INTRODUCTION
Since the first description of Primary Sclerosing Cholangitis over a century ago by Hoffman in 1867, the disease has remained an uncommonly diagnosed syndrome of unknown cause, characterized by chronic fibrosing inflammation of bile ducts, usually affecting both the extrahepatic and intrahepatic biliary ductal systems. The etiology of this condition is related to both genetic predisposition and aberrant immunological response. Disease associated HLA variants and autoantibodies have been detected in this disorder, and approximately 75-90% of patients with have concurrent inflammatory bowel disease. In Western countries, the incidence and prevalence rates for PSC range from 0 to 1.3 per 100,000 inhabitants/year and 0-16.2 per 100,000 inhabitants, respectively. The prevalence appears to be on the increase possibly due to increased awareness of the disease coupled with improved accuracy of biliary imaging.

The natural history of PSC is characterized by slow and relentless progression from an asymptomatic stage to a condition characterized by symptoms of cholestasis and complicated by cirrhosis, portal hypertension, liver failure and possibly carcinoma of the bile ducts. Although this progression may take over a decade or longer, the time course is unpredictable. Early non-invasive and pre-icteric Identification of this condition requires magnetic resonance or endoscopic cholangiopancreatography (MRCP or ERCP). We report here a case of a PSC in a Nigerian woman to highlight the occurrence of this unusual condition in Tropical Africa and also to discuss the challenges in patient evaluation.

CASE REPORT
A 47-year old woman presented with a 6-month history of right upper quadrant pain, associated with intermittent jaundice, and generalized pruritus and weight loss. She also complained of intermittent loose stools 4 to 6 times daily, associated with mucus. She
has no prior history of surgery or abdominal trauma. She did not take alcohol or smoke cigarettes and was not on any medications or herbal preparations.

On clinical evaluation, she had a tinge of jaundice, hard hepatomegaly of 8cm and liver span of 18cm. There was no ascites, no splenomegaly or features of portal hypertension. Initial investigations done revealed a predominantly conjugated hyperbilirubinemia with total bilirubin 177 mmol/l (normal range 2-20 mmol/l), conjugated bilirubin 107 mmol/l (normal range 0-8 mmol/l) and cholestatic pattern of liver enzymes with serum alkaline phosphatase and gamma glutamyl transferase increased by 4.8 and 8 times the upper limit of normal respectively (579 u/l, normal range 40-120u/l and 548u/l, normal range 7-64u/l respectively). The alanine and aspartate transaminases (ALT, AST) were moderately elevated (139 u/l, and 199 u/l respectively, normal range 10-42 u/l). There was also hypergammaglobulinaemia (64g/l, normal range 0.9-2.7) and hypoalbuminaemia (26g/l, normal range 37-52 g/l). The protein electrophoretic pattern showed a polyclonal gammopathy, with total gammaglobulin level 2 times ULN (26.9 g/l, normal range 8-13.5 g/l). She had mild normocytic normochromic anaemia. Laboratory testing was negative for hepatitis B and C biomarkers (HBsAg, anti-HBsAb, anti HBc, anti HBe, anti-HCV) and HIV.

A clinical diagnosis of cholestatic liver disease was made after initial investigations. Auto-immune antibodies reported were anti-nuclear factor, anti-mitochondrial antibodies, and anti-neutrophil cytoplasmic antibodies (p-ANCA, c-ANCA) all of which were negative. Abdominopelvic ultrasound scan using a 4MHz curvilinear transducer showed a hepatomegaly with coarse echotexture. The portal vein and hepatic veins showed normal spectral tracing. An abdominal CT scan showed isolated areas of dilated peripheral bile ducts suggestive of sclerosing cholangitis. Histological evaluation of liver biopsy sample obtained on percutaneous liver biopsy showed multiple portal tracts expanded with proliferated bile ducts exhibiting fibro-obliterative cholangitis. There was concentric periductal fibrosis with dense inflammatory infiltrate, mainly lymphocytes (figure 1,2). Sigmoidoscopy was done later in the course of the disease revealed friable oedematous mucosa and multiple superficial ulcers in the rectum and sigmoid colon. Histological examination showed epithelial erosions, cryptitis and architectural distortion.

Fig. 1: H&E LPx200- Medium power micrograph showing hepatic nodular regeneration and proliferated bile ducts exhibiting fibro-obliterative cholangitis. H&E, x200

Fig. 2: H&E HPx400- High power micrograph showing periportal fibrosis (arrow) with lining cell degeneration and surrounding dense lymphocytic infiltrates. H&E x400
Fig. 3: H&E HP- Micrograph showing large area of epithelial erosion on colonic mucosa. 
(a) There is crypt distortion with evidence of cryptitis. Many of the crypts show goblet cell depletion. H&E, x200
(b) The lamina propria is intensely infiltrated by plasma cells, lymphocytes and some polymorphs with extension of inflammation into the muscularis mucosa H&E, x400. The features are suggestive of ulcerative colitis

of the crypts consistent with ulcerative colitis (figure 3).

