

HISTOPATHOLOGICAL ANALYSIS OF SCHISTOSOMIASIS IN THE GASTROINTESTINAL TRACT WITH FIRST RECORD OF SCHISTOSOMAL APPENDICITIS FROM SOHAG, UPPER EGYPT

By

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Abstract

Schistosomiasis is a chronic granulomatous inflammation that affects many systems in the body including the gastrointestinal tract. Appendiceal schistosomiasis is also described and can be a precursor lesion of schistosomal appendicitis. The present study was done to make a retrospective analysis of histopathological changes in the gastrointestinal tract affected by *Schistosoma mansoni* among patients attending Sohag University Hospital, Sohag Governorate between June 2013 and June 2016. A total of 150 colon and 30 appendix specimens were collected through out the period from male infected patients aged between 35-50 years and suffering from abdominal pain and dysentery. Histopathological examination of the tissue biopsies was performed. 5µ tissue sections were prepared and examined microscopically. Ten specimens were documented to have intestinal schistosomiasis, nine of the colon 9/150 (6%) were diagnosed as chronic schistosomal colitis and one of the appendix 1/30 (3.3%) as chronic schistosomal appendicitis. Microphotographs of the tissue sections were prepared for histopathological observations. Histopathological examination of all specimens revealed degenerated pinkish and calcified bluish bilharzial eggs in the submucosa and even musculosa with surrounding granulomatous reaction. Bilharzial polyps of the colon were detected in two specimens (20%) and bilharzial worms within venules of the muscle layer in two specimens (20%). During the present study, *S. mansoni* was documented as a not uncommon cause of chronic colitis and for the first time from Sohag as a cause of chronic appendicitis. All specimens did not show any malignant or premalignant cells.

Key words: Sohag Governorate, *Schistosoma mansoni*, chronic colitis, chronic appendicitis,

Introduction

Schistosomiasis is an endemic disease in Egypt caused by different *Schistosoma* spp. (Elbaz and Esmat, 2013) that affects hundreds millions of people and accounts for more than 40% of global health burden as one of the neglected tropical diseases (Nalugwa *et al*, 2015). WHO considered schistosomiasis as the second to malaria in socio-economic importance worldwide and the third more frequent parasitic disease in public health importance (Sarvel *et al*, 2011).

Schistosomiasis is a chronic granulomatous inflammation that affects many systems in the body including the gastrointestinal tract (Badmos *et al*, 2006). Gastrointestinal schistosomiasis is known to be caused by *Schistosoma mansoni*, *S. japonicum*, *S. mekongi*, *S. guineensis* and/or *S. intercalatum* (WHO, 2016). From ancient time *Schisto-*

soma mansoni was considered to be the most prevalent species being endemic in 55 countries e.g. Arab peninsula, Egypt, Libya, Sudan, Sub-Saharan Africa, Brazil, some Caribbean islands, Suriname and Venezuela (Chitsulo *et al*, 2000). In Egypt, *S. mansoni* was estimated to infect 60% of the population in the Northern and Eastern parts of the Nile Delta and 6% in the Southern part (Barakat, 2013). Pathological changes associated with intestinal schistosomiasis are predominately brought out by detriment of the immunological responses to eggs, which become trapped in host tissues. Migration of eggs through the intestinal wall stimulates an initial eosinophilia inflammatory reaction in the mucosa. Granulomas eventually form around the eggs if they are not voided and fibrosis ensues to form large non-malignant granulomas (Montes *et al*, 2004). Egg depo-

sition and granuloma formation eventually lead to acute followed by chronic schistosomal colitis and is commonly associated with polyp formation (Elbaz and Esmat, 2013).

Schistosomiasis of the appendix is a rare disease and presents mostly as a chronic granulomatous inflammation (Ahmed *et al*, 2014). The exact pathogenesis of appendicitis secondary to schistosomiasis is uncertain. The most common hypothesis is that eggs in the appendix wall stimulate inflammation and thus fibrosis and narrowing of the appendicular lumen (Badmos *et al*, 2006). Other hypotheses include schistosomal egg emboli causing ischemia, and granulomatous inflammation of the peri-appendicular intestine, causing fibrosis and disruption of the intestinal wall leading to obstruction of the appendix and acute appendicitis (Cox and Yates, 2010).

The present study was done to make a retrospective analysis of histopathological changes in the gastrointestinal tract affected by *Schistosoma mansoni* among patients attending Sohag University Hospital, Sohag Governorate from June 2013 to June 2016.

