Recurrent acute pancreatitis

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Goal

- Define RAP
- Etiology
- Diagnostic algorithm
- Management strategy

Definitions

Acute pancreatitis

clinical syndrome of an episode of acute inflammation originating in the pancreas diagnosed according to the Revised Atlanta Criteria presence of 2 of the 3 following criteria

- (a) abdominal pain suggestive of pancreatitis
- (b) serum amylase or lipase levels 3 or more times normal
- (c) characteristic findings on (CT), (MRI), or(US).

Definitions

Recurrent acute pancreatitis

Is defined as 2 or more well-documented separate attacks of AP with complete resolutionf with or more than 3 months between attacks.

It usually occurs in the setting of normal morpho functional gland with self-limited edematous changes

Definitions

Chronic pancreatitis

pathologic fibro-inflammatory syndrome of the pancreas in individuals with genetic, environmental and/or other risk factors who develop persistent parenchymal injury include pancreatic atrophy, fibrosis, pain syndromes, duct distortion and strictures, calcifications, pancreatic exocrine dysfunction, pancreatic endocrine dysfunction and dysplasia."

Recurrent acute pancreatitis

- (RAP) is a clinically significant problem globally.
- The etiology remains unclear in approximately 10% to15% of patients
- Data on natural history and efficacy of treatments are limited
- Approximately 10% to 30% of patients with AP develop recurrent attacks In most studies male predominance is seen (male constitutes 63-79% of RAP cases)
- Idiopathic recurrent acute pancreatitis is defined as RAP after exclusion of readily apparent causes by history, routine laboratory tests, and conventional imaging
- Mean age of RAP varies from 33 to 43, years

ETIOLOGY

- AP, RAP, and CP share multiple risk factors and clinical features
- Any condition causing a single episode of AP has the potential to cause recurrent episodes
- Treating the underlying cause has the potential to reduce or eliminate recurrent Attacks

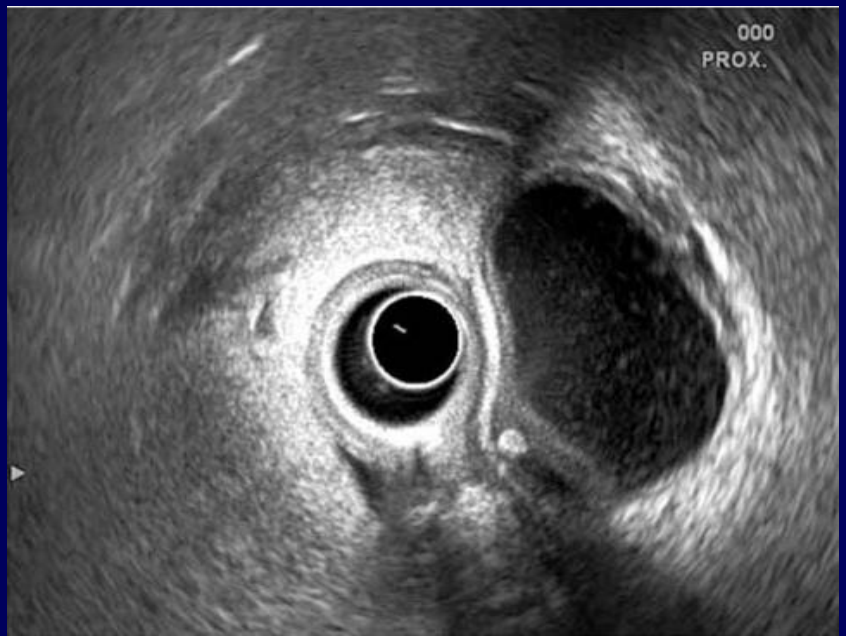
- Effective management of RAP requires identification of etologic factors and pathogenic processes.
- Etiology can be identified by first-line testing (history, blood work, standard imaging) in approximately 70% of cases 10% of patients remain truly idiopathic and should be followed expectantly

ETIOLOGY

Mechanical	Metabolic	toxic	miscellaneous	infection	Genetic
Microlithiasis Sphincter of Oddi Dysfunction Pancreas Divisum Anatomic Abnormalities Tumer ampullary tumours cystic neoplasms	Hypertriglyceridaemia (HTG; >1000 mg/dL) hypercalcaemia	Alcohol medication	Vasculitis SLE AIP Celiac	Ascariasis HIV	Mutations in CFTR SPINK1 PRSS1 CTRC •Hereditary pancreatitis

MICROLITHIASIS

- small gallstones less than 3 mm.
- Microlithiasis and sludge can co-occur
- prevalence of microlithiasis ranging from 6% to 16%.
- microlithiasis should be suspected as a cause of AP, when it is demonstrated on imaging ideally on EUS, and LFTs are abnormal at the time of pancreatitis



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alcohol

- Excess alcohol consumption is responsible for 30% of adult cases of AP in the United States History of over 5 years of heavy consumption.“Heavy” alcohol consumption is generally considered to be > 50 g per day
- Prevalence estimates for RAP in alcoholics are approximately 16.9% in men and 5.5% in women

smokers + alcoholics → ARP → CP

Sphincter of Oddi Dysfunction (SOD)

Benign obstructive disorder of the Sphincter of Oddi due to fibrosis, inflammation or hypertonic sphincter

SOD has been found in 25% to 60% of patients with IRAP.