A final diagnosis of Primary Sclerosing Cholangitis and concurrent ulcerating colitis was made based on the clinical presentation, imaging and histological characteristics. The patient was commenced on symptomatic management for pruritus initially with cholestyramine, but now on ursodeoxycholic acid (UDCA) and antihistamines with good clinical and biochemical response. She is currently attending the outpatient follow up clinic and has been counseled on nature of disease, need for colon cancer surveillance and future possible requirement for liver transplantation abroad.

DISCUSSION

Primary Sclerosing Cholangitis (PSC) is an unusual cause of chronic liver disease worldwide. It is even less common in many parts of Africa where viral hepatitis B and C are endemic and ulcerative colitis uncommon in Western populations. PSC is thought to occur predominantly in men, with an average age of 40 years at diagnosis and with auto antibodies occurring in up to 53% of these subjects. In contrast, various studies done in Western countries suggest that among patients of African descent, females appear more susceptible than males and have less concurrent IBD.

There is no epidemiological data or case series on PSC from Tropical Africa. Jones et al, (1979) report the case of a 39-year old Tanzanian man who presented with cholestatic jaundice and required diagnostic laparotomy, intraoperative cholangiography and liver biopsy for establishing the diagnosis of PSC. Our patient also presented with cholestatic jaundice, but was female and required liver and colonic biopsies to establish the diagnosis. In developed Western countries, diagnosis of PSC is currently made using ERCP. The advent of MRCP as a screening tool for suspected patients has made non-invasive, early and pre-icteric diagnosis possible. In these subjects, localized areas of dilatation proximal to multifocal biliary strictures produces a characteristic beaded appearance on cholangiography. These cholangiographic tools are unavailable at our Center as in most of Tropical Africa.
From the foregoing, it is evident that highly technical equipment and invasive skills appear to be a prerequisite for evaluation. Although regarded as rare, it is plausible that PSC is under diagnosed in many parts of Africa due to lack of adequate facilities.

The close association of PSC and IBD is well recognized worldwide. Jorgensen et al in one of the largest multicenter case series, reviewed 439 patients who received liver transplantation at the Nordic Liver transplant group over a 22 year period (1984 and 2006). A total of 353 patients (80%) had associated inflammatory bowel disease (IBD) at the time of transplantation. Our finding of concurrent IBD in the patient with PSC thus conforms to the established prevalence of dual disease. Although no correlation between the severity of ulcerative colitis and that of primary sclerosing cholangitis has been established, patients with dual disease have been shown to have a high risk of colorectal cancer and require surveillance for colorectal cancer.

In Tropical Africa, AIDS cholangiopathy is an important differential of cholestatic jaundice. Similarly, Autoimmune hepatitis, hepato-biliary tuberculosis and biliary obstruction must be considered. In our patient, the negative HIV serology, absence of autoimmune markers, absence of typical features of biliary dilatation on abdominal imaging and liver biopsy findings helped to exclude these.

The role of supportive and symptomatic therapy is very important, as no effective therapy exists for limiting disease progression. Specific clinical conditions associated with chronic cholestasis such as pruritus is managed with ursododeoxycholic acid, cholestyramine and antihistamines with variable responses. Vitamin replacement therapy is given to subjects with vitamins A, D, E and K deficiency whilst low fat diet and medium chain triglycerides is recommended to improve steatorrhoea. Liver transplantation is the most effective treatment option in PSC and now accounts for 5-10% of liver transplants done in the United States with 5-year survival rates of 86.4%. Most patients in Tropical Africa do not have access to these facilities and will likely progress to end-stage liver disease with its associated complications and dismal outcomes.

In conclusion, although a rare disease worldwide, we establish that PSC exists in Tropical Africa, corroborating the evidence from East Africa and highlight the importance of considering this diagnosis in patients with cholestatic jaundice. Challenges in identification and unavailability of MRCP imaging and advanced endoscopic procedures like ERCP make the diagnosis a challenge. The present report emphasizes the important role of abdominal CT scan and percutaneous liver biopsy in the diagnosis of persistent cholestasis. The treatment of PSC remains unsatisfactory and the possibility of liver transplantation in Africa remains remote except centers of excellence are established and supported.

REFERENCES


