Treatment of Schistosomiasis: Gathering Stones Together

JR Lambertucci

Departamento de Clínica Médica, Faculdade de Medicina da UFMG,
Av. Alfredo Balena 190, 30130-100 Belo Horizonte, MG, Brasil

In this paper the treatment of schistosomiasis is examined under the following headings: cercarial dermatitis, Katayama fever, schistosomiasis in the immunosuppressed host and treatment of therapeutic failures.

Key words: schistosomiasis - praziquantel - oxamniquine - corticosteroids

CERCARIAL DERMATITIS

Cercarial dermatitis results from incomplete infection by small mammal or avian schistosomes and occurs in immune populations from endemic areas following heavy reexposure to *Schistosoma mansoni* (Amer 1982)

Schistosome dermatitis is difficult to distinguish from other forms of dermatitis. The lesions are commonly confused with those of contact dermatitis, poison ivy, scabies, impetigo, and insect bites.

This stage also includes migration and development of the schistosomes and symptoms may start as early as two or three days after infection with fever, pulmonary symptoms (cough) and infiltrates, myalgia, abdominal pain, eosinophilia and moderate splenomegaly (Pedroso et al. 1984).

The diagnosis of schistosomiasis at this stage is quite difficult. Treatment is usually not needed. Palliative topical agents, e.g., corticosteroids creams can be applied, and in severe cases, oral or parenteral antihistamines can be administered. There have been no clinical reports on the efficacy of schistosomicides at this stage but experimental work in mice supports the viewpoint that praziquantel, oxamniquine or steroids when given during the first week of infection, in the usual doses, are efficient in aborting the development of the worms (Coker 1957, Harrison & Doenhoff 1983, Sabah et al. 1986).

TREATMENT OF ACUTE SCHISTOSOMIASIS (KATAYAMA FEVER)

Four main approaches have been proposed for the treatment of acute schistosomiasis (Fig. 1): (1)

