 main criteria:

1. Imaging

Diffuse or segmental narrowing of the main pancreatic duct with irregular wall and diffuse or segmental enlargement of

the pancreas with imaging studies such as: Ultrasound, CT, MRI or ERP (Endoscopic Retrograde Pancreatography).

2. Serology

High serum gammaglobulin IgG or IgG4, or the presence of autoantibodies, such as antinuclear antibodies or rheumatoid factor.

3. Histology

Marked inter-lobular fibrosis and prominent infiltration of lymphocytes and plasma cells in the periductal area, occasionally with lymphoid follicles in the pancreas. For the diagnosis to be confirmed, criterion 1 must be present along with criterion 2 and/or criterion 3. There is an optional criterion for patients fulfilling criterion 1 alone: a response to steroid therapy, with the caveat that malignancy of the pancreas or biliary tract must be excluded. In 2006, a mandatory ERP became part of these guidelines.

Data was collected and tabulated. Categorical variables were expressed as percentages/ proportions and continuous variables as mean (SD). Fischer exact test/Chi-square test was used to compare categorical variables between groups. An alpha level of 5% was taken, i.e. if *p* value is less than 0.05 it was considered as significant. The statistical software SPSS version 20 was used for the analysis and Microsoft Excel 2007 to make the diagrams.

Results

Table 1: Comparison of no. of cases diagnosed using MRCP and EUS

	MRCP	EUS
CBD Microliths	02 (2.56%)	07 (10%)
CBD Sludge	(0)	02 (2.86%)
GB Microliths	01 (1.28%)	02 (1.43%)
GB Sludge	01 (1.28%)	02 (4.29%)

5 patients had pancreas divisum. Diagnosis of pancreas divisum was made by performing MRCP, EUS, and confirmed by ERCP which was done on 4 out of 5 patients for minor papillotomy. MRCP performed on 5 patients, out of which 4 showed the dorsal pancreatic duct draining separately in to the minor papilla and there was no communication with the ventral duct suggestive of pancreatic divisum along with dilated duct. 1 patient showed above with features of chronic pancreatitis. EUS was done on 4 patients but stack sign was not seen in any of them. 1 patient along with this showed hyperechoic foci, lobularity, dilated dorsal duct with presence of side branches and hyperechoic main pancreatic duct wall suggestive of chronic pancreatitis.

2 patients had autoimmune pancreatitis. Both patients had increased IgG4 levels. In both these patients contrast enhanced CT (CECT), MRCP and EUS was performed. CECT abdomen showed diffuse parenchymal enlargement with a capsule-like rim, and diffuse narrowing of the pancreatic duct. MRCP showed hypointense and swollen pancreas with loss of normal peripheral lobulations with dilated CBD distally and stricture in the intrapancreatic course with mildly dilated main pancreatic duct. EUS in 1 patient showed pancreas is intensely hypoechoic well demarcated and enlarged in head, body and tail, including the uncinate process. Main pancreatic duct was mildly dilated

with presence of side branches and hyperechoic main pancreatic duct wall. CBD was dilated 8mm from hilum to intrapancreatic part with smooth tapering in the intrapancreatic course suggestive of autoimmune pancreatitis with terminal CBD narrowing. Another patient showed pancreas with normal echotexture in distal body and tail. The uncinate process, head, neck and proximal body was grossly hyperechoic. MPD was prominent in involved portion but not dilated, no mass seen. CBD was dilated with terminal narrowing suggestive of focal non-calcific with benign biliary stricture and 1 patient was diagnosed to have choledochocoele on MRCP. No statistically significant difference was observed between MRCP and EUS in diagnosing the conditions.

Table 2: Comparison of the no. of cases diagnosed using MRCP vs EUS

	MRCP	EUS	p Value
Pancreatic divisum	5 (6.41%)	4 (5.71%)	0.859*
Autoimmune	2 (2.56%)	2 (2.86%)	0.913*
Choledochocoele	1 (1.28%)	0 (0)	0.314*

*Not statistically significant

In the present study EUS was performed on total 70 patients and found 11 to have CP out of 80 patients which was not detected by routine investigations.

