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Clinical case

Primary sclerosing cholangitis: about a series of 3 cases in Brazzaville (Congo)

La cholangite sclérosante primitive : à propos d'une série de 3 cas à Brazzaville (Congo)

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Résumé

Les troubles hépatobiliaires d'origine inflammatoire sont rarement décrits en Afrique subsaharienne. Le but de ce travail était d'étudier les caractéristiques épidémiologiques, cliniques, thérapeutiques et évolutives de la cholangite sclérosante primitive (CSP) au CHU de Brazzaville en 2023. Nous rapportons une série de trois cas de CSP diagnostiqués sur une période de 13 ans. L'ictère, présent chez tous les patients, était le principal motif de consultation. Elle était précédée ou suivie de signes de cholestase (prurit, urines foncées, selles décolorées ou bradycardie). Une IRM biliaire chez un patient a montré une sténose unilatérale gauche de la convergence biliaire et une dilatation en amont. Nous avons noté un cas de rectocolite hémorragique (RCH) et un cas de colite chronique non spécifique. Un patient a été traité par Salazopyrine. Tous les patients ont été traités par acide ursodésoxycholique (AUDC). L'évolution a été marquée par la disparition de l'ictère et des signes de cholestase. Le décès est survenu chez un patient présentant un cancer sténosant de l'angle colique droit, après 8 ans de progression de la CU. Un patient a été perdu de vue et chez le troisième patient, une réduction de la sténose et de la dilatation des voies biliaires intra-hépatiques a été notée après 12 mois de suivi. En conclusion, le diagnostic de CSP ne doit pas être ignoré dans notre contexte, où les ressources diagnostiques et thérapeutiques sont limitées. Une coloscopie avec biopsies échelonnées doit être réalisée systématiquement.

Mots-clés : cholangite sclérosante primitive, MICI, cancer du côlon, AUDC.

Abstract

Hepatobiliary disorders of inflammatory origin are rarely described in sub-Saharan Africa. The aim of this work was to study the epidemiological, clinical, therapeutic and evolutionary characteristics of primary sclerosing cholangitis (PSC) at Brazzaville University Hospital in 2023. We report a series of three cases of PSC diagnosed over a 13-year period. Jaundice, present in all patients, was the main reason for consultation. It was preceded or followed by signs of cholestasis (pruritus, dark urine, discolored stools or bradycardia). A biliary MRI in one patient

showed unilateral left-sided stenosis of the biliary convergence and upstream dilatation. We noted one case of haemorrhagic rectocolitis (UC) and one case of chronic non- specific colitis. One patient was treated with Salazopyrin. All patients were treated with ursodeoxycholic acid (AUDC). The course was marked by the disappearance of jaundice and signs of cholestasis. Death occurred in one patient who presented with stenosing cancer of the right colonic angle, after 8 years of UC progression. One patient was lost to follow-up, and in the third patient, a reduction in stenosis and dilatation of the intrahepatic bile ducts was noted after 12 months of follow-up. In conclusion, the diagnosis of PSC should not be ignored in our context, where diagnostic and therapeutic resources are limited. Colonoscopy with staged biopsies should be performed systematically.
Keywords: primary sclerosing cholangitis, IBD, colonic cancer, AUDC.

Introduction

Acute and chronic viral hepatitis are the most frequent hepatopathies in sub-Saharan Africa.
(1) where inflammatory liver diseases such as primary sclerosing cholangitis (PSC), autoimmune hepatitis (HAI) or primary biliary cholangitis (PBC) are rarely described (2,3). In North Africa, the frequency of inflammatory liver disease appears to be higher than in the rest of Africa (4). Primary sclerosing cholangitis (PSC) is a potentially serious liver disease that can be complicated by cirrhosis, hepatocellular carcinoma or cholangiocarcinoma, and is often associated with chronic inflammatory bowel disease (IBD), which can be the starting point for colonic cancers. (5). Unlike HAI and PBC, magnetic resonance imaging (MRI) of the bile ducts (bili-MRI) is the key diagnostic test for PSC. However, this examination is not performed in many African countries, which could partly explain the low prevalence of PSC in this region and is a limitation in their management. We report a series of cases of PSC diagnosed in the gastroenterology department of Brazzaville University Hospital. The aim was to study the epidemiological, diagnostic, therapeutic and evolutionary aspects of PSC in Congo Brazzaville in 2023.

