Original Paper

# The Differential Diagnosis of Chronic Pancreatitis

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**ABSTRACT** BACKGROUND Chronic pancreatitis is an inflammatory disease of the pancreas with a physiopathology that is yet to be fully understood, with a multifactorial etiology, of which alcohol abuse causes the majority of cases. PATIENTS AND METHOD We included 80 patients diagnosed with chronic pancreatitis, admitted in the Gastroenterology Clinic of the University of Medicine and Pharmacy Craiova. In each patient, demographic parameters, family and personal history were recorded. All patients were initially evaluated by transabdominal ultrasound. In selected cases other imagistic methods were used: computed tomography, endoscopic ultrasound with fine needle aspiration, endoscopic retrograde cholangiopancreatography. RESULTS The mean age in the studied group ranged between 26 and 76 years with a mean age of 52.9 years. The male to female ratio was 3.6:1. The most frequent presenting symptom was abdominal pain (93.75%), followed by fatigue (70%), anorexia (50%); fewer patients presented with emesis, loss of weight, diarrhea, meteorism and flatulence. The most frequent etiologic factor of chronic pancreatitis in the studied group was alcohol abuse. Using imaging methods the following complications of chronic pancreatitis were diagnosed in the studied group: complicated or uncomplicated pseudocysts (31.57%), pancreatic cancer (18.75%), obstructive jaundice (10%), segmental portal hypertension (2.5%), and pseudoaneurysm (1.25%).CONCLUSSIONS Transabdominal ultrasound is quite accurate in diagnosing chronic pancreatitis and its morbidities and its non-invasiveness makes it the method of choice in the initial assessment of the disease. EUS has the advantage of visualizing not just the modifications of the pancreatic ducts, but also the parenchyma. Moreover, it can be used as EUS-FNA in order to increase the sensitivity of the differential diagnosis between pseudotumoral chronic pancreatitis and pancreatic cancer.

**KEY WORDS** *chronic pancreatitis; transabdominal ultrasound; endoscopic ultrasound; endoscopic ultrasound guided fine needle aspiration biopsykeywords*

## Introduction

Chronic pancreatitis is characterized by recurrent episodes of abdominal pain associated with both exocrine and endocrine pancreatic failure and progressive atrophy of the pancreatic parenchyma. The etiologic factors involved in the occurrence of the disease are: chronic alcohol abuse, genetic factors, autoimmune injuries, as well as obstructions of pancreatic and bile ducts. Apparently, two main mechanisms are responsible for pain in chronic pancreatitis: increased intraductal pressure and neural as well as perineural inflammation. Differentiating non-ulcerous epigastric pain in chronic pancreatitis is difficult, as it can be mistaken for epigastric pain in duodenal ulcer, hiatal hernia, irritable bowel syndrome and other pancreatic and billiary diseases. Acute episodes can be easily mistaken for acute edematous pancreatitis.

The adequate treatment of chronic pancreatitis remains a challenge. For the majority of patients a medical instead of surgical approach is the best option, especially for those who necessitate a substitutive therapy in order to correct the exocrine and endocrine failure of the pancreas. Pain control is by far more difficult, and, although a medical approach might solve this problem as well, surgery needs to be performed if antialgic therapy fails. Besides pain, chronic pancreatitis can lead to pseudocysts, fistulae, upper gastrointestinal bleeding due to ruptured esophageal varices (caused by portal or splenic vein thrombosis), bile duct or duodenal stenosis, ascites and pancreatic cancer.

## Patients and method

We included in this study 80 patients diagnosed with chronic pancreatitis, admitted in the Gastroenterology Clinic of the University of Medicine and Pharmacy Craiova between January 2004 and December 2007. The eligibility criteria were: age between 26 and 76 years and the diagnosis of chronic pancreatitis established on both clinical criteria (abdominal pain, signs and symptoms of exocrine and endocrine pancreatic failure) and imaging data.

In each patient the following parameters were taken into consideration: age, sex, social background, family history of pancreatic disease, alcohol abuse, smoking, reasons of presentation, Body Mass Index, laboratory and imagistic tests.

All patients were evaluated by transabdominal ultrasound; in cases with a difficult diagnosis, especially the ones that necessitated a differential diagnosis with pseudotumoral chronic pancreatitis, other imagistic methods were used: computed tomography (CT), endoscopic ultrasound (EUS) with fine needle aspiration (EUS-FNA), and in selected cases, endoscopic retrograde cholangiopancreatography (ERCP).

