

CASE REPORT

Diagnosis and Therapeutic Management of Cystic Dystrophy of the Duodenal Wall in Heterotopic Pancreas. A Case Report and Revision of the Literature

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ABSTRACT

Context Cystic dystrophy in heterotopic pancreas is a rare and serious condition. Diagnosis is difficult because of non-specific clinical manifestations and radiologic and endoscopic imaging are pivotal. Therapeutic management is still under debate.

Case report We describe a case of cystic dystrophy of the duodenal wall in heterotopic pancreas complicated with chronic pancreatitis and pancreatic cystadenoma.

Discussion Computed tomography and magnetic resonance are very useful in demonstrating the presence of cysts in a thickened duodenal wall but, for the most part, endoscopic ultrasonography is the most useful imaging examination. The choice of different therapeutic options is still under debate; although some authors have proposed a medical approach using octreotide or endoscopic treatment for selected patients, a pancreaticoduodenectomy is usually proposed for symptomatic patients.

Conclusion When surgery is needed, a pancreaticoduodenectomy is preferred, reserving by-pass procedures for high risk patients. Because of the non-specific clinical manifestation and the very difficult diagnosis

and therapeutic management, these patients should be studied and treated in specialized and dedicated centers.

INTRODUCTION

Cystic dystrophy in heterotopic pancreas is a rare condition, described for the first time by Potet and Duclert in 1970 [1], it is characterized by the development of true cysts from heterotopic pancreatic tissue localized in the gastro-enteric wall. Its incidence ranges from 0.5 to 14% on necroscopic examination [2, 3] and the most common locations are the duodenum, stomach and jejunum [4, 5].

The disease can often be associated with signs of upper digestive obstruction, sometimes by jaundice or by signs of acute pancreatitis. Nevertheless, the symptoms are also compatible with chronic alcoholic pancreatitis with which it is associated in the majority of patients [6]. The disease has also been observed in young patients with a healthy pancreas [7].

Computed tomography (CT) and magnetic resonance imaging (MRI) are very useful in demonstrating the presence of cysts in a thickened duodenal wall but mainly endoscopic ultrasonography (EUS) is the

principal means of reaching a correct diagnosis [6, 8].

The choice of different therapeutic options is still under debate: a pancreaticoduodenectomy is usually proposed for symptomatic patients [1, 6]; however, some authors have proposed a medical approach using octreotide [9, 10] or endoscopic treatment [11, 12] for selected patients.

The purpose of this paper is to describe the clinical and therapeutic features of a rare case of cystic dystrophy of the duodenal wall associated with chronic pancreatitis and pancreatic cystadenoma and to evaluate the

