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ARTÍCULO ORIGINAL

Role of interferon - γ on the immunosuppression during Toxoplasma gondii ***infection by*** *Trypanosoma lewisi*

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ABSTRACT

On the basis of previous studies on ***Trypanosoma lewisi*** *immunosuppression model groups of 5 Wistar rats were infected with.* ***T. gondii*** *and* ***T. lewisi*** *according to the following protocol. One group was inoculated i.p. with 10^6* ***T. lewisi*** *tripanomastigotes and 4 days later with 10^7* ***T. gondii*** *tachyzoites. The second and third groups were infected only with* ***T. lewisi*** *or* ***T. gondii*** *respectively. The fourth group was not infected and served as control. Rats were bled before the infection and then every day for seven days. Serum samples were collected and the levels of IFN-γ, IL-2 and TNF-α were measured. The results indicates that the level of IFN-γ is very high 24 hour after infection in rats inoculated with* ***T. gondii*** *only, while in those animals infected with both parasites (first group), IFN-γ was not detected 24 hours after infections with* ***T. gondii****. These data give evidence that a reduction of IFN-γ levels is one of the reasons for the immunosuppressive effect induced by* ***T. lewisi****, increasing* ***T. gondii*** *multiplication in an animal as the rat, which is remarkable resistant to this parasite.*

Key words: *Interferon γ , immunosuppression,* ***Toxoplasma gondii, Trypanosoma lewisi****, white rats natural resistance.*

INTRODUCTION

Immunosuppression events have been observed after infection with *T. brucei*[1], *T. congolense*[2] and others[3], as well as in tripanosomes from rodents[4,5]. It appears that citokines play an important role in this effect, specially IFN-γ, TNFα factor and IL-10[1,3,6].

We have observed that infection of white rats with *T. lewisi* makes these animals, which usually are very resistant to *T. gondii* infections[7], as susceptible as mice, either in *vivo* or *in vitro*[8,9].

According to these observations, the present study was performed in order to determine the role of INF-γ, IL-2 and TNFα in the immunosuppression effect exerted by *T. lewisi* against *T. gondii* infections.

MATERIAL AND METHODS

Wistar white rats (150-200 g body weigth) obtained from the Animal house of the México

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Hospital were caged in 4 groups of 5 animals each. Rats of the first group were inoculated i.p. with 10^6 *T. lewisi* tripomastigotes and 4 days later the animals were infected i. p. with 10^7 *T. gondii* (RH strain) tachyzoites. Rats of the second and third groups were infected with *T. lewisi* and *T. gondii* respectively. A fourth group was not infected and served as control. All the animals were bled from the tail vein in serum separation tubes (Becton Dickinson, Vacutainer Systems) before the infection and then every 24 h until for 7 days.

Sera were stored at -20^0 C and IFN-γ, IL-2 and TNFα determinations were done two months later. For the quantitative determination of rat IFN-γ, IL-2 and TNF-α concentration in serum, a quantitative ELISA technique (Quantikine^R M murine, R & D Systems, Minneapolis, MN, USA) was used.

RESULTS AND DISCUSSION

Figure 1 shows that in the animals infected only with *T. gondii*, there were high IFN-γ levels starting at 24 h after infection. These values diminished to one half after 48 h. On the other hand, in rats previously infected with *T. lewisi* and then inoculated with *T. gondii* 4 days later, IFN-γ was detected only after 48 h of *T. gondii* infection. This lymphokine was not found in animals infected only with *T. lewisi.* Neither IL-2 or TNF-α were detected in the samples.

These findings appear to demonstrate that IFN-γ plays an important role in this immuno suppressive model caused by *T. lewisi.* This has also been observed in intracellular parasites[10]. Regarding to *T. gondii,* Lüder *et al*[11], made an interesting relation between the role of IFN-γ and IL-4 and their effect on the natural resistance of Lewis strain rats to this parasite.

The results showed in Figure 1 indicate an inhibitory effect of IFN-γ production apparently due to the previous presence of *T. lewisi* in *T. gondii* infected white rats. Since it has been found some immunosuppressive action exerted by *T. brucei* soluble fragments[2], it is possible that protein fractions or excretion products from *T. lewisi* could be in part responsible, of the immune phenomena observed. To this respect, Ndarathi studies[12,13] presented some promissory data. In fact they found that epimastigote extracts probably containing exoantigens of this parasite, caused immunosuppression in infected rats. Since epimastigote forms appear early in the life cycle of this parasite[14], and the effect observed in the present study occurs four days after *T. lewisi* infection, a relation between both events, immunosuppressive action and epimastigote extracts can be established. This immune effect could be the result of a INF-γ reduction after 4 or 5 days after *T. lewisi* infection and not due to an IL-2 inhibition as suggested by Ndarathi[13]. Production of IL-10 is another possibility since it has been shown that this lymphokine can be secreted as response to *T. congolense* extracts[6]. More studies on this model are currently in progress.

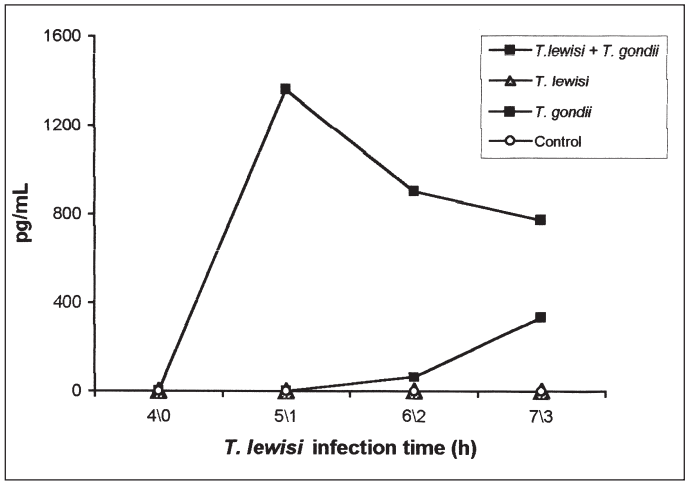

Figure 1. *T. gondii* was inoculated on day 4 after *T. lewisi* infection. 4/0 = *T. lewisi* infection time/ *T. gondii* infection time. Determination of INF gamma in rats infected with *T. gondii* or *T. lewisi.*

RESUMEN

De acuerdo con estudios anteriores, en donde se ha demostrado el efecto de inmunosupresión producido por *Trypanosoma lewisi* sobre infecciones con *Toxoplasma gondii,* grupos de 5 ratas Wistar fueron inoculadas según el siguiente protocolo. Un grupo fue inoculado i.p. con 10^6 tripomastigotos de *T. lewisi* y 4 días después con 10^7 taquizoitos de *T. gondii.* El segundo y el tercer grupo fueron inoculados sólo con *T. gondii* o con *T. lewisi* respectivamente. Un cuarto grupo no fue infectado y sirvió como control. Las ratas fueron sangradas antes de la infección y luego cada día durante 7 días. Los sueron fueron colectados para determinar la presencia de IFN-γ, IL-2 y TNF-α .El nivel de IFN-γ fue muy alto después de 24 h de infección en las ratas inoculadas únicamente con *T. gondii*, mientras que en los animales infectados con ambos parásitos (el primer grupo) el IFN-γ no fue detectado en el mismo período de infección con *T. gondii*; IL-2 y TNF-α no fueron detectados. Estos datos son una evidencia preliminar de que en este proceso de inmunosupresión, existe una reducción en los niveles deIFN-γ, inducida por *T. lewisi*, lo cual es probablemente una de las razones por las que la rata se ve disminuida en su resistencia natural al *T. gondii.*

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