Acute Human Schistosomiasis Mansoni

Ana Rabello

Centro de Pesquisas René Rachou - FIOCRUZ, Av. Augusto de Lima 1715, 30190 002 Belo Horizonte, MG, Brasil

The acute schistosomiasis is the toxemic disease that follow the Schistosoma *cercariae active penetration trough screen in the immunologicaly naive vertebrate host.The clinical picture starts two to eight weeks after the first contact with the contaminated water. Susceptible patients present a syndrome comprising fever, diarrhea, toxemia and hepatosplenomegaly. Diagnosis is based on epidemiological and clinical features, presence of* Schistosoma *eggs in the feces, enlargement of abdominal lymph nodes by ultrasonography and by detection of high antibodies levels against the antigen keyhole limpet haemocyanin. Different rates of cure have been observed with specific medication and for the most severe clinical presentations the use of steroids reduces the systemic and allergic manifestations.*

Key words: schistosomiasis - schistosomiasis mansoni - acute phase

The initial phase of the S*chistosoma* infection incorporates a large group of signs and symptoms which follows the *Schistosoma* sp. cercariae active penetration through skin. It comprises the prepostural period and the variable acute form which in the most severe presentation corresponds to the *Katayama fever* of *S. japonicum* infection. The acute form is a self-limiting clinical picture resultant mainly from the underlying immune systemic response occurring in the immunologicaly naive vertebrate host.

The assumption that the basis of the toxemic illness of the initial period of the *Schistosoma* infection is mainly caused by a immune reaction against *parasite toxins* has been accorded since the first reports of this condition in monkeys (Fairly 1920) and humans (Dias Rivera et al. 1956, Ferreira et al.1966). Although the acute form can be rarely observed in re-infection (Katz & Bittencourt 1965) there is an agreement on the fact that the susceptible organism prone to develop a severe toxemic disease is the prime infected patient (Dias Rivera et al.1956, Neves 1965, Ferreira et al. 1966, Hiatt et al. 1979) and that the disease is predominantly self-limiting, mostly benign, and invariably proceeds to chronification (Dias Rivera et al. 1956, Neves 1965, Ferreira et al. 1966).

EPIDEMIOLOGY

The incidence of the acute form of schistosomiasis mansoni is certainly underestimated. This illness has been mainly described as a disease of travelers. Many scientific publications concerning this acute disease refer to groups of tourists, fishermen or sailors originally from an non-endemic country who have visited a tropical zone (Lunde & Ottsen 1980, Evengard et al. 1990). However, as schistosomiasis is a focally distributed disease (Pessoa & Amorim 1957, Kloetzel 1989), the acute form is also diagnosed in inhabitants from endemic countries who do not live in endemic areas. Nevertheless, acute disease is seldom recognized in infected patients from endemic areas.

CLINICAL ASPECTS

Different intensities of clinical manifestation are observed; some patients evolve with a relatively severe picture while others develop mild symptoms. The development of non-apparent clinical form characterized by blood cosinophilia and a positive immediate cutaneous reaction in the initial phase has been described by Rocha et al. (1993).

Two to eight weeks after a first contact with natural water infested by *Schistosoma* cercariae, susceptible infected patients present a syndrome comprising a period of 2 to 30 days of fever (100%), diarrhea (94.4%), toxemia and weakness (62%), weight loss (50%), abdominal pain (55.5%), cough (66.7%), myalgia and arthralgia (61.1%), edema (50%), urticaria (44.4%), nausea and vomiting (28.8%) and hepatosplenomegaly the patients sought physician and/or hospital (Rabello et al. 1995). The clinical findings associated with the acute disease may be confounded with a number of infections such as visceral leishmaniasis, typhoid fever, malaria, miliary tuberculosis, viral hepatitis, mononucleosis and bacterial infections (Neves 1986, Chapman et al.1988).

