PARASITIC DISEASE OF THE LIVER AND BILIARY TREE

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Several parasites infest liver or biliary tree, either during their maturation stages or as adult worms. Biliary tree parasites may cause pancreatitis, cholecystitis, biliary tree obstruction, recurrent cholangitis, biliary tree strictures and some may lead to cholangiocarcinoma. This review discusses the hepatobiliary parasites, and shows our experience in diagnosis and management of these parasites. Ultrasonography of the liver is diagnostic in schistosomiasis, hydatid cysts, amebic liver abscess, ascariasis and other biliary tree parasites showing bile duct dilatation. Percutaneous aspiration under ultrasonography guidance of hydatid liver cysts or amebic abscess are effective measures in management. Endoscopic retrograde cholangiopancreatography (ERCP) is safe and effective in diagnosis and management of biliary tree parasites. (Saudi J Gastroenterol 1997; 3 (1):22-28).

Intestinal parasites are among the most common microorganism to affect humans. Although most infections occur in developing countries, developed ones are also affected by migrants and travelers (1). Previously, the final diagnosis of most hepatobiliary and gastrointestinal parasitic diseases was based on the detection of the parasites larva, ova or cysts in the stools (2). Eosinophilia may indicate the presence of a parasite. Serological tests are not available for all parasitic diseases and some of these serological tests are neither sensitive nor specific. Many parasites may inhabit the upper or lower gastrointestinal tract, pancreas, liver, gallbladder and biliary tree (3). It is estimated that approximately 25% of the Third World population is infested with Ascaris lumbricoides (4). More than 200 million people are infected with schistosomiasis throughout the world and 500-600 million are exposed to the risk of infection (5).

The extent of the disease depends on the parasite burden and stage of infestation, the type of tissue response and host immunity. Patients suffering from immuno-deficiency syndromes may develop severe and fatal forms of parasitic disease. Modern techniques are important for the diagnosis and treatment of parasitic disease. These techniques include imaging techniques such as barium studies, ultrasonography, computed tomography and magnetic resonance imaging (6,7). Fibreoptic endoscopies have been shown to play an important role in the diagnosis and treatment of parasitic infestations of gastrointestinal tract and biliary tree (8).
Parasitic Disease

Amebiasis

The major clinical manifestation of Entameba histolytica infestation is liver abscess (9). In order to distinguish pathogenic strains of Entameba histolytica from nonpathogenic strains of Entameba dispar, a simple and rapid DNA extraction method on a fecal sample has been developed (10). A specific probe, using a monoclonal antibody technique, has been used to detect defined antigen in necrotic liver material in E. histolytica infection (11); Amebiasis cause tender hepatormegaly during the acute phase (amebic hepatitis) which is more common in chronic carriers, and an amebic abscess may develop. Hepatic amebiasis is the commonest extraintestinal complication. The diagnosis is usually reached by history and clinical examination together with ultrasonography of liver which will show the abscess (Fig 1). Patients may also present with picture of obstructive jaundice (12).

A study reported the prevalence of amebiasis in patients with schistosomal colonic polyposis is 37% compared to 15% in schistosomal patients without polyposis and 11% in non-schistosomal patients (13). Amebiasis can stimulate malignancy in barium enemas but the diagnosis is made by endoscopic biopsies (14-15).

In a previous study of 1775 lower gastrointestinal tract endoscopies, 31% of the colonic biopsies were abnormal including five patients with amebic colitis which was severe in one patient, who developed later a rectal stricture that required dilatation (16). In our hospital population, amebiasis is rare (2). We treated three patients with amebic liver abscess by percutaneous drainage. Percutaneous drainage is also helpful to differentiate amebic from a pyrogenic liver abscess. Amebiasis responds well to metronidazole treatment. Addition of diloxanide furate is useful for cysts eradication.

Hydatid Cyst

Echinococcus granulosis is the most common form of hydatid disease in humans. In endemic areas, the incidence might reach up to 5% as in Turkana area in Kenya (17). The incidence directly correlates with the number of infected dogs and the definitive hosts. Cysts caused by E. granulosis grow slowly and develop over many years. The effects are mainly those of a space occupying lesion (18). There are recent developments diagnosis of hydatid disease as in serological tests (using Elisa technique) and in radiological using ultrasound classification (19). A liver cyst may rupture into the biliary tree causing obstructive jaundice (20) and a lung cyst may rupture into pleural cavity presenting with a pleural effusion (21). Surgery used to be the definitive type of treatment but this carries risk of morbidity, recurrence and mortality (22).