Diagnosis : noninvasive MRCP/EUS with Secretin Stimulation.

invasive Manometry (gold standard)

Therapy: sphincterotomy

Pancreas divisum

- 5 to 10 % of papulation
- Pancreas divisum has been associated with RAP and CP
- increased prevalence of genetic abnormalities (specially SPINK1and CFTR)

in patients with both PD and RAP suggesting that PD is a cofactor rather than a cause

DONOT MISS TUMER

- 10% of IRAP are diagnosed with mass
- Common tumours include ampullary tumours and cystic neoplasms of the pancreas, especially intraductal papillary mucinous tumour (IPMT)
- EUS has the highest sensitivity for identifying small pancreatic neoplasms.

Medications

Drug-induced pancreatitis is classified (class I-IV) based on:
1-Number of cases reported.
2-Consistent latency period (time from initiation of drug to development of pancreatitis)
3-Reaction with rechallenge

Summary of drug-induced acute pancreatitis based on drug class

Class Ia	Class Ib	Class II	Class III	Class IV
α-methyldopa	All-trans-retinoic acid	Acetaminophen	Alendronate	Adrenocorticotrophic hormone
Azodisalicylate	Amiodarone	Chlorothiazide	Atorvastatin	Ampicillin
Bezafibrate	Azathioprine	Clozapine	Carbamazepine	Bendroflumethiazide
Cannabis	Clomiphene	Didanosine	Captopril	Benazepril
Carbimazole	Dexamethasone	Erythromycin	Ceftriaxone	Betamethasone
Codeine	Ifosfamide	Estrogen	Chlorthalidone	Capecitabine
Cytosine Arabinoside	Lamivudine	L-asparaginase	Cimetidine	Cisplatin
Dapsone	Losartan	Pegaspargase	Clarithromycin	Colchicine
Enalapril	Lynestrenol/methoxyethinylestradiol	Propofol	Cyclosporin	Cyclophosphamide
Furosemide	6-mercaptopurine	Tamoxifen	Gold	Cyproheptadine
Isoniazid	Meglumine		Hydrochlorothiazide	Danazol
Mesalamine	Methimazole		Indomethacin	Diazoxide
Metronidazole	Nelfinavir		Interferon/ribavirin	Diclofenac
Pentamidine	Norethindronate/mestranol		Irbesartan	Diphenoxylate
Pravastatin	Omeprazole		Isotretinoin	Doxorubicin
Procainamide	Premarin		Ketorolac	Ethacrynic acid
	Trimethoprimsulfamethazole		Lisinopril	

Early chronic pancreatitis

- Early CP may be present as ARP (pancreatic duct is typically normal in early)
- Pancreatic function tests may help establish the diagnosis at an earlier stage
- Risk for progression to CP in patients with AP and RAP are higher among smokers and alcoholics.

Work up

When a patient of RAP (RAP) presents initially should be to

Level I evaluation

history taking (especially alcohol, trauma, drug and family history)

biochemistry evaluation (LFT, CA, TG)

crosssectional imaging by US or pancreatic protocol CT.

If etiology could not be found after level I evaluation patient are labelled as having IRAP and need level II evaluation.

Level II evaluation

EUS with or without (FNA)

MRCP

ERCP (with or without bile aspiration, sphincter of Oddi manometry, secretin test, intraductal US).

bile microscopy

Tropical Gastroenterology 2013;34(3):123–135

Work up

70-90% of cases by level I evaluation only,

after extensive evaluation (level I & II evaluation) few patients remain undiagnosed

This group of patient should be go to

level III evaluation

- Genetic testing indicated in patients with a family history of pancreatitis and those with subtle changes of CP
- IG4

