MEDICAL REVIEWS

Clinical Aspects of Hepatosplenic Schistosomiasis: A Contrast with Cirrhosis

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The clinical picture of liver disease in endemic areas of Schistosomiasis mansoni differs in many ways from that observed in alcoholic and other types of cirrhosis. In hepatosplenic schistosomiasis there is predominance of the clinical manifestations of portal hypertension, e.g., bleeding esophageal varices, while ascites, jaundice, and hepatic precoma or coma are much less common. Ammonia tolerance is usually normal and helps explain the low mortality rate during bleeding. Of special interest is the observation of a high incidence of persistent hepatitis B surface antigenemia among patients with hepatosplenic schistosomiasis, suggesting increased susceptibility of such patients to the development of virus-induced chronic active hepatitis.

INTRODUCTION

Schistosomiasis is a disease caused by trematodes. These organisms alternate generations between fresh water snails that are the intermediate hosts in which they multiply and mammals that are the definitive hosts in which they cause the disease. Patients with low worm burdens have silent schistosomiasis. Such patients exhibit no evidence of disease, and the existence of the infestation can be determined only by the presence of the ova in the stools. Although ova can sometimes be demonstrated in the liver, there are no signs or symptoms of hepatic involvement. Hepatosplenic schistosomiasis (HSS) exists when the hepatic worm burden is great enough to cause clinical liver disease. In the compensated state HSS is characterized by hepatomagaly, typically of the left lobe, splenomegaly and portal hypertension. Liver function is usually normal. Decompensated HSS is the late stage of the disease when advanced fibrosis complicated by malnutrition, increasing age, or other factors induces ascites, portal-systemic encephalopathy, and liver failure.

Schistosomal liver disease is a benign process. Between 6 and 10% of all infected persons in an endemic region have the hepatosplenic form of schistosomiasis, and most of them lead an entirely normal life. Since there are approximately 200 million infected persons in the world (1), the number of patients with the hepatosplenic form of the disease is overwhelming. The common idea that liver involvement by schistosomiasis is a bad disease derives from the description of patients hospitalized in major medical centers, a highly selected sample of the most severe cases. Observation of these advanced cases led many clinical investigators to the conclusion

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that hepatosplenic schistosomiasis was clinically similar to hepatic cirrhosis of other etiologies, thus coining the erroneous term schistosomotic cirrhosis.

Despite some superficial similarities, there are marked clinical differences between hepatosplenic schistosomiasis and cirrhosis.

Aside from the pathological picture, which is unmistakably different, these diseases differ enormously in the clinical features that characterize them.

CLINICAL FEATURES

1. Clinical Appearance

The major clinical difference between hepatosplenic schistosomiasis (HSS) and cirrhosis is the predominance of the clinical manifestations of portal hypertension over impairment of hepatic function.

The stigmata of chronic liver disease are generally absent, and the liver function tests are usually within normal limits. Occasionally an elevation of the \( \gamma \)-globulins

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FIG. 1. Compensated hepatosplenic schistosomiasis. The grossly enlarged spleen is shown by the crosshatched markings. The left lobe of the liver is indicated. The right lobe of the liver is not palpable. Otherwise the patient looks healthy.
and moderate elevation of the alkaline phosphatase exist. Such individuals are said to have compensated hepatosplenic schistosomiasis (2). The large spleen and the prominent, hard left lobe of the liver are the only clinical clues that the disease exists (Fig. 1). These cases are much more like extrahepatic portal vein thrombosis than like cirrhosis.

A small minority of cases, with the same degree of portal hypertension, will present with ascites and a few or all of the clinical stigmata of chronic liver disease (Fig. 2). The laboratory tests in these patients often show hypoalbuminemia and variable degrees of derangement of all other tests of liver function. These are the cases of decompensated hepatosplenic schistosomiasis. It is sometimes clinically impossible to ascertain the nature of the liver disease without the help of a liver biopsy. All gradations of intermediate forms between the well-compensated and the severely decompensated cases occur.

