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Portal Cavernoma Cholangiopathy: A Case Series With Literature Review

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Abstract
Background and study aims :
Our work aimed to describe the epidemiological, clinical, and para-clinical aspects as well as the therapeutic modalities of the portal cavernoma cholangiopathy (PCC).
Patients and methods:
This was a retrospective single-center descriptive study over 7 years (2016-2023). We included all patients presenting Portal cavernoma cholangiopathy .
Results :
19 had PCC so an incidence of 41,3%. The median age was 41.5 (20-76) with a clear female predominance and sex ratio of 3.13 . Patients were asymptomatic in 13 patients (68,4%). Upper endoscopy revealed signs of portal hypertension (PH) in 12 cases (63.15%). Abdominal ultrasound coupled with Doppler and Cholangio-pancreatic-MRI (CP-MRI) confirmed the diagnosis in all cases . The radiological abnormalities found were according to the Chandra classification : type I in 04 cases (21,05%) with lithiasis in two cases, Type II in 08 cases (42,1%) and type III in 07 cases (36,84%) . Therapeutically, endoscopic treatment was indicated in 6 patients, surgical treatment was indicated in 6 patients. During the monitoring, Two patients were lost to follow-up, and 3 patients died postoperatively. For the other patient, a simple monitoring was applied
Conclusions :
Our study shows an of PCC of incidence 41,3 % in the presence of portal cavernoma . Endoscopic treatment is a cornerstone in the management either as definitive or waiting treatment .
Keywords: *Portal cavernoma , Portal Cholangiopathy ,Cholangio-pancreatic-MRI , biliary Stent .*

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I. Background

Portal cavernoma cholangiopathy (PCC) is a group of abnormalities of the extra-hepatic bile ducts with or without abnormalities of the intra-hepatic bile ducts in patients with non-neoplastic and non-cirrhotic extra-hepatic portal venous thrombosis. Our work aimed to describe the epidemiological, clinical, and para-clinical aspects as well as the therapeutic modalities of this disease .

II. Patients And Method

This was a retrospective single-center descriptive study over 7 years (2016-2023).
Inclusion criteria : all patients over 18 years old , presenting a portal cavernoma complicated by Portal cavernoma cholangiopathy (symptomatic or not) with or without biological cholestasis in whom carried out cross-sectional imaging a Cholangio-pancreatic-MRI (CP-MRI) and CT scan .
Exclusion criteria : under 18 years old, with doubt of diagnosis of cavernoma , or thrombosis of tumor origin , patient known with chronic liver disease complicated by thrombosis or with a known cholangiopathy .
Clinical, biological, morphological, and evolutionary data were collected retrospectively and anonymously from data register .

Descriptive analysis
The qualitative variables are expressed as numbers and percentages. Quantitative variables are expressed as means and standard deviations (± SD) if the variable is normally distributed , or median and interquartile if the variable is not normally distributed . The analysis was carried out by the SPSS Software .

Ethical considerations

The patient data were anonymously collected from a uniform structured reporting used in our department and the study protocol was conducted following the Helsinki declaration. As database does not include patient identifiers, the Institutional Review Board (IRB) approval was not required. An informed consent was obtained from two participants for the publication of their imaging .