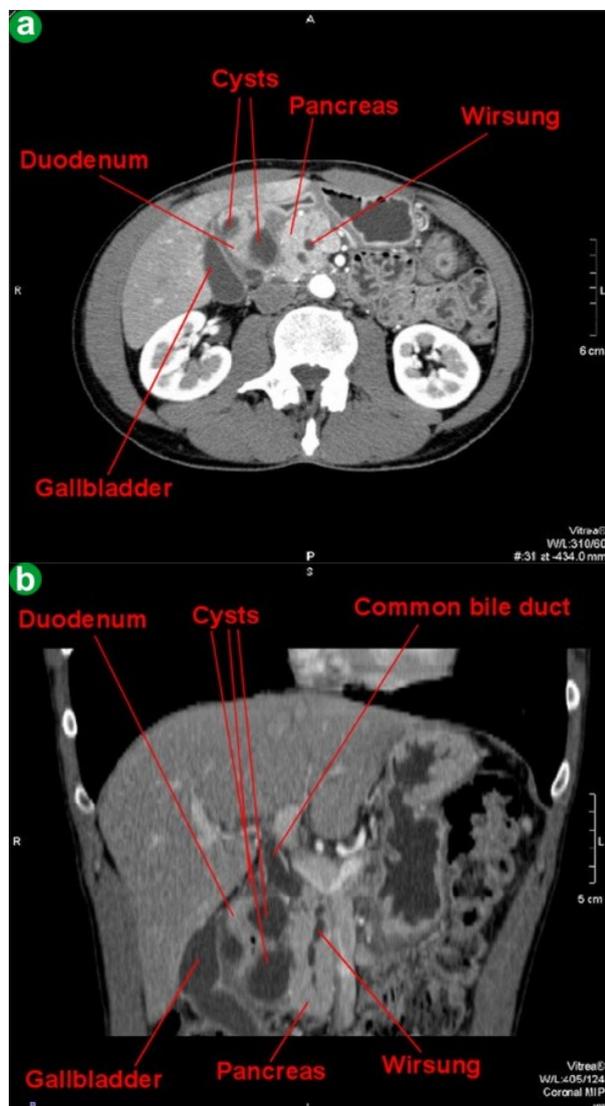


Figure 1. Computed tomography scans (a. axial; b. coronal multiplanar) reveal an inhomogeneous thickening of the duodenal wall by multiple cystic lesions compressing the duodenal lumen, common bile duct and Wirsung duct.

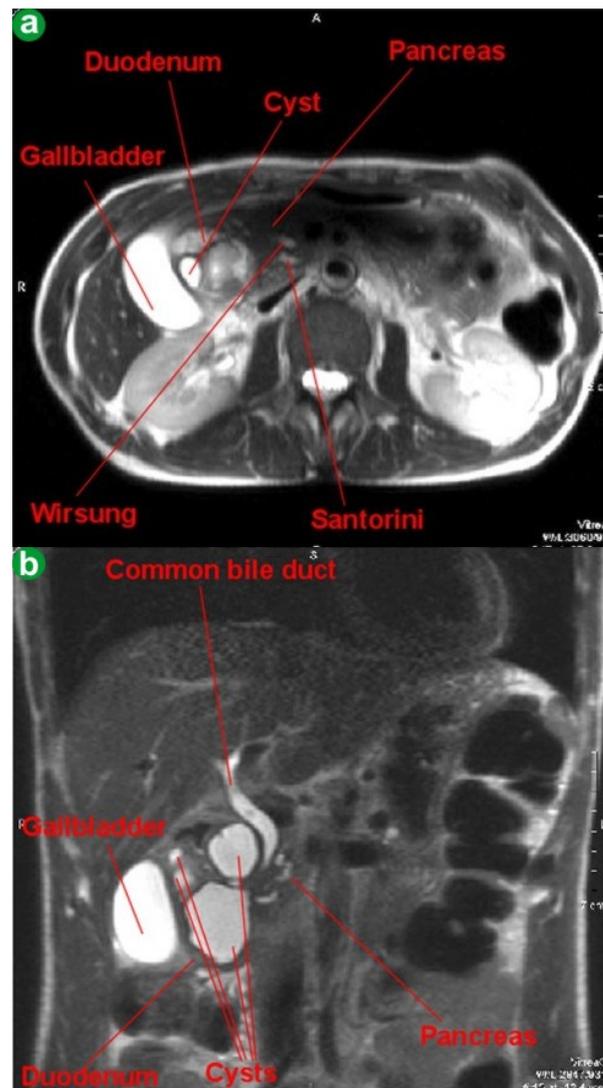


Figure 2. Magnetic resonance scans (a. axial; b. coronal) reveal the thickened duodenal wall with multiple cystic lesions compriming the duodenal lumen, common bile duct and the Wirsung duct.

role of pancreaticoduodenectomy as primary therapeutic option on the basis of the literature.

CASE REPORT

A 44-year-old Caucasian man was admitted to the Gastroenterology Unit of our university hospital with recurrent epigastric pain and weight loss (12 kg in 5 months). He said that, during the previous two months, the pain had become continuous, increasing after meals and being relieved only after vomiting.

The patient was a smoker (40 cigarettes/day) and an alcoholic (250 g/day).

