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ACUTE SCHISTOSOMIASIS: CLINICAL, DIAGNOSTIC AND THERAPEUTIC FEATURES

J. R. LAMBERTUCCI

SUMMARY

Three distinct syndromes caused by schistosomiasis have been described: cercarial dermatitis or swimmer's itch, acute schistosomiasis or Katayama fever, and chronic schistosomiasis. Complications of acute schistosomiasis have also been reported. The absence of a serological marker for the acute stage has hindered early diagnosis and treatment. Recently, an ELISA test using KLH (keyhole limpet haemocyanin) as antigen, has proved useful in differentiating acute from chronic schistosomiasis mansoni. Clinical and experimental evidence indicate that steroids act synergistically with schistosomicides in the treatment of Katayama syndrome. In this paper, clinical, diagnostic and therapeutic features of acute schistosomiasis are updated.

KEY WORDS: Acute schistosomiasis; Oxamniquine; Praziquantel; Corticosteroids.

CLINICAL ASPECTS

Acute schistosomiasis or Katayama fever is a serum sickness-like syndrome that occurs four to nine weeks after infection. This period coincides with the onset of egg production. In some patients, though, a pre-egg-laying phase has been described, where symptoms and signs of the acute stage are present, together with a nonspecific hepatitis [6].

Acute schistosomiasis is most marked in primary infection in non-immune individuals. Among people living in endemic areas the acute phase may pass undiagnosed. It has been suggested that in endemic conditions exposure to infection occurs early in life, symptoms would be inconspicuous and diagnosis not suspected. Acute schistosomiasis superimposed on chronic *S. japonicum* or *S. mansoni* has been reported [5, 8, 18, 30, 38].

Symptoms of the acute phase are due to hypersensitivity [13]. Large-sized immune complexes, usually cleared by reticuloendothelial cells, are probably responsible for hypertrophy of lymphoreticular tissue and other signs and symptoms of this stage [27].

The most common manifestations are fever, chills, weakness, weight loss, headache, anorexia, nausea, vomiting, diarrhoea, dry cough, hepatosplenomegaly, and eosinophilia. A small proportion of patients also have bloody diarrhoea, urticaria, periorbital oedema, bronchospasm and mental dullness [20]. Erythematous or purpuric lesions on the skin have been described on rare occasions [3].

Symptoms last for a few weeks to two or three months and gradually abate without therapeutic intervention. No evidence of renal disease has been found in patients with acute schistosomiasis. Heavy primary infection in non-immune individuals can rarely be fatal.

Address for correspondence: Prof. J. R. Lambertucci' Department of Internal Medicine, Federal University of Minas Gerais 30.130-100 Belo Horizonte, MG, Brazil.

LAMBERTUCCI et al [26] described 2 patients with acute schistosomiasis that developed multiple pyogenic liver abscesses caused by *Staphylococcus aureus*. They also reproduced the syndrome in mice concomitantly infected with both agents. Their patients were children, and they had had skin pustules beginning some time before the appearance of symptoms of liver abscesses. Except for the presence of striking pain on the right side of the abdomen, the symptomatology, reported by both patients, was that found in acute schistosomiasis. Eosinophilia was absent at the time of the diagnosis but reached high levels after successful treatment with antibiotics. Another 10 similar cases have been examined by the author since the first report in 1990.

DIAGNOSTIC ASPECTS

The finding of necrotic-exudative granulomata in liver biopsy has been used to define the diagnosis of Katayama fever in doubtful cases [5] (Figure 1).

Other helpful data include: epidemiological (recent contact with stream water in a schistosomiasis endemic area); clinical (acute enterocolitis, high fever, toxaemia, hepatosplenomegaly), laboratory studies (eosinophilia above 1000/mm^3 in leucocyte differential count, and viable schistosome eggs in stool). Excluding the characteristic granuloma in liver histology, the other findings are nonspecific. Typhoid fever, brucellosis, mononucleosis, miliary tuberculosis, visceral larva migrans, and Churg-Strauss disease may resemble acute schistosomiasis. In addition, patients with less well-defined clinical pictures (low fever, few bowel movements, non-toxaemic), moderate eosinophilia and/ or with negative stool examination for parasite ova may pass unnoticed [11]. Faecal examination is superior to rectal biopsy in acute schistosomiasis. In light infections, however, when parasitological stool examination failed in disclosing eggs of the parasite, rectal biopsy should be tried.

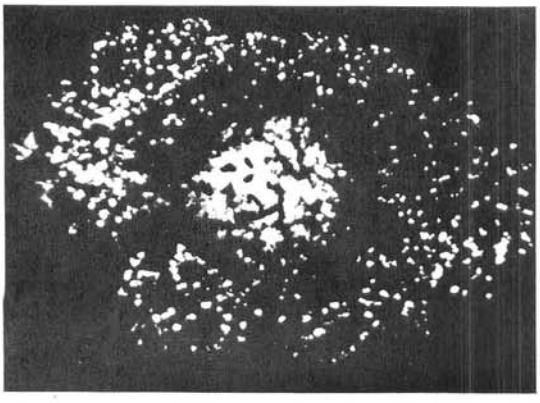

Fig. 1 - Immunofluorescence of a necrotic-exudative granuloma in the liver of a patient with acute schistosomiasis. Anti-human IgA labelled with fluorescein (250x).