III. Result

Out of the 46 patients with chronic portal thrombosis, 19 had PCC so an incidence of 41,3%. The median age was 41.5 (20-76) with a clear female predominance and sex ratio of 3. Clinically, 13 patients were asymptomatic (68,4%), and 06 patients (31.6%) were symptomatic: hepatic colic in 2 cases (33%) and jaundice in 4 cases (67%). A history of upper digestive bleeding was present in 5 cases (26.31%) and an anemic syndrome in 4 cases (21.05%) . The clinical examination revealed splenomegaly in 13 cases (68.42%) , collateral venous circulation (CVC) at the level of both flanks and basithoracic in 8 cases (42,1%) , an overloaded liver in 5 cases (26.31%), and hepatomegaly in one case (5.2 %). The liver function tests (LFT) assessment showed cholestasis in 5 cases (26.31%) , cytolysis in 4 cases (21.05%) , hypersplenism in 9 cases (47,36 %), and hepatocellular insufficiency in one case (5.2 %). Upper endoscopy revealed signs of portal hypertension (PH) in 12 cases (63.15%). Abdominal ultrasound coupled with Doppler and CP-MRI confirmed the diagnosis in all cases. The radiological abnormalities found in our patients were, according to the Chandra classification: type I in 04 cases (21,05%) **(Figure 1)** with lithiasis in two cases, Type II in 08 cases (42,1%) and type III in 07 cases (36,84%) **(Figure 2).** The etiologies of the portal thrombosis are presented in **Table 1.** Endoscopic treatment was indicated in 6 patients, all of them had cholangitis: 04 patients had a plastic biliary stent, 2 were permanent with iterative exchanging and 3 were in preparation for a surgical procedure, and one patient benefited from an endoscopic sphincterotomy with stone extraction. Endoscopic retrograde cholangiopancreatogram (ERCP) , when carried out, showed type I of Chandra in 5 patients **(Figure 3)** and type III of Chandra in one patient , **Table 2** summarizes the finding results. Surgical treatment was indicated in 6 patients. One patient refused the intervention and 4 patients benefited from a vascular diversion: splenorenal (Warren intervention) in 2 cases and mesenteric-caval (Drapanas intervention) in 2 cases then bilio-digestive diversion in one case. 1 patient benefited from bilio-digestive diversion. **figure 4** summarizes the treatment in our series . The complications of these treatments were as follows : Post-ERCP cholangitis in 3 cases, a splenic infarction in 1 case and ascites with digestive hemorrhage in 1 case and an obstruction of the vascular stent requiring anticoagulant treatment with favorable outcome . During the monitoring, Two patients were lost to follow-up, and 3 patients died postoperatively. For the other patient, a simple monitoring was applied.

case	ERCP finding	Chandra classification
1	Multiple CBD strictures	Grade I
2	Narrowing of the middle part of CBD , dilation of the IHBD and the proximal CBD upstream	Grade I
3	Dilation of EHBD and IHBD , multiple CBD and cystic stones	Grade I
4	A located stenosis on the CBD.	Grade I
5	Dilation of the proximal CBD secondary to the fibrotic stenosis of the distal CBD with stones upstream	Grade I
6	Narrowing of the middle part of CBD with dilation of the proximal EHBD and IHBD upstream , stenosis of the left hepatic ducts	Grade III

Table 2: ERCP finding in our serie

ERCP: Endoscopic retrograde cholangiopancreatogram
EHBD: extrahepatic ducts
IHBD: intra hepatic ducts
CBD: common bile duct

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ETIOLOGIES	Number (%)
protein C and S deficiency	**2 (10.5)**
Iatrogenic cause	**2 (10.5)**
Polycythemia Vera (PV)	**1(5,2)**
Paroxysmal nocturnal hemoglobinuria (HPN)	**1(5,2)**
Antiphospholipid syndrome (APS)	**1(5,2)**
Hyperhomocysteinemia due to vitamin B12 deficiency in Biermer's disease	**1(5,2)**
Undetermined	**6 (31,57)**
Combined causes	**4 (21,05)**
- protein C and S deficiency + PV	**1(5,2)**
-Protein C and S deficiency + (APS) + Celiac disease	**1(5,2)**
- protein C and S deficiency + (APS)	**1(5,2)**
- celiac disease + (APS)	**1(5,2)**

Table 1: Etiologies of portal thrombosis

Antiphospholipid syndrome (APS)
paroxysmal nocturnal hemoglobinuria (PNH)
Polycythemia Vera (PV)