However there are new modalities of treatment that might replace surgery in the future and these include medical therapy with albendazole and praziquantel, endoscopic management in biliary tree obstruction and percutaneous aspiration of the cyst (20). Liver ultrasonography is diagnostic for hydatid cyst and recently the ultrasonic appearance has been classified into four groups depending on cyst appearance, cyst consistency and presence of septations (23). Hydatid cysts of the liver are usually single but can be multiple. They may be large and cause pressure effect on the liver or may rupture into the biliary tree leading to biliary obstruction by daughter cysts. In our unit since 1985 we have introduced endoscopic management for such cases and successfully treated 10 patients with complete cure (Fig 2). Installation of hypertonic saline through nasobiliary tube with tip close to main liver cysts ruptured into the biliary tree is used as sclodial agent in the treatment of hydatid disease of biliary tree and liver cysts (6,20). Hydatid cysts may regress or disappear under medical therapy. Between 1985-1991 we treated 22 patients with albendazole alone (24). Subsequently combination therapy using albendazole and praziquantel was found to be more effective (25).
in 91% and 41% of the individuals passed more than 1000 eggs per gram of feces. Abdominal discomfort was reported by 60%, and diarrhea by 33%. The frequency of symptoms did not correlate significantly with egg counts while 70% of patients had hepatomegaly, only 0.5% had splenomegaly (27).

Schistosomiasis may involve the liver early in the disease in about 30% of the patients (schistosomal hepatitis) or more commonly 5-10 years after initial infection leading to periportal fibrosis and portal hypertension due to ova migration and development of hepatic granulomas followed by fibrosis. This results in increase of portal pressure and development of esophageal or gastric varices and portal hypertensive gastropathy (28).

We studied 72 patients with hepatosplenic schistosomiasis, liver ultrasonography showed perportal fibrosis in 58 of these patients (Fig 4). The liver functions are usually well preserved till late in the disease. Liver biopsy in 16 of these patients showed schistosoma granuloma or fibrosis. The gallbladder may be involved (29). In schistosomiasis, cirrhosis may occur as a result of anoxia following massive gastrointestinal bleeding or as a result of co-existing hepatitis B or C infection. Hepatocellular carcinoma or other malignancies have not been reported with Schistosoma mansoni but reported with Schistosoma japonicum (30). The main cause of death is gastrointestinal bleeding from esophageal or gastric varices and sclerotherapy may be effective in these patients (31). Upper abdominal ultrasonography is important in the diagnosis of schistosomiasis of the liver. The extent of perportal fibrosis is classified into four groups and this findings was found to be correlated well with liver biopsy findings (32). Ultrasonography has been used to assess hepatic fibrosis in 176 S. mansoni-infected individuals in northeastern Brazil. The severity of perportal fibrosis correlated significantly with the clinical stage of disease (P 0.0001), and the extent of esophageal varices (determined by upper gastrointestinal endoscopy (P 0.0001); furthermore the degree of esophageal varices correlated significantly with presence of hemorrhage (P 0.0001) (33). Reversibility of schistosoma induced hepatic fibrosis is increasingly accepted. Serial liver biopsy histology to assess liver collagen content, collagen biosynthesis, and collagenase activity in S.

Schistosomiasis

In human, morbidity resulting from Schistosoma mansoni infestation has been studied in a random population of 422 individuals at a newly established focus in northern Senegal. Egg counts were positive (Fig 3). Since 1993, we used a one stage percutaneous drainage of liver cysts and this was found successful in 12 patients (26).
japonicum infected rabbits, led a group of investigators in the United States and Brazil to conclude that "...advanced liver fibrosis... is slowly reversible after cure of senescence of the infection possibly resultant on persistently increased collagenolysis as collagen synthesis diminishes" (34). Drugs used for treatment of schistosomiasis, such as praziquantel are safe and effective and may stop the progress of liver fibrosis.

