

LIGHT MICROSCOPIC STUDY ON *SCHISTOSOMA MANSONI* INDUCED HEPATIC AND SPLENIC LESIONS FOLLOWING PRAZIQUANTEL TREATMENT

By

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ABSTRACT

Hepatic and splenic lesions were developed in mice of both sexes following their exposure to cercariae of *Schistosoma mansoni* (70 cercariae / animal). After 12 weeks of infection, the liver showed the formation of typical egg granuloma infiltrated with abundant bilharzial pigments. Meanwhile, paraganuloma hepatocytes displayed abnormal alterations. However, no egg lesions were observed in the spleen of infected mice and the only detectable change was distortion of splenic parenchyma with deposited bilharzial pigments. The present investigation was extended to include the effect of praziquantel administration on the liver and spleen of non infected and schistosome infected mice. The study revealed that, the drug induced areas of focal necrosis in the liver, whereas it was found to have no marked effect on the spleen of non infected mice. In addition, the drug administration to schistosome infected mice circumvented induced lesions in both liver and spleen.

INTRODUCTION

Development of the syndrome in the mice after *Schistosoma mansoni* infection, an attempt has been made to study whether praziquantel administration will be effective in treating induced hepatic and splenic lesions in mice. Praziquantel is an antischistosomal drug with very high cure rates and with low toxicity if compared with other schistosomicides (Omar, 1981 and Mc Mahon, 1983). In this work hepatic and splenic tissues of test animals were microscopically examined.

MATERIAL AND METHODS

Adult Swiss albino male and female mice were used. They were provided with food and water *ad libitum*. The animals were maintained in four groups : (1) control (uninfected and non treated), (2) *Schistosoma mansoni* infected, (3) Praziquantel treated; one dose of the drug was orally applied (4mg / 100g body weight). (4) both schistosome infected and praziquantel treated.

In groups (2) and (4), mice infection was produced by exposing them to about 70 cercariae / animal of the Egyptian strain of *S. mansoni*, according to the method of Peters and Warren (1959). Furthermore, group (4) was praziquantel treated four weeks after the infection. A single dose of praziquantel (25mg / 100g body weight) was orally administered as a suspension via polyethylene stomach tube.

Test mice were sacrificed 12 weeks after the beginning of the experiment. Specimens of liver and spleen were taken, fixed in 10% neutral formalin and processed for histopathological investigation. Tissue sections, 5 μ thick, were stained with Harris's Haematoxylin and Eosin.

RESULTS

Liver examination

Liver of schistosome infected mice, shows the formation of granulomatous lesion, in which the ovum appears to be surrounded by a fibrotic capsule, with abundant bilharzial pigments infiltrated into its outer surface. Abnormal alterations in the paraganuloma hepatocytes were also observed (fig. 2).

In the liver of praziquantel treated mice, areas of focal necrosis were observed (fig. 3).

The liver of *S. mansoni* infected and praziquantel treated mice, exhibits the effective action of the used drug in repairing induced egg lesions (Fig. 4).

Spleen Examination

The spleen of schistosome infected mice, shows distortion of splenic architecture and presence of bilharzial pigments (Fig. 6).

Praziquantel administration, was found to exhibit no discernible influence on the spleen of non infected mice (Fig. 7). In addition, the splenic lesion produced by *S. mansoni* in mice, was found to be improved after giving praziquantel (Fig. 8).

