

Laparoscopic cyst fenestration in the treatment of polycystic liver disease



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INTRODUCTION: *The PLD, included in the group of malformative lesions of ductal plate, is characterized by progressive development of multiple parenchymal cysts. Different surgical treatments have been proposed for symptomatic patients with PLD: percutaneous aspiration, fenestration, hepatic resection and liver transplantation. The aim of this report is to outline the treatment of polycystic liver disease with laparoscopic fenestration.*

MATERIALS AND METHODS: *Of thirteen patients with PLD, in all cases associated with polycystic kidney disease, 7 patients underwent to laparoscopic treatment of cysts fenestration, and 6, asymptomatic and not amenable to surgical treatment, underwent to clinical follow-up. Of the 7 patients, 5 have symptoms related to "effect mass" ¹⁻²⁻³ of hepatic cysts while in the 2 asymptomatics the fenestration of the cysts was performed during the procedure of laparoscopic cholecystectomy for cholelithiasis.*

DISCUSSION: *The best indication for laparoscopic fenestration are those cases of PLD characterized by a relatively limited number of large cysts, preferably situated in the anterior segments of the liver and in the left lobe; in this patients, laparoscopic fenestration reduces significantly the volume of the liver and relieves symptoms. The laparoscopic fenestration of hepatic cyst, in carefully selected patients, is an effective technique in terms of morbidity, mortality, conversion rate and recurrence rates; while in patients with cyst diffuse in liver parenchyma is indicated the hepatic resection or liver transplantation. The optimal surgical approach is still evolving, the type of approach is related to extent and distribution of the cysts, and vascular anatomy of normal segment of the liver.*

KEY WORDS : Laparoscopic fenestration, Polycystic liver

Introduction

Polycystic liver disease (PLD), malformative pathology of "ductal plate", is characterized by the progressive development of multiple intraparenchymal cysts.

The disease can occur as an isolated form (autosomal dominant trait) or in association with polycystic kidney

disease, as autosomal dominant (ADPKD) or recessive (ARPKD).¹

In the majority of patients (80%), PLD remains usually asymptomatic with no alterations of hepatic function, and it is often diagnosed incidentally during imaging examinations performed for other pathologies. When present, clinical signs and symptoms are related to the space occupying effect of the cysts on the liver or on the adjacent viscera.

Different approaches have been proposed for the treatment of symptomatic patients, including percutaneous (echo/CT) aspiration (PEI), surgical procedures of drainage, fenestration and, in severe cases, hepatic resection or liver transplantation ².

The aim of this report, is to outline the treatment of polycystic liver disease with laparoscopic fenestration.

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Materials and Methods

Thirteen patients (10 women and 3 men; age range 39-71 years, mean age 55 years) with PLD associated with polycystic kidney disease were admitted in the Department of General Surgery of the University of Messina during the period November 2006- June 2011. Seven patients (53.84%), 5 women and 2 men, with a mean age of 59.4 years underwent to laparoscopic treatment of cysts fenestration, the remaining 6 patients, after careful examination, asymptomatic for PLD and not amenable to surgical treatment are in clinical follow-up. Of the 7 patients treated, 5 (71.43%) had symptoms related to "effect mass" of the hepatic cysts while in two (28.57%) asymptomatic the fenestration of the cysts was performed during the procedure of laparoscopic cholecystectomy for symptomatic cholelithiasis. Physical examination of symptomatic patients revealed hepatomegaly (23 cm) all these patients had normal renal and hepatic function except one case in whom cholestasis enzyme levels were abnormal (109 U/L gamma-glutamyl transferase and 321 U/L alkaline phosphatase) due to compression of bile duct confluence by a cyst (size 9 cm). Hepatomegaly was responsible for pain in the right hypochondrium, severe in three patients and moderate in two (Wong-Baker FACES Pain Rating Scale). All patients complained of fatigue and dyspepsia, including abdominal fullness dyspnea in supine position in two cases and abdominal distension in another two. The diagnostic evidence of non-parasitic cysts was carefully reviewed in all cases; sonographic and tomographic (Fig. 1) findings were suggestive showing cysts of various sizes without septae, calcifications or papillary intracystic lesions. In all cases serological tests for hydatid disease were negative. The inferior margin of the liver descends in five cases at level of umbilicus and in two cases below it.

Hence the optic 30° forward oblique telescope was inserted 2-8 cm below the umbilicus on the xiphoid - pubic line.



Fig 1: Image CT shows Polycystic liver disease (PLD).



Fig 2: The image documents a stage laparoscopic fenestration of the massive hepatic cyst.



Fig 3: Laparoscopic maneuvers in order to reduce the exposure of the secretory epithelium and therefore the effluvium of secretions.