**Biliary Tree Parasites**

Biliary parasites can cause obstruction and dilatation of the common bile duct or hepatic ducts. Biliary lithiasis can develop secondary to ascaris, Fasciola hepatica and clonorchis sinensis (35-36). The stones related to ascaris are thought to form in the gallbladder and not the ducts (37). Hemobilia, sclerosing cholangitis and cholangiocarcinoma are complications of biliary parasites (38-40). Parasites may also lead to pancreatic duct obstruction or dilatation (41).

**Liver Flukes**

Liver flukes such as Fasciola hepatica, C sinensis and opisthorchis infest liver and can cause biliary tree obstruction with recurrent cholangitis. One patient from Thailand presented to our unit with obstructive jaundice. ERCP showed multifocal cholangiocarcinoma and drainage from nasobiliary tube revealed multiple C sinensis worms and ova (Fig 5 A, B) (39). Previously surgical treatment has been necessary for management of biliary parasites. However, recently ERCP and endoscopic papillotomy proved to be successful and replaced unnecessary operations. It has been recommended as first line in diagnosis and treatment (19,36,42,43).
Endoscopic extraction of biliary tree parasites will relieve the obstruction and decompress the dilated biliary tree and help in treatment of cholangitis. Pancreatitis secondary to parasites will settle also after worm extraction. Papillotomy and insertion of nasobiliary tube or stents will lead to decompression of obstructed biliary tree. Instillation of drugs through nasobiliary tube may be effective. Intestinal ascariasis can be treated with anthimetics but drugs have no enterohepatic circulation and has no effect on the worms inside the biliary tree. Instillation of piperazine citrate through a nasobiliary tube has been used successfully.

Hemoperitoneum had been reported as a rare complication of liver flukes. During three years we have studied 208 patients with human Dicrocoeliasis. Of these, 16 patients had disturbed liver function and 10 patients had gallbladder or biliary tree disease due to Dicrocoelium dentriticum (44). Biliary tree parasites can cause cholecystitis, cholangitis, biliary tree strictures, liver abscess, sclerosing cholangitis and cholangiocarcinoma.

**Other Parasites**

The reticuloendothelial system of the liver may be involved in leishmaniasis, malaria and others. Visceral leishmaniasis is destined to become and increasingly important problem worldwide. It has been clearly established as an "opportunistic" infection in HIV and AIDS sufferers.

During an eight-year period, 65 patients have been diagnosed in a single department in France (45). Fifty-six of these were infected locally, most by the Leishmania infantum MON-1. An increase in prevalence is suggested between 1985 and 1992; 19 cases of coinfection with Leishmania spp and HTLV-1 have been recorded since 1986. Clearly visceral leishmaniasis is an infection which the hepatologist will be encountering to an increased extent in the future, and a precise geographic history is of paramount importance in clinical diagnosis.

Multiple calcification may be seen in liver or peritoneum in porocephalasis due to calcified nymphs of the tongue worm (linguatulidae). Eosinophilic syndrome is a frequent sequel to most helminthic infection especially with hepatic involvement (46,47).

In malaria especially with Plasmodium falciparum hepatomegaly can develop early and subsides with treatment. In complicated falciparum malaria, patients can present with acute biliary remittent fever. Tropical splenomegaly syndrome develops in chronic malaria and might cause confusion with portal hypertension (48).

**Conclusion**

Parasitic involvement of liver and biliary tree is an important differential diagnosis in patients with jaundice especially those from tropical or subtropical continents. Biliary tree parasites can cause cholecystitis, recurrent cholangitis, biliary obstruction, stone formation and biliary tree strictures. ERCP is an important diagnostic and therapeutic method in these cases. Liver flukes if not diagnosed and managed early, may later lead to cholangiocarcinoma. Schistosomal liver disease is a major problem in endemic areas. Ultrasonography is an important diagnostic tool and can help in identifying the degree and stage of fibrosis. Antischistosomal drugs if given early may stop the progression of disease. In hydatid disease, the endoscopic management is effective in cases where liver cyst rupture into the biliary tree. Combined medical treatment with albendazole and praziquantel is effective in all forms of hydatid disease. Percutaneous drainage of liver cyst is effective and should be considered in such patients. New methods of management of hydatid disease may replace surgery in the future.

**References**

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42. Jessen K, Al Mofleh I, Al Mofereh M. Endoscopic treatment
of ascaris causing acute obstructive cholangitis.