Clinical cases

Case n°1

A patient born on June 17, 1977, married with three children, reported a history of rectal bleeding in 2010 associated with diffuse hemorrhagic rectocolitis (image 1), for which he was treated with Salazopyrin 3g/d for one month, then 1.5 g/day continuously. Treatment was initially effective, but the patient was lost to follow-up. He was hospitalized in 2016 for icterus of progressive evolution with periods of remission, associated with generalized pruritus of variable intensity. On clinical examination, he presented with medium-weight ascites with citrine fluid. On laboratory examination, total bilirubin was 83.3 mg/l (N<12), direct bilirubin
76.3 mg/l. Alkaline phosphatase (ALP), gamma glutamyl transpeptidase (GGT), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were elevated to 390 IU/l (N: 30- 130), 1309 IU/l (N < 50), 86.43 mg/l and 79.50 mg/l (N < 40) respectively. Prothrombin rate (PT) was 41%, factor V 45% (N: 70-100). HBsAg, anti-HBc IgG, anti-HBs and anti-HCV antibodies were negative. Anti-smooth muscle, anti-LKM and anti-mitochondrial autoantibodies were negative. Upper GI endoscopy was normal. Bili-MRI was not performed, as it was not available in Congo Brazzaville. The diagnosis was probably primary sclerosing cholangitis associated with ulcerative colitis (UC), complicated by cirrhosis. The patient was treated with ursodeoxycholic acid (AUDC) at a dose of 15 mg/Kg/d, a low-salt diet and Salazopyrin. Liver transplantation was indicated but not feasible in our country. Progression under this treatment was marked by regression of ascites and pruritus. The patient was again lost to follow-up before being rehospitalized in 2018 for colicky abdominal pain, intermittent rectorrhagia

complicated by anemia, and ascites of low abundance. Hemoglobin was 4.5 g/dl, GMV 84 fl, MCHT 20.9 pg. Colonoscopy showed congestive and erosive rectocolitis, colonic pseudopolyps extending into the transverse colon, and irregular tight stenosis of the right colonic angle. Colonic biopsies of the stenosis revealed a well-differentiated liberkühnian adenocarcinoma. Thoracoabdominal and pelvic CT scans revealed a tumour in the right colonic angle, obstructing the colonic lumen, measuring approximately 17.4 mm in long axis (image2), with no upstream colonic dilatation; there was no evidence of distant metastases. There was no evidence of distant metastases. The diagnosis was primary sclerosing cholangitis associated with chronic UC, complicated by cirrhosis, a stenosing tumour of the right colonic angle and severe anaemia. After a blood transfusion of three erythrocyte units, the patient was transferred to digestive surgery. He died in 2019 before the surgery was performed.

Case n°2

patient born on September 10, 1970, aged 51 at diagnosis, known diabetic since 2013, initially on oral antidiabetics (Metformin 850 mg morning and evening and Glimepiride 3g in the morning) then on insulin therapy (Insuline humaine rapide 100 UI according to glycemia and Insuline rapide/Isophane 30/70). She was hospitalized from June 04 to 27, 2021 for jaundice that progressively set in over a week, preceded three months earlier by generalized and permanent pruritus. On clinical examination, general condition was preserved, WHO score was 2, and physical examination revealed frank jaundice, diffuse hyperchromic macules, scratchy skin lesions and discreetly tender global hepatomegaly. On laboratory examination, PAL was elevated to 1,283 IU/l, ASAT to 135 IU/l, GGT to 899 IU/l, ALAT to 125 IU/l, total bilirubin to 77.43 mg/l, direct to 55.33 mg/l. PT and factor V were normal. Blood count, creatinine level and ionogram were normal. Anti-mitochondrial, anti-smooth muscle, anti- nuclear, anti-LKM and anti-cytosol antibodies were negative. Viral markers for hepatitis A, B, C and E were negative. Abdominal ultrasound revealed homogeneous hepatomegaly. Abdominal CT showed homogeneous hepatomegaly without dilatation of the intra- and extra- hepatic bile ducts. No biliary MRI or colonoscopy had been performed. Histology of liver biopsies after liver biopsy was consistent with lesions of non-specific, mildly active chronic hepatitis. By elimination, the diagnosis of primary sclerosing cholangitis was retained, and the patient was put on AUDC 13 mg/Kg/d. The evolution was marked by the regression of jaundice and the disappearance of pruritus, justifying discharge from hospital. The patient was regularly followed in the department until January 2022, when she was lost to follow-up.