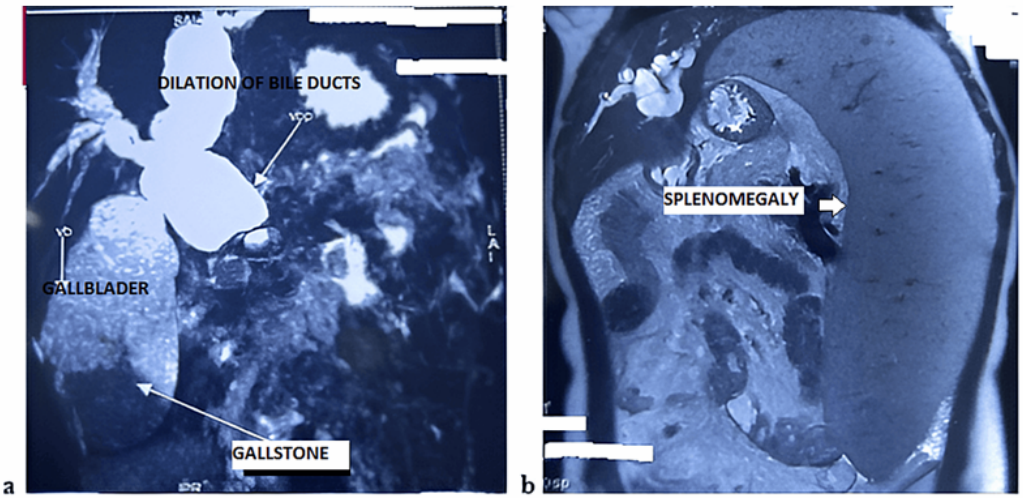

Figure 1: a) an enlarged gallbladder with stones, and monstrous dilation of the intra and extrahepatic proximal bile ducts (Grade III of liop, type I of Chandra). b) enormous splenomegaly with dilation of intra and extrahepatic ducts.

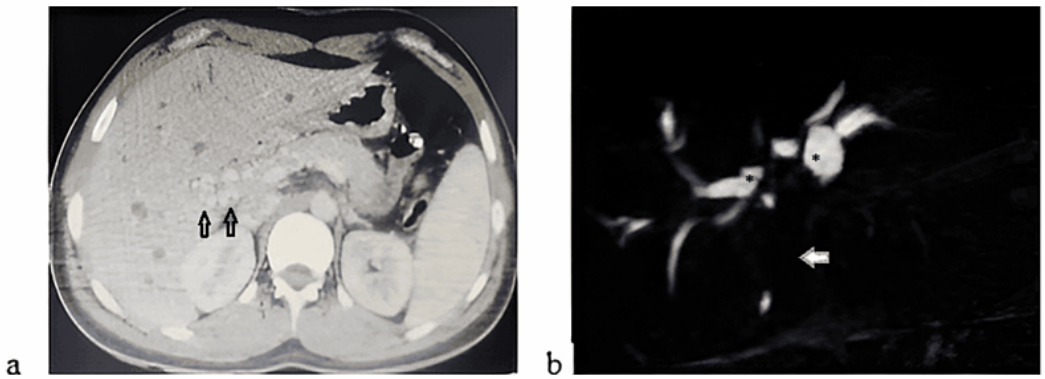

Figure 2: a : portal cavernoma (arrow)replacing the portal vein with dilation of the intrahepatic bile ducts . b: stenosis of the CBD (arrow) and the both heptic ducts (asterix) (type III of Chandra)
CBD : common bile duct

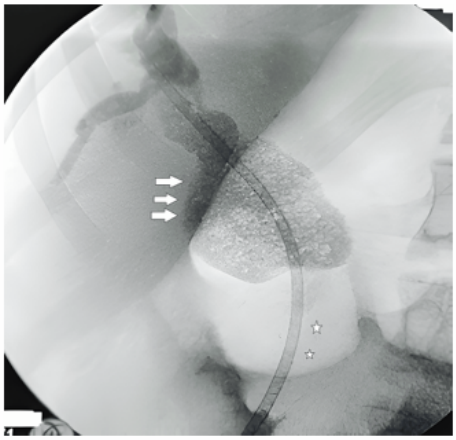

Figure 3: ERCP showing monstrous dilation of the proximal CBD(arrow) (Grade I of chadra) secondary to the stenosis of the fibrotic distal CBD with plastic stent (asterix)