Transabdominal ultrasound was performed with an Aloka SSD 5000 ultrasonography system, using a convex transducer with a frequency of 3,5-5 MHz.

EUS was performed a jéun, with a system of liniar endoscopic ultrasound and an Olimpus UCT echoendoscopic transducer with variable frequency (5-10 MHz) connected to the same Aloka SSD 5000 ultrasonography system. All patients were sedated with intravenous Midazolam (Dormicum). Butilscopolamin (Buscopan) was used in order to decrease duodenal motility. All patients were informed about the risks and the benefits of the procedure and they signed informed consent prior to it.

All the patients included in the study were evaluated by transabdominal ultrasound **(figure 1),** which showed ultrasonographic signs of chronic pancreatitis.

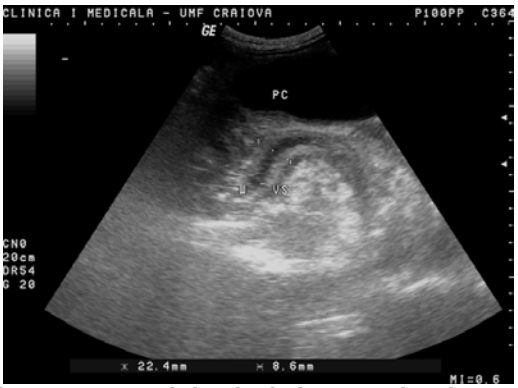


***Figure 1: Transabdominal ultrasound –advanced chronic pancreatitis***

EUS-FNA was performed according to a common protocol which included a minimum of 3 passages with 10 to-and-fro movements, aspiration being performed simultaneously. The needle (Olympus NA-10J-1) could be visualized directly, in real time, during the procedure, in order to place it correctly inside the suspected pancreatic tumoral mass. EUS-FNA was done in several points of the lesion, both in the center and peripherally, by subtly adjusting the endoscope and the needle in order to increase the probability of obtaining tissue for biopsy. A cytologist was permanently present during the procedure, assessing the quality of the extracted biopsy material and prompting supplementary passages if necessary. Smears were prepared out of the aspirated material obtained via fine-needle biopsy and they were stained using Giemsa or Papanicolau method. The Papanicolau staining was applied after moist fixing in ethanol for at least 5 minutes, while the Giemsa staining was done after moist fixing and postfixing with methanol. In describing the smears, several factors were taken into consideration: cellularity, nuclei, nucleoli, chromatin in order to interpret lesions as benign or malign.

Contrast enhanced CT was undertaken in Imaging Department of the Emergency Hospital Craiova, using special protocols in order to visualize the pancreatic masses.

## Results

The mean age in the studied group ranged between 26 and 76 years with a mean age of 52.9 years. The male to female ratio was 3.6:1. The social background of the patients was either rural or urban, in equal proportions. The most frequent presenting symptom was abdominal pain (93.75%), predominantly in the epigastrium, followed by fatigue (70%), anorexia (50%); fewer patients presented with emesis, loss of weight, diarrhea, meteorism and flatulence. Endocrine pancreatic failure (diabetes mellitus) occurred in 13.15% of the patients. 65% of the patients had a normal BMI, 28.75% of them were overweight, while 6.25% had a lower than normal BMI.

The most frequent etiologic factor of chronic pancreatitis in the studied group was alcohol abuse: 38.75% of the patients were alcoholics, 22.5% were moderate alcohol consumers, 16.25% were occasional alcohol consumers, while only 22.5% of the patients had not drunk alcohol. Other causes of chronic pancreatitis were: repeated bile duct obstructions by migrated gallstones (18.75% of the patients had a history of calculous cholecistitis, treated by cholecystectomy), pancreas divisium, autoimmune or idiopathic pancreatitis, etc.

Of the patients who were diagnosed with chronic pancreatitis in the 3 years of the study, most were admitted for pancreatitis-associated symptomatology, while in a lesser percentage (25%) of the patients pancreatitis was diagnosed by chance during imagistic exploration for other digestive tract conditions (only 21.25% of the major alcohol consumers in the studied group developed concomitant cirrhosis and chronic pancreatitis).

