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SCHISTOSOMA MANSONI: IMMUNODEPRESSION OF HEPATIC SCHISTOSOME GRANULOMA FORMATION IN MICE INFECTED BY *TRYPANOSOMA CRUZI* *

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Infection by Trypanosoma cruzi *in mice depresses hepatic granuloma formation around* Schistosoma mansoni *eggs. This immunodepressive effect occurred in mice with Chagas' disease at the acute and/or chronic phases, granulomas being significantly smaller than those in controls. Data suggest that Chagas' disease depresses the delayed hypersensitivity immune response directly.*

Key words: *Schistosoma mansoni.* Immunodepression. Granuloma. *Trypanosoma cruzi.*

Immunodepression during infection by *Trypanosoma cruzi* was first described by Clinton et al.[5], who noted a reduction of early response of antibodies to donkey red blood cells in infected mice. Later, depression of immune response to different antigens in mice infected by *T. cruzi*[17 18] and in men[22] was demonstrated. The mechanisms of this immune depression in Chagas' disease have been studied by a number of authors[6 8 21]. Macknika and Choromanski[14] showed that *T. cruzi* induces nonespecific immunodepression in mice reducing humoral and cellular response to antigens of *Hymenolepis diminuta.* A marked depression of humoral and cellular response coincidently with the peak of parasitemia occurs during the acute phase of infection by *T. cruzi*[7].

In the present study we studied the effect of infection by *T. cruzi* (acute and chronic phases) on granuloma formation in mice with concomitant infection by *Schistosoma mansoni.*

MATERIAL AND METHODS

Swiss albino mice weighing 18-20 g were used. *S. mansoni* cercariae (LE strain, coming from Belo Horizonte, Brazil) were obtained from *Biomphalaria glabrata*[13 16]. Mice were inoculated with about 40 cercariae subcutaneously. Three strains of *T. cruzi* were used: Y strain[20], CL strain[4], and Colombian strain[12]. Induction of the chronic phase in CL and Colombian strains was performed according to Brener and Chiari[3]. An inoculum of about 1 x 10^4 blood trypomastigotes, given by the intraperitoneal route, was the standard challenge. Using these methods, granuloma formation was studied in two groups of mice: a) infected by both *S. mansoni* and *T. cruzi*; b) infected by *S. mansoni* only. Control groups of uninfected animals and those only infected with *T. cruzi* were maintained concurrently.

In experiment I, designed to study the effect of acute phase of Chagas' disease on schistosome granuloma formation, 20 mice were inoculated with *S. mansoni.* On the 43rd day after infection, 10 out of those 20 mice, plus 10 normal ones, were inoculated with *T. cruzi* (Y strain). Since this strain is highly virulent, with a high mortality rate after the peak of parasitemia, this experiment was of short duration.

In experiments II and III, mice chronically infected by *T. cruzi* (CL and Colombian strains), and their respective controls, were distributed in 4 different groups. At 98 and 185-day-intervals after infection by *T. cruzi* animals from groups A and C were infected by *S. mansoni.*

At the end of each experiment, surviving mice were killed and necropsy performed. Snips from the liver of infected mice were fixed in 10% formol-saline, embedded in parafin, sliced into sections of 5 µm thickness (with a 500 µm interval), and stained with Hematoxilin-Eosin. The size of each granuloma was determined by the measure of two diameters intersecting at right angle, by means of an ocular micrometer.

RESULTS

Table 1 shows the mean diameter of schistosome granulomas in the liver of mice from group A (*S. mansoni* + *T. cruzi* and group C (*S. mansoni* only) in

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Table 1 – *Diameter of hepatic granulomas in mice with concomitant infection by* Trypanosoma cruzi *and* Schistosoma mansoni

Phase of infection by T. cruzi	*Strain*	*Interval between infections (days)*	*Duration of infection by* S. mansoni *(days)*	*Duration of infection by* T. cruzi *(days)*	*Mean diameter of granulomas (μm)**		*% reduction of granulomas in size*	*Student's t test*
					Group A T. cruzi+S. mansoni	*Group B* S. mansoni only		
I acute	Y	43	54	11	164.5±5.3	324.5±4.5	49.3	$P < 0.001$
II chronic	CL	68	62	130	195.7±5.9	368.8±11.1	46.9	$P < 0.001$
III chronic	Colombian	185	135	320	192.5±15.6	305.9±49.0	37.0	$P < 0.01$

* Mean diameter of granulomas of five mice (measured 40 granulomas per animal)

the three experiments. As can be seen, the diameters of granulomas in *T. cruzi* infected animals are significantly smaller than those in controls, with a reduction rate varying from 37 to 49.3% from the normal size of granulomas in control group.

DISCUSSION

Granulomatous reactivity around *S. mansoni* eggs has been demonstrated to be a form of delayed cell-mediated hypersensitivity[24]. These authors showed that this kind of hypersensitivity could be transferable to non-infected mice with lymphnode cells or the spleen of immune animals, but not with serum. This hypothesis was reinforced by suppression of schistosome granuloma formation in mice, using effective techniques against delayed cell-mediated reaction, such as immunodepressive drugs[11], neonatal thymectomy[9], heterologous antilymphocytic serum[10] moderate or severe disease like Hodgkins[23], and antimacrophage serum[2]. Abdel-Wahab et al.[1] first demonstrated that parasitic infections such as *Plasmodium yoelii* had direct influence on granulomatous reactivity around *S. mansoni* eggs reducing the size of granulomas. Later, Mahmoud et al.[15] verified that infection by *Toxoplasma gondii* also induced a marked reduction of schistosome granuloma in size.

In the present investigation, infection by *T. cruzi* produced an intense effect on schistosome granuloma size. Depression of the delayed hypersensitivity immune response was showed by reduction of hepatic granulomas in size occurring in mice infected by *T. cruzi* (Y strain) at the acute phase. This finding agrees with those of Rowland & Kuhn[19] and Costa[7], who verified depression of cellular response by *T. cruzi* at the acute phase of infection. Further, it shows that such immunodepression also appears in Chagas' disease during the chronic phase, as observed with CL and Colombian strains of *T. cruzi*.

RESUMO

A infecção de camundongos pelo *Trypanosoma cruzi* inibe a formação do granuloma hepático esquistossomótico. Este efeito imunodepressor ocorreu em camundongos com a fase aguda ou crônica da doença de Chagas, sendo os granulomas significativamente menores que nos animais controles. Os dados sugerem que a doença de Chagas deprime diretamente a imunidade celular.

Palavras chaves: *Schistosoma mansoni*. Imunodepressão. Granuloma. *Trypanosoma cruzi*.

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