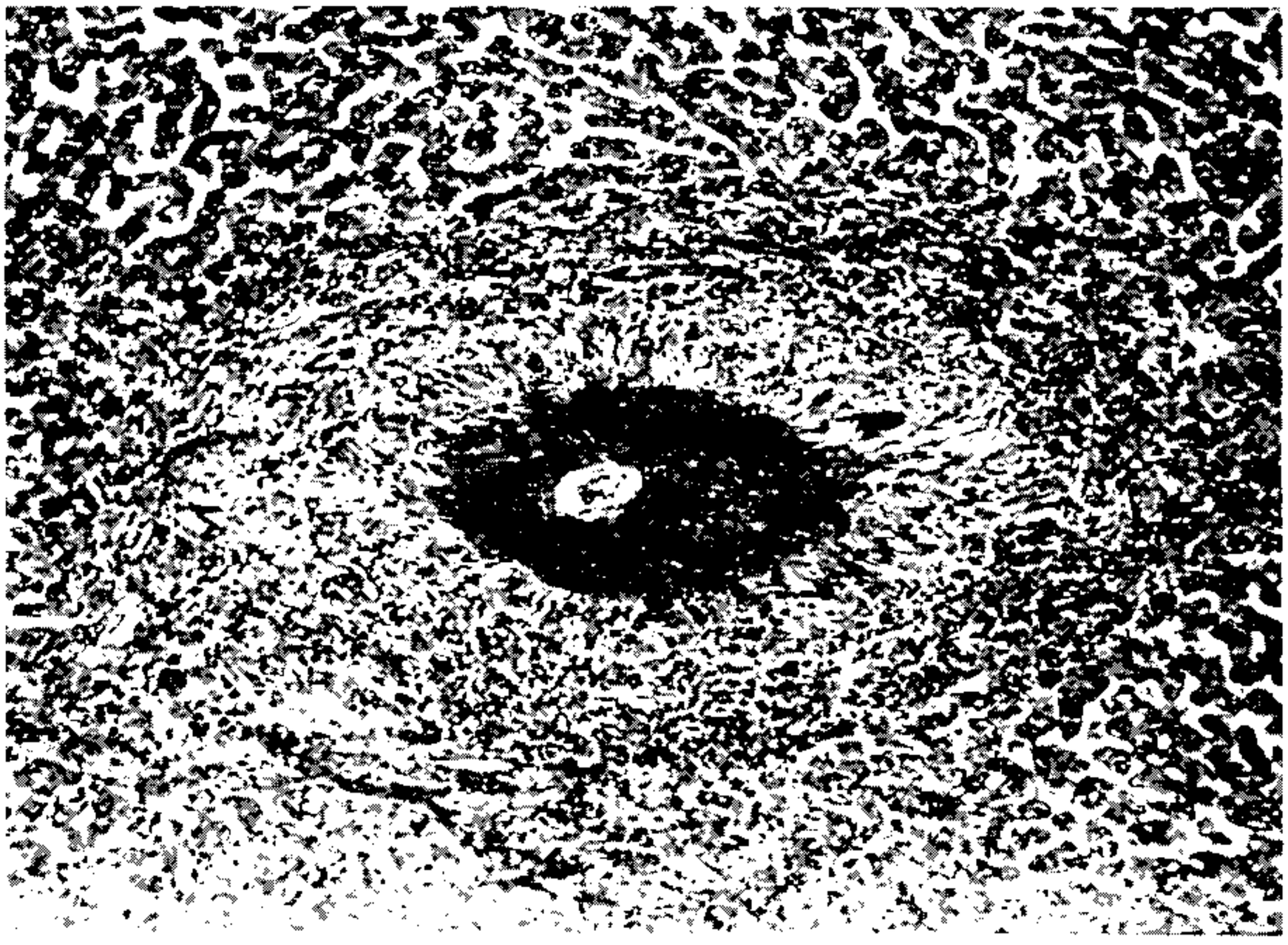

Fig. 1: a necrotic-exudative granuloma in the liver of a patient with acute schistosomiasis.

Wait for the chronic stage - Due to the low efficacy of all schistosomicides in the toxaemic phase of schistosomiasis, it has been suggested that specific treatment should be postponed until the disease has entered its chronic stage (Lambertucci 1993); (2) *Use of schistosomicides alone* - Oxamniquine and praziquantel are potent schistosomicidal agents against mature *Schistosoma mansoni* (Lambertucci et al. 1982). They have also been used for the treatment of acute schistosomiasis. A reduced efficacy of these drugs against immature worms in experimentally infected mice has been demonstrated (Sabah et al. 1986). In at least two reports it has been shown that treatment with praziquantel alone aggravates the clinical picture of acute schistosomiasis (Harries & Cook 1987, Chapman et al. 1988). Schistosomicides alone should be given only to asymptomatic or paucisymptomatic patients (Lambertucci et al. 1980); (3) *Steroids alone* - Mice experimentally infected with *Schistosoma mansoni* and treated with corticosteroids alone form incomplete granulomas around *S. mansoni* eggs and develop diffuse and severe hepatitis, and mortality is high in the infected group. Steroids should not be used alone in the treatment of acute schistosomiasis (Neves & Raso 1963); (4) *Association of steroids and schistosomicides* - The association of steroids and 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 (Lambertucci et al. 1989).

THE IMMUNE DEPENDENCE OF CHEMOTHERAPY

The number of people immunosuppressed by drugs (cytotoxic chemotherapy, other imunosuppressive agents including steroids and irradiation) or affected by diseases that cause immunodepression (AIDS, neoplasia, malnutrition, chronic renal failure) is growing fast. In thc immunocompromised host there have been changes in the approach to most associated infectious diseases.

Data on the behaviour of schistosomiasis mansoni in the immunosuppressed host are rather few (Hillyer & Cangiano 1979, Doenhoff et al. 1986, 1991, Hillyer & Climent 1988).

Immunosuppressed individuals tend to have disseminated infection with *S. mansoni* (eggs) involving lung, liver, spleen, intestine, pancreas, and testis (Hillyer & Climent 1988, Lambertucci & Neves 1993). The migration of worms to different organs in the human body may explain the finding of a great number of eggs in unusual places. This hypothesis implies that the immune system is important in keeping the adult worms of *S. mansoni* confined to the mesenteric vessels.

The efficacy of schistosomicides, in mice infected with *S. mansoni* and immunosuppressed by thymectomy and administration of rabbit anti-mouse thymocyte serum, is decreased. The schistosomicidal power of antimony, oxamniquine, and praziquantel is enhanced by passive transfer of immune serum simultaneously with drug administration to *S. mansoni*-infected mice, thus indicating a role for humoral immune effector mechanisms in this phenomenon (Brindley & Sher 1987, Lambertucci et al. 1989). Modha et al. (1990), using scanning and transmission electron microscopy, examined the immunodependence of praziquantel for the treatment of schistosomiasis mansoni in mice. The damage seen in male parasites harvested from mice that had been treated with praziquantel plus rabbit immune serum was more dramatic than that observed in worms from mice given either treatment alone (Fig. 2).

Failure to respond to oxamniquine or praziquantel, in the usual doses, is to bc expected in the immunocompromised host infected with *S. mansoni*. Most infections in patients with AIDS, for example, have been treated with higher doses of chemotherapeutic agents and they have also been given for longer periods of time.

If it can be proven that the immune status of human patients influences the outcome of chemotherapy in the manner described for rodent models of schistosomiasis, there would be a strong case for the development of a vaccine that would enhance the efficacy of schistosomicidal drugs (Doenhoff et al. 1991).

TREATMENT OF THERAPEUTIC FAILURES

The approach to patients infected with *S. mansoni* who did not respond to previous treatment for schistosomiasis is still unsettled. In order to minimize the risk of the development of drug resistance, Katz and colleagues (1991) have suggested that infected patients should be treated with one drug, and therapeutic failures with another.