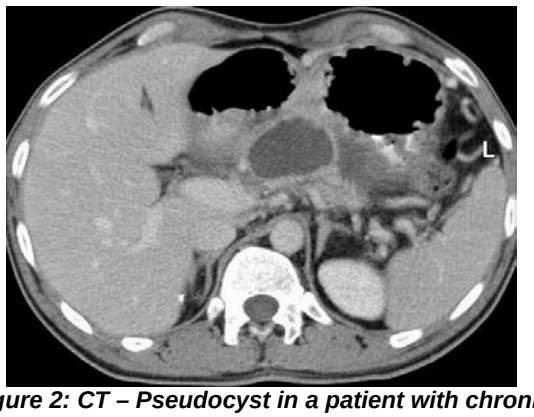

***Figure 2: CT – Pseudocyst in a patient with chronic pancreatitis***

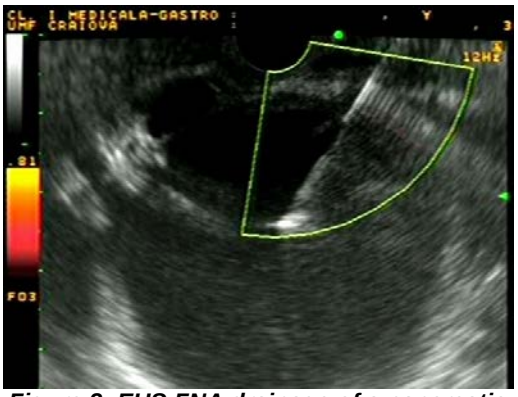


***Figure 3: EUS-FNA drainage of a pancreatic pseudocyst***

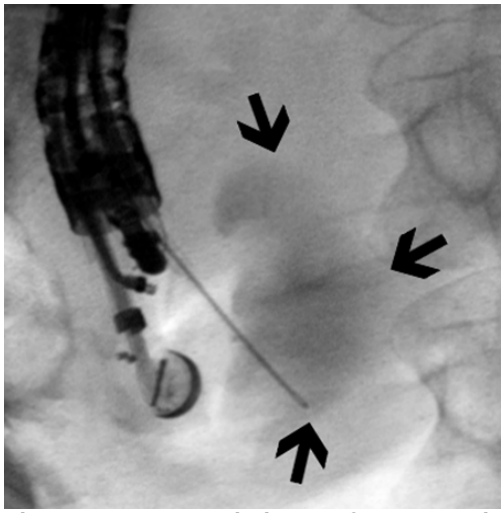

***Figure 4: EUS-FNA drainage of a pancreatic pseudocyst (Rx aspect)***

***Figure 5: ERCP – the aspect of the Wirsung duct in chronic pancreatitis***

Thus, a nonhomogenous pancreatic echostructure appeared in 56.25% of the patients, pancreatic calcifications occurred in 55% of them, a visible or dilated Wirsung duct in 47.5% and transonic pancreatic masses (pseudocysts) were visualized in 31.25% of the patients.Visualizing transonic pancreatic masses by transabdominal ultrasound prompted for further investigations meant to establish a certain diagnosis between a pseudocyst and a pancreatic cystadenocarcinoma. Contrast enhanced CT **(figure 2)** was the first imagistic investigation performed after transabdominal ultrasound; EUS-FNA was carried out in uncertain cases, in order to try and aspirate the pseudocysts. **(figures 3,4)**. In case EUS-FNA failed to solve the problem, ERCP was used in order to place a stent in Wirsung duct **(figures 5, 6**).

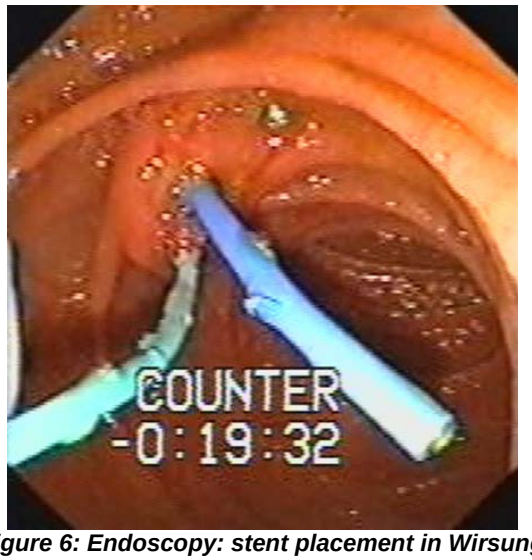


***Figure 6: Endoscopy: stent placement in Wirsung duct by ERCP***

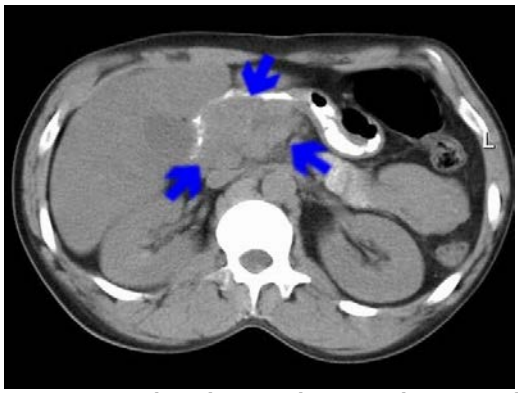

***Figure 7: CT – chronic pseudotumoral pancreatitis***

Patients with pseudotumoral chronic pancreatitis **(figure 7)** underwent EUS-FNA **(figure 8)** of the suspect pancreatic masses, in order to exclude pancreatic cancer, one of the complications of chronic pancreatitis **(figure 9)**.

