



Contribution of Endoscopic Ultrasound in the Etiological Diagnosis of Acute Pancreatitis

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Abstract

Introduction: Acute Pancreatitis (AP) is a self-digestion of the pancreatic gland. Its aetiologies are multiple, dominated by lithiasic biliary disease and alcoholism. In case of acute pancreatitis of undetermined origin by different biological and radiological assessments, Endoscopic Ultrasound (EUS) plays an important role. The aim is to study the contribution of EUS in the etiological diagnosis of AP.

Material and Methods: From October 2015 to October 2019, were included all patients with acute pancreatitis of which etiology is either suspected or remains undetermined after an initial radiobiological assessment. The epidemiological, clinical, biological and endoscopic ultrasound data were collected from EUS records.

Results: 53 cases of patients were explored (20%). The average age of the patients was 51.5 years, with a female predominance 58.5%; 47 patients (87.5%) were explored by EUS after 1 episode of AP, 3 patients (6.25%) after 2 episodes and 3 patients after 4 episodes (6.25%). The time to perform EUS was <1 week in 2 patients (3.77%), 2 weeks to 8 weeks in 37 patients (70%) and more than 8 weeks in 14 patients (62.5). Gallstones were objectified in 59.28% of cases: Biliary microlithiasis without choledocholithiasis (68%), biliary microlithiasis with choledocholithiasis (42%), IPMN in 20% of cases, 2 cases (3.78%) of chronic early pancreatitis, 1 case of Vaterian ampulloma (1.88%), an appearance of cholangitis in a patient (1.88%), 1 case of hydatid material in the CBD (1.88%) in a patient operated for a LHC who presents calcified peritoneal HC, 1 case of pancreas divisum (1.88%) and in 4 cases (7.54%) EUS was normal, including 1 young patient in whom a genetic origin was suspected.

Discussion and Conclusion: These preliminary results confirm that endoscopic ultrasound remains essential in the case of acute pancreatitis of unknown etiology after a negative radiobiological assessment, however, larger series are desirable to confirm our results.

Keywords: Acute pancreatitis; Etiology; Endoscopic ultrasound; Gallstone; Tumor

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Introduction

Acute Pancreatitis (AP) is a frequent condition since its annual incidence is 13 cases to 45 cases per 100,000 inhabitants [1]. Nearly 80% of APs are benign without serious complication (s) or sequela (s), the remaining 20% are said to be serious as they are associated with locoregional and/or general complications with a risk of mortality still significant in 2018. Indeed, the overall mortality of AP is 5% to 7% [2], most often by multiple organ failure secondary or not to an infection of intra- and/or extra pancreatic necrosis. Even if the clinical course is most often mild, AP is a painful condition, requiring hospital stay, sometimes at the intensive care unit. It is therefore important to know its cause in order to treat it if possible, and thus avoid recurrence that occurs in more than half of the cases, responsible for the picture of "recurrent" APs [3-5]. Its aetiologies are multiple, dominated by lithiasic biliary disease and alcoholism but it is also necessary to know how to look for an obstructive tumor origin. Urgently or at a distance of the acute episode, EUS plays an important role in the etiological assessment of AP.

The aim of this work is to study the contribution of EUS in the etiological diagnosis of AP through a monocentric series.

Materials and Methods

This is a descriptive, retrospective study carried out over a period of 4 years ranging between October 2015 and October 2019, collecting all patients with acute pancreatitis of which etiology

is either suspected or remains undetermined after an initial radiobiological assessment.

The epidemiological, clinical, biological, radiological and Endoscopic Ultrasound data were collected from EUS records of the Functional Digestive Explorations and Hepato-Gastroenterology Department (FDE-HGE) of the Ibn Sina University Hospital - Mohammed V University of Rabat.

Out of a total of 265 bilio-pancreatic EUSs performed during the study period, 53 patients with AP were explored by endoscopic ultrasound.

Were included all patients who were hospitalized for acute, persistent abdominal pain and lipasemia greater than three times the normal with or without imaging.

Were excluded acute pancreatitis of metabolic, infectious, toxic, medicinal, post-ERCP or post-surgery origins.

Results

Epidemiology

From October 2015 to October 2019, 53 cases of patients with acute pancreatitis were collected in our study.

Age: The average age of our patients was 51.55 years with extremes ranging from 16 years to 84 years.

Gender: These are 31 women (58.5%) and 22 men (41.5%), with a female predominance.