CBD : common bile duct

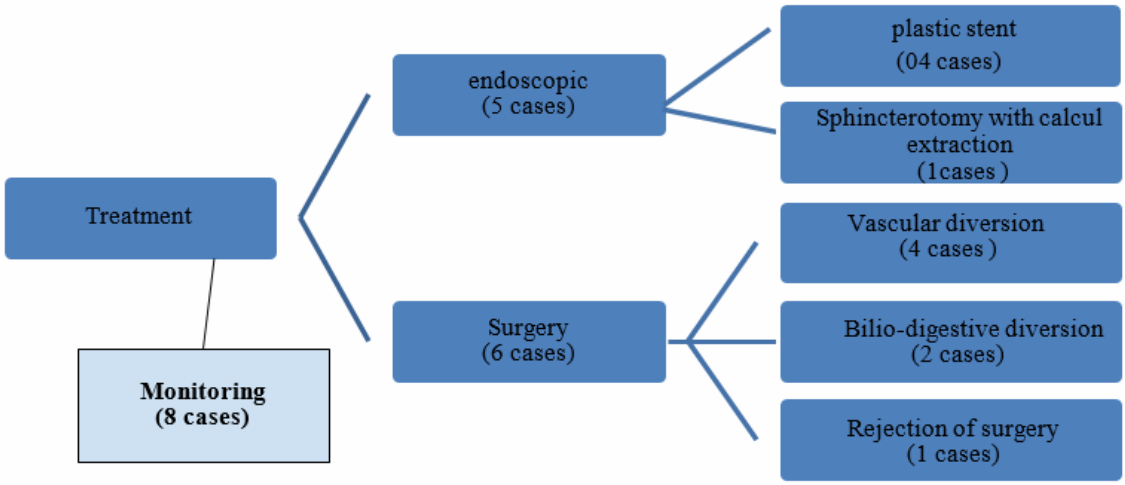

Figure 4: Summary of treatment in our serie

IV. Discussion

In 1944, Fraser and Brown were the first to discuss the relationship between symptomatic biliary obstruction and collateral veins in patients with extra-hepatic portal venous thrombosis [1]. The first description of cholangiographic changes in patients with portal thrombosis was made by Williams et al in 1982 [2]. The first prospective study of biliary abnormalities on endoscopic retrograde cholangiopancreatography in patients with deep vein thrombosis (DVT) was published by Dilawari and Chawla in 1992 [3]. Since then several case series of portal cavernoma cholangiopathy have been published in the literature [4]. The term portal biliopathy was then used until 2014 when a consensus (Radha K Dhiman et al., 2014) was established, proposing the name: Cavernoma portal cholangiopathy (CCP) with the following diagnostic criteria: 1) Presence of a portal cavernoma 2) Presence of cholangiographic abnormality and 3) Absence of differential diagnosis [1].

In response to DVT, porto-portal bypass tracts develop giving what is called portal cavernoma. Two venous system participate in the extrinsic compression of the bile ducts: para-choledochal veins (of Petren) on either side of the CBP and the epi-choledochal plexus (of Saint) on the surface of the biliary tree [5] . The pathogenesis of biliary abnormalities during DVT with portal cavernoma is multifactorial. These anomalies include a reversible component upon surgical decompression and a fixed component that persists even after surgical decompression. According to the ischemia theory, long-term DVT leads to sclerosis of the draining veins of the bile ducts, which is responsible for ductal ischemia which is the cause of stenosis, angulations and ductal ectasia which do not regress after portal decompression surgery [4]. The incidence of portal cavernoma cholangiopathy is difficult to determine on the one hand because of its rarity and on the other hand because of its symptomatic nature in only 5 to 50% of cases. [1, 6,7].

In the literature, portal cavernoma cholangiopathy is often diagnosed in adulthood with an average age varying between 29.5 and 49.5 years . As opposed of our series ,the male sex is the most affected in the majority of published cases. [4,6-9] In our series the median age was 47.4 years . The majority of patients with CCP are asymptomatic, the bile duct abnormality is then diagnosed accidentally. In our series 76% were asymptomatic and the rest of the patients had non-specific symptoms. The average time between the diagnosis of (DVT) and symptomatic portal cavernoma cholangiopathy is approximately 10 years [6,8]. The functional signs are dominated by cholestatic jaundice found in 76.16% of cases, followed by hepatic colic in 39.78% of cases, cholangitis in 33.94% of cases, and by pruritus in 23.57% of cases . Besides biliary manifestations, signs of portal hypertension such as bleeding due to rupture of gastroesophageal or hemorrhoidal varices and splenomegaly are often found [5]. In our series , they are present in approximately 70% of cases [5].The majority of patients with portal cavernoma cholangiopathy in the symptomatic phase (in the presence of stenosis and/or gallstones) have biological cholestasis, hepatic cytolysis is observed in advanced stages of the disease. In case of secondary biliary cirrhosis, a drop in PT (prothrombin time) and albumin can be observed [6], in our series, 26,3% had cholestasis, 21.05 % had cytolysis, hypersplenism in 47% and insufficiency hepatocellular in a 5.9%.