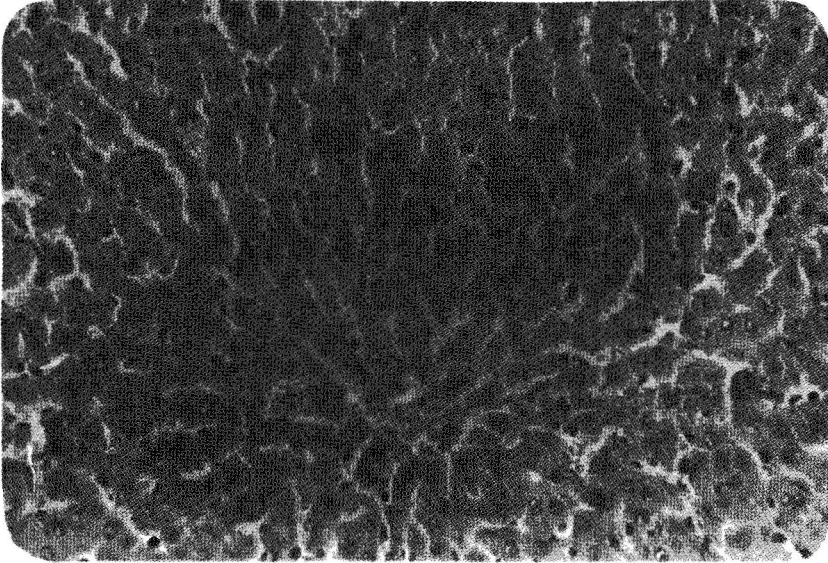


Fig. 1: Section in the liver of control mice. HX. X250

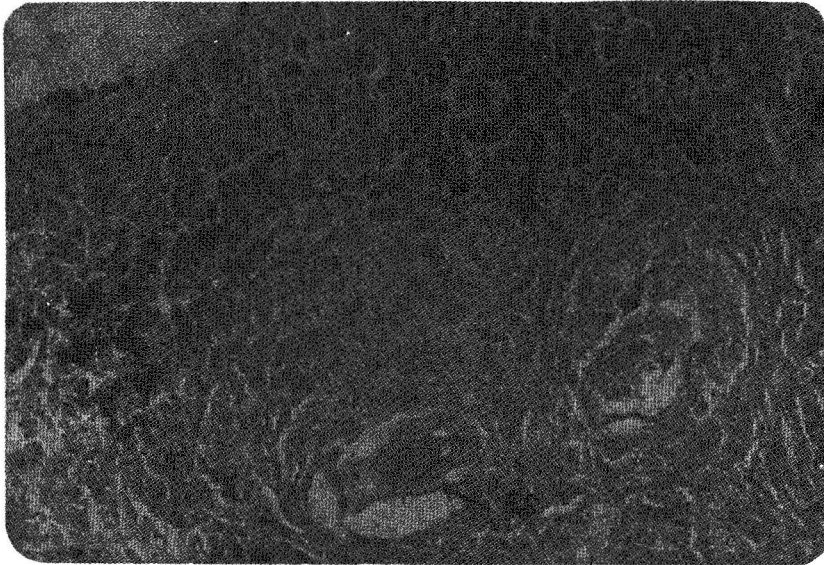


Fig. 2: Section through two adjacent granulomas in liver of schistosoma infected mice. Note the egg shell (ES) with the miracidium inside it being disintegrated. The outer surface of granuloma (heavy arrow) contains few granulocytic elements and bilharzial pigments. Hepatic, cells in the vicinity of the granulomas exhibit early fibrosis. HX. X 250

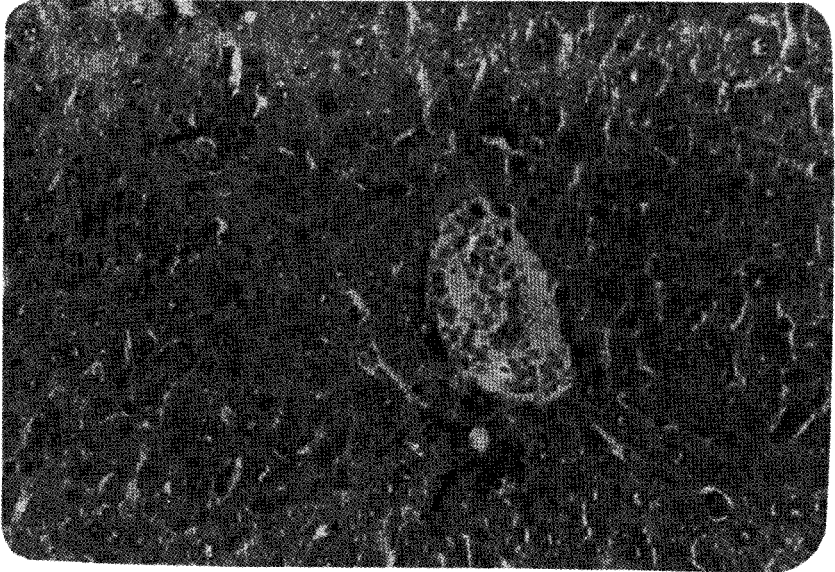


Fig. 3: Section in the liver of noninfected praziquantel treated mice. Note the presence of focal necrosis (arrow). HX X 250.