History and/or co-morbidities

Seventeen patients (32%) have a medical history and/or comorbidity:

- Cholecystectomy: 09 cases (16.96%)
- Chronic alcoholism: 02 cases (3.76%)
- Diabetes: 02 cases (3.76%)
- Celiac disease: 01 case (1.88%)
- Myeloma: 01 case (1.88%)
- Hydatid cyst of the liver: 01 case (1.88%)
- Good Pasture Syndrome: 01 case (1.88%)
- 36 patients (68%) do not have any particular pathological history or comorbidities.

Severity of AP using the Balthazar score

Abdomen and Pelvis CT scan with contrast was performed 48 h to 72 h on average after the onset of pancreatic pain and showed severe acute pancreatitis in 14 patients (26.4%), it also made it possible to objectify a cholelithiasis without gallstones at the level of the CBD in 1 case, dilatation of the CBD without visible obstacle in 1 case, and an IPMN in another case.

According to the Balthazar score, patients were classified into:

- Grade A: 7 patients (13.2%)
- Grade B: 13 patients (24.5%)
- Grade C: 10 patients (18.9%)
- Grade D: 8 patients (15%)
- Grade E: 6 patients (11.4%)

The Balthazar score was not specified in 9 patients or 17% of the cases.

Imaging techniques performed before EUS (other than CT scan)

Abdominal ultrasound: Ultrasound was normal in 42 cases (79.24%) and showed abnormalities in 9 cases (20.76%): Cholelithiasis without gallstones in the common bile duct in 5 patients, dilatation of the CBD with no apparent obstacle in 4 patients with an average caliber of 10.5 mm.

MR Cholangiography: Twenty one patients (39.6%) benefited from a Magnetic Resonance Cholangiography which showed a gallstone origin in 38.1% of the cases: Cholelithiasis with gallstone migration in 2 cases (9.53%) and choledocholithiasis in 6 cases (28.57%), dilated CBD without obstacle in 4 cases (19.04%), 5 IPMN cases (23.8%) and 4 MR Cholangiographies were normal (19%).

Number of episodes before endoscopic ultrasound: The number of acute episodes before EUS was performed was the following:

- 1 episode: 47 cases (87, 50%)
- 2 episodes: 3 cases (6.25%)
- 4 episodes: 3 cases (6.25%)

Time period before performing endoscopic ultrasound: EUS was performed early (<1 week) in 2 patients (3.77%), from 1 week to 8 weeks in 37 patients (70%) and > than 8 weeks in 14 patients (26.3%).

Implementation periods of endoscopic ultrasound: 53 patients with acute pancreatitis explored by EUS were divided into 4 periods:

- 6 patients from October 2015 to October 2016 (11, 32%)
- 11 patients from October 2016 to October 2017 (20.75%)
- 8 patients from October 2017 to October 2018 (15.1%)
- 28 patients from October 2018 to October 2019 (52.83%)

Lipase levels at the time of endoscopic ultrasound: Lipasemia was >3N with an average of 1640 IU/L and extremes of 438 IU/L to 12000 IU/L in 7 patients (18.7%).

Lipasaemia was normal at the time of EUS in 45 patients (81.3%)

Results of endoscopic ultrasound: EUS showed lesions responsible for acute pancreatitis in 49 cases (92.45%):

- Gallstones were objectified in 59.28% of cases in the form of biliary microlithiasis (Figure 1) without choledocholithiasis in 68% and biliary microlithiasis associated with choledocholithiasis in 42% of cases with a dilated CBD in 6 patients (11.32%) to an average caliber of 11.55 mm and extremes of 9.6 mm to 20.6 mm

- an IPMN in 20% of cases
- early chronic pancreatitis in 2 cases (3.78%)
- a vaterian ampulloma in 1 case (1.88%)
- an appearance of cholangitis in 1 patient (1.88%)
- hydatid material in the CBD in 1 case (1.88%) of a patient operated for a liver hydatid cyst who presents calcified peritoneal HC.
- a pancreas divisum in 1 case (1.88%)
- a genetic origin was strongly suspected in 4 cases (7.54%) where

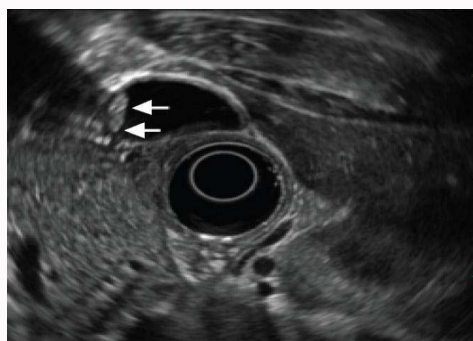


Figure 1: EUS revealing biliary microlithiasis with two gallstones of 3 mm in diameter (two white arrows).