Laboratory evaluation revealed leukocytosis (WBC: 14,000 μL^{-1} ; reference range: 4,800-

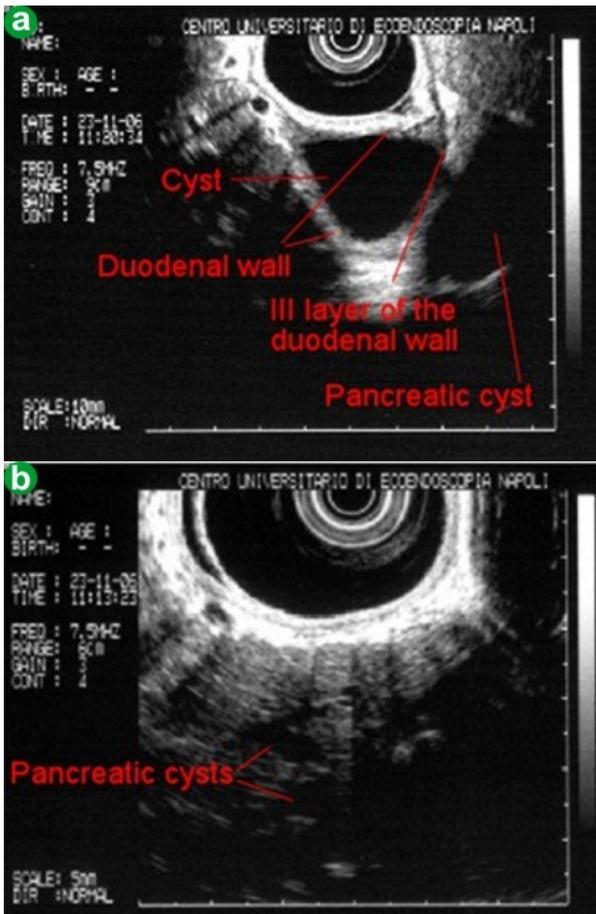


Figure 3. Endoscopic ultrasonography reveals: **a.** thickening of the duodenal wall and the presence, within the wall of first and second duodenum, of a cyst arising from the third layer of the duodenal wall; **b.** enlargement of pancreatic head, with evidence of a small thin-walled cystic lesion.

10,800 μL^{-1}), a decrease in pseudo-cholinesterase (4,153 U/L; reference range: 5,400-13,200), and an increase in amylase (409 U/L; reference range: 28-100 U/L), lipase (785 U/L; reference range: 13-60 U/L) and CA 19-9 (82 U/mL; reference range: 0-37 U/mL).

An upper endoscopy showed a gastric dilation and a stenosis of the second part of the duodenum, by extrinsic compression.

An abdominal ultrasonography was performed revealing a normal gallbladder, a slightly ectatic common bile duct without stones and a complex multi-cystic lesion (9.5x5 cm) between the duodenum and the head of the pancreas whose origin was impossible to define.

A multislice iodinate contrast-enhanced CT scan (Figure 1) and an MRI (Figure 2)

revealed an inhomogeneous thickening of the duodenal wall by multiple, coarse, septate cysts compressing the common bile duct, the Wirsung duct and the duodenal lumen.

In order to explore the pancreatic and the duodenal areas better, we performed radial endoscopic ultrasonography (EUS) (Figure 3) which showed:

- thickening of the duodenal wall;
- the presence of multiple, intramural septate cysts within the wall of the first and the second duodenum which seemed to arise from the third layer of the duodenal wall;
- enlargement of the pancreatic head, with evidence of a small thin-walled cystic lesion;
- slight dilation and calcification of the Wirsung duct in the head as well as in the body and the tail of the pancreas.

On the basis of all these findings, we diagnosed cystic dystrophy of the duodenal wall associated with chronic pancreatitis and a pancreatic cystic neoplasm.

Because of the cystic features, the case was not eligible for endoscopic treatment; moreover, the presence of an associated pancreatic cystic neoplasm indicated surgery as the primary choice of therapy. Therefore, the patient underwent a duodenopancreatectomy with a Whipple reconstruction.