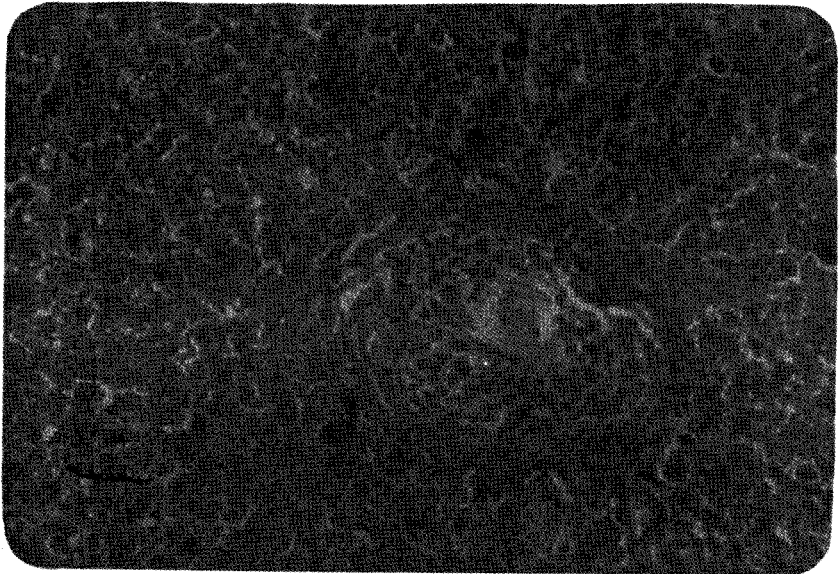


Fig. 4: Section in the liver of schistosoma infected and praziquantel treated mice. The granuloma has considerably shrunken (compare with Fig. 2). HX X 250.

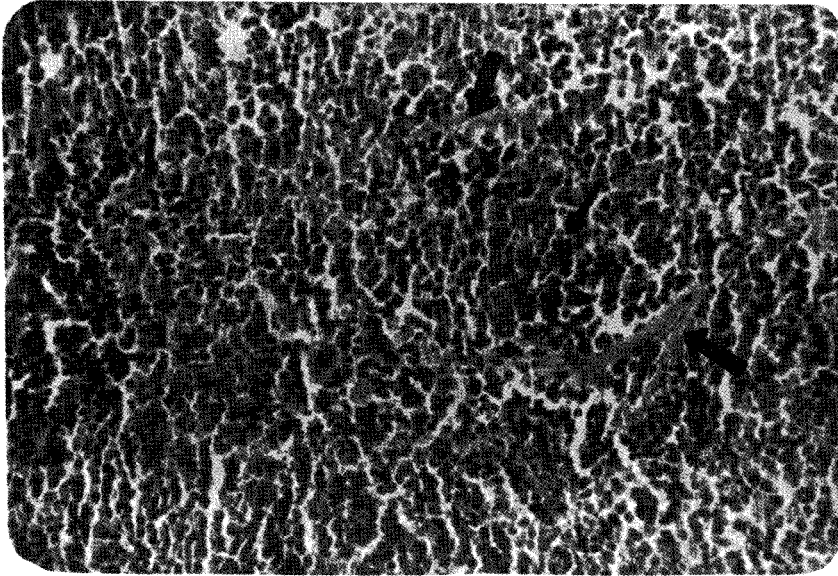


Fig. 5: Tissue section of the spleen in control mice. The splenic parenchyma was observed with normal shaped red pulp (light arrow) and extending trabeculae into the body of spleen (heavy arrows) HX X 250.

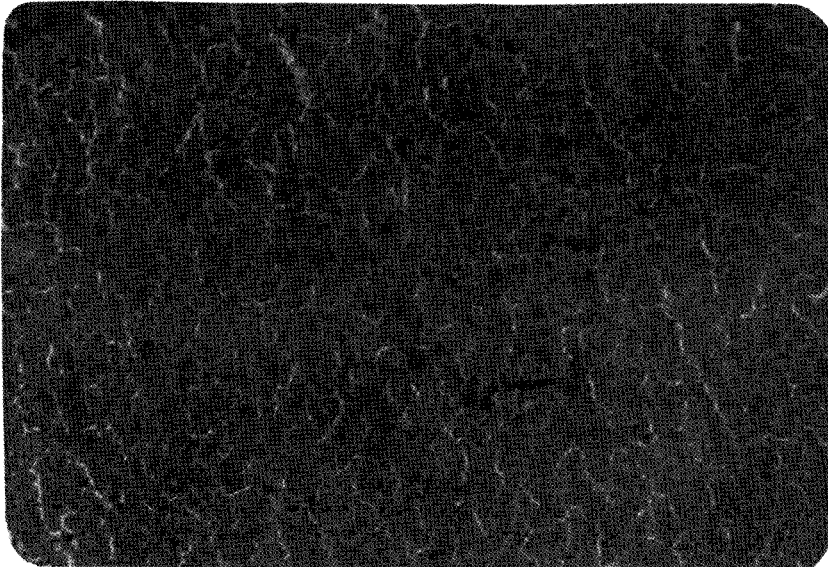


Fig. 6: Tissue section of the spleen in schistosoma infected mice. Note the presence of considerable fibrosis within the irregularly shaped red pulp and the presence of bilharzial pigments as well (arrow) HX X 250