Figure 2: EUS revealing 2 gallstones in the CBD with acoustic shadowing.

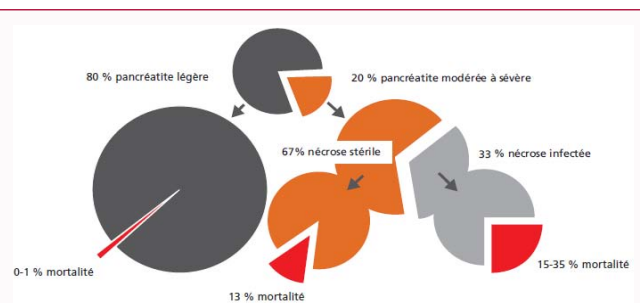


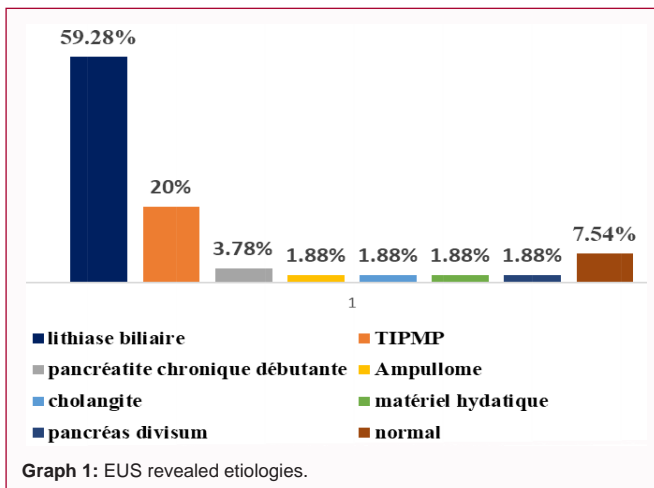
Figure 3: Mortality rates in AP [11].

EUS was normal

In addition, EUS objectified a pancreatic pseudocyst in 5 patients (9.43%) associated with necrosis in 2 cases (3.77%) (Graph 1).

Discussion

The annual incidence of Acute Pancreatitis (AP) is 13 cases to 45 cases per 100,000 people [1]. There are variations between countries with an incidence of 10 per 100,000 in England, 15 to 37 per 100,000 in northern European countries, and 44 per 100,000 in the United States [6,7]. An increased incidence of AP has been noted worldwide over the past ten years, linked to an increase in obesity and in the biliary cause of pancreatitis [8]. Thus, in the United States, AP represents 275,000 hospital admissions per year, a figure that is constantly increasing. In France, an evaluation based on data from the ISMP (Information System Medicalization Program) reported 27,550 hospital admissions for AP in 2013 [9]. Mortality associated with AP is less than 5% in mild forms, but can reach 30% in necrotizing forms (Figure 1) [10,11]. In our series there are 26.4% necrotizing forms.



Graph 1: EUS revealed etiologies.

Gallstones and alcohol represent the causes of AP in 60% to 80% [12]. The biliary origin of AP was first demonstrated in 1901 when Opie et al. [12] reported a case of AP with a gallstone lodged in the papilla [4].

Pathophysiology of AP is based on two mechanisms: The obstruction of the pancreatic duct at the level of the ampulla of Vater by a gallstone or by papillary edema secondary to its passage causing an increase in pancreatic duct pressure or a bile reflux into the pancreatic duct. The clinical diagnosis of a biliary origin has no major peculiarity, except than an age greater than 50 years, an excess weight, a female gender and a history of biliary colic or cholangitis will be very suggestive [13,14]. In our series, the average age was 51.55 years with a female predominance (58.5%). Biologically, an elevation of liver enzymes (namely ALT and GGT) is also a good marker of the biliary origin of pancreatitis [14]. Ultrasound of the Hepatobiliary system, although hampered by an intestinal ileus often present in the initial phase of AP, will attempt to detect cholelithiasis (although its mere presence is not always a formal argument in favor of the biliary origin of AP) or dilatation of the bile ducts. In our series, ultrasound found a cholelithiasis in 9.4% and a dilatation of the CBD in 7.54% with an average caliber of 10.5 mm.

Computed tomography (performed 72 h to 96 h after admission), also makes it possible to visualize cholelithiasis, dilatation of the bile ducts and more rarely a choledocholithiasis, but its sensitivity is also low (60% to 87%), with a specificity of 97% to 100% [15]. It has allowed in another series to objectify a lithiasic origin in 1.88% of the cases.

