

Evolution of Rosemont's indeterminate for chronic pancreatitis in recurrent acute pancreatitis patients with 1-year follow-up: A prospective case series



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ABSTRACT

Some patients presenting with recurrent acute pancreatitis (RAP), while undergoing endoscopic ultrasound (EUS), are classified as indeterminate for chronic pancreatitis (CP) according to Rosemont criteria. We are describing the clinical and radiological evolution of 14 such patients for 1 year. All the patients were closely followed up at 3 monthly intervals and subjected to ultrasound abdomen and blood sugar profile 6 monthly and EUS after 12 months. Males were 93%. Median age was 26 years. Most common etiology of RAP was idiopathic followed by ethanol and hypertriglyceridemia. On 1-year follow-up, 35.7% remained pain free and 28.6% had acute pancreatitis attack. Endocrine and exocrine insufficiency seen in one and two patients, respectively. Follow-up EUS in eight patients revealed Rosemont "normal" in 1, "Indeterminate" in 2, suggestive of CP in 3, and consistent with CP in two patients. Therefore, Rosemont's "Indeterminate" progress to suggestive/consistent with CP in majority of patients.

Key words: Pancreatitis; Indeterminate; Idiopathic; Endoscopic ultrasound; Rosemont

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INTRODUCTION

Recurrent acute pancreatitis (RAP) and chronic pancreatitis (CP) are common clinical entities in gastroenterology. Early CP can present initially as RAP.¹ It is important to diagnose CP early and definitively to avoid repeated imaging and unwanted procedure. An early aggressive lifestyle changes such as smoking and alcohol abstinence could possibly alter the course of disease.²

Endoscopic ultrasound (EUS) was first reported for CP in 1986.³ Rosemont criteria⁴ integrate pancreatic parenchymal and ductal features into a four-level diagnostic stratification system that grades the likelihood of CP (normal,

indeterminate, suggestive, and consistent with CP). Catalano et al.,⁵ reported that a sensitivity of 88% and a specificity of 100% when threshold of ≥ 3 features to diagnose CP were used. The pathologic EUS changes of CP correlate to extent of exocrine dysfunction and histopathology findings.⁶ A study by Trikudanathan et al.,⁷ demonstrated that 25/26 (96.2%) patients with features suggestive of CP and 12/15 (80%) with indeterminate for CP based on Rosemont criteria on EUS had evidence of CP on histopathology.

Till date, there is no follow-up study on the evolution of indeterminate for CP. Hence, we are presenting this case series to describe clinical and radiological outcome of Rosemont's indeterminate for CP in RAP patients on 1-year follow-up.

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Aims and objectives

To study clinical and radiological evolution of Rosemont's indeterminate for CP in RAP patients on a 1-year follow-up.

MATERIALS AND METHODS

Study design

This was a prospective case series from Department of Gastroenterology at SSKM Hospital, Kolkata and this study was approved by the Institutional Ethics Committee of IPGME and R, Kolkata.

Patients

Data were collected between June 2019 and February 2021. All the patients of RAP above 12 years with normal CT abdomen and magnetic resonance cholangiopancreatography (MRCP) were subjected to EUS. Those who fulfilled diagnostic criteria of Indeterminate for CP according to Rosemont criteria were prospectively followed up. Patients or whose guardians not willing to give consent, pregnant females, and patients with medical contraindication for EUS were excluded from the study. Proper written consent was obtained. EUS was performed after 6–8 weeks of acute attack of pancreatitis if it occurred recently.

Data collection

Demographic data, smoking habits (either active or past), alcohol consumption (≥ 2 drinks per day for males and ≥ 1 drink per day for females for at least 6 months), and relevant medical and surgical history were noted. RAP was defined as two or more episodes of documented acute pancreatitis (AP), separated by at least 3 months.⁸ All EUS examinations were performed by two expert gastroenterologists with experience of more than 2000 EUS procedures using “Pentax” linear echoendoscope at 7.5 MHz in the left lateral position under conscious sedation using iv. Midazolam and iv. Propofol given by post-doctoral trainee. EUS findings were noted and assessed according to Rosemont criteria which included Major A, Major B, and minor criteria as described by Catalano et al.,⁴ Major A criteria included main pancreatic duct calculi and hyperechoic foci with shadowing. Major B criteria included lobularity with honeycombing. Minor criteria included cysts, dilated ducts (body ≥ 3.5 mm and tail ≥ 1.5 mm), irregular pancreatic duct contour, dilated side branches ≥ 1 mm, hyperechoic duct wall, strands, non-shadowing hyperechoic foci, and lobularity with non-contiguous lobules. The final interpretation was made as normal, indeterminate, suggestive, and consistent with CP based on Rosemont criteria.⁴ All the patients were subjected to liver function tests, serum calcium, lipid profile, HbA1c, and blood sugar profile and imaging including abdominal

ultrasound, CT abdomen, and MRCP before EUS. Patients were followed up at 3 months interval in pancreatic clinic for 1 year after enrollment. Pain pattern, severity, analgesic requirements, AP, and hospitalization history were noted at enrollment and during follow-up. Information was gathered through telephonic conversation in patients who missed follow-up visits due to lockdown or other reasons owing to COVID pandemic. All patients were subjected to ultrasound abdomen to look for gallstones/sludge and signs of CP and blood sugar profile at 6 monthly intervals. A follow-up EUS was performed 12 months after baseline EUS by the same endosonographer who had done baseline EUS earlier in that patient.

