Hepatic schistosomiasis with massive splenomegaly: a case report and literature review

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Abstract

Schistosomiasis is a parasitic disease caused by Schistosoma species. Intestinal and hepatic schistosomiases are the most common forms of chronic disease. We describe a case of a 26-year old patient from Eritrea who was referred to our hospital with abdominal pain and diarrhea. The diagnosis of hepatosplenic schistosomiasis was made by liver biopsy and the patient was treated with praziquantel. Hepatic schistosomiasis is characterised by deposition of schistosomal eggs in the liver which results in a host cell immune response and leads to granuloma formation and neo-angiogenesis. This is hallmarked by different grades of periportal fibrosis with portal hypertension leading to splenomegaly. Normal liver architecture is preserved and periportal fibrosis can be reversible if treated adequately and timely.

With a recent native schistosomiasis cluster report from France and the expected influx to Europe of persons from regions endemic for schistosomiasis, increased awareness of this disease in healthcare practitioners is needed. We review the epidemiology, pathogenesis, clinical presentation and treatment of schistosomiasis. (Acta gastroenterol. belg., **2018**, 81, **93-96**)

Key words : Schistosoma, S. mansoni, hepatic fibrosis, splenomegaly

Introduction

Infections with Schistosoma species have been recorded throughout human history (1). 240 million people are currently affected by schistosomiasis, most of them live in Sub-Saharan Africa where annually 200 000 deaths are attributed to this parasitic disease (2-3). The geographic distribution of the different schistosomiasis forms is shown in Table 1. There are six main species causing two forms of schistosomiasis: intestinal and urogenital schistosomiasis (2). S. haematobium, S. mansoni and S. japonicum are the dominant causes of intestinal schistosomiasis. Less prevalent species include S. mekongi, S. intercalatum and S. guineensis (4). S. mansoni, S. japonicum and S. mekongi infections can result in hepatic fibrosis which occurs in 5-10% of the infections (5). Prevention by means of praziquantel is the key public-health strategy to combat schistosomiasis. Reduction in transmission is achieved by snail control. In 2010, 34.8 million people were treated for schistosomiasis in 30 countries. The transmission has reportedly been interrupted in 19 countries (3).

Case report

A 26-year old male patient from Eritrea was admitted to our emergency department with abdominal pain and diarrhea since a few months. The patient had no medical history and was in Belgium since ninety days. His physical examination revealed abdominal tenderness with splenomegaly. Haematology results showed a pancytopenia with haemoglobin levels of 8.6 g/dl (13.2-17.3 g/dl), a total white blood cell count of 1.5 x 10^9/ L (4.5-11.0 x 10^9/L) and platelets of 64 x 10^9/L (150-400 10^9/L). Differential white blood count was normal. Liver tests were normal except of an elevation of alkaline phosphatase to 135 U/l (30-120 U/l). C-reactive protein was 30 mg/l (< 5 mg/l). IgG was 39 g/l (7-16 g/1 (polyclonal). Anti-HCV antibodies were positive but PCR HCV RNA remained negative. ANA and ANCA were 1/1280 and 1/320 respectively. ASMA was negative.

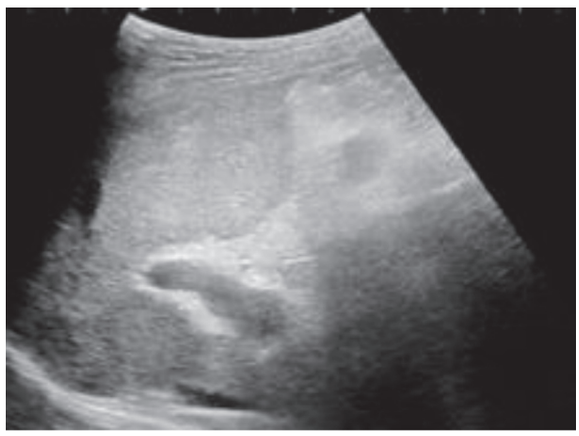

Figure 1. — Hepatic ultrasound showing periportal fibrosis (0.62 cm).