MR Cholangiography or bili-MRI, a non-invasive method but expensive and not available in all hospital structures, has a sensitivity greater than 90% for the diagnosis of CBD stones of more than 6 mm in diameter, but drops to 55% for gallstones <6 mm which is frequently the case for biliary AP [16,17]. In our series, bili-MRI diagnosed abnormalities in 17 cases of which a lithiasic origin in 15% of the cases on 21 MRI performed, 4 were normal (7.54%) including 2 cases that involved gallstones on EUS.

Endoscopic ultrasound has a sensitivity and specificity close to 100% for the diagnosis of CBD stones [18], making this technique more precise than MRI for the detection of small gallstones (<6 mm) [19]. A systematic review of seven studies [19] (six prospective, one retrospective) [18-20] including 545 patients with suspected biliary AP found sensitivity, specificity, NPV and PPV of endoscopic

ultrasound respectively at 86% to 100%, 85% to 100%, 92% to 100% and 92% to 100%, with almost zero morbidity. Another study evaluated prospectively the role of early endoscopic ultrasound in biliary AP [21]. EUS was performed within 48 h of admission. In the group of patients at a low risk for residual lithiasis, EUS allowed the diagnosis of a CBD stone in 20% of cases. Among high-risk patients, 50% had no CBD stones on endoscopic ultrasound. This technique also revealed microlithiasis of the gallbladder in 20% of patients who showed an acalculous gallbladder on transcutaneous ultrasound. In our series, EUS made it possible to diagnose a biliary origin in 59.28% of the cases, which joins the literature data.

Intraductal Papillary Mucinous Neoplasms (IPMN) of the pancreas reveals themselves in 20% to 60% of cases with AP. They develop from the main pancreatic duct alone, the secondary ducts alone or both (mixed-type IPMN). Diagnosis can be made with CT scan, but the addition of EUS and MRCP increases diagnostic performance [22]. In our series, EUS revealed IPMN in 20% of cases, about half of which were objectified by MR cholangiography.

Pancreatic adenocarcinoma can be revealed in 3% to 9% of cases by an acute episode of AP. AP precedes the diagnosis of cancer by a few weeks to a few months. This last element should draw the clinician's attention for an earlier diagnosis of the cancer in question. It is important to think of this possibility in case of any non-alcoholic non-biliary AP occurring after the age of 50 or recurrent after cholecystectomy for an AP "labeled" as biliary and even in the presence of cholelithiasis. In our series, one case of Vaterian ampulloma was found, but no case of pancreatic adenocarcinoma was identified.

Pancreas divisum is the most frequent pancreatic malformation observed in 10% to 15% of subjects examined by MRCP, a figure close to that of autoptotic series. It comes from the defect of embryonic fusion of the dorsal (Santorini) and ventral (Wirsung) pancreatic ducts. Thus, most of the pancreas is drained through the dorsal duct to the accessory papilla. The accountability of pancreas divisum in the genesis of recurrent AP remains controversial [23]. Before incriminating pancreas divisum as a cause of AP, it is still important to eliminate more frequent causes or to look for co-factors (nutritional, genetic, and toxic). A pancreas divisum was found in 1.88% of cases in our series.

Conclusion

Etiological assessment of acute pancreatitis at the initial phase includes a thorough anamnesis, a biological assessment, an ultrasound of the Hepatobiliary system and an abdominal CT scan. Biliary and alcoholic causes will be identified in 60% of cases, 10% of aetiologies of acute pancreatitis will be identified of type non-A non-B but in 30% no cause will be clearly recognized imposing an etiological assessment to be carried out. This assessment will include autoimmune tests, a genetic testing in young adults, a MRCP and an endoscopic ultrasound in search of a biliary etiology but also to look for other causes in particular tumors or malformations, in this case, a period of 6 weeks to 8 weeks after the acute episode of pancreatitis and the normalization of lipasemia is necessary to properly explore the pancreas.

In our study, the etiological profile of acute pancreatitis in our patients is a middle-aged woman in whom the most common etiology is a biliary disease followed by the intraductal papillary mucinous neoplasm of the pancreas.

In fact, in acute pancreatitis, the biliary cause is retained

when ALT is increased and ultrasound reveals gallstones. MR Cholangiography and Endoscopic Ultrasound are the most effective investigative techniques in the diagnosis of choledocholithiasis. The latter technique seems more sensitive and more specific for the diagnosis of small gallstones often involved in biliary AP. However, other larger multicentric studies are desirable to confirm our results.

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