Macroscopic examination of the surgical specimen (Figure 4) showed the presence of multiple cysts within the thickened duodenal wall and a cystic pancreatic mass.

Histologic examination confirmed the diagnosis of cystic dystrophy of the duodenal

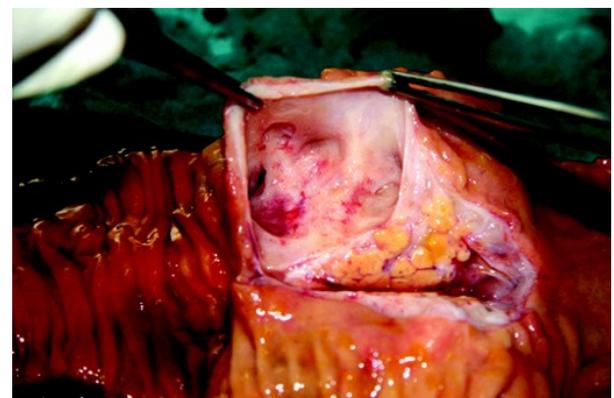


Figure 4. Duodenopancreatectomy specimen showing cystic lesions of the duodenal wall and a cystic mass of the pancreatic head.

wall, pancreatic mucinous cystadenoma and chronic pancreatitis (Figure 5). There were no postoperative complications; the course was uneventful and the patient was discharged after 14 days.

Complete alcohol withdrawal was achieved and today, after 14 months of follow-up, the patient has not had a relapse nor have there been any recurrences.

DISCUSSION

Cystic dystrophy is an almost exclusive complication of heterotopic pancreas located in the peri-papillary duodenum [13]. Ectopic exocrine lobules may have excretion ducts which are too small to function; the accumulation of pancreatic secretions can lead to recurrent episodes of acute obstructive pancreatitis and, then, to the formation of retention cysts [14].

Cystic dystrophy, generally observed in Caucasian males in their fifth decade, can be associated with a healthy pancreas but, very often (75%), it is associated with alcoholic chronic pancreatitis [13]. For some authors, cystic dystrophy is an extension of pre-existing chronic pancreatitis in an ectopic localization [15]; for others, the chronic pancreatitis evolves independently in the ectopic gland, leading to upstream compression of the pancreatic duct [1]. An alcoholic etiology of chronic pancreatitis is considered when alcohol intake is more than 60 g/day during the preceding five year period [16].

The patients are often misdiagnosed or diagnosed late [13] because of non-specific clinical manifestation and difficult nosologic analysis of the cystic wall lesions. In fact, some reports describe patients with cystic lesions of the duodenal wall considered to be duplications or heterogeneous cysts in spite of the absence of intestinal and gastric epithelium [17] and the presence of ectopic pancreatic tissue in some cases [18, 19]. In many of these cases, a careful evaluation can demonstrate the presence of cystic dystrophy in heterotopic pancreas [14].

Symptoms can be epigastric pain, vomiting and nausea from intolerance of food intake

(by duodenal compression) or jaundice (by biliary compression). Weight loss can be related to pain, leading to auto-limitation of food intake and vomiting due to duodenal stenosis.

Upper digestive endoscopy can show duodenal or gastric (antral or pyloric) stenosis by extrinsic compression with intact mucosa. In some cases, endoscopic lesions are described as enlarged folds with edema and congestion, usually without ulcerations. In several patients, sessile polyps are described [2,14].

Barium ingestion shows stenosis of the duodenum or, in a few cases, of the gastric antrum [14].

Abdominal ultrasonography and CT are less sensitive and specific than EUS but are able to visualize duodenal wall thickening and, sometimes, the presence of cyst-like lesions; moreover, ultrasonography can also be useful in the evaluation of biliary and pancreatic ducts [13].