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Table 1. — **Geographic distribution of human schistosomiasis**

Parasite species		**Geographic region**		
	Africa	America	Asia	Europe
S. mansoni (hepatic- and intestinal schistosomiasis)	- Southern Africa - sub-Saharan - the Nile River valley	- South-America - Caribbean (low)	/	/
S. haematobium (urogenital schistosomiasis)	-Southern-Africa - sub-Saharan Africa - the Maghreb region - Nile River valley	/	- Middle East	-Corsica
S. japonicum (hepatic- and intestinal schistosomiasis)l	/	/	- Indonesia - parts of China - the Philippines - South-East Asia	/
S. mekongi (hepatic- and intestinal schistosomiasis)	/	/	- Cambodia - Laos	/
S. intercalatum *S. guineensis (intestinal schistosomiasis)*	- Central Africa - West Africa	/	/	/

Abdominal ultrasonography showed a massively enlarged spleen (22.8 x 9.1 x 16 cm) and hypertrophy of the left liver lobe with a dilated portal vein and prominent periportal fibrosis (Figure 1). There was no evidence of portal vein thrombosis or ascites. Hepatic veins were normal. Abdominal CT scan confirmed the ultrasound findings. Gastroscopy revealed a hypertensive gastropathy without esophageal varices. Rectosigmoidoscopy showed a patchy erythema. Histological examination of colon biopsy samples revealed a moderately active colitis. The presence of prominent periportal fibrosis with normal appearance of the hepatic veins, together with the origin of the patient and the clinical presentation with splenomegaly suggested hepatosplenic schistosomiasis but serial stool samples initially remained negative. Because the patient also had significantly altered ANA and ANCA, a percutaneous liver biopsy was performed. The biopsy showed Schistosoma eggs with surrounding eosinophils and multi-nucleated giant cells in combination with periportal fibrosis and sparse fibrous septa (Figure 2a). This diagnosis was subsequently confirmed by positive serology. Meanwhile renewed serial stools samples showed S.mansoni eggs. Treatment with praziquantel 40 mg/kg po was administered, repeated with the same dose two weeks later. Six months post-treatment the abdominal pain and diarrhea resolved but the radiological and laboratory abnormalities remained as before with unchanged periportal fibrosis, splenomegaly and pancytopenia.

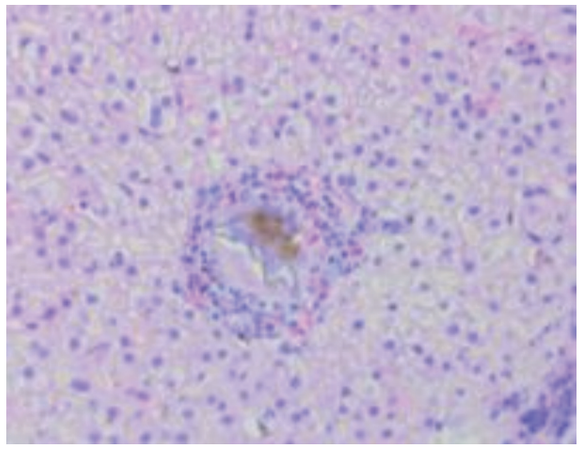

Figure 2. — a. Histological section showing a live Schistosoma egg, surrounded by eosinophils (H&E) (courtesy P. Van Eyken (5).

Discussion

Life cycle and epidemiology

Transmission of Schistosoma species occurs when infected humans contaminate fresh water with their excreta. When the eggs hatch in fresh water they discharge miracidia. These free-living motile forms penetrate specific freshwater snails, where the cercariae are produced. After release of the cercariae, they can be attracted by human skin secretions and penetrate the skin.