We used two 10 mm trocars for better visualization of liver during the procedure and two 5 mm trocars; the position of additional trocars, usually laterally to the outer edges of rectus muscle in the lower quadrants of abdomen, is related to the size of liver and location of cysts.

After identification of the cysts and confirmation of its nature through puncture and aspiration of the serous fluid, the wall of the cysts was dissected and its content completely aspirated (Fig. 2). Fenestration of cysts was performed using the Ultracision Harmonic Scalpel in six patients, while in one patient we used the PKS Cutting Forceps.

We proceeded to resection of the wall of the cyst, sent for histological examination, up to about 3 mm from liver parenchyma.

Following the complete fenestration of the cysts was performed, a careful haemostasis of liver and a washing of the peritoneal cavity; the procedure was completed in five cases with an omentoplasty after apposition of human fibrin glue, while in two cases the clotting of bottom of cysts was performed with argon - laser spray-



Fig 4: Follow-up CT at 12 months post laparoscopic fenestration .

ing. These maneuvers were done in order to reduce the exposure of the secretory epithelium and therefore the effluvium of secretions (Fig. 3). For such reasons we consistently placed a tubular drainage for 48 h. There was no need to laparotomic conversion under any circumstances. The mean operative time was 98 min. with a range of 75-130 min.

The average hospital stay was 6 days, with a range from 3 to 13 days; we did not observed mortality and post-operative morbidity is limited to the development of ascites in four patients (57.1%) for about two weeks. The long-term follow-up showed the recurrence of clinical symptoms in two patients (28.6 %) at 12 and 19 months after the procedure

The follow-up, variable from 2 to 7 years (ultrasound every 6 months and CT every year) (Fig. 4), showed relapse of liver cysts in two patients (28.6%), asymptomatic and not appropriate to a new surgical approach.

Discussion

In the last decade, an isolated form of polycystic liver disease, which occurs with an incidence of 0.01% has been recognised⁴. The disease has an autosomal-dominant inheritance pattern and develops without the association with polycystic kidney. At the molecular level, the disease is characterized by mutation of PRKCSH and SEC63 genes, which encode respectively⁵ for the hepatocystin and protein SEC63, PLD is most frequently associated with polycystic kidney disease in the trait autosomal dominant (ADPKD) or recessive (ARPKD), as described for the first time by Bristowe in 1856; polycystic liver disease is the most common extra-renal manifestation. The liver cysts develop with greater frequency in patients with advanced renal cystic disease and impaired renal function; are present in 65-70% of patients on dialysis and in these patients the PLD represents an important factor of morbidity and mortality⁶. The preva-

lence of macroscopic liver cyst associated with adult polycystic kidney disease increases with the age of the patients, from 0% in patients younger than 20 years to about 80% among those over 60 years. In the form associated with ADPKD the hepatic parenchymal cysts are linked to mutations of the PKD1 or PKD2 gene, which encodes respectively for the polycystin 1 and 2, basic proteins for structure and function of the primary cilia localized in the apex of cholangiocytes⁷ that play a key role in the pathogenesis of polycystic liver⁸.

Experimental data suggest that other mechanisms are involved in the genesis of cystic formations such increase of cell proliferation, apoptosis and fluid secretion, abnormal interaction between cells and matrix and alterations of cellular polarity⁹.

Recently, the composition of fluid secreted by the cystic epithelial cells has been also analyzed. The results indicate the presence of cytokines and growth factors, which are likely involved in mediating the transmission of signals autocrine / paracrine and thus to promote cell growth¹⁰.

In addition to these molecular mechanisms, the cysts that characterize the disease are likely caused by micro-hamartoma or complex of Von Meyenburg, which originate from evolutive alterations of intralobular biliary ducts⁴. Cysts located in the peripheral regions of the liver have a common origin with micro-hamartomas, while morphologic studies have demonstrated that the cysts located centrally derive instead from the expansion of peri-biliary glands⁹.

In 80% of cases, polycystic liver disease is asymptomatic, often diagnosed incidentally, with a progressive natural course. When present, symptoms are caused by the so-called "mass effect" of the cysts or by the development of complications such as rupture, bleeding or infection¹¹. The clinical manifestations can result from a single or a limited number of large dominant cysts or by the involvement of a large portion of liver parenchyma or by cysts that compress the intrahepatic structures¹³. Symptoms include dyspnea, early satiety, gastro-oesophageal reflux, nausea, abdominal pain, ascites caused by obstructed outflow of the hepatic venous system, edema of the lower limbs caused by compression of the inferior vena cava, portal hypertension caused by compression of the portal vein and jaundice by obstruction of the bile ducts¹².