Recent analysis of a group of 25 individuals simultaneously exposed to *S. mansoni* cercariae showed that morbidity (measured by the clinical-sonographic index) is more severe in children than in adults independent of level of water contact and also more severe in patients with high egg output irrespective of age or level of water contact (Rabello et al. 1995).

PATHOLOGY

According to anatomic *post mortem* reports (Bogliolo 1958), acute clinical form corresponds to an acute generalized miliar dissemination of granulomas and *S. mansoni* eggs, predominantly in the liver, the subserous layer of the small and large intestines, lungs, spleen and in the lymph nodes of the mesentery, epiploon, retroperitoneum, as well as in the lymph nodes of the hilus of the liver, pancreas, lung and spleen. The granulomas are observed uniformly in the initial phase of formation, with local histolysis and granulocytic exudation. The liver is enlarged with a softened consistency presenting necrotic-exudative granulomas and degeneration of the hepatocytes. The spleen presents as the "acute infectious tumor" (acute splenits).

The liver biopsy which displays the above mentioned granulomata consists on the firm diagnostic of acute schistosomiasis. Of course, this invasive procedure is seldom indicated.

Chronification of disease happens due to immunomodulatory mechanisms dependent on cell-mediated immunity (Boros et al. 1975) results in progressive reduction and organization of the granulomas (Raso & Neves 1965).

LABORATORIAL DIAGNOSIS

Untill recently, acute schistosomiasis diagnosis was only based on epidemiological and clinical features, presence of *S. mansoni* eggs in stools and eosinophilia. Many times this situation consists on a challenge to physicians, since chronic infected patients from an endemic area may present an adjacent disease with a clinical picture similar to the acute schistosomiasis.

Different patterns of specific humoral responses have been described for acute and chronic schistosomiasis. Although IgG, IgM and IgE responses against egg and worm antigens using indirect immunofluorescence were shown to be equivalent in acute, intestinal, hepatointestinal and hepatosplenic patients (Kanamura et al. 1979), the higher levels of IgG, IgM and IgE anti-cercariae adult worm antigens ratios in acute patients disclosed serological differences antigen-stage related between different clinical phases (Lunde & Ottesen 1980). Indeed, the presence of a circulating cercariae 41 KD molecular weight glicoprotein antigen was detected in experimentally infected mice as soon as three days after infection while increased levels of IgM levels to this antigen were detectable since one week post-infection (Hayunga et al. 1986).

High IgA responses to the gut associated antigens in acute as compared to the chronic schistosomiasis using sections of liver granulomata (Kanamura et al. 1979) and paraffin sections of adult worm and by an indirect immunofluorescence technique been previously shown (Kanamura et al. 1991). High levels of IgA1 against adult worm and egg antigens have been demonstrated in a small number of recently infected patients by Evengard et al. (1990).

More recently, the high levels of IgG and IgM response antikeyhole limpet hemocyanin (KLH) were shown to be a diagnostic simple and useful tool for the acute and chronic differentiation achieving high sensitivity and specificity for *S. hematobium* (Mansour et al. 1989), *S. mansoni* (Alves Brito et al. 1992) and *S. japonicum* (Yusheng et al. 1994). It has been demonstrated the existence of a shared carbohydrate epitope between the 38 KDa antigen which is expressed at the miracidia and schistosomula surface and the KLH (Dissous et al. 1986). Based on anti-SEA and anti-KLH detection dipsticks dot-ELISA and dot-DIA (dot-dye immunoassay) tests for the serological differentiation of acute and chronic forms were successfuly described, presenting efficacies of 90.2%, 89.0% respectively compared to an efficacy of 92.7% of the ELISA test using the same antigens (Rabello et al. 1993).

The diagnostic usefulness of the detection of circulating IgA anti-SEA in ELISA for the serological differentiation between acute and chronic clinical forms has been recently stablished. Sensitivity and specificity proved to be as high as 100% for the acute serological definition. Moreover, it has been found that the specific immune response of anti-KLH antibodies and anti-SEA IgA and IgM antibodies correlate with morbidity allowing for age and levels of water contact (Rabello et al. 1995).