Materials and Methods

Collection of tissue samples: In a retrospective study, a total of 150 colon and 30 appendix specimens were collected from June 2013 to June 2016 from male patients aged between 35-50 years; suffering from abdominal pain and dysentery. Endoscopic biopsies of the colon specimens, referred from the Gastroenterology Unit, Department of Internal Medicine and specimens of the appendix referred from Department of Surgery, Sohag University Hospital, were examined to study the histopathological effect of *S. mansoni* on the gastrointestinal tract. The research Team followed the ethical standards of confidentiality and freedom to participate. The respondents were informed that the study was voluntary and they were assured that their privacy would be protected and all of them gave a written consent for taking and studying the specimens.

Histopathological examination: The specimens were fixed in 10% formalin, and sections of 5µm thickness were prepared with paraffin embedded tissue by using standard histological techniques (Culling, 1993). Sections were stained with Haematoxylin and Eosin and mounted permanently in DPX. Microphotographs of tissue sections were prepared for histopathological observations. The slides were examined using compound microscope.

Results

Through histopathological examination of all biopsies of the colon; nine cases (6%) and one biopsy of appendix (one case) (3.3%) were found to be due to intestinal schistosomiasis (*S. mansoni*) as documented by the Medical Parasitology and Pathology Departments, Faculty of Medicine, Sohag University. The surrounding tissue of the colon specimens showed deposits of degenerated and calcified bilharzial eggs surrounded by granulomatous reaction (Fig.1) while degenerated pinkish and calcified bluish bilharzial eggs were seen in the sub mucosa and even musculosa with surrounding granulomatous reaction rich in macrophages and eosinophils in addition to lymphocytes, plasma cells and fibroblasts (Fig.2,3,4). Bilharzial polyp of the colon composed of vascular connective tissue core in 2 specimens (20%) showing large number of degenerated and calcified bilharzial eggs with surrounding granulomatous reaction (Fig.4) and sectioned bilharzial worms were detected within in venules of the muscle layer in 2 specimens (20%) (Fig.5). Chronically inflamed appendix showed *Schistosoma* eggs in the musculosa and granulomata reaction in the submucosa (Fig. 6).

Discussion

Schistosomiasis is one of the neglected tropical diseases caused by a trematode *Schistosoma* spp, and affects many systems in the body including the gastrointestinal tract (Ahmed *et al*, 2014). *S. mansoni* is the main agent causing intestinal schistosomiasis in Africa (WHO, 2016). Schistosomiasis

is more rampant in poor rural communities, especially places where fishing and agricultural activities are dominant (Adenowo *et al*, 2015).

The pathogenesis of schistosomiasis is related to the host cellular immune response. This leads to granuloma formation. Egg deposition and granuloma formation eventually leading to acute followed by chronic schistosomal colitis and is commonly associated with polyp formation (Elbaz and Esmat, 2013).

In the present study egg deposition in the submucosa and even musculosa with surrounding granulomatous reaction rich in macrophages and eosinophils in addition to lymphocytes, plasma cells and fibroblasts were detected in 100% of specimens while 20% of specimens had bilharzial polyps and 20% of specimens had bilharzial worms within venules of the muscle layer. As regards Sohag Governorate, this three years retrospective study demonstrated (6%) prevalence rate of *S. mansoni* infection which was diagnosed as chronic schistosomal colitis. This correlates with Barakat (2013) who detected that *S. mansoni* infected only 6% in the Southern part of Egypt and 60% of the population in the Northern and Eastern parts of the Nile Delta. As regards Lower Egypt, the average prevalence rate of *S. mansoni* infection was 36.45% (Nooman *et al*, 2000) while in Upper Egypt Governorates; *S. mansoni* was rare being consequential in El-Fayoum only, which had a prevalence of 4.3% (Abdel-Wahab *et al*, 2000).

Endoscopic and histopathological study in Delta region of Egypt from 2004 to 2009 covering 984 individuals presented with gastrointestinal manifestations demonstrated typical schistosomiasis colorectal lesions in 20.33 % of them (Gad *et al*, 2011). While *S. haematobium* continues to decline sharply in the Nile Delta, *S. mansoni* transmission is continuing at an appreciable level, in addition to evidence of extension of *S. mansoni* to Upper Egypt (Barakat, 2013). Variability in prevalence of infection between villages

is due to variations in the socioeconomic standards and access to health services (Barakat *et al*, 2000).