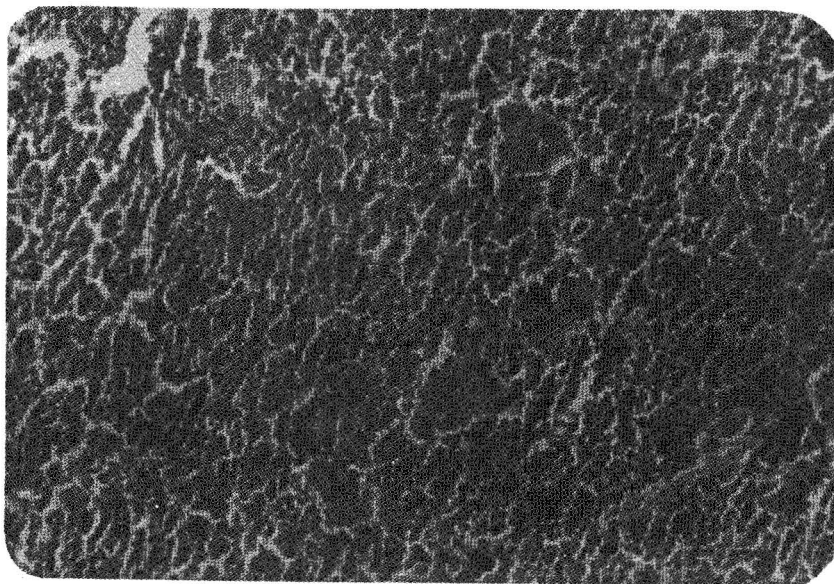


Fig. 7: Tissue section of the spleen in praziquantel treated mice. There was no lesions or alterations in the red pulp region. HX X 250.

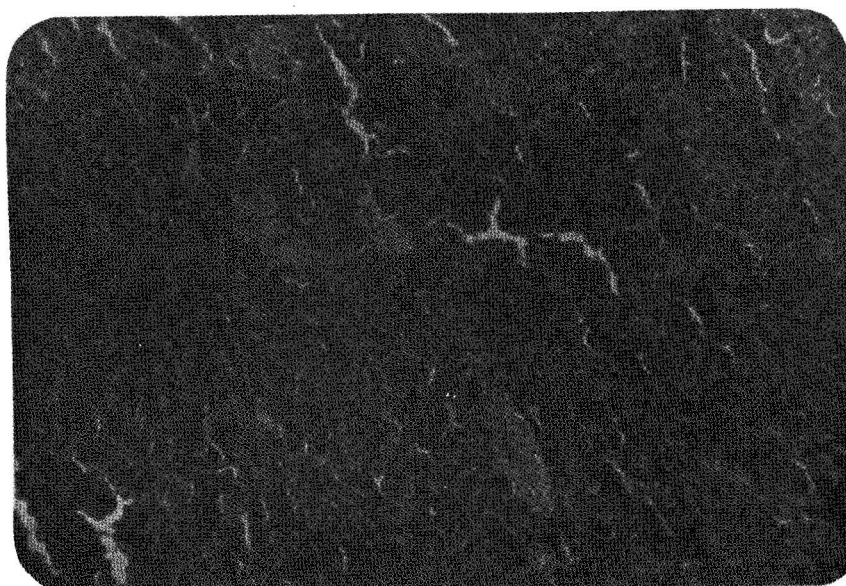


Fig. 8: Tissue section of the spleen in schistosoma infected and praziquantel treated mice. Note that the normal appearance of the splenic parenchymal cells began to be restored, HX X 250.

DISCUSSION

Schistosoma mansoni infection in mice develops many complications. The major one is the hepatosplenic schistosomiasis disease. Several factors may be involved in the pathogenesis of this disease. Dewitt and Warren, 1959 and Stenger *et al.*, 1967, ascribed the cause to schistosome eggs. Others have proposed that toxins and dead worms might be important etiologic factors (Warren, 1961, El-Shakankery, 1979).

In the present work, livers of schistosome infected mice showed the typical egg granuloma in which the ovum is surrounded by a fibrotic capsule infiltrated with the granular schistosomal pigments. Early fibrosis of the paragonuloma hepatocytes was also observed (Fig. 2). The antigenic materials arising from schistosome ova may be of much greater importance in the pathogenesis of liver lesions in the hepatosplenic disease. This view has been implicated by Stenger *et al.*, (1967). The evidence from the present study, might corroborate this view, since the only hepatocytes displaying significant structural alterations were those in the vicinity of egg granuloma. In addition, the detected alterations in the hepatocytes contiguous to egg granuloma, may be attributed to the mechanical pressure exerted by expanding granuloma (Stenger *et al.*, 1967).

