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HISTOPATHOLOGICAL ALTERATIONS IN INTESTINE OF MICE INFECTED WITH OF SCHISTOSOMA MANSONI

Mohamed F Hamed* and Moustafa A. Al-Araby**

**Lecturer of pathology, pathology department, Mansoura University, Egypt, 35516*
*** Lecturer of parasitology, parasitology department, Mansoura University, Egypt, 35516*

ABSTRACT

Schistosomiasis remains an important health problem in many tropical countries and developing countries. It has serious pathological lesions in different tissues particularly liver. The aim of this study is to demonstrate histopathological alterations in intestine of mice infected with S. mansoni as model for human schistosomiasis. Twenty mice were infected by tail immersion technique (80±10 cercariae per mouse of Egyptian strain of S. mansoni). Animals were clinically observed for 7 weeks and then they were sacrificed. Gross and histological examination was done, in addition to Masson trichrome and scoring of fibrosis by image J analysis were performed. The results revealed severe weight loss of infected mice compared to control one, large number of neutrophiles in granuloma of S mansoni in intestinal submucosa, extensive fibrosis, about 12% from total area of intestine, that penetrate deeply into muscle layer. it was concluded that S. mansoni caused pyogranulomatous enteritis and extensive fibrosis that extended deeply into muscle layer of intestine.

INTRODUCTION

Schistosomiasis is a parasitic disease caused by blood flukes (trematodes) of the genus *Schistosoma.* After malaria and intestinal helminthiasis, schistosomiasis is the third most devastating tropical disease in the world, being a major source of morbidity and mortality for developing countries in Africa, South America, the Caribbean, the Middle East, and Asia **(Gray, 2010)**.

In Egypt, the disease is not only a prime health problem, but it is also an economic one, as it affects million of farmers at the early age diminishing their productivity and exerting a serious socioeconomic problem. In intestinal schistosomiasis, eggs become lodged in the intestinal wall and cause an immune system reaction called a granulomatous reaction **(Tamer and Gamal, 2013)**. This immune response can lead to obstruction of the colon and hemorrhage. The infected individual may have what appears to be a potbelly. Eggs can also become lodged in the liver, leading to high blood pressure through the liver, enlarged spleen, the buildup of fluid in the abdomen (ascites), and potentially life-threatening dilations or swollen areas in the esophagus or gastrointestinal tract that can tear and bleed profusely (esophageal varices). Rarely, the central nervous system may be affected. Individuals with chronic active schistosomiasis may not complain of typical symptoms. Although various research on schistosomiasis and huge number of methods and new protocol in the treatment were evaluated but the full pathological effect on the intestine isn't fully described. So the aim of this is to study the histopathological deterioration in intestine in mice infected with *Schistosoma mansoni*.

MATERIAL AND METHODS

Animals

Twenty male Swiss albino mice, weighing 18–20 gm bred at the Experimental Research centre of Theodor Bilharz Institute, Cairo, Egypt, were used for the study. They were housed with free access to standard lab chow and tap water and ten negative control animals were separated.

Infection of animals

Twenty mice were infected by tail immersion technique according to the method of **Olivier and Stirewalt (1952)** with 80±10 cercariae per mouse of the Egyptian strain of *S. mansoni*.

Clinical observation

The mice were observed clinically allover the period of experiment (7 weeks).

Sample collection and gross examination

After 7 weeks (at the end of infection) the mice were sacrificed, necropsy were done and intestine were collected and gross examination were done.

Intestine histopathology

Tissue samples were immersed in 10% formalin for measurement of granuloma diameter. Samples were embedded in paraffin, sectioned and stained with Haematoxylin and Eosin. **Bancroft, 1996**.

Scoring of fibrosis

Using Imaje J anlaysis to detect the amount of fibrosis present in wall of granuloma.

RESULTS

Clinical examination

Mice in *S. mansoni* infected group showed chronic diarrhea, and in last days severe dysentery, loss of body weight of infected mice, alopecia dehydration start after the 5 th week of infection, compared to control group.

Gross examination

Intestine showed grayish white areas on serosal surface and became hard on pressure, when opened. The lumen was pluged with mucous tinged with blood, narrowed lumen was noticed, also showing ulceration on mucosal surface that studded with multiple raised foci. On cutting section through these foci revealed circumscribed nodules its wall has whitish color and lumen brown to grey one.