Although acute and chronic schistosome infections can be distinguished serologically on the basis of specific immunoglobulin and immunoglobulin ratios [17, 31], a rapid and simple test specific for acute schistosomiasis is not yet available.

In 1989, MANSOUR et al. [28] demonstrated that an ELISA test using KLH (keyhole limpet haemocyanin) as antigen was efficient in differentiating acute from chronic schistosomiasis in patients living in endemic areas of Egypt. The haemocyanin of the keyhole limpet (*Megathura crenulata*), shares a well defined carbohydrate epitope with the surface of *S. mansoni* schistosomula [14]. The good results reported for Egypt have been reproduced in Brazil using the same antigen and methods [1]. These findings represent an important advance in the clinical diagnosis of acute schistosomiasis.

Sonography of the liver is an excellent technique to demonstrate periportal fibrosis in hepatosplenic schistosomiasis [32]. In acute schistosomiasis, however, ultrasonographic findings are nonspecific and similar to those found in other systemic infectious diseases: hepatomegaly, splenomegaly and increase in the size and in the number of intra-abdominal lymph nodes.

THERAPEUTIC ASPECTS

Four main approaches have been proposed for the treatment of acute schistosomiasis:

1). ***Wait for the chronic stage.*** Due to the low efficacy of all schistosomicides in the toxaemic phase of schistosomiasis, some authors [5, 16] have suggested that specific treatment should be postponed until the disease has entered its chronic stage. This recommendation was introduced before the advent of the new schistosomicides, praziquantel and oxamniquine. The toxic effects of antimonial drugs, niridazole and hycanthone justified the viewpoint that treatment would be disadvantageous for patients with toxaemia. In fact, many patients with acute schistosomiasis died during treatment with antimonials [4, 38].

2). ***Use of schistosomicides alone.*** Oxamniquine and praziquantel are potent schistosomicidal agents against mature *Schistosoma mansoni* in man [25, 37]. They have also been used for the treatment of acute schistosomiasis [4]. A reduced efficacy of these drugs against immature worms in experimentally infected mice has been demonstrated [29, 35]. In at least two reports it has been suggested that treatment with praziquantel alone aggravates the clinical picture of acute schistosomiasis [7, 16].

LAMBERTUCCI [22, 23] gave oxamniquine to 19 patients with acute toxaemic schistosomiasis mansoni (55-77 days after infection) and only nine (47%) were cured (parasitological stool negativation in a follow-up of six to 10 months post-treatment). Eight out of nine patients, later on considered to be cured, continued to present signs and symptoms of acute schistosomiasis for 8 to 15 days after treatment (Figure 2); similar findings have been reported by DIAZ-RIVERA et al. [9] for antimonials. KATZ et al [19] treating patients recently infected but asymptomatic on the occasion of treatment (90 days after infection), reported cure rates of more than 90% for oxamniquine or praziquantel.

Schistosomicides alone should be given only to asymptomatic or paucisymptomatic patients.

3). ***Steroids alone.*** Mice experimentally infected with *S. mansoni* and treated with corticosteroids alone do not form granuloma around *S. mansoni* eggs and develop diffuse and severe hepatitis, and mortality is high in the infected group [24, 34].

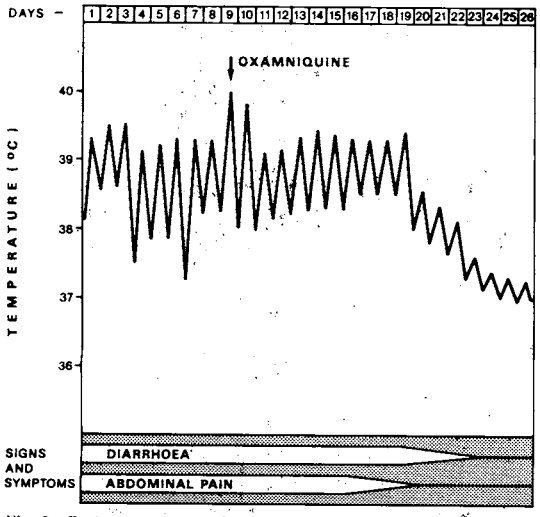

Fig. 2 - Body temperature, signs and symptoms in acute schistosomiasis before and after treatment with oxamniquine.

Three patients with acute schistosomiasis treated with dexamethasone by NEVES [34] died during treatment or some time after stopping the steroid. The deaths were linked to the use of steroids and in the author's opinion, corticosteroids should not be used alone in the treatment of acute schistosomiasis.