Parasitic acute appendicitis was reported by da Silva *et al*, (2007) to be usually and primarily caused by *Enterobius vermicularis* in 95.8% out of 1600 appendectomies while schistosomiasis of the appendix is a not uncommon disease and presents as a chronic granulomatous inflammation (Ahmed *et al*, 2014) although it was reported by Doudier *et al*, 2004) as an unusual cause of appendicitis. The pathogenesis of schistosomal appendicitis has been described as one from two mechanisms. The first mechanism is schistosomal obstructive acute appendicitis, believed to be a result of fibrosis around eggs leading to obstruction followed by bacterial infection. This mechanism presents pathologically with no tissue eosinophils or granulomas. This is seen more often in the late stages of infection. The second mechanism is schistosomal granulomatous acute appendicitis, was believed to be a result of immunological granulomatous reactions to newly deposited eggs. This mechanism presents pathologically with tissue necrosis leading to perforation. These patients have tissue granulomas and eosinophilia. This mechanism is seen more often in the early stages of infection (Satti *et al*, 1987). The pathogenesis is most probably due to a peri-appendicular granulomatous inflammatory reaction of the host against the schistosome (Adebamowo *et al*, 1991). Inflammation and repair cause scarring and structural deformation of the appendiceal wall leading to luminal obstruction and acute appendicitis (Paulson *et al*, 2003).

In the present study, 3.3% of surgically removed appendices were diagnosed as chronic schistosomal appendicitis. This correlated with Abdellatif *et al*. (2015) who detected 3% bilharzial granulomas of the appendix and Hedaya *et al*. (2012) who reported that the retrospective study of appendectomies revealed 11/251 (4.38%) with para-

sitic infection, 1.19% of them had *Schistosoma* spp. eggs.

Several records implicated *S. haematobium* (Duvie *et al*, 1987; Opara *et al*, 2003; Doudier *et al*, 2004; Hobson *et al*, 2007; Webb and Thomas, 2009; Gundlapali *et al*, 2012; Ouédraogo *et al*, 2013; Ahmed *et al*, 2014), while *S. haematobium* and *S. mansoni* were rarely implicated together (Ahmed *et al*, 2014; Galli *et al*, 2016) in the granulomatous reactions in the appendix. It is interesting that *S. mansoni* was never reported alone as the cause of appendicitis. As *S. haematobium* inhabit the genitourinary system in the body, it is difficult to find its eggs in the vermiform appendix. As most of the previously mentioned studies which identified *S. haematobium* as the cause of appendicitis were from African countries, the present authors believe that the causative agent may be *S. intercalatum* which is a terminal-spined intestinal schistosome common in Central and South African countries. Also, it was often difficult to distinguish between terminal and lateral spined eggs in cross sections, many reports of schistosomal appendicitis were recorded as to be due to schistosomal eggs without identifying the species (Badmos *et al*, 2006; Kalyana *et al*, 2008; Adisa *et al*, 2009; Nwagbara *et al*, 2011; Hedaya *et al*, 2012; Zakaria *et al*, 2013; Abdeed Latif *et al*, 2015; Abo-Alha-ssan *et al*, 2016). Hence, the present authors recommend the use of acid fast staining technique during histopathological studies that easily differentiate between eggs of *S. haematobium* and *S. intercalatum*.

The present study revealed the importance of histopathological examination of surgically removed inflamed appendices and illustrated the characteristic schistosoma eggs surrounded by granulomata. The result showed the occurrence of schistosomal appendicitis as the mere presence of the parasite eggs in stool or urine do not confirm them as the cause of appendicitis; particularly in Egypt where the parasite is common. Hence, it is recommended to do hisopathological studies

of removed appendices with special concern to presence of parasitic infestation.

Conclusion

During the present study, *S. mansoni* was documented as a not uncommon cause of chronic colitis and polyp formation. We reported chronic schistosomal appendicitis due to a specific trait of *S. mansoni* infection in Sohag for the first time. Moreover, all examined specimens did not show any malignant or premalignant cells.

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Explanation of figures

Fig. 1: Degenerated and calcified eggs surrounded by granulomatous reaction

Fig. 2, 3 & 4: Degenerated pinkish & calcified bluish eggs in sub mucosa and musculus with surrounding granulomatous reaction rich in macrophages and eosinophils in addition to lymphocytes, plasma cells and fibroblasts.

Fig. 4: Polyp of colon composed of vascular connective tissue core showing large number of degenerated and calcified eggs with surrounding granulomatous reaction

Fig. 5: Sectioned worms within venules of muscle layers.

Fig. 6: Chronically inflamed appendix showed *Schistosoma* eggs in musculus and granulomata reaction in sub mucosa.