Although isolated cases of oxamniquine resistance have been reported (Dias et al. 1982), a community with a serious problem of resistance has not yet been described. There are no similar reports for tolerance or resistance in *S. mansoni* infected individuals to praziquantel.

Lambertucci and Carvalho (unpublished data) treated 220 children (ages 7 to 14), infected with *S. mansoni* in Brazil, with oxamniquine (20 mg/kg/body weight, single dose). Those children still passing eggs 1-3 months after therapy received oxamniquine again. Therapeutic failures were retreated three times during the following 9 months. Two successive quantitative stool examinations were performed after each treatment. Eight chil-

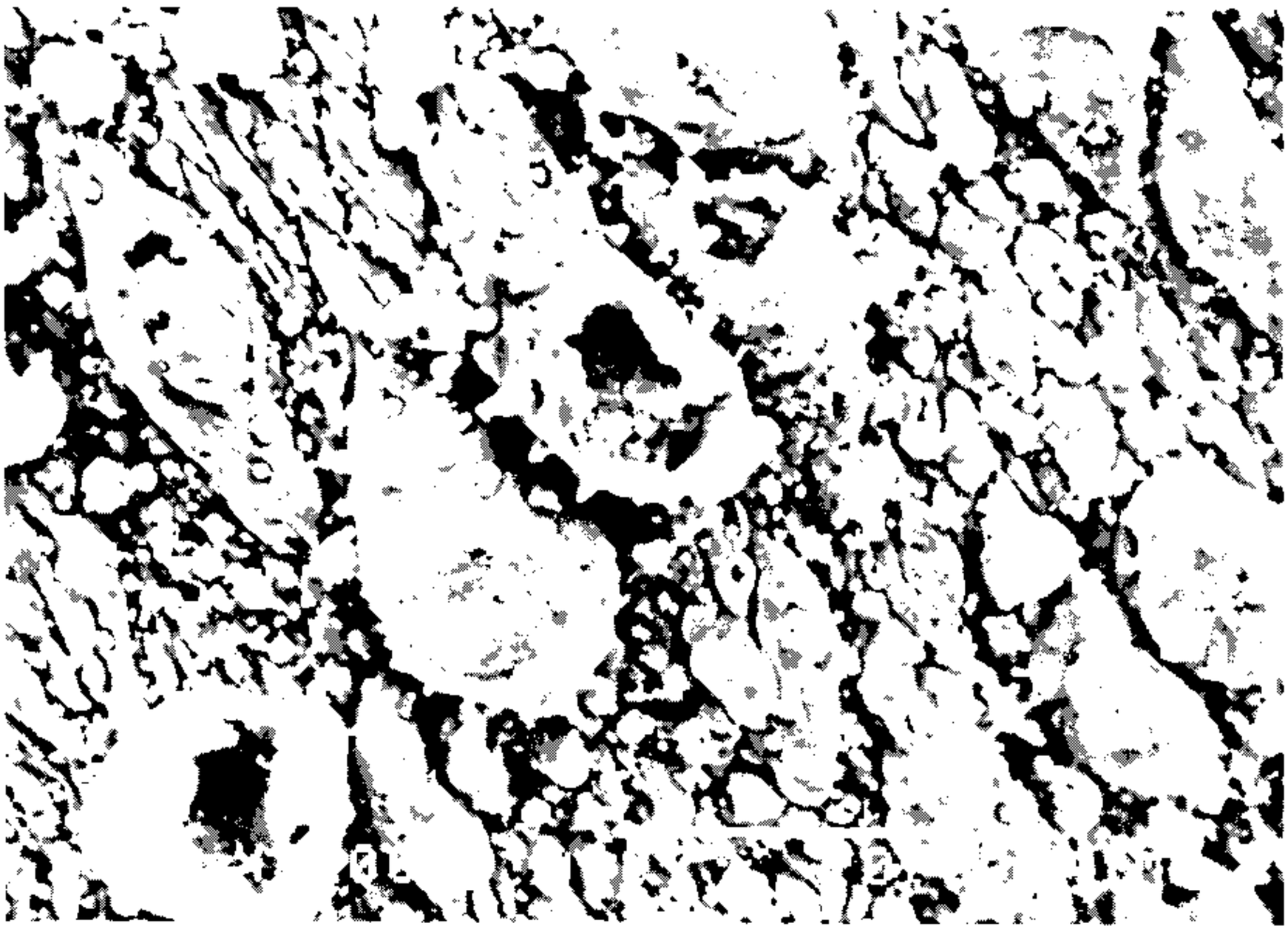

Fig. 2: scanning electron micrograph showing exploded surface protuberances on the dorsal tubercles of a worm harvested from a mouse treated with praziquantel and immune serum.

dren presented viable eggs of the worm in their stools after the fourth treatment with oxamniquine. The percentage reduction in egg counts in children not cured was above 80%. Our data suggest that repeat treatment with oxamniquine is curative in most children infected with *S. mansoni* in Brazil.

Other well-designed prospective studies are needed to define the best approach to therapeutic failures in patients with schistosomiasis mansoni.

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