QUALITATIVE AND QUANTITATIVE FEATURES OF IMMNOMODULATION OF GRANULOMAS OF HEPATIC MURINE SCHISTOSOMIASIS MANSONI

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ABSTRACT

The development and immunomodulation of hepatic granulomas formed around Schistosoma mansoni eggs was investigated in mice over a period of 32 weeks following their infection with cercariae Development of granulomas occured 6 weeks after the onset of infection. These granulomas were first large, irregular and entirely cellular, with evidence of a hypersensitivity type of inflammatory reaction, then progressively changed into fibrocellular and ultimately fibrous (healed) granulomas. In mice infected for 16 or more weeks, immunomodulation was evidenced qualitatively by the smaller size and regular contours of the recently developing granulomas as well as by an immune type of reaction, and quantitatively by failure of increase in the number of granulomas inspite of continuous trapping of eggs in the liver.

INTRODUCTION

Several investigators described the phenomenon of immunomodulation of hepatic granulomas developing around mature Schistosoma mansoni eggs in mice with prolonged infection. These modulated granulomas are characterized by their smaller sizes, round contours and their composition of a few histiocytes and fibroblasts, in contrast to the granulomas that develop during the early stages of infection which appear large, irregular and exhibit a necrotic, exudative proliferative reaction (Andrade and Warren, 1964, De Brito et al., 1984 and Grimaud et al., 1987).

The mechanisms involved in the process of immunomodulation of hepatic granulomas involve both cellular and humoral factors. Specific T-cell subsets possibly act as suppressor cells leading to modulation of the granulomatous hypersensitivity reactions (Doughty et al., 1984). Inhibition of collagen synthesis by specific lymphokines, monokines and collagenases may sometimes contribute to the process of granulomatous modulation (Wahl et al., 1974 and Jimenez et al., 1979). Suppression of the cell mediated immune response by circulating antibodies to eggs and worms is another possible factor, supported by the finding that decrease of granuloma size was coincident with higher levels of circulating antibodies (Boros et al., 1975, Oberlien and Weiss, 1977 and De Brito et al., (1983).

The present investigation was designed to delineate the process of immunomodulation of hepatic granulomas in mice infected with schistosomiasis mansoni for up to 32 weeks, through study of the duration-related qualitative and quantitative changes of the developing granulomas.

MATERIALS AND METHODS

Infection of mice and organ sampling:

Five weeks old female, CBA/J mice were obtained from the animal house of Theodor Bilharz Research Institute and infected subcutaneously with 60 cercariae of Schistosoma mansoni. Groups of 5-10 mice were sacrificed at intervals of 5,6,8,10,12,14,16,18,22,26,28 and 32 weeks after the onset of infection, making a total of 82 mice. The livers of these animals were excised, fixed in buffered formalin and processed for paraffin sections and histology using haematoxylin and eosin and Masson trichrome stains.

Morphometry of the granulomas:

Taking into consideration that the longest diameter (LD) of granuloma varies according to the plane of sectioning, estimation of the LD was restricted to those granulomas which contained an egg within or nearly within their centers. Estimation of the LD was avoided in granulomas with many or eccentric eggs and in confluent granulomas. The LD of all granulomas fulfilling the previous requirements in all liver sections of each mice group was