Histopathological examination

Routine Hematoxyline and Eosin (HE) staining showed characterstic egg granuloma in the intestinal submucosa where one or more Schistosoma eggs were loaded and sometimes forming nests surrounded by aggregations of esinophiles, macrophages, plasma cells, lymphocytes also neutrophiles were noticed replacing the intestinal crypts and villi, causing thickening of the wall of mucosa and submucosa. Laminated Fibrous tissue was proliferated forming thick wall which is extended throughout intestinal mucosa, submucosa and also deeply into muscular layer of intestine (Fig. 1).

Masson trichrome staining indicated bluish stained fibrous connective tissue in the wall of granuloma that proliferated and extended in all directions and extended deeply into muscular layer of intestine (Fig. 2)

Image J analysis for scoring declared of 12.5% fibrosis of intestinal wall.

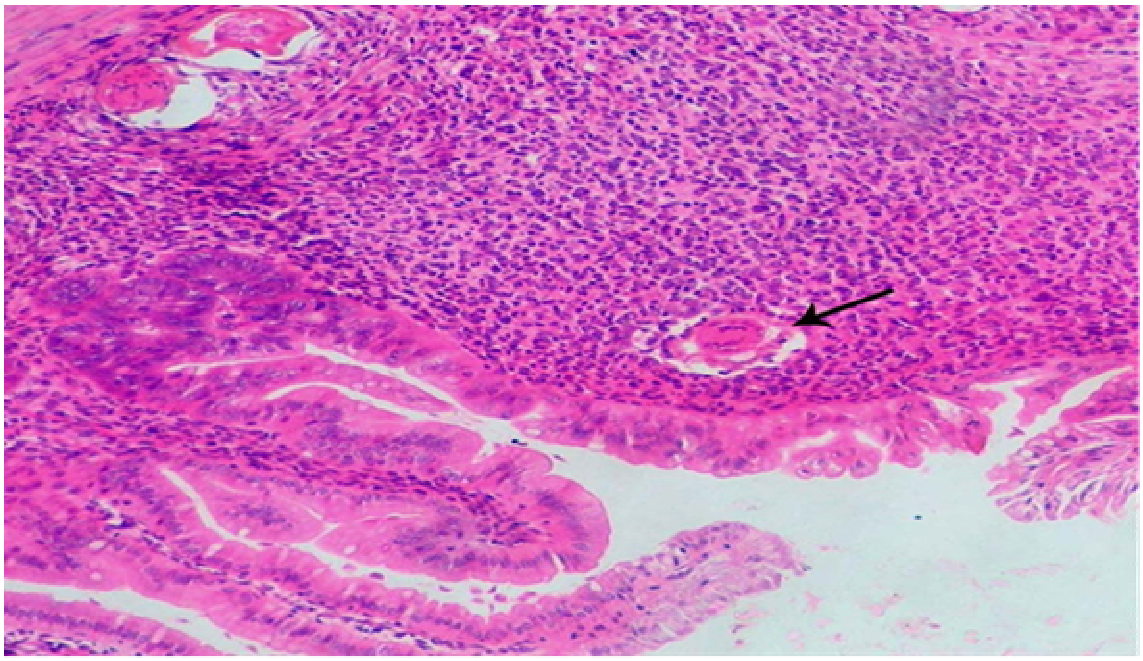

Fig. (1): intestine displays scistosoma egg embedded in the lamina propia of intestine (arrow) surrounded by granulomatous reaction and fibroblastic proliferation (HE t, 40x)