The purpose of imaging is twofold, it makes it possible to evaluate the degree and extent of portal vein thrombosis and to describe the different collateral venous circulations and to objectify the resulting biliary abnormalities . Abdominal ultrasound coupled with Doppler shows the absence of the portal vein which is replaced by periportal collaterals called portal cavernoma , it's look like multiple tortuous anechoic structures which can be interpreted as a solid tissue mass surrounding the CBD , but the Doppler allows easy identification of the vascular nature of this mass by showing the absence of flow in the thrombosed portal vein with hepatopetal flow in these collaterals [10]. Although abdominal Doppler ultrasound can show most of the radiological abnormalities of PCC, other imaging techniques (CT and MRI) are necessary to confirm the disease. Abdominal CT shows the dilation of the common bile duct (CBD) and IHBD (intrahepatic bile ducts) due to extrinsic compression by collateral veins and gallstones, but does not allow detailed identification of the extent and degree of biliary stricture. It plays an important role in the preoperative evaluation of vascular bypass surgery and also postoperatively to assess the patency of the vascular bypass. CT also makes it possible to show portal hepatopathy which is characterized by dysmorphia associating hypertrophy of the "central liver" segments IV and I, preferentially irrigated by the cavernoma and perfusion changes with hyper arterialization of the peripheral territories of the liver (left lobe and subcapsular region of the right liver) [10]. Currently CP-MRI is the imaging of choice, it is a complete examination including angio-MRI sequences which provide vascular mapping useful for diagnosis and for the choice of the most appropriate derivation technique and sequence. Cholangio-MRI allowing the mapping of biliary anomalies and thus characterizing the type of biliary impact by showing the direct relationship of biliary stenosis with the veins of the portal cavernoma . It is also useful in elucidating the cause of bile duct stenosis, allowing the distinction between neoplastic thickening which is characterized by early enhancement and fibrosis by ductal ischemia which is characterized by late enhancement [7,8,11]. Biliary abnormalities described are ripples, irregularity of the bile duct wall, biliary stricture, stenosis with or without prestenotic dilation, thickening of the wall of the gallbladder and bile ducts, angulation of CBD, gallstones [10]. The wavy appearance of the biliary wall is probably due to extrinsic compression of the CBD by the periportal collaterals, whereas the thickening of the wall of the bile ducts and gallbladder is due to ischemic fibrosis , focal stenosis (short (<2 cm) or long (>2 cm)) can be secondary to compression or ischemia. In a retrospective study of 16 patients with portal cavernoma, all patients had evidence of portal cavernoma cholangiopathy on MRI . Liop et al [9] proposed a classification of PCC into 3 grades based on the degree of dilation of the bile ducts on the MRI results of 67 patients with (DVT), of whom only 52 patients had PCC: Grade I: Presence of bile duct irregularities; Grade : Presence of bile duct strictures without dilation; Grade : Presence of stenosis with dilation of the bile ducts . Dilation was defined by a diameter greater than 7 mm for extrahepatic bile ducts (EHBD) and greater than 4 mm for intrahepatic bile ducts (IHBD) , they found that grade III was the most common: Grade III (51%), Grade II (18%), grade I (9%) . Shin et al classified the radiological abnormalities of PCC into 3 types: varicoid, fibrotic and mixed, according to the mechanism and