Table 3: Management and follow up of patients

Etiology	Management	Frequency	Follow up	Frequency
Alcohol	Abstinence	28 (100%)	Admitted for recurrent episode	8 (28.6%)
			Improved	20 (71.4%)
Autoimmune	Steroids	2 (100%)	Improved	1 (50%)
			Lost follow-up	1 (50%)
Choledochocoele	Sphincterotomy	01 (100%)	Improved	1 (100%)
Hypertriglyceridemia	Lipid lowering drugs	06 (100%)	Admitted for recurrent episode	1 (16.7%)
			Improved	5 (84.3%)
Idiopathic	Symptomatic	24 (100%)	Admitted for recurrent episode	2 (8.3%)
			Symptomatic	3 (12.5%)
			Symptomatic	19 (79.2%)
Microliths	Cholecystectomy	03 (21.4%)	Improved	9 (64.3%)
	Sphincterotomy	08 (57.1%)	Admitted for recurrent episode	5 (35.7%): 3 pts on drugs and 2 pts who underwent spincterotomy
	Drugs	03 (21.4%)		
P. divisum	Sphincterotomy	04 (80%)	Admitted for recurrent episode	1 (20%)
			Improved	3 (60%)
	Symptomatic	01 (20%)	Symptomatic	1 (20%)

EUS and MRCP combined, diagnosed 14 patients to have GB & CBD Microliths/Sludge. EUS diagnosed more number of cases as compared to MRCP.

Discussion

In this study, EUS and MRCP combined, diagnosed 14 patients to have GB & CBD Microliths/Sludge. EUS diagnosed more number of cases as compared to MRCP.

Garg *et al.* [1], prospectively evaluated patients of RAP with ERCP, EUS or bile microscopy and showed that 46% patient had some evidence of Chronic pancreatitis on imaging. Microlithiasis and pancreatic divisum were present in 13% and 5.3%, respectively. Mean age was 33 yrs. with male preponderance in there group. One fourth patients remained idiopathic after application of these three investigations. These results are consistent with our study except that 12% of the patients showed evidence of chronic pancreatitis by EUS and/or MRCP [8].

No cause could be found after extensive investigations in 30% of RAP patients (idiopathic). This was similar to (27%) Gao *et al.* [9], (22%) Sherman *et al.* [10], (27%) Sajith *et al.* [11]. However Gullo *et al.* [10], found 10.4% of patients had IRAP which was low compared to this study. Saraswat *et al.* [8], observed microlithiasis as a common cause for idiopathic recurrent acute pancreatitis by examining bile microscopy in 70 patients for cholesterol monohydrate crystals (CMC) and calcium bilirubinate granules (CBG). Bile microscopy was abnormal in 75% patients with RAP (18/24; CMC in 10, CBG in six, CMC and CBG in two), 83.3% patients with

unexplained biliary pain (10/12; CMC in seven, CBG in one, CMC and CBG in two) and 95.4% patients with gallstones (21/22; CMC in 12, CBG in one, CMC and CBG in eight). None of the controls without gallstone disease had CMC while three patients had low counts of CBG [3, 8]. These observation were different from our study, where we found microliths in 17.5% of our RAP patients using performed EUS/MRCP.

EUS diagnosed more cases of microliths/sludge after combined application which is similar to other studies.

Our study found low prevalence of pancreas divisum 5% by using MRCP and EUS which was similar to the study by Sajith *et al.* [11], (8.5%) Garg *et al.* [7], (5%) in contrast to study done by Gono *et al.* [13].

The recurrence of acute pancreatitis in alcoholic patients is similar to the study conducted by Pelli *et al.* [14], in which they concluded risk factors for recurrences include increased dependency on alcohol, mild first attack, and young age at the time of the first attack. Alcohol consumed after the first attack has been identified as a dose-dependent risk factor, and total abstinence has been suggested to protect against recurrences according to a preliminary short-term follow-up. In the present study endoscopic minor papilla sphincterotomy was performed with dorsal duct stenting on 4 patients. 1 out of the 4 patients treated (sphincterotomy group) was admitted with recurrent attacks whereas the other 3 did not report another attack during the follow up. These observation are similar to other studies in which they had shown 68%-75% improvement on patient who

underwent endotherapy during follow up. We observed that the patients who improved had dilated pancreatic ductal diameter prior to therapy. This could mean that documented intrapancreatic ductal hypertension may be related to effectiveness of endoscopic therapy and more patients required to prove the hypothesis. 85% patients of sphincterotomy group and 100% of cholecystectomy group showed improvement similar to Ros *et al.* [16], in which significant decline in the recurrence (from 66%–75% to <1%) was observed after cholecystectomy.

Conclusion

All patients with hypertriglyceridemia responded to treatment by diet, exercise, lipid lowering agents. These observations are similar to another Indian study where prevalence of hypertriglyceridaemia was 4.2% in 188 RAP patients and response to lipid lowering agent was also similar. 2 patients of autoimmune pancreatitis treated on steroids showed marked improvement in terms of jaundice and imaging.

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