EUS is the most useful imaging examination [10, 13, 20, 21], allowing the separation of any layer from the duodenal mucosa up to the duodenal serosa and, deeper, up to pancreatic tissue. In fact, it can diagnose the three specific signs of the duodenal wall (thickening, the presence of cysts predominantly in the fourth hypoechoic layer of the duodenal wall and a network of channels around the cysts) and it allows

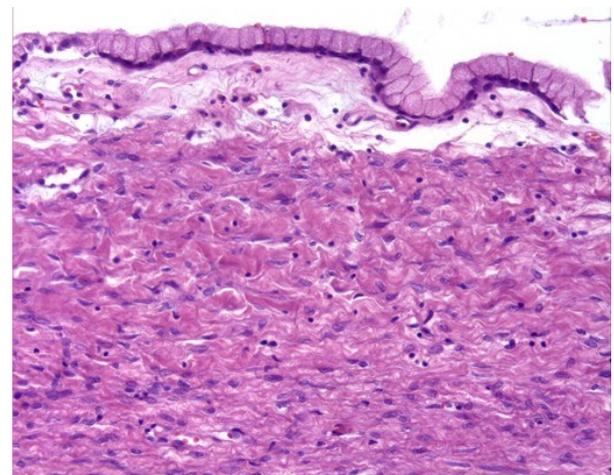


Figure 5. Cystic wall, with a cylindrical mucinous epithelium, showing ovarian-like stroma (hematoxylin-eosin stain; 40x).

reaching a differential diagnosis with duodenal duplication, necrotic duodenal tumors, pancreatic pseudocysts or cystic tumors [13]. EUS with miniprbes may be useful in patients with duodenal stenosis in which passage beyond the genu superior is not possible [6, 20, 22].

MRI with cholangiopancreatography must still be evaluated, particularly in comparison to EUS. However, it can demonstrate the presence of cysts within the duodenal wall (high intensity signal on T2 sequences) and interposition between the duodenum and the head of the pancreas (low intensity signal on all sequences) [23, 24].

Regarding treatment of cystic dystrophy of the duodenal wall, the role of different therapeutic options are still under debate. The relief of symptoms, particularly pain relapse, can be achieved by fasting, alcohol abstention and gastric aspiration.

Pharmacologic treatment with octreotide (200-400 µg *bid* by subcutaneous injection) has been proposed but is the subject of debate because of its variable effect on pain, reduction of cyst size and weight improvement [10, 13, 22]. Moreover, the delayed efficacy, the short time of action and the unknown long-term effects render this of therapy questionable [25]. A study [9] reports an improvement in 100% of cases treated with octreotide (9 patients) but with a follow-up of just 90 days. Jouannaud *et al.* [6] reports 7 patients treated with octreotide: one alcohol abstinent patient remained symptom-free for 87 months, one non-abstinent patient developed recurrent symptoms and 5 underwent surgery after the recurrence of symptoms 0 to 25 months following interruption of the octreotide regimen.

Endoscopic treatment by cystogastrostomy has been proposed [26] after the failure of medical therapy. The endoscopic fenestration of cysts has been proposed for selected cases: few, voluminous and superficial cysts [11, 12]. Nevertheless, in cystic dystrophy, the cysts are numerous, small and develop within the thickening of the duodenal wall; for these reasons, endoscopic treatment provides temporary and often incomplete results [13],

with a high percentage of recurrence [6, 11, 12].

The surgical approach has the best results. Formerly, it was widely used for the diagnostic and therapeutic management of cystic dystrophy of the duodenal wall but nowadays, due to the improvement of preoperative imaging, it is being used less frequently as a first line option. Some authors reserve this approach for resistant or relapsing cases after medical or endoscopic treatment; others propose it as a primary choice of therapy.

Regarding the outcome of the different surgical options, a pancreaticoduodenectomy remains the most effective since the affected tissue is removed. The other procedures are designed to relieve the symptoms by draining the cysts or fashioning a biliary or digestive by-pass but cannot prevent recurrent flare-ups [6].