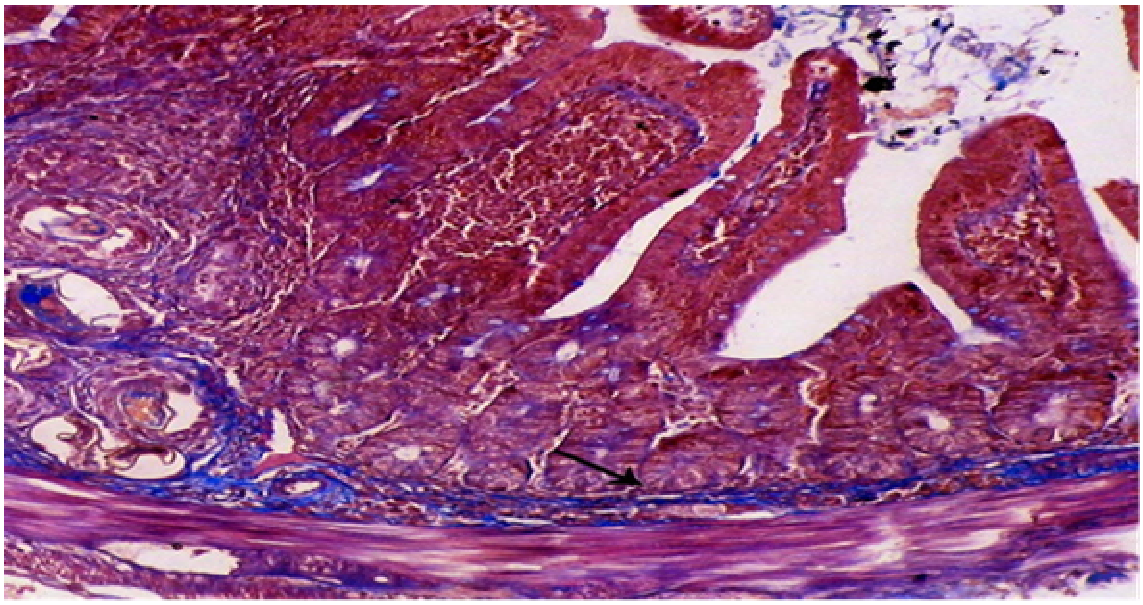

Fig. (2): bluish stained fibrous connective tissue in the wall of granuloma that proliferated and extended in all directions and extended in the deep layers of intestine. (Masson trichrome, 40x)

DISCUSSION

Histopathological alterations in intestine of mice was evaluated as a models for human infected with schistosomiasis, where intestinal schistosomiasis caused by *S mansoni* occurs in 52 nations, including Caribbean countries, eastern Mediterranean countries, South American countries and most countries in Africa **(John et al., 2008)**.

The study revealed aggregation of large number of neutrophiles besides esinophiles, macrophages, lymphocytes and plasma cells which indicate severe pyogranulomatous reaction against *S. mansoni* eggs in intestine that is contradicts **Ernesto, 1969,** who demonstrates that eggs become lodged in the intestinal wall and cause an immune system reaction called a granulomatous reaction.

Severe pyogranulomatous reaction may be due to secondary bacterial infection that agreed with **Argemi et al, 2009** who reported that patients with heavy bowel wall involvement have an increased rate of recurrent *Salmonella* infection, generally with positive blood cultures and negative stool cultures.

Extensive fibrous tissue that extended deeply into the muscular layer cause severe weakness in intestine wall that may be liable to serious pathological sequelae, as approved by **Badmos, 2006 and Terada 2009,** who reported that chronic intestinal schistosomiasis can present with acute complications of appendicitis, perforation, and bleeding long after travel-related (or endemic) exposure.

In conclusion, *S. mansoni* causing pyogranulomatous enteritis and extensive fibrous tissue proliferation that extended deeply into muscle layer of intestine.

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الملخص العربي
التغيرات الباثولوجيا فى الامعاء نتيجه الاصابه بلهارسيا مانسونى

محمد فوزى محمد حامد* – مصطفى العربى**

*المدرس بقسم الباثولوجيا – كلية الطب البيطرى
** المدرس بقسم الطفيليات – كلية الطب البيطرى

تعتبر الاصابه بلبهارسيا من المشاكل الخطيره على صحه المجتمع فى الدول الناميه ولها تغيرات مرضيه مهمه على معظم الانسجه وخصوصا الكبد. وكان الهدف من التجربه معرفه التغيرات المرضيه التى تحدت فى الامعاء نتيجه الاصابه بلبهارسيا مانسونى فى الفئران كنموذج للاصابه للانسان. وتم عمل تجربه على ٢٠ من الفئران تم اصابتهم بالسركاريا عن طريق الديل وتم ملاحظتهم وذبحهم بعد ٧ اسابيع . وتم عمل الفحوص الهستوباثولوجيا وتم قياس نسبه التليف فى الامعاء. اثبتت النتائج ان وجود تجمعات كبيره من الخلايا الالتهابيه وخلايا ليفيه حول بيضه البلهارسيا فى جدار الامعاء وبعمل الصبغات الخاصه بالتليف وجد زياده فى كميه وحجم النسيج الليفى المنتشر فى جميع اجزاء الامعاء الذى تصل نسبته الى ١٢% من مساحه الامعاء. واثبتت التجربه ان البلهارسيا مانسونى لها تاثيرات باثولوجيا ضاره وسبب فى ظهور تليفات فى الامعاء.