the presence or absence of biliary strictures . The varicoid type : characterized by an irregular and wavy biliary wall secondary to multiple extrinsic compressions by dilated collateral veins, this type simulates a cholangiocarcinoma giving rise to the sign of "pseudo-cholangiocarcinoma".The fibrotic type: characterized by localized stenosis of the bile ducts with upstream dilation of variable degree secondary to ductal ischemia ,CBD is often involved . The mixed type: characterized by the association of the two varicoid and fibrotic types.The importance of this classification lies in the therapeutic attitude because the varicoid type is reversible after portal decompression surgery unlike the fibrotic type [12]. The classification proposed by Chandra et al [13] to describe biliary abnormalities on ERCP can also be applied to classify biliary abnormalities on CP-MRI. Type I : involvement of EHBD ;Type II : involvement of IHBD only; Type III a : EHBD involvement and unilateral IHBD involvement.Type III b : EHBD involvement and bilateral IHBD involvement. The anomalies found in our patients were: type I in 17.6%, Type II in 47% and type III in 35.3%.Currently, ERCP is reserved only for therapeutic indications : Biliary drainage in cases of cholangitis, Extraction of stones from the CBD , dilation of stenosis of the CBD and placement of biliary prosthesis (stents) [11].Ultrasound endoscopy is indicated if there is doubt about the diagnosis, but in cases of cholangiopathy it allows a detailed assessment of the bile duct collaterals before ERCP [10,14]. Liver biopsy remains necessary to exclude an associated anomaly, particularly vascular disease. Generally, the pathological study of the liver biopsy is normal or almost normal, sometimes it shows dilation of the portal vein or segmental narrowing of the bile ducts with slight dilation of the IHBD. [15]
In the literature, the etiology of DVT is most often idiopathic (23 to 68%) of cases. In the rest of the cases, it is most often associated with coagulation disorders, a myeloproliferative syndrome, abdominal sepsis in 5 to 36% of cases, pancreatitis, and can also be associated with local causes (trauma or malformation portal vein, abdominal surgery, after splenectomy, liver abscess and umbilical vein catheterization in childhood) [16]. Table *1* summarizes the etiologies found in our series . Without treatment secondary biliary cirrhosis is the natural evolution of PCC. It is secondary to fibrous biliary strictures due to the ischemic mechanism [6] .
Therapeutically, the principle of treatment is to drain the bile ducts. First the medical treatment, with ursodeoxycholic acid, some authors have used it , in some of their patients with stenosis or after endoscopic treatment with insufficient clinico-biological improvement but its use remains limited in current practice and not indicated in first intention [1].
In the current era, endoscopy occupies a central place in the management of symptomatic PCC: first line of treatment either as a temporary treatment in preparation for a surgical procedure or as a definitive treatment if surgical treatment cannot be carried out . Endoscopic treatment includes the extraction of stones after endoscopic sphincterotomy (ES) associated or not with mechanical lithotripsy and the dilation of biliary strictures which are often associated with the placement of biliary endoprostheses [16]. Gallbladder lithiasis is observed in 8 to 69% of cases and CBD lithiasis in 7 to 77% of cases. The treatment of CBD lithiasis in patients with portal cavernoma cholangiopathy was first described in 1995 by Bhatia and Sarin who performed (ES) with extraction of multiple CBD stones in 3 patients [11]. Few data in the literature have been reported on large balloon dilation of sphincter of oddi and cholangioscopy with intraductal lithotripsy using laser or electrohydraulic probes in PCC .The treatment of biliary stenosis consists of biliary dilation followed by repeated placement of a biliary prosthesis. The first report of biliary prosthesis placement for common bile duct stenosis was published in 1993 [17]. The stents used are plastic (single or multiple) and covered metal stents. Their implementation reduces the risk of re-stenosis and recurrence of gallstones but exposes the patient to the risk of recurrent cholangitis and secondary biliary cirrhosis, which requires them to be changed regularly [16]. Oo et al reported their experience with self-expanding metal stent placement in 3 PCC patients who were not candidates for portal bypass surgery and had difficult access to tertiary care centers for repeated changes of plastic stents.The result was satisfactory, after 6 years of evolution, endoprosthesis occlusion was noted in only 1 patient [18] . In a more recent series of 12 patients with a median follow-up of 3 years. Completely covered metal prostheses is an effective method in biliary strictures as an initial treatment. Acute cholecystitis was a common complication, but the majority of patients responded to medical treatment [19]. ERCP is mainly complicated by hemobilia. It is attributed to an accident at the time of stent placement with peri-choledochal varices, sphincterotomy, balloon sweeping, balloon dilation. Bleeding can be perfectly managed by a covered metal prosthesis but often treatment with Terlipressin or sandostatin can be sufficient. [14]. In a retrospective review of 35 patients for patients eligible for surgery or who had failed surgery and an average follow-up of 46 months who benefited from endoscopic treatment. A total of 363 endoscopic procedures were performed with a median of 9 for each patient (3-29). hemobilia was the main complication (6.06%), secondary cirrhosis in 11.4% and death in 2 patients. [20]