During penetration, the cercariae lose their tail and are then labelled as schistosomula. The schistosomula are carried in blood and/or lymph nodes to the portal vessels in the liver where they develop into adult schistosomes (1,6). Adult worms live in the mesenteric veins or in the veins of the urogenital system where the female schistosomes deposit their eggs. By moving to the lumen of the intestine or bladder, the eggs can be released from the human body (1,6).

The geographic distribution of human schistomiasis is linked to the specific habitats of their intermediate snail hosts which live in still or slow-flowing waters in (sub) tropical regions (Table 1) (1-2,6).

Pathogenesis and clinical presentation

The course of the disease can be divided in three stages : a migratory, an acute and a chronic stage. The first migratory stage starts when cercariae migrate through the skin which may cause a maculopapular eruption, also called "swimmer's itch". The second stage, referred to as Katayama fever, occurs approximately within four to six weeks after the initial infection when the eggs are released (4). The symptoms are due to an acute systemic hypersensitivity response which results in fever, chills, tiredness, diarrhea, arthralgia and myalgia (7). Respiratory symptoms have been reported in up to 70 percent of persons infected with S.mansoni. Physical examination may reveal lymphadenopathies, hepatosplenomegaly or rash. Biochemistry shows eosinophilia and high levels of IgG and IgE (4).

The third or chronic phase is characterised by the cumulative deposition of eggs. The eggs who don't penetrate the lumen of the gut or bladder are swept away in the circulation. Those lost eggs become trapped in the circulation of organs where they provoke a granulomatous response. As a result the ova are destroyed but the immune response leads to fibrosis (1-2,4,8).The different effects on the host organs are summarised in Table 2 (1-2).

Clinical and pathologic findings in hepatosplenic schistosomiasis

The early inflammatory reaction is due to ova trapped in the pre-sinusoidal periportal spaces. Typical clinical features include hypertrophy of the left liver lobe and nodular splenomegaly (9).

The chronic phase of hepatic schistosomiasis has two major disease forms: hepatointestinal and hepatosplenic schistosomiasis. The majority of patients infected with S.mansoni or S.japonicum develop hepatointestinal schistosomiasis, which is a mild disease with only a few hepatic granulomas. This form presents as abdominal pain, diarrhea and rectal bleeding (10). Approximately 5 to 10% of individuals develop a more severe form of the disease in which progressive periportal fibrosis occurs over years, which is described as hepatosplenic

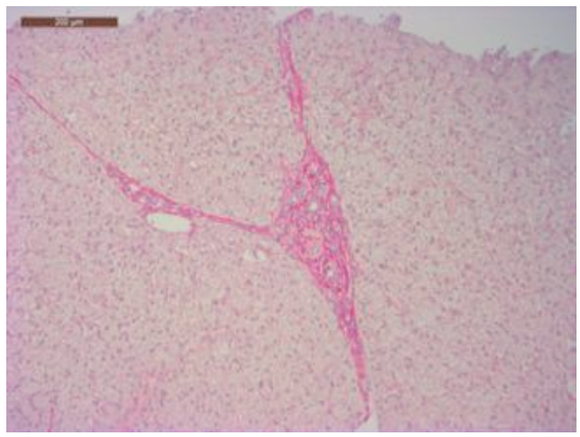

Figure 2. — b. Sirius Red stain showing the portal spaces with periportal fibrosis (courtesy P. Van Eyken (5)).

Table 2. — **Characteristics of schistosomiasis**

Organ system	**Effects and symptoms**
Gastro-intestinal	Intestinal polyposis, abdominal pain, diarrhea
Hepatic	Periportal fibrosis, presinusoidal portal hypertension which leads to hepato-splenomegaly, ascites, esophageal varices
Pulmonary	Pulmonary arteritis
Cardiovascular	Heart failure
Neurologic	Cerebral granulomas resulting in epileptic convulsions, spinal granulomas resulting in transverse myelitis
Renal	Glomerulonephritis
Urogenital	Hematuria, fibrosis of bladder and ureter, squamous cell carcinoma, vaginal bleeding, dyspareunia, genital lesions, infertility

schistosomiasis. Worm load, infection during infancy and multiple re-infections are the most important risk factors for hepatosplenic schistosomiasis (11).