Considering the effect of praziquantel administration on test animals, the present investigation indicates its hepatotoxicity in the form of focal necrosis (Fig. 3). Such histopathological changes could be responsible for the rise in the mean SGOT and SGPT values noticed by the authors in an earlier paper (El-Wakf *et al.*, 1987). However, the hepatotoxic effect of praziquantel was minimal if compared with the reported side effects of other antischistosomal drugs on the liver. El-Wakf (1983), found that vansil treatment produces severe hydropic degeneration along with mild fatty changes in the hepatocytes. Moreover, Halawany (1964), reported the occurrence of centrilobular zonal necrosis along with hydropic and fatty changes of liver cells after antimonials treatment.

Subsequently, the liver of both schistosome infected and praziquantel treated mice showed resolution of induced lesions (Fig. 4). The drug seemed to be highly effective in regressing egg granulomas of liver. Regression of egg lesions in mice with *S. mansoni* infection after praziquantel treatment, has been reported by Mehlhorn *et al.*, 1982.

On the other hand, histopathological studies on the spleen of *S. mansoni* infected mice reveals distortion of splenic architecture with deposited bilharzial pigments within splenic parenchymal cells (Fig. 6). This observation supports the work of Ashry (1967). Observed alterations in the splenic cells may be attributed to toxins produced by the worms. This view is in agreement with that of Stenger *et al.* (1967), who reported that toxins from adult worms might be involved in antigen-antibody reactions that would injure the spleen in schistosome infected mice.

In the present investigation, localization of bilharzial pigments in the granulomatous areas in the liver and throughout the splenic tissue, has been considered to be due to a home derivative, which is thought to arise by the digestive breakdown of host erythrocytes in the adult schistosome worms. The excretion of heme pigments by the schistosome into the circulating blood of the host, leads to its deposition in the liver, spleen and other organs (El-Aaser *et al.* 1978).

Studying the effect of praziquantel treatment on the spleen in experimental animals, revealed that the splenic parenchymal cells are apparently unaffected by the drug (Fig. 7). This finding concurs with that of El-Tahry (1984). Hereinafter, praziquantel administration to the schistosome infected mice, circumvented the induced splenic affection (Fig. 8), Disappearance of bilharzial pigments was also noticed. The stated drug efficacy in repairing splenic lesions detected in the present investigation (Fig. 6), may be attributed to the drug's rapid onset of action on the schistosomes through its specific effect on the permeability of their teguments (Andrew, 1981).

In the light of the present discussion, it is concluded that, infected liver provides the best tissue in which to observe the development of lesions associated with eggs, whereas no egg lesions were detected in the infected spleen. Moreover, praziquantel application seems to be quite effective in treating the experimentally induced hepatosplenic schistosomiasis in mice.

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دراسة التغيرات الهستوباثولوجية المحدثه في أنسجة
الكبد والطحال في حيوانات الفأر الصغير المعدة
بالبلهارسيا وكذلك في حيوانات معداة ومعاملة
بعقار البرازيكانثيل

عزة محمد الوقف و أبو بكر الصديق عثمان

يستهدف البحث دراسة طبيعة التغيرات الهستوباثولوجية المحدثه في أنسجة الكبد والطحال للفأر الصغير المصاب بحوالي ٧٠ من سركاريا المستقيم وكذلك تهدف الدراسة إلى معرفة تأثير عقار البرازيكانثيل المضاد للبلهارسيا على كل من الكبد والطحال في حيوانات تجارب معداة وغير معداة بالبلهارسيا . وقد أجريت هذه الدراسة على إناث وذكور حيوانات التجارب . وكانت تقتل هذه الحيوانات بعد ثلاثة أشهر من بداية العدوى . وقد أوضحت هذه الدراسة ظهور تليفات نسيجية تحيط بويضات البلهارسيا المتجمعة في أكباد الفئران المعدات وكذلك ظهور تليفات تتخلل نسيج الطحال .

وعند دراسة تأثير البرازيكانثيل على حيوانات التجارب غير المعداة لوحظ وجود نكروز في الكبد وعدم وجود تغيرات هستوباثولوجية في الطحال . أما بالنسبة لتأثير العقار على الحيوانات المعداة فقد أثبتت هذه الدراسة فاعلية هذا العقار في علاج التغيرات النسيجية المحدثه في كُلى من الكبد والطحال نتيجة العدوى بالبلهارسيا .