Case n°3

This patient was born on May 28, 1986, aged 35 at the time of diagnosis, married with two children, and presented with progressive pruritus followed by progressive jaundice. Stools were normo-colored. The patient was apyretic, with no notable medical or surgical history. He had been drinking alcohol at an average rate of 50-60 g/day for five years. Clinical examination revealed a weight loss of 6.5% in one month, frank conjunctival jaundice, and itchy skin lesions. On laboratory examination, GGT, PAL, total bilirubin, direct bilirubin, AST and ALT were elevated to 299 IU/l, 739 IU/l, 39.4 mg/l, 26.5 mg/L, 78 IU and 152 IU respectively. PT and factor V were normal at 79% and 97%. Hepatitis B and C viral markers were negative. Anti-smooth muscle, anti-LKM, anti-cytosol and anti-mitochondrial autoantibodies were negative. Abdominal ultrasound was normal, as was the injected abdominal CT scan. Biliary MRI, performed in Dakar, showed dilatation of the intra- and extra-hepatic bile ducts, with clear disparity of the common hepatic duct (image 3). Systematic colonoscopy revealed superficial ulcerations of the right colon and cecum. Histology of colonic biopsies showed a colonic mucosa with a fibrous chorion, reworked by a polymorphic infiltrate of lymphocytes and polynuclears, accentuated glandular regeneration

and cryptitis suggestive of chronic non- specific relapsing colitis. Treatment consisted of AUDC 13 mg/Kg/d. The course was marked by the disappearance of jaundice and pruritus, and normalization of GGT and PAL. In the absence of intestinal manifestations, no treatment had been instituted for chronic colitis. A bili- MRI was performed after 12 months of evolution, showing an improvement in the stenosis of the left hepatic convergence and a decrease in the dilatation of the left bile ducts. The evolution of GGT, alkaline phosphatases and transaminases was illustrated in figure 1. The patient is regularly monitored to this day, with colonoscopy performed every 2 years.

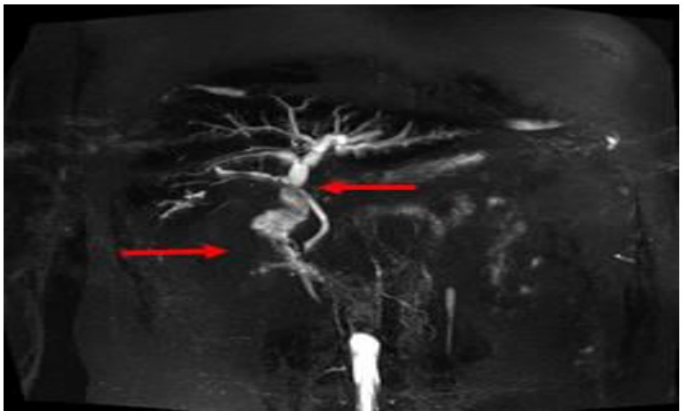

Image 3: biliary MRI, biliary strictures predominantly on left hepatic convergence, dilatation of the bile ducts Left biliary