The reason why some cases decompensate is not known. Repeated hemorrhages from varices may lead to ischemic necrosis of the liver (3, 4), but it is common to

FIG. 2. Decompensated hepatosplenic schistosomiasis. The left lobe of the liver and the spleen are enlarged as outlined. In addition, the patient shows gross ascites, gynecomastia, and emaciation.
TABLE 1
Esophageal Varices in Hepatosplenic Schistosomiasis

|                      | Esophagoscopy | Barium swallow |
|----------------------|---------------|----------------|
|                      | Number examined | Varices present | Number examined | Varices present |
| All patients         | 153           | 143 (93%)       | 94             | 73 (78%)        |
| History of bleeding  | 103           | 102 (99%)       | 68             | 60 (88%)        |
| No history of bleeding | 50          | 41 (82%)        | 26             | 13 (50%)        |

find well-compensated cases with a history of many episodes of variceal bleeding and decompensated patients who have never bled. In a blind histologic evaluation of autopsy material, Cheever and Andrade (5) reported active inflammation of the portal triads with destruction of the limiting plate and piecemeal necrosis in patients with decompensated hepatosplenic schistosomiasis. This pattern, which is typical of chronic active hepatitis, was not seen in compensated HSS.

2. Esophageal Varices

Esophageal varices occur twice as frequently in HSS as they do in Laennec's cirrhosis (6, 7). Indeed, of 153 patients with hepatosplenic schistosomiasis in our own experience, esophageal varices were demonstrated by direct visualization with an Eder-Hufford esophagoscope in 93% compared to less than 50% in patients with alcoholic cirrhosis (8, 9). This high incidence might have been influenced by selection, since many of these patients sought hospital attention because of upper gastrointestinal hemorrhage. When we examined 50 patients in the same series who did not have a history of bleeding, the incidence of varices by esophagoscopy was 82% (Table 1). The pattern was similar for varices diagnosed by barium swallow, but the incidence of varices was lower in all categories, probably reflecting the diagnostic superiority of endoscopy.

3. Tolerance to Gastrointestinal Hemorrhage

Because of their extensive deep portal collateral circulation and high incidence of esophageal varices, gastrointestinal hemorrhage is a common event among patients with schistosomiasis and often is the only reason for which compensated cases seek medical care. Tolerance to hemorrhage is well established, and the mortality rate from bleeding varices is far below that observed in cirrhotic patients. In cirrhosis the mortality varies from 30 to 80% (10-12); in a small, controlled series in schistosomiasis it was only 8% (Table 2).

4. Variceal Bleeding: Response to Medical Treatment

Because of their good tolerance to hemorrhage, the medical management of ruptured esophageal varices in schistosomiasis seems to be very effective. Spontaneous

TABLE 2
Gastrointestinal Hemorrhage in Hepatosplenic Schistosomiasis

|                      | Total |
|----------------------|-------|
|                      | Number | Percent |
| Patients             | 35     |        |
| Hemorrhages          | 49     |        |
| Spontaneous cessation| 14     | 29     |
| Precoma or coma      | 4      | 8      |
| Deaths               | 4      | 8      |
cessation of the hemorrhage before any treatment is started occurs in about one-third of the cases. In our controlled trial, intravenous injection of vasopressin and esophageal tamponade with the Sengstaken–Blakemore tube were equally successful in controlling the hemorrhage (Table 3). Despite the absence of a significant difference in efficacy between the two methods, we favor the use of vasopressin in these patients because of its simplicity and the absence of serious complications.

5. hepatic coma and ammonia tolerance

The low mortality rate during hemorrhage reflects the rarity with which patients with schistosomiasis develop hepatic coma (Table 2). The majority of these patients, who belong in the compensated category, tolerate well the overload of ammonia in blood brought about by the hemorrhage into the gut. Only patients with decompensated HSS show a rise in their arterial blood ammonia (13). A similar pattern has been observed after the administration of ammonium chloride (Fig. 3).

6. abdominal wall collaterals

Despite their extensive deep portal collateral circulation as shown by esophagoscopy or splenoportography, superficial collaterals such as dilated veins on the abdominal wall are uncommon. The classical “caput medusae” is practically never seen. Venous collaterals on the abdominal wall are clearly not a sensitive clinical index of portal hypertension.

