Lack of Urothelial Topical Tumorigenicity and Cotumorigenicity of Schistosome Ova in Mice

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Summary

Lyophilized Schistosoma haematobium ova in mineral oil suspension did not exert a topical carcinogenic effect on mouse bladder epithelium in 44 weeks. When methylcholanthrene was incorporated in the ova suspension, small numbers of transitional and squamous neoplasms were observed.

Introduction

In certain endemic areas significant correlation exists between bladder cancer and Schistosoma haematobium infestation in rural males. The clinical presentation of bladder cancer associated with chronic vesical schistosomiasis further supports the belief that neoplasia is a sequel to chronic inflammation with metaplasia. Ferguson (6), Makar (7), Aboul Naser et al. (1), and Al-Waith (2) have reported that unique clinical and histopathologic features characterize bladder cancer in areas where schistosomiasis is endemic. In these areas the high incidence of bladder cancer parallels the high incidence of schistosomiasis. A history of bilharzial cystitis frequently antedates the detection of bladder cancer. Aboul Naser et al. (1) reported finding bilharzial cystitis in 97% of 700 cases of bladder cancer in Egypt. The age distribution of bladder cancer in areas where bilharzial cystitis is prevalent favors a much younger population than that which obtains in nonendemic areas. Al-Waith (2) found that the mean age of occurrence of bladder cancer in Iraq was in the 3rd decade. El-Mofty (4) reported that the mean age of occurrence in Egypt was 41.2 years. The histopathology of bladder cancer in areas of endemic bilharziasis differs from nonendemic locales. Squamous carcinomas constituted more than 50% of bladder cancers in endemic areas of bilharziasis (1, 2, 4, 8).

Hypotheses on the etiologic role played by the parasite have been advanced. Fairley (5) reported development of adenomalignomas of the bladder in experimental bilharzial infestation in monkeys. These lesions were found mainly in S. haematobium infestations. They were interpreted to be the result of toxins liberated by the ova and the cellular infiltrate in the bladder wall.

Shimkin et al. (9) were unable to demonstrate carcinogenicity of injected lyophilized material from Schistosoma mansoni worms and S. haematobium worms and ova.

Results

The present study was conducted in an attempt to determine whether schistosome ova, either as the dry ova alone or in the presence of a chemical carcinogen, exhibit a tumorigenic action on mouse urothelium.

Materials and Methods

Washed, lyophilized S. haematobium ova obtained from human urine were suspended in mineral oil so that approximately 1000 ova were present in 0.15 ml. 3-Methylcholanthrene was suspended in mineral oil at a concentration of 0.5%. Chapman's method (3) was used to permit long contact of the test substances with the bladder epithelium. Male BALB/c mice 3–4 weeks old were the test species used. Under light ether anesthesia a lower abdominal incision was made in the donor mouse. The bladder was exteriorized. The test material was injected and allowed to float up to the bladder dome. A 4–0 silk ligature was tied just above the site of needle puncture. The bladder cyst thus formed was excised below the ligature and transplanted subcutaneously in the ventral part of the recipient mouse. In between injections the syringe, which contained a Teflon stirrer bar and several small glass beads, was kept on a magnetic stirrer to keep the suspension from settling out. Each pouch received an injection of 0.15 ml of mineral oil containing the following ingredients: Group 1, 29 animals had bladder cysts containing mineral oil only; Group 2, 30 animals had cysts containing about 1000 lyophilized S. haematobium ova suspended in mineral oil; Group 3, 30 animals had cysts containing 0.5% 3-methylcholanthrene suspended in mineral oil; Group 4, 31 animals had cysts containing 0.5% 3-methylcholanthrene and about 1000 lyophilized ova suspended in mineral oil.

Groups were kept in separate cages which were checked daily. Animals were weighed weekly. Purina laboratory diet was given with water ad libitum. All animals were sacrificed at the end of 44 weeks; the bladder pouches were removed, fixed, and examined.

Results

The fibrosarcomas in Groups 3 and 4 were probably a direct effect of the 3-methylcholanthrene on the subcutaneous tissue, through seepage from the cyst. We were unable to recognize the bladder epithelium in the sections, so they were excluded from the percentage of tumor yield in Table 1.

The squamous changes were not of significance in our opinion not only because of the low percentage but also because of the possibility that the lyophilized ova acted as a foreign body on the bladder epithelium.
TABLE 1

**TUMORIGENICITY OF SCHISTOSOMA HAEMATOBIUM OVA IN MOUSE BLADDER EPITHELIUM**

<table>
<thead>
<tr>
<th>GROUPS</th>
<th>NO. OF ANIMALS</th>
<th>CYST RECOVERED AFTER 44 WK.</th>
<th>HISTOLOGIC FINDINGS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>SARCOMA</td>
</tr>
<tr>
<td>1</td>
<td>29</td>
<td>23</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>30</td>
<td>19</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
<td>20</td>
<td>0*</td>
</tr>
<tr>
<td>4</td>
<td>31</td>
<td>20</td>
<td>3*</td>
</tr>
</tbody>
</table>

* See text for group identification.  
* Not included in % (see text).

There was no difference in the time of appearance of palpable tumors in any of the groups studied. From the results of our experiments it is apparent that the lyophilized *S. haematobium* ova did not produce a significant number of tumors in mouse bladders.

**Acknowledgments**

The authors are grateful to Dr. E. McConnell, head of the Parasitology Department, USN Medical Research Unit No. 3, for the supply of the lyophilized ova which made this study possible.

**References**


FEBRUARY 1967
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