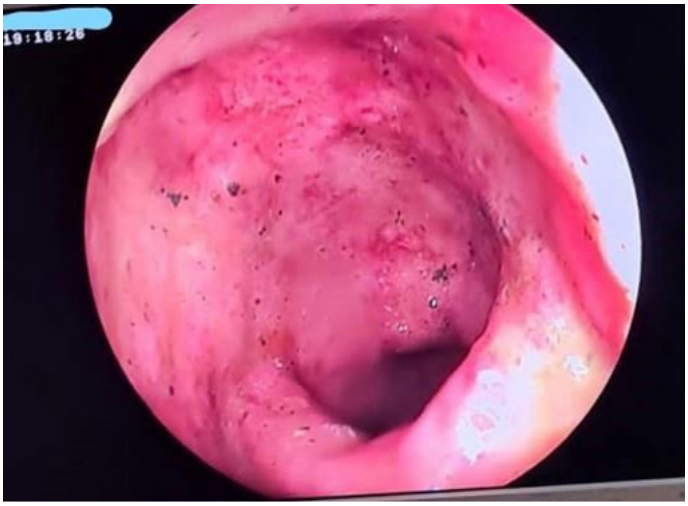

Image 1: congestive and erosive aspect of the colon

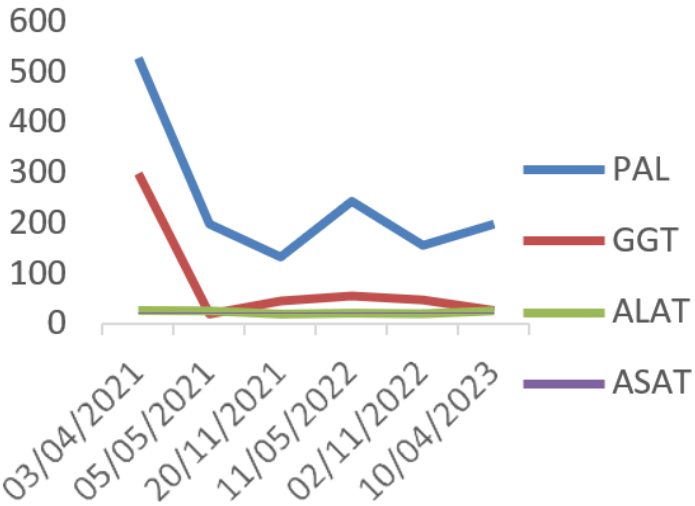

Figure 1: Evolution of biological markers

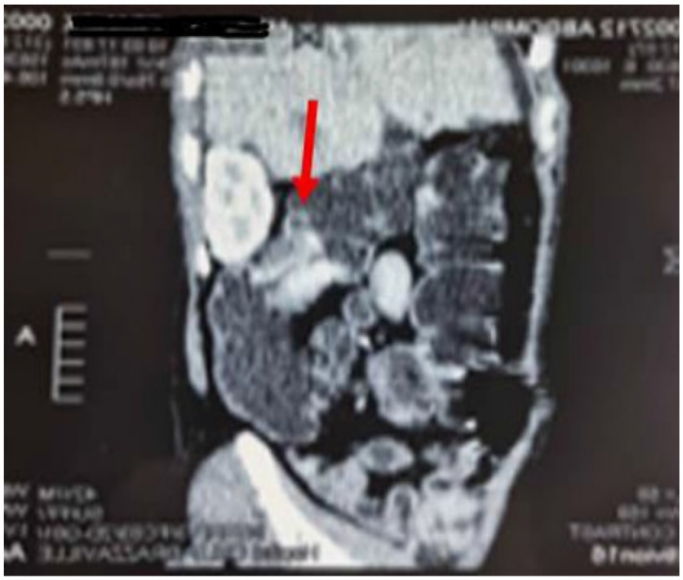

Image 2: Injected abdominal CT scan, stenosing tumor right colonic angle (red arrow)

Discussion

PSC is characterized by inflammation and fibrosis of the intra- and/or extra-hepatic bile ducts, leading to biliary stasis. (1). It is common in the West (6) but rarely reported in Africa (2,4). Its clinical features are polymorphic and non-specific, to the extent that PSC should be considered in the presence of any cholestatic disease of undetermined cause (7). It more often affects males, with a median age of 40 years (1,7,8). In our series, all patients were registered in an adult medicine department, and were between 35 and 51 years of age. Vijay et al in the USA found a predominance in black adults under 40 years of age (9). In the literature (10,11) pediatric forms are rare.