A gastro-entero anastomosis without resection is suggested in the case of obstructive lesions with vomiting without painful episodes [14, 27]. The advantages of this strategy are low morbidity and sparing of the pancreatic tissue; nevertheless, the lesions are left in place and can become painful later on, with new episodes of acute pancreatitis. For this reason, some patients undergo a secondary pancreaticoduodenectomy [13]. A primary pancreaticoduodenectomy removes the lesions and any risk of recurrence, and is indicated when there is diagnostic doubt of an associated pancreatic neoplasm. However, this intervention is characterized by a high mortality and morbidity rate, and some hesitate to propose it for a benign, though serious, condition. For this reason, some authors, only in the case of suprapapillary localization of the cystic lesions, proposed a segmental resection of the second part of the duodenum without a pancreatectomy [28].

Pancreaticoduodenectomy specimens show duodenal lumen stenosis because of appreciable thickening of the duodenal wall. It was predominant on the pancreatic side of the duodenum, above or below the papilla of Vater, or both. The mucosa overlying the abnormal areas is often intact but irregular

with giant folds or sessile polypoid lesions, or both, similar to a pseudotumor [3, 29]. The main and constant feature reported by several authors is the presence of multiple cysts of variable size measuring up to 3 cm in diameter. These cysts are located in the thickened duodenal wall and contain either clear fluid or thick yellow material, with stones in some patients [14]. In a few cases, the macroscopic appearance of the gastrectomy specimens is very similar to that observed on pancreaticoduodenectomy specimens. The lesions are present on the greater curvature, in the antrum and the mucosa can appear pseudovillous and hemorrhagic; cysts are present in the antropyloric wall and appear related to whitish nodules on the serosa [14].

The smaller cysts are often detectable only on microscopy and correspond to dilated ducts with a clear cell columnar epithelium. The larger the cysts, the more flattened the lining epithelium. In the larger cysts, the epithelium can be partially or totally eroded, and there can be surrounding inflammatory granulation tissue [19]. The lumina of the larger cysts often contains degenerated polymorphonuclear cells; in some cases, protein plugs and stones can be present [14].

The cystic lesions are located in the submucosa and muscularis propria. Hyperplastic Brunner's glands are frequently observed. Very often, fibrosis and chronic inflammatory changes are present, with features similar to those described in chronic pancreatitis of the normal gland [30, 31].

The relationship between cystic dystrophy in heterotopic pancreas and chronic pancreatitis, very often associated with it, is still under debate but it is possible that cystic dystrophy might provoke a stenosis of the pancreatic duct and might be responsible for chronic pancreatitis [14, 32]. In fact, when pancreaticoduodenectomy specimens showing chronic pancreatitis have been reprocessed and investigated for dystrophic heterotopic pancreas of the duodenal wall, the lesion was found in 27% of patients in the study of Martin [33] and in 34% of patients in the study of Vankemmel *et al.* [16].

Cystic dystrophy of the duodenal wall on heterotopic pancreas is a rare disease with variables and non-specific clinical manifestations. Nowadays, EUS and MRI are the instrumental examinations of choice for a correct and rapid diagnosis. Therapeutic management is still under debate but it is also very important to remember that relapses or recurrences are very frequent if alcohol withdrawal is not achieved.

Pharmacologic treatment with octreotide (200-400 µg *bid* by subcutaneous injection) has been proposed as a first therapeutic option but, because of its variable effects, delayed efficacy, its short period of action and short follow-up, this kind of therapy is questionable.

An endoscopic cystogastrostomy has been proposed after the failure of medical therapy in selected cases: few, voluminous and superficial cysts [11, 12]. Nevertheless, in cystic dystrophy, the cysts are numerous, small and deep.

CONCLUSION

Surgical resection provides the best longlasting results. When surgery is needed, a pancreaticoduodenectomy is preferred, reserving by-pass procedures for high risk patients.

Because of the non-specific clinical manifestation and the very difficult diagnosis and therapeutic management, these patients should be studied and treated in specialized and dedicated centers.

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