Bacterial infections of the cysts are rare, but when present are characterized by fever, leukocytosis and pain in the right abdominal quadrant. This is a severe complication that must be promptly treated to prevent the rapid development of bacteremia, sepsis and death¹. Abscal reported a morbidity rate of 3% and a mortality of 2% in patients with infection of liver cysts. Notably, infections of the cysts may be facilitated by immunosuppressive drugs administered to renal transplant recipient. PLD can occur in association with other diseases; the combination of ADPLD with intracranial aneurysm is

about 10%¹⁴. The presence of intracranial aneurysm must be investigated in any patient that is considered for abdominal surgery. Other diseases associated with PLD are insufficiency or prolapse of mitral valve¹⁴.

Quia reported the presence of mitral valve prolapse or insufficiency respectively in 26% and 30% of patients with ADPLD. These patients may also present asymptomatic cysts of the pancreas, spleen, ovaries and lungs¹⁵.

For the diagnosis of polycystic liver is made using common techniques of imaging, such as ultrasound, MR and CT.

The ultrasound is able to establish site, size and number of cysts, and also provides significant information for the differential diagnosis, which includes hydatid and / or neoplastic cysts; is also used as a real-time guide for conservative therapeutic procedures of liver cysts¹⁶. Computerized tomography is considered the most reliable in the simple or complicated forms of polycystic liver¹⁷ and also in the follow-up after surgery¹⁸. The contrast-enhanced CT and MR are important for the valuation of vascular anatomy of liver in order to identify pre-operatively anatomic arterial variants¹⁹. The "mass effect" that polycystic liver can elicit, is well evidenced by CT and MRI, in particular with the multiplanar reconstructions or coronal sections, while the cholangio-MR can be diriment for the study of the biliary tree. The treatment is indicated only in symptomatic patients²⁰; the choice of procedure is related to size, site and number of cyst and to the total volume of residual liver parenchyma²¹. A reliable guide for the planning the treatment of patients with polycystic liver disease is the classification of Gigot. Recently Schneedorfer has proposed a new classification where for each class is suggested a specific therapeutic option; the parameters used are the entity of the symptoms, the distribution of the cysts and vascular anatomy of the normal segments of liver³².

For symptomatic patients there are various therapeutic conservative or surgical strategies related to the severity of the clinical picture.

Among conservative treatments, PEI (percutaneous echo or CT) is the most effective procedure indicated for the management of dominant cysts, with a diameter greater than 6 cm and for the treatment of cyst relapse²³.

Among surgical techniques the laparotomic fenestration was for the first time described by Lin et al. in 1968 and in 1991 was introduced the laparoscopic approach^{24,27}.

The advantages of the laparoscopic treatment are represented by a decrease of morbidity and mortality, by a reduction of operative time (below 60 minutes) and an hospital stay of approximately 72 hours²⁵. The open procedure results in the formation of adhesions that limit the possibility of a re-operation or of a future liver transplant²⁶.

The objective of the fenestration of the cysts is that to reduce the volume of the liver while maintaining an adequate amount of remnant functioning liver, to improve

the quality of life of patients and to reduce the recurrence²⁷.

The asymptomatic cysts, centrally localized, are also considered for fenestration, even if they are less than 5 cm in size, or in case of hilar compression and all those greater than 10 cm for the high risk of complications^{28,29}. According to Konstadoulakis we considered that laparoscopic fenestration should be limited to the treatment of cysts located superficially in anterior segments of the liver avoiding those in the segments I-VII-VIII (30); patients with cysts in the posterior segments are not candidates for the procedure of fenestration (28,31,32). Patients with multiple cysts of 5 cm or more have a higher relapse rate compared to patients with smaller cysts and occupying less parenchyma (27% vs 13%)³⁵.

The fenestration procedure must be performed for each cyst; this step can be tedious and lengthen the time of surgery, but it is important that all cysts identified by laparoscopy are fenestrated; the success of the operation depends just from the careful treatment of each cyst^{34,35}. In case of deep cysts, which appear blue at vision, it is necessary to perform an intra-operative ultrasound color Doppler to establish relations with the vascular elements of the liver before proceeding to the fenestration. In laparoscopic and open fenestration was not recorded mortality and the more frequent postoperative complication is ascites. The fluid secreted by the cysts has properties similar to plasma, never contains bile because aren't in continuity with biliary tract, therefore isn't toxic and reabsorbed by the peritoneum. For the huge post-operative ascites, renal insufficiency is a contraindication to fenestration because the large surface exposed epithelium the risk of transient post-operative ascites is high.

We agree that the technique of laparoscopic fenestration has evolved over the last decade as an effective treatment in selected patients with PLD that can replace the open technique, because it is safe and effective, with a comparable recurrence rate, mortality and morbidity.