However, in Sao Paulo, Brazil, cases of PSC have been described (10) in children aged 10 to 12. In general, the diagnosis of PSC is based on a number of factors: chronic cholestasis, biliary stenosis associated with upstream biliary dilatation or histological hepato-biliary abnormalities, and the absence of arguments in favour of secondary sclerosing cholangitis. (7,8). Bilio-MRI or cholangio-MRI has become the key diagnostic test, showing biliary stenosis and dilatation, although sometimes absent. It can also be used to assess the impact on the liver (4,8). Endoscopic retrograde cholangiopancreatography (ERCP) is essential when endoscopic dilatation of the bile ducts is indicated, and enables cytological sampling of the bile ducts in search of cholangiocarcinoma (8,9). In Congo Brazzaville, biliary MRI was not available, making it difficult to confirm radiological abnormalities in two patients. Only one patient was able to undergo bili-MRI, but in another country. In the literature, bili-MRI was diagnostic in 61% of cases in Tunisia (4). The availability of bili-MRI in our context will undoubtedly help to diagnose more cases of PSC. Regarding PBH, literature data stipulate that normal histology can be seen during the course of PSC and does not exclude the diagnosis as described in one of our patients. The association between PSC and IBD is frequently described, but less frequently in Africa (1,4,8). Kchir et al in Tunisia found 33% IBD, while David Laharie et al in France showed that 70% of patients with PSC had associated IBD, and 10% of IBD occurred during the course of PSC. We reported two cases of IBD in three patients, including one case of UC and one case of non-specific chronic inflammatory colitis. In Tunisia (4) and South Africa (13) Crohn's disease was the IBD most frequently associated with PSC. In these cases, the association with HLA-B27 was incriminated in women. As a result, colonoscopy is strongly recommended in PSC (7,12). Treatment of PSC is usually symptomatic, and there is no specific medical therapy. AUDC at a dosage of 15-20 mg/Kg/d is generally used, with good results in reducing cholestasis without improving the hepatic prognosis of the disease (3,8,11). The administration of AUDC 20 mg/Kg/d is debated (7) and does not appear to provide any further benefit. In all patients reported in this series, AUDC at 13 or 15 mg/Kg/d improved cholestasis-related signs, and no patient required higher doses of AUDC. Sometimes, systemic corticosteroids are combined when there is an association with another inflammatory disease such as autoimmune hepatitis, IBD or hemolytic anemia (7,14). Endoscopic balloon dilatations are performed in cases of symptomatic tight stenosis (7,8,12). Endoscopic dilatation has not been performed in patients with biliary convergence stenosis, as cholestasis-related symptoms were ameliorated under AUDC. Liver transplantation is indicated in over 50% of cases after 10-15 years of disease progression, and remains the most effective treatment in 40% of cases at the cirrhosis stage, but is not accessible in many African countries. However, recurrence remains possible after liver transplantation (1,8,12,15). Liver transplantation was indicated for a patient with cirrhosis, but this surgery is not feasible in our country. PSC is monitored clinically, biologically and morphologically (4,6,7). The most frequently described hepato- biliary complications are angiocholitis, vesicular lithiasis, cirrhosis and cholangiocarcinoma (1,6,8). Vesicular lithiasis was the mode of revelation in a study of three children in Brazil (10). The cumulative risk of cholangiocarcinoma and colorectal cancer is respectively 10% and 25%. (15). In our series, no cases of cholangiocarcinoma were observed. However, we noted one case of lieberkühnian adenocarcinoma of the right colon during the course of UC. This complication was not promptly managed, as the patient was lost to follow-up for several years. This data confirms the value of close surveillance with annual colonoscopies in the course of PSC associated with colonic IBD. Because of the difficulties of early diagnosis of cholangiocarcinoma, there is no specific strategy for cholangiocarcinoma screening. Chazouillères et al recommend biannual clinical and biological surveillance, and annual morphological monitoring. (7). Close endoscopic surveillance by colonoscopy and upper GI endoscopy

for signs of portal hypertension is also recommended in the follow-up of PSC (12).

Conclusion

With this case series and review of the literature, we confirm the rarity of PSC in Brazzaville, where we have reported three cases in 16 years of practice. However, the lack of diagnostic resources partly explains this trend. In cases of PSC, AUDC was effective in all patients. The association with IBD and recto-colic cancer is frequently described, requiring close endoscopic surveillance. We urge you to systematically search for PSC in the presence of any cholestasis of undetermined cause.

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