![Oral Ammonia Tolerance Test](image)

FIG. 3. Ammonia tolerance test in schistosomiasis. Increment above fasting levels of arterial ammonia concentration 45 min after 5 g of ammonium citrate is small in patients with compensated hepatosplenic schistosomiasis and large in patients with decompensated disease. Increments are not further increased when cirrhosis develops.
7. Ascites

The presence of ascites is the major clinical sign of decompensation. It is absent in all compensated cases and is independent of the severity of the portal hypertension. Occasionally, severe hemorrhage induces the development of transient ascites and represents temporary decompensation of a borderline case. In such cases there is usually a prompt response to salt restriction and to diuretics, and the patients may go back to a normal diet after the bleeding episode.

8. Jaundice

Mild to moderate hyperbilirubinemia in schistosomiasis occurs in only a few of the uncompensated cases, and its presence always raises the suspicion of chronic active hepatitis. In patients with schistosomal cor pulmonale and passive congestion of the liver, deep jaundice may ensue. After portacaval shunts jaundice may also appear due to hepatic failure, hemolysis, and other factors (14).

9. Diabetes

Unlike Laennec's cirrhosis (15), the incidence of diabetes does not seem to be increased among patients with hepatosplenic schistosomiasis, at least in the compensated form. This subject is now under investigation in our and other laboratories (16).

10. Dwarfism

Adolescents with hepatosplenic schistosomiasis may present with variable degrees of dwarfism and sexual immaturity (17). Protein undernutrition may be responsible for the lack of normal growth. Although the production of hypophyseal hormones has been shown to be normal in such patients (18), the hypothesis of a peripheral blockade to the action of growth hormone and gonadotrophins has not been excluded.

11. Prolonged Salmonella Septicemia

While patients with Laennec's cirrhosis may have gram-negative peritonitis, patients with hepatosplenic schistosomiasis may develop prolonged septicemia caused by Salmonella (19, 20) and, perhaps, other gram-negative bacteria. The duration of the bacteraemia seems to be associated with the schistosome parasite per se rather than an immunological defect of the host, since it has been demonstrated that the bacteria adhere to the cuticula of the worm and can be entirely eliminated by the treatment of the parasite (19, 21, 22). Unlike cirrhosis, bacterial peritonitis is not a common event, probably due to the relative rarity of ascites, the sine qua non of cirrhotic peritonitis.

12. Response to Surgical Treatment of Portal Hypertension

For the elective surgical treatment of the portal hypertension in schistosomiasis, the major procedures such as portacaval anastomosis have practically been abandoned by most Brazilian surgeons. This type of operation, although very efficient in preventing variceal hemorrhage, may result in progressive hepatic dysfunction (18), leading to death in liver failure in a high proportion of patients, and is probably worse than the basic disease. Curiously, the splenectomy, which does not seem to decrease the chance of further hemorrhagic episodes significantly, presents a much better survival rate. The splenorenal shunt, which still has the preference of some surgeons, occupies an intermediary position, probably because it is not so
efficient as the direct portacaval shunt in decreasing the hepatic blood flow. Most specialists will give preference to a combination of splenectomy plus either trans-esophageal ligation of the varices or another type of azygoportal disconnection. It should be emphasized, however, that there is no well-controlled prospective study to justify these surgical preferences.

13. Association of Hepatosplenic Schistosomiasis with Hepatitis B Antigenemia

In a study in progress in our laboratory, Lyra (25) has found a high incidence of persistent hepatitis B surface antigenemia (HB, Ag) among cases with hepatosplenic schistosomiasis. Decompensated cases showed a higher proportion of positive HB, Ag (12%) than compensated cases (7.7%). Both, however, had antigenemia in a much higher incidence than a large control group (1.4%), which included patients with intestinal schistosomiasis. It is of interest to note that the antigenemia has proven to be persistent in all cases for at least several months and that active inflammation on the liver biopsy was also more prevalent among the cases positive for the Au antigen (26). It seems possible that patients with hepatosplenic schistosomiasis may be especially susceptible to the development of hepatitis B virus-induced chronic active hepatitis, thus explaining the progression of some cases to a full blown picture of cirrhosis.

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