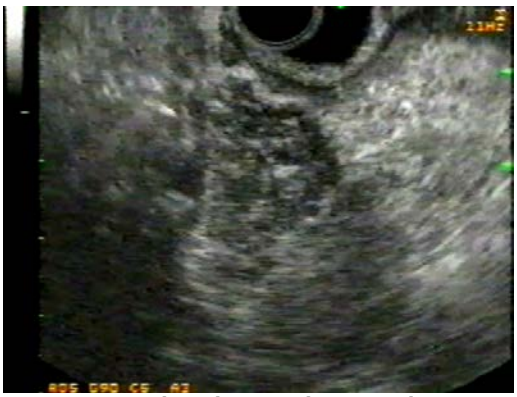

*Figure 8: EUS – chronic pseudotumoral pancreatitis*

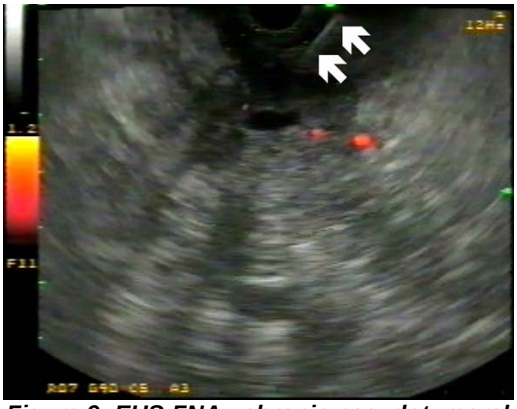

*Figure 9: EUS-FNA - chronic pseudotumoral pancreatitis*

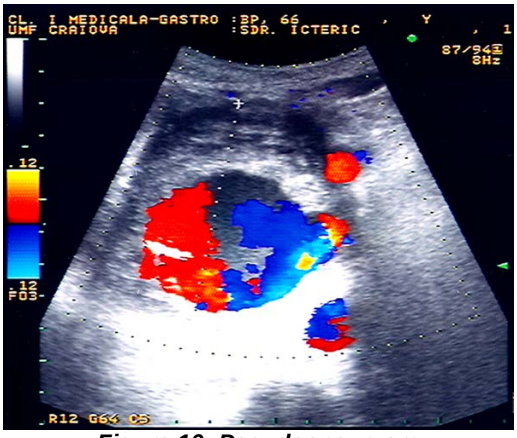


*Figure 10: Pseudoaneurysm*

The following complications of chronic pancreatitis were found in the studied group of patients: complicated or uncomplicated pseudocysts (31.57%), pancreatic cancer (18.75%), obstructive jaundice (10%), segmental portal hypertension (2.5%), pseudoaneurysm (1.25%) **(figure 10)**. In the cases of chronic pancreatitis that presented pancreatic cancer as a complication, EUS criteria were used in order to stage the chronic pancreatitis. Thus, all stages of chronic pancreatitis were encountered: severe (46.66%), moderate (33.33%), while mild pancreatitis was showed a looser association with pancreatic cancer (20%).

## Discussions

Chronic pancreatitis is an inflammatory disease that leads to definitive structural alterations of the pancreas, with the eventual loss the exocrine and endocrine functions [1,2]. Even though pain is a cardinal symptom in chronic pancreatitis, its presence might vary significant from one patient to another. Classically, pain is located in the epigastrium and irradiates in the back being accompanied by nausea end emesis. Many patients with chronic pancreatitis do not have this specific pattern of pain, therefore it has to be included in the differential diagnosis of upper abdominal pain, provoked by: gastric ulcer, duodenal ulcer, billiary tree diseases, irritable bowel syndrome, etc. Approximately 20% of the patients have an endocrine or exocrine dysfunction in the absence of abdominal pain [3]. Exocrine dysfunction leads to maldigestion, causing diarrhea, steatorrhea and loss of weight. Steatorrhea typically occurs before the protein deficit. The malabsortion of liposoluble vitamins and vitamin B12 may occur, yet a clinically significant deficit is seldom the case.