For patients who fail endoscopic treatment, a second line of treatment, this time radiological or surgical, is indicated. The objective is to reduce portal hypertension to reduce the pressure in the collateral veins which contribute to the obstruction of the bile ducts in addition to reducing the pressure in esophageal varices or splenomegaly. [21]

Interventional radiology is promising in PCC, the reduction of portal hypertension within the cavernoma collaterals can be achieved through the establishment of a (TIPS) (Transjugular Intrahepatic Portosystemic Shunt). There are not yet clear recommendations on its use and few data are available in the literature. [10]
Two types of surgery have been reported for the treatment of symptomatic PCC: portal diversion surgery (spleno-renal or mesenteric-caval), which aims to reduce the pressure in the portal collaterals and therefore resolve the biliary obstruction. It also helps treat digestive bleeding and hypersplenism. [22] biliary drainage surgery is necessary to bypass biliary obstruction in symptomatic patients without resolution of biliary anomalies after portal diversion surgery [23] : there are 02 techniques: choledocho-duodenal anastomosis or hepatico-jejunal anastomosis [1]. Surgical treatment also includes cholecystectomy: in cases of gallbladder lithiasis or cholecystitis [22]. Liver transplantation is indicated only in cases of secondary biliary cirrhosis according to classic indications.
Apart from the specific treatment of portal cavernoma cholangiopathy and in the presence of an underlying thrombophilic condition, anticoagulant treatment may be indicated [15] , Likewise symptomatic treatment of portal hypertension. To date, there is no appropriate therapeutic consensus for the choice and priority of this or that treatment . The choice of treatment must be guided and adjusted according to the clinical and radiological characteristics of each patient .
Referring to the therapeutic management algorithm recently proposed by Frenceschet Irene in 2016 [23]: Asymptomatic patients require simple monitoring, no treatment is indicated. For symptomatic patients: Endoscopic treatment is indicated as first-line treatment in cases of CBD lithiasis or gallstone cholangitis or secondary to choledochal stenosis. Portal cavernoma cholangiopathy of the varicoid type (by extrinsic compression): portal diversion or radiological (TIPS) allows the resolution of biliary stenosis. Portal cavernoma cholangiopathy of the mixed type (by ischemia and compression), diversion portal alone will not resolve the problem, which in this case requires other endoscopic biliary interventions, and if biliary symptoms persist, biliary drainage surgery must be performed. Portal cavernoma cholangiopathy of the fibrotic type (by ischemic mechanism) , portal diversion does not resolve the biliary abnormalities. In this case, resolution of the PCC is difficult to achieve and multiple biliary treatments (endoscopic and surgical) are necessary. Cholecystectomy is recommended in cases of gallstone disease or cholecystitis. Liver transplantation is indicated in cases of secondary biliary cirrhosis . In total, each case must be discussed in a multidisciplinary meeting between hepatologists, endoscopists, radiologists and surgeons in order to define the best management .

Limitations of our study:
The retrospective study design could induce a bias of selection and a bias of gathering information. However, the data were collected prospectively and made these biases minimal.
Our study includes a small sample , so a large randomized study is needed to better know this pathology and therefore codifies its management .

V. Conclusions

PCC is a progressive pathology often diagnosed after a long period of progression of extra-hepatic portal venous thrombosis. Symptomatic forms are found in only 5 to 50% of cases, and cholestatic jaundice is the predominant sign. The diagnosis is confirmed by imaging: Abdominal Doppler ultrasound which is the first-line screening examination in patients with portal venous thrombosis and suspected of having PCC. Magnetic resonance imaging is the gold standard for diagnosis and makes it possible to identify biliary abnormalities and to confirm its compressive or ischemic mechanism on the other hand . Definitive treatment of portal cavernoma cholangiopathy often requires multiple, combined interventions on both the vascular and biliary systems. Treatment is indicated only in symptomatic patients, without forgetting the etiological treatment of portal thrombosis and the treatment of portal hypertension. If left untreated, PCC can be complicated by secondary biliary cirrhosis.