Abdominal Ultrasonography - The usefulness of the abdominal ultrasonography on the diagnosis of acute schistosomiasis was recently described (Lambertucci et al. 1994, Rabello et al. 1994). The most typical sonographic findings of acute clinical schistosomiasis mansoni are hepatosplenomegaly and periportal and peripancreatic lymphadenomegaly. Peri-portal lymphnodes may be seen surrounding the portal vein and the hepatic artery in the hepatic hilus. Size of peri-portal lymph nodes varies from 10 x 5 to 36 x 12 mm. They are round or ovoid, sharply delimited, with thin surrounding hypoechoic halus and internal medium intensity echos. The liver presents homogeneously enlarged in all acute patients. All chronic control patients presented a normal liver echogenicity. The spleen is enlarged with a diffusely increased echogenicity in all acute patients, presenting preserved shape and contours. No lymph nodes can be seen in the chronic and non-infected control groups. The sonographic aspects of lymph nodes, liver and spleen are not specific and can also be

also be seen in other infectious diseases such as acute hepatitis and other viral diseases with mesenteric adenitis. The differential sonographic aspects of acute schistosomiasis is detailed discussed elsewhere (Rabello et al. 1994).

TREATMENT

Hospitalization may be necessary for patients presenting the more severe clinical manifestations. Intense toxemia, fever, vomits and diarrheia frequently provoque dehydratation. Clinical support and strict attention should be provided to the acutely infected patient.

Reduced therapeutic efficacy of schistosomicides drugs during acute disease has been inputed to their relatively inactivity against immature worms. However, althoug the majority of these drugs are relatively inative in mice three to four weeks after infection, at the earliest stage of patency (five to six weeks after infection) high cure rate is achieved (Sabah et al. 1986). Thus when diagnosis of the infection through detection of *Schistosoma* eggs in the feces becomes possible the antischistosomal action of usual drugs is similar to that observed in the chronic stage. Patency was shown to happen between 45 and 48 days after infection in baboons (Damian et al. 1992)

Different rates of cure from 45% in children (Lambertucci et al. 1988) to 90% in adults (Katz et al. 1983) have been observed with the use of oxamniquine for the acute schistosomiasis. Praziquantel offerred 90% of cure rate in a series of adult patients treated three months after infection (Katz et al. 1983). In a recent opportunity, therapeutical efficacy of 85.7 % of 14 patients in the acute patent phase treated with oxamniquine (20 mg/kg of body weigh) was observed (Rabello et al. 1995). One patient from this group had been treated with praziquantel (60 mg/kg of body weigh) in association with prednisone (1 mg/kg/day for five days beggining two days before oxamniquine) 37 days after water contact based on clinical-epidemiological features. He presented symptoms and *S. mansoni* eggs in his stools 60 days after treatment. Retreatment with oxamniquine alone was efficient at this occasion.

Severe adverse reactions have been observed in some occasions when the patient with the acute phase was treated with niridazole, hycanthone or praziquantel (Bogliolo 1958, Harries & Cook 1987, Chapman et al. 1988). Some authors suggest that clinical deterioration after treatment could be due to the liberation of antigens from the dead worms and consequent increased formation of immune complexes (Harries & Cook 1987).

A number of case reports refer to an improvement of symptoms with the use of steroids during this stage of the disease (Gelfand et al. 1981, Farid et al. 1989) and some authors recommend the administration of prednisone associated with schistosomicides (Lambertucci et al. 1989). Contrary opinion refers to that possible deleterious effect with the use of dexamethasone has been observed (Raso & Neves 1965). Steroids can reduce the size of liver granuloma during the acute diasease in mice (Lambertucci et al. 1989). Although there is no case-control study available in the literature it seems that for the most severe clinical presentations the use of steroids for a short period of time reduces the systemic and allergic manifestations.

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