Liver Function and Plasma Protein Metabolism in Rodent Model of Filariasis

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Abstract

Rodent model of filariasis was developed by infecting Wistar rats with *Litomosoides carinii*. Liver function tests, plasma protein concentrations, and synthesis rates of liver-formed proteins were estimated in these rats at 63 and 90 days post-infection.

At 63 days post-infection, aspartate aminotransferase and alkaline phosphatase were significantly increased. Alanine aminotransferase, plasma total proteins and plasma albumin were in the normal range. However, at 90 days post-infection all these parameters were affected, reflecting progressive liver involvement. Hyperalbuminemia at 90 days post-infection did not appear to be due to decreased synthesis rate, indicating higher catabolism and/or altered distribution in pools.

Key words: Helminths, protein synthesis

Introduction

Some studies on the immunological changes associated with filariasis have helped in understanding the pathophysiology of this disease. However, biochemical data in hosts, both human and animal models, are scanty. A definite evidence associating filariasis with liver dysfunction is lacking, even though the passage of the nematode parasites through the host may indirectly affect the liver. Scattered reports indicate elevated transaminases in humans with chronic filariasis. However, invariably filariasis is superimposed by other infections in humans. This can be avoided in rodent filariasis models where controlled studies on the involvement of the liver, uncomplicated by simultaneous infections, can be done.

We have carried out such a study in a Wistar rat- *Litomosoides carinii* model system. This mite-borne filarial infection in cotton rats differs slightly from the mosquito-borne infection of man due to *Wuchereria bancrofti* or *Brugia malayi*. Cotton rat filariasis bears resemblance in certain respects to infections by the Culicoides-transmitted *Dipterocera pomeris* in man. In addition to liver function tests, we have also studied the circulating levels and synthesis rates of discrete plasma protein fractions to explore whether any specific protein is affected in this infection, as found in other helminthic and parasitic infections in rodents, like hookworms and malaria (unpublished observations).

Material and Methods

Induction of infection: Cotton rats (*Sigmodon hispidus*) served as pool animals. They were infected naturally by exposing them for 2-3 hours to a population of vector mite *Ornithonyssus bacoti*, which had been infected 10-12 days before. Male Wistar rats of 130-150 g body weight were exposed to infected mite (30 mites per rat) for 3rd stage larval transmission. At different time-intervals after infection (21, 63 and 90 days), necropsies were performed and all the recovered parasitic worms were counted.

Initial studies revealed that no parasite worms could be recovered at 21 days post-infection. The liver function tests (transaminases and alkaline phosphatase) were also within normal range. Hence, detailed studies were done at 63 days and 90 days post-infection.

Biochemical studies: At required post-infection time intervals rats were injected intraperitoneally with 

\[ ^{14}C \text{-labelled chlorella protein hydrolysate (370 KDa) 100 g, 962 MBq/atom C, Isotope Division, Bhabha Atomic Research Centre, Trombay.} \]

Within two hours of this injection, all the liver and plasma proteins were labelled. Albumin, fibrinogen and seromucoid fraction from plasma were isolated and their specific activity (cpm/mg) was determined as described previously. Likewise, the total mixed proteins from the liver tissue homogenate were precipitated by trichloroacetic acid and their specific activity was obtained. From the protein-free filtrate of the liver homogenate the concentration of liver free amino acids and their specific activity was determined. The fractional synthesis rate (FSR) of different proteins was calculated as the ratio of specific activity of protein to the specific activity of liver free amino acid pool. The relative synthesis rate (RSR) was expressed as:

\[
\text{RSR (3)} = \frac{\text{FSR in infected animal}}{\text{FSR in control animal}} \times 100
\]

This is a meaningful comparison of protein synthesis rate based on amino acid incorporation, since it takes into account the specific activity of the precursor amino acid pool in the liver.

Plasma transaminases and alkaline phosphatases were estimated by the methods described by Bergmeyer. Means were compared by Student's *t* test.

Results

Our studies show that at 63 days post-infection aspartate aminotransferase and alkaline phosphatase were signi-
significantly elevated. At 90 days post-infection there was
significant increase in serum aspartate and alanine
aminotransferases, as well as alkaline phosphatase
(Table 1). By this time, the rats also manifested hypo-
proteinemia, hypalbuminemia and decreased relative
liver weight; this may suggest progressive liver involve-
ment. The reason for elevated serum transaminases and
alkaline phosphatase, which are indicative of liver
impairment, is unclear. Furthermore, there was decrease
in relative liver weight in infected animals. It is possible
that the host may respond to the infection by increasing
oxidants. It has recently been postulated that helminths
may have their antioxidant enzymes as a protective
mechanism against host oxidants. If this is true, then
the host's response in the form of increased oxidants and free radicals may have deleterious effects
on the host's organs. This aspect requires further study.