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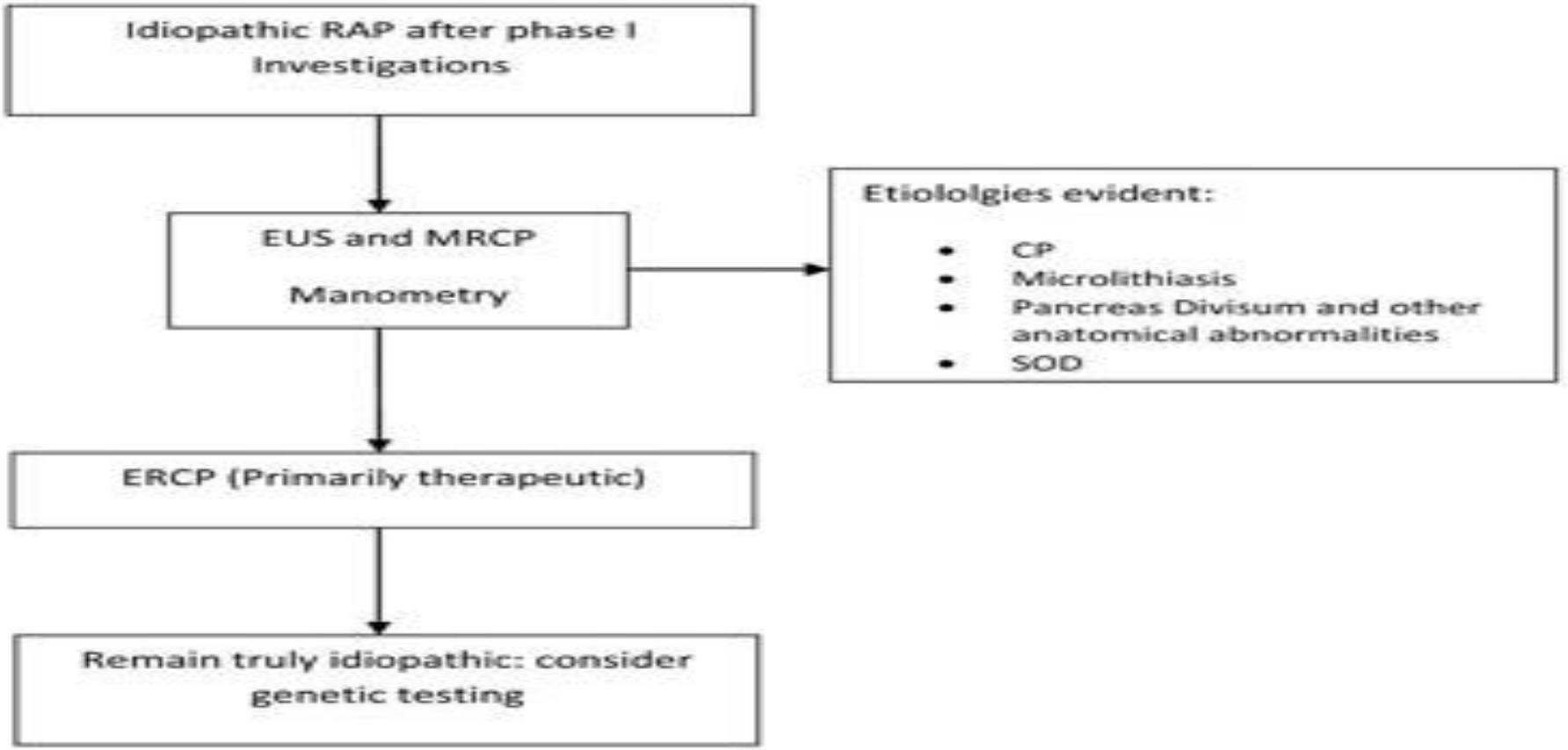

Figure 6: Algorithm for evaluation of patients with Idiopathic pancreatitis RAP recurrent acute pancreatitis EUS endoscopic ultrasound MRCP magnetic resonance cholangiopancreatography CP chronic pancreatitis SOD spincter of Oiddi dysfunction ERCP endoscopic retrography cholangiopancreatography PD pancreas divisum

EUS

Safe less invasive than ERCP

Most accurate for diagnosis

- GB CBD stones / sludge
- Tumor (Occult ampullary and pancreatic tumors)
- P divisum (80 – 90 % accuracy)
- CP

ERCP

- With the availability of EUS, ERCP is rarely used now-a-days for purpose only except for sphincter of Oddi manometry (SOM) and intraductal US.
- Main advantage of ERCP over MRCP or EUS is the ability to perform therapeutic measures in the same session of procedure if abnormality detected.

(SOM)

- Sphincter of oddi manometry (SOM) is still the gold standard for the diagnosis of SOD performed during ERCP

Genetic testing

- Genetic testing (mutations in CFTR, SPINK1, PRSS1, CTRC, and other genes) is indicated in most younger (<35 years old) with IRAP
- Genetic testing should routinely be performed in patients with PD and RAP

IgG4

- Autoimmune pancreatitis is a rare (<5%) cause of IRAP
- Routine serological testing for IgG4 should not be done in patients with RAP in the absence of imaging features suggestive of AIP

Management of patients with RAP

- Attack of AP should be treated well regardless of the aetiology. Recurrence is prevented by removing the cause of pancreatitis
- microlithiasis treat by cholecystectomy but in patients with high surgical risk, endoscopic sphincterotomy or ursodeoxycholic acid are other treatment options.
- cessation of alcohol intake and smoking

- Treatment for SOD includes biliary and/or pancreatic sphincterotomy, which might lead to relief in >50% patients Prophylactic pancreatic stenting for 2 weeks after sphincterotomy has shown to reduce the incidence of post- ERCP pancreatitis

Treatment for PD consists of endoscopic or surgical therapy. Endoscopic therapy consists of minor papilla sphincterotomy with or without stenting

Management of patients with RAP

- RAP is the most important risk factor for progression to end-stage CP.

- Effective manage RAP, beginning with the sentinel AP

- AP patients with unexplained etiology should follow-up patients with EUS and CT for a long period of time for at least 12 month specially in patients over the age of 40.


Thank you