Annual incidence of chronic pancreatitis was estimated in some retrospective studies to 3 up to 9 cases per 100.000 persons [4]. Alcohol abuse seems to play a role in more than two thirds of the cases of chronic pancreatitis. The incidence of autoimmune pancreatitis is much larger than estimated in the past; this form of the disease is spread all over the world, with a higher incidence in Japan [5].

The main imaging investigation in patients with abdominal pain is transabdominal ultrasound (TUS), which, at the same time, is able to diagnose other associated conditions (alcoholic hepatic cirrhosis), select the type of interventional method and assess for possible complications after invasive interventional techniques [6]. TUS cannot detect early-stage pancreatitis and is limited by patient-dependent factors: overweight and abdominal meteorism [7,8]. Ultrasound criteria predictive for chronic pancreatitis are: increased pancreatic volume, modified pancreatic shape and echostructure, pancreatic calcifications, pseudocysts and dilations of the Wirsung duct [9,10]. Provided for a good quality of the image, the method has a sensitivity of 70% and a specificity of almost 90% [6]. Pancreatic calcifications appear as multiple or solitary hyperechogenic structures of varied dimensions, located in the parenchyma or in the pancreatic duct. However, TUS has a lower sensitivity in detecting pancreatic calcifications in comparison with CT. Pseudocysts occur in chronic pancreatitis

as a consequence of the stenoses of peripheral ramifications of the Wirsung duct; therefore, they appear as small (10-20 mm), numerous pancreatic masses. Large, symptomatic pseudocysts can be drained percutaneously by endoscopic or surgical maneuvers [11]. The former technique is not yet unanimously accepted, even though transpapillary endoscpic drainage, using ERCP, or transmural endoscopic drainage, using EUS-FNA have a rate of success compared to the surgical approach [12-16], but with a significantly lower morbidity rate [15,17].

EUS is superior compared to TUS because it uses high frequency transducers, it visualizes the entire pancreas and it is not obstructed by the gaseous interface. EUS is able to explore both the alterations of the parenchyma (hyperechogenic foci and bands, calcifications, pseudocysts larger than 2 mm), as well as those of the main pancreatic duct and its branches (increased echogenity, irregularities, stenoses, calcifications) [6,18]. The advantage over ERCP consists in visualizing not only the ductal system, but also the pancreatic parenchyma. Also, EUS is a lot safer: the risk of acute pancreatitis after ERCP is approximately 6.7%, whereas EUS for diagnostic purposes causes acute pancreatitis in an estimate of only 0.5% [19]. The sensitivity and the specificity of EUS in comparison to ERCP are 97% and 60%, respectively [20].

Patients suffering from chronic pancreatitis have an increased risk of pancreatic cancer compared to the healthy population. The prolonged inflammation of the pancreas probably initiates and promotes carcinogenesis. The differential diagnosis of pseudotumoral chronic pancreatitis and pancreatic cancer is still difficult despite the progress in medical imaging. Although EUS has a high sensitivity in detecting pancreatic tumors, it is possesses a limited capability in differentiating between inflammatory processes and cancer [21]. EUS-FNA is especially useful in detecting pancreatic tumors and in differentiating between the benign and malignant ones. The accuracy of EUS-FNA in differentiating between pseudotumoral chronic pancreatitis and pancreatic cancer ranges between 90 and 95% [22-26]. Most studies have reported a high specificity, close to 100%, but a rather low sensitivity, because of a large number of false negative cases, which may influence the patients' therapy with potentially disastrous effects [13]. The result may also be influenced by the experience of the endoscopist, that of the cytopathologist, and by factors decreasing the cellularity of the aspirate: extensive fibrosis, tumor necrosis and degree of differentiation [18,26].

In conclusion, chronic pancreatitis is an inflammatory disease of the pancreas with a physiopathology that is yet to be fully understood, with a multifactorial etiology, of which alcohol abuse causes the majority of cases. Presenting symptoms are quite diverse, varying from abdominal pain to symptoms caused by the morbidity (e.g. pseudocysts, pancreatic cancer, etc.). TUS is quite accurate in diagnosing chronic pancreatitis and its morbidities and its non-invasiveness makes it the method of choice in the initial assessment of the disease. Unlike ERCP, EUS has the advantage of visualizing not just the modifications of the pancreatic ducts, but also the parenchyma. Moreover, it can be used as EUS-FNA in order to increase the sensitivity of the differential diagnosis between pseudotumoral chronic pancreatitis and pancreatic cancer.

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