Progressive obstruction of blood flow results in portal hypertension, leading to splenomegaly due to chronic passive congestion but also hyperplasia of the reticuloendothelial system (8,12). The compensated stage of hepatosplenic schistosomiasis is characterised by enlargement of the left hepatic lobe and moderate splenomegaly. In the decompensated stage, patients present with a small liver, massive splenomegaly, esophageal varices, hepatic encephalopathy and ascites (11).

On microscopic evaluation the eggs are often detectable inside portal veins radicles. In early lesions they are surrounded by eosinophils, later on there is granuloma formation (Figure 2a). The hepatic fibrosis surrounds the portal vein branches and leads tot fibrous expansion of the portal tracts (Figure 2b). This characteristic portal fibrosis is called Symmers clay-pipe stem fibrosis (13). Within the fibrosed and enlarged portal space, there are

partially or totally obstructive vascular lesions. Lobular architecture remains intact (5).

Diagnosis

Faeces analysis, abdominal ultrasound, serology and liver biopsy are the preferred tools to confirm hepatosplenic schistosomiasis. Microscopic detection of schistosome eggs in excreta remains the gold standard for diagnosis (9). Anyway, the presence of schistosomes cannot be ruled out definitively because of the low sensitivity of standard faecal examinations and the fluctuation in shedding of eggs (8,10). Molecular tests to detect schistanaemiaosome DNA in faecal specimens show greater sensitivity compared to light microscopy (10). When urine and faeces samples are negative, bladder, rectal or liver biopsy can lead to the diagnosis (5).

Antibody testing is sensitive, but its use is limited in endemic areas since antibodies remain detectable after parasitological cure and the possibility of cross-reaction with other helminth infections (5,8-9). Seroconversion generally happens within 4-8 weeks of infection (9). Schistosome antigens can be detected and quantified with labelled monoclonal antibodies in serum or urine of infected patients (9).

Biochemistry may show anemia, eosinophilia, pancytopenia, hypoalbuminemia, elevated urea and creatinine levels and hypergammaglobulinemia (5,8). Periportal fibrosis in hepatic schistosomiasis is demonstrated on ultrasonography, computed tomography or magnetic resonance imaging (8). An ultrasonographic grading system for periportal fibrosis was proposed by Abdel-Wahab and is defined as follows: grade I for mild (3-5 mm) echogenic thickening of peripheral portal vein radicals; grade II for moderate (5-7 mm) echogenic thickening and grade III for marked (> 7 mm) echogenic thickening of portal vein radicals, scattered throughout the liver with a central lucency that is obliterated in severe cases (14).

Treatment

Praziquantel, a pyrazinoisoquinoline derivative, is the standard treatment of choice. The recommended regime for S. mansoni is 40 mg/kg bodyweight in a single dose (9). Because the ineffectiveness of the drug against immature schistosomal forms it is recommended to repeat the administration of praziquantel after 3-6 weeks (10). Artemisin derivates are also effective against cercariae and can be used in conjunction with praziquantel to improve infection control. The initial inflammatory response is considered reversible (4). Despite this, collagen deposition and fibrosis is only partially reversible (4). The granulomas may disappear after cessation of parasitic activity (5).

Conclusion

Hepatosplenic schistosomiasis is a parasitic disease which is rarely diagnosed in industrialised countries. It is caused by trapped schistosome eggs in the liver which provoke a host cell immune response leading to periportal fibrosis and portal hypertension. The treatment of choice consists of anti-parasitic drugs as praziquantel but patients do not always benefit from it as periportal fibrosis is only partially reversible.

As there might be a larger migration of patients from regions endemic for schistosomiasis, an increased awareness of this disease is needed in Western countries.

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