Statistical analysis

Data analyses were done using SPSS version 23.0. Demographic and clinical data were analyzed using descriptive statistics and reported as mean with standard deviation and median with range for continuous variables and as frequencies and percentage for categorical variables.

RESULTS

EUS was performed in 21 RAP patients and 14 patients were found be Rosemont's “indeterminate for CP” and followed up. Normal pancreas was seen in three patients and rest four patients were suggestive of CP.

Table 1 outlines basic characteristics and clinical and radiological follow up of indeterminate for CP patients. Among 14 patients of Indeterminate for CP, males were 13 (92.9%) along with 1 female (7.1%). Mean age was 29.4 ± 12 years. The age varied from 16 to 54 years. The median of documented attacks of AP before EUS was 4 with range 2–10. Case 4 had history of severe AP. The mean duration between first pain attack and EUS examination was 39 months and range 5–96 months. Mean duration between first documented attack of AP and EUS examination was 34 months and range 5–96 months. At enrolment, pain pattern was continuous in 4 (28.6 %) and episodic in 10 (71.4%) patients. Mean and median of analgesics requirement was 4.5 and 2.5 per month with range 0–20 per month. Case 1, 2, 5, 7, and 8 had history of smoking. Case 8 had history of cholecystectomy before AP attacks. Diabetes mellitus at baseline was present in Case 1.

Clinical follow-up of 1 year

On 1-year follow-up, five (35.7%) patients remained pain free throughout the year. AP occurred in four (28.6%) (Case 6, 7, 9, and 12) patients. Case 9 had moderately severe AP and developed Walled off necrosis requiring endoscopic drainage. Rest all had mild AP. Hospitalization required in five (35.7%) patients, out of which Case 3 required for

Table 1: Baseline characteristics and clinical and radiological follow-up of indeterminate for chronic pancreatitis patients

Case number	Baseline characteristics					1 year follow-up					EUS outcome		
	Age (years)	Sex	Number of AP attack before EUS	Pain pattern	Smoking	Etiology of RAP	Pain attack	AP attack	Hospitalization	Endocrine insufficiency		Exocrine insufficiency	Gall stones/sludge
1	54	M	2	C	Yes	Ethanol	No	No	No	Yes	No	No	Indeterminate for CP
2	45	M	2	C	Yes	Ethanol	Yes	No	No	No	No	Gall stones	Not done
3	28	M	10	E	No	Idiopathic	Yes	No	Yes	No	No	No	Normal
4	21	M	3	E	No	Idiopathic	Yes	No	No	No	No	No	Consistent with CP
5	23	M	3	E	Yes	Idiopathic	No	No	No	No	No	No	Not done
6	17	F	6	E	No	Idiopathic	Yes	Yes	Yes	No	No	No	Suggestive of CP
7	26	M	3	E	Yes	Idiopathic	Yes	Yes	Yes	No	No	No	Suggestive of CP
8	48	M	7	E	Yes	Idiopathic	Yes	No	No	No	No	No	Indeterminate for CP
9	23	M	3	C	No	Idiopathic	Yes	Yes	Yes	Yes	Yes	Sludge	Suggestive of CP
10	27	M	8	C	No	Hypertriglyceridemia	Yes	No	No	No	No	Sludge	Not done
11	20	M	5	E	No	Idiopathic	No	No	No	No	No	No	Not done
12	37	M	2	E	No	Idiopathic	Yes	Yes	Yes	No	Yes	No	Consistent with CP
13	16	M	2	E	No	Idiopathic	No	No	No	No	No	No	Not done
14	26	M	5	E	No	Idiopathic	No	No	No	No	No	No	Not done

M: Male, F: Female, C: Continuous, E: Episodic

pain control and rest for AP episode. The mean analgesic requirement throughout the year was 1.3 days per month with range (0–20). Case 9 was diagnosed with endocrine insufficiency. Exocrine insufficiency was seen in Cases 9 and 12 with fecal elastase levels <100.

Radiological follow-up at 1 year

On 1-year follow-up, pancreatic calcification was present in Cases 4 and 12 on ultrasound abdomen. Gallbladder sludge and stones were seen in Cases 9 and 10 and case 2, respectively.