In a more recent report [21], a patient with cerebral schistosomiasis (*S. japonicum*), during the acute stage, was treated with corticosteroid alone; all neurological alterations disappeared. In such cases, however, the use of schistosomicides in conjunction with corticosteroids is recommended. Schistosomicides eradicate adult worms living in sites close to the central nervous system and in other organs, thus preventing further deposition of eggs.

4). ***Association of steroids and schistosomicides.*** Clinical and experimental evidence indicate that steroids act synergistically with schistosomicides in the treatment of Katayama syndrome [24]. In one study [23], the association of prednisone (1 mg/kg body weight for one week, beginning one day before oxamniquine, followed by 0.5 mg/kg during the second week and 0.25 mg/kg in the third week) with oxamniquine resulted in rapid improvement of acute schistosomiasis and raised the index of cure above 90%. Signs and symptoms of acute schistosomiasis disappeared 24 to 48 hours after starting prednisone (Figure 3). Similar results have been reported for praziquantel [12]. The association of steroids with schistosomicides in the treatment of acute toxaemic schistosomiasis augment cure rates, speed the recovery time (reducing the demand for inhospital treatment) and improve the quality of medical care.

NEUROSCHISTOSOMIASIS

Neurological symptoms occasionaly appear during Katayama syndrome. Fever with eosinophilia is usually present. Patients may become confused, develop focal or generalized seizures or become stuporose [8]. Visual impairment and papilloedema may occur; more rarely, other signs of encephalopathy such as hemiplegia and opisthotonus with extensor plantar responses. Evidence of mielopathy has included ataxia, weakness of the legs, paraestesiae, sensory loss and sphincter disturbances. Usually, when the Katayama syndrome subsides, or after specific treatment, the central neurological symptoms disappear.

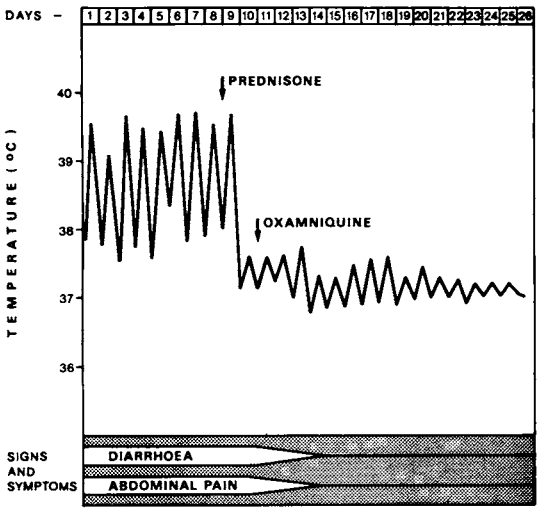

Fig. 3 - Body temperature, signs and symptoms in acute schistosomiasis before and after treatment with prednisone followed by oxamniquine.

There have been several reports of successful recoveries after treatment of cerebral or spinal schistosomiasis with antischistosomal drugs. Oxamniquine and praziquantel are the agents available to treat *S. mansoni* infection [10, 36]. Steroids are used to suppress the host response around the ectopic eggs [4].

The administration of corticosteroid drugs in the early stages of myelopathy, ie, within the first few days or weeks following the appearance of neurological symptoms, can markedly improve the clinical picture, even before schistosomicidal treatment is started [21], and patients often make a full recovery. A reduction of the inflammatory reaction to schistosomal ova is only effective before nervous tissue destruction by necrotic-exudative granulomata has occurred. When administered many weeks or months after the initial neurological symptoms, steroids do not significantly alter the evolution of the disease.

Prompt diagnosis and treatment with schistosomicides plus steroids leads to recovery; residual defects may occur in cases which have gross pathology at presentation. Because of the potential benefit of the recommended therapy, presumptive treatment of patients with diagnosis of neuroschistosomiasis and histories of water exposure in endemic areas should be initiated while awaiting results of parasitologic or serologic tests [15, 33].

RESUMO

Esquistossomose aguda: aspectos clínicos, diagnósticos e terapêuticos

A esquistossomose apresenta-se clinicamente em três formas distintas: dermatite cercariana, esquistossomose aguda ou febre de Katayama e esquistossomose crônica. Há na literatura relatos de complicações da fase aguda. A ausência de um marcador sorológico simples e confiável tem dificultado o diagnóstico precoce e, como consequência, o tratamento adequado de pacientes na fase aguda da doença. Recentemente, o teste de ELISA, realizado com o antígeno KLH (hemocianina do caramujo *Megathura crenulata*), tem se mostrado util na identificação dos pacientes com febre de Katayama. Evidências clínicas e experimentais apontam no sentido de uma ação sinérgica entre os corticosteróides e os esquistossomicidas no tratamento da esquistossomose toxêmica. Neste artigo, alguns aspectos clínicos, diagnósticos e terapêuticos da esquistossomose aguda são atualizados.

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