Table 1: Liver weights and liver function parameters in rodent filarial model at two different post-infection time intervals

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Relative liver weight (g/100 g)</th>
<th>SGOT (ASAT) (U/L)</th>
<th>SGPT (ALAT) (U/L)</th>
<th>Alkaline Phosphatase (U/L)</th>
<th>Plasma total proteins (g/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (63 d)</td>
<td>3.69 ± 0.23</td>
<td>23.9 ± 1.7</td>
<td>13.6 ± 3.5</td>
<td>92 ± 7</td>
<td>6.13 ± 0.27</td>
</tr>
<tr>
<td>Infected (63 d)</td>
<td>3.72 ± 0.30</td>
<td>32.4 ± 4.1*</td>
<td>16.3 ± 2.1</td>
<td>156 ± 3*</td>
<td>5.52 ± 0.25</td>
</tr>
<tr>
<td>Control (90 d)</td>
<td>3.24 ± 0.19</td>
<td>15.5 ± 2.3</td>
<td>12.9 ± 3.5</td>
<td>59 ± 14</td>
<td>5.75 ± 0.23</td>
</tr>
<tr>
<td>Infected (90 d)</td>
<td>2.84 ± 0.07*</td>
<td>27.8 ± 3.2*</td>
<td>16.4 ± 0.9*</td>
<td>132 ± 15*</td>
<td>5.22 ± 0.21</td>
</tr>
</tbody>
</table>

Values represent Mean ± SD for 10 rats. *p<0.05 (vs respective controls).

Though there was a tendency towards elevation of
circulating levels and synthesis rates of other proteins
studied, the changes were statistically not significant,
except for the relative synthesis rate of seromucoids in
rats 63 days post-infection (Table 2).

Table 2: Circulating levels and synthesis rates of specific plasma proteins and liver mixed proteins in rodent filarial model at two different post-infection time intervals

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control (63 d)</th>
<th>Infected (63 d)</th>
<th>Control (90 d)</th>
<th>Infected (90 d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conc (g/dL)</td>
<td>3.13 ± 0.39</td>
<td>2.98 ± 0.21</td>
<td>3.20 ± 0.11</td>
<td>2.66 ± 0.25*</td>
</tr>
<tr>
<td>RSR (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibrinogen</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conc (mg/dL)</td>
<td>263</td>
<td>309</td>
<td>357</td>
<td>423</td>
</tr>
<tr>
<td>RSR (%)</td>
<td>100</td>
<td>107.7</td>
<td>107.7</td>
<td>111.2</td>
</tr>
<tr>
<td>Serumucoids</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conc (mg/dL)</td>
<td>45.2 ± 9.9</td>
<td>61.3 ± 4.9</td>
<td>52.2 ± 4.6</td>
<td>64.3 ± 9.9</td>
</tr>
<tr>
<td>RSR (%)</td>
<td>100</td>
<td>112.3 ± 12.0*</td>
<td>100</td>
<td>121.7 ± 22.2*</td>
</tr>
<tr>
<td>Liver proteins</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conc (mg/g)</td>
<td>114.4 ± 7.6</td>
<td>120.0 ± 5.0</td>
<td>132.9 ± 7.4</td>
<td>129.8 ± 4.6</td>
</tr>
<tr>
<td>RSR (%)</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

Values represent Mean ± SD for 10 rats. *p<0.05 (vs respective controls).

Discussion
Information on the relationship of filariasis with hepatic
involvement and dysfunction is scanty. However, ham-
ters infected with filarial worms develop liver cirrhosis.10
Filarial-infected dogs have shown elevated transami-
nas.11 There is electron microscopic evidence to
suggest that microfilaria inhabit the liver.12 Further
human studies reveal increased serum transaminases in
chronic filariasis.13 Based on liver function tests our
results suggest progressive liver involvement.

Our studies also included circulating levels and
synthesis rates of specific plasma proteins of hepatic
origin, apart from albumin. Two of these proteins,
fibrinogen and serumucoids, are sensitive to infection
and inflammation.14 Another reason for studying these
mixed proteins and their synthesis.

References
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NEWS AND NOTICES


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Those who have not received the Second Circular, please write to Dr Jayaram.

CORRECTION

In the article “Efficacy of Tinidazole...” (Indian J Gastroenterol 1989; 8: 103-4), in the last sentence in Results, the value 8.23 ± 1.6 should read as 28.3 ± 1.6. The error is regretted.— Editor.