Follow-up EUS in indeterminate for CP at 1 year

Follow-up EUS was performed in eight patients after 1 year. Cases 5, 10, 11, 13, and 14 refused to undergo follow-up EUS. Case 2 had features of groove pancreatitis on initial imaging; therefore, follow-up EUS was deferred. Follow-up EUS revealed Rosemont's "normal" in Case 3 "indeterminate" in Cases 1 and 8, "suggestive of CP" in Cases 6, 7, and 9 and "consistent with CP" in Cases 4 and 12. Both the patients with findings of consistent with CP had pancreatic parenchymal calcification (Major A). No patient had microlithiasis or gall stone/sludge.

DISCUSSION

Till date, no study has been done on outcome of indeterminate for CP on EUS in RAP. Majority were young adults, comparable to study by Sajith et al.,⁹ studies done by Gullo et al.,¹⁰ Gao et al.,¹¹ and Zhang et al.,¹² showed 10–20 years higher age of presentation. Younger age of presentation can be attributed to more patients with idiopathic etiology which is relatively common in younger population. Around 91% patients were male. Higher prevalence of RAP in males was also shown in other studies^{9–11} attributed to more cases of alcoholic RAP in those studies.

Majority patients presented after or during fourth episode of AP, also observed in study by Tepox-Padrón et al.,¹³ In contrast, majority patients in study by Sajith et al.,⁹ presented during third episode and in European and Chinese studies^{10–12} during second episode. Mean duration between first AP episode and EUS examination was 39 months. This delayed presentation at tertiary care center was due to delay in referral by primary care physicians and patient's negligence. RAP is associated with high morbidity as median hospital admissions before presentation was 3. Therefore, it is important to educate doctors and patients about RAP and nature of disease to improve outcome and decrease morbidity.

Most common identified etiology of RAP was alcohol seen in 14.3% patients. Alcohol etiology was found in 6.4 % in study

by Sajith et al.,⁹ and in 57 % patients in European study.¹⁰ In our study, majority alcoholic RAP patients had definitive evidence of CP on baseline CT abdomen or MRCP and hence excluded. In 79% patients, no cause could be identified despite thorough laboratory investigations and imaging including EUS and such patients were labeled "idiopathic." Biliary etiology was not found in any patient which may be due to early cholecystectomy or biliary sphincterotomy done nowadays after an episode of biliary AP.

Smoking is considered as important risk factor for RAP and its progression to CP and 35.7% patients were smokers. Case 8 had repeated AP attacks post cholecystectomy. Therefore, recurrence may still occur despite cholecystectomy as shown in previous study¹⁴ probably due to genetic predisposition. Severe AP history was present in Case 4 with progression to definitive CP. Severe AP is associated with progression of RAP to CP as necrotizing pancreatitis can lead to permanent ductal lesions and development of exocrine insufficiency.¹⁵

During 1 year of follow-up, no patient had continuous pain pattern and 35.7% remained pain free. Mean analgesics requirement reduced to 1 day/month from 4.5 days/month. All the patients were counseled regarding diet and lifestyle modifications including smoking and alcohol abstinence. Only one patient continued smoking and had episodic pain attacks. Rest all patients with smoking and alcohol history who were abstinent remained pain free. Gall bladder stones and sludge were detected on follow-up ultrasound. Therefore, these patients had biliary RAP and repeating ultrasound imaging periodically can be useful. Total five patients refused to undergo follow-up EUS attributed to COVID-19 pandemic. Follow-up EUS in eight patients revealed Rosemont "normal" in 12.5%, indeterminate in 25%, suggestive of CP in 37.5%, and consistent with CP in 25%. Thus, findings improved in 12.5% and 62.5% patients progressed, while 25% remained Indeterminate. Case 3 with normal study on follow-up EUS continued to have pain attacks attributed to functional chronic abdominal pain syndrome. Cases 1 and 8 who remained indeterminate were smokers and one of them was alcoholic and both remained abstinent. All patients who progressed were Idiopathic RAP and Case 7 was smoker who continued smoking. Thus, alcohol and smoking cessation can halt the progression and ongoing smoking can lead to progression to definitive CP. Four of five patients who progressed to definitive CP had repeat AP attack during follow-up; probably, these patients had CP at baseline not diagnosed by EUS. Thus, repeating EUS after a period of time can be useful in such patients.

Limitations of the study

Our study has several limitations. First, smaller number of patients, and second, high dropout rate for follow-

up EUS. Third, EUS findings were interpreted by single endosonographer and interobserver variation was not taken care of. Fourth, genetic testing was not done in idiopathic RAP. Strength of our study is close follow-up of patients.

CONCLUSION

Indeterminate for CP is common in young idiopathic RAP. Majority were found to be suggestive/consistent with CP at 1 year on EUS. Close follow-up and alcohol and smoking cessation can improve clinical outcome. More follow-up studies are required with larger sample size to determine natural history of Rosemont's Indeterminate for CP.

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AV- Concept and design of study, reviewed literature, interpreted results, statistical analysis, preparation and revision of manuscript; **PSP-** Concept and design of study, coordination and revision of manuscript.

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