The most recent reports show a significant reduction in morbidity (10%) in patients treated with laparoscopic fenestration, likely due to technological innovations of the instruments and to the increased experience of surgeons. The conversion rate for laparotomy stands at 7%, most often due to bleeding that cannot be completely controlled.

Patients treated by laparotomy present a relatively high morbidity (27%), because this approach is reserved to the most challenging cases, cysts in the segment VII and VIII or fenestrations associated with surgery in the other lobe of liver; the mortality in recent studies is equal to 0%. We suggest that criteria to obtain a satisfactory result are indication for surgery, patient selection and definition of the extent of the disease²¹. In a follow-up of 75 months the recurrence rate was similar in both groups (13% vs 11%) .

Meta-analysis reveals important data on the incidence of relapses; the rates are around 5% for open surgery and

6% for the laparoscopic approach; most cysts don't require re-operation.

According to Yu Tan Men laparoscopic fenestration is the procedure of choice in the treatment of symptomatic hepatic cysts in the PLD; the technique has been successfully performed and 88% of patients did not relapse in the long term follow-up. Laparoscopic management has several advantages: less invasiveness than laparotomy, rapid recovery, tissue sampling for histopathology, inspection of the cyst wall exposure, ablation by sclerosis or omentoplasty of the residual cyst lining.

To avoid complications and recurrences must be careful to make a complete resection of the dome of the cyst and accurate hemostasis of resection margins of liver, the use of ultracision or bipolar forceps allow to perform this technique with considerable safety.

In agreement with Armitage and Blumgart, in patients with PCLD type II or III according to classification of Gigot the best treatment option is likely partial resection of the liver associated with the fenestration of the cysts¹¹.

We believe that technique for hepatic resection in patients with PLD presents various peculiar aspects. The liver is not only large but rigid so mobility is decreased and access to vascular supply more difficult; exposure and mobilization are facilitated by fenestration of selected cysts. Essential for division of the liver is in particular the fenestration of cysts along the transection plane; of those that determine displacement of hepatic vessels and bile ducts for facilitate hepatic venous exposure and optimize post-operative patency³².

In large polycystic liver with cysts scattered throughout the liver parenchyma the ability to perform a complete resection appear difficult, because of the currently reported morbidity (37-67%) and mortality rates (3-11%).

We believe that in polycystic liver disease the laparoscopic fenestration of hepatic cysts in carefully selected patients is a minimally invasive technique effective in terms of morbidity, mortality and recurrence rates while in cases with cysts diffuse to the liver parenchyma is indicated the hepatic resection or, in severe cases, liver transplantation. Current data on the natural history of PLD suggest that progression of cystic disease is slow and fenestration / resection offers the possibility of prolonged benefit.

In conclusion we retain that the optimal surgical approach for this disease is still evolving; the type of treatment is mainly related to the extent and distribution of the cysts, sectorial vascular patency, parenchymal preservation and hepatic reserve.

Riassunto

INTRODUZIONE: La malattia del fegato policistico (PLD) è una patologia ad etiologia genetica, che rientra nelle patologie malformative del "ductal plate"¹. Solo nell'20%

dei casi la PLD è sintomatica. I sintomi possono essere causati dall' "effetto massa" della cisti o dalle sue complicanze (rottura, emorragia o infezione).

Lo scopo di questo studio è inquadrare lo stato dell'arte per la fenestrazione laparoscopica nella policistosi epatica.

MATERIALI E METODI: Nel periodo 2007/12 presso l'U.O.C. di Chirurgia Generale dell'A.O.U. "G. Martino" sono stati osservati 13 soggetti con PLD; trattavasi di 7 pazienti (53,84%), 5 donne e 2 uomini, con età media 55 anni (range 39-71 anni) suscettibili di trattamento chirurgico. La fenestrazione laparoscopica è stata eseguita in 6 (85,71%) casi mediante Ultracision Harmonic Scalpel e nel caso restante (14,28%) mediante PKSTM Cutting Forceps (Gyrus). La degenza media è stata di tre giorni. Non si è registrata né morbidità né mortalità.

DISCUSSIONE E CONCLUSIONE: La tecnica di fenestrazione di cisti del fegato, descritta da Lin et al. nel 1968 ed eseguita con approccio laparoscopico nel 1991, risulta dai dati in letteratura come il "gold standard" soprattutto nei pazienti con cisti singole o fegato policistico con ADPKD.

L'obiettivo della fenestrazione delle cisti nel PLD è ridurre il volume del fegato, mantenendo un'adeguata quantità di fegato residuo funzionante. Nella PLD la fenestrazione laparoscopica in pazienti accuratamente selezionati rappresenta una tecnica miniminvasiva efficace in termini di morbidità, tassi di recidiva e mortalità.

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