Appendicular schistosomiasis: a cause of clinical acute appendicitis?

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SUMMARY The role of schistosomes in the pathogenesis of acute appendicitis in an endemic area was investigated. Of 1600 appendicectomies received in our laboratory, 26 showed appendiceal schistosomiasis, which prompted what we believe to be the first detailed histopathological evaluation of all appendices with schistosomal infestation, without prior knowledge of the clinical and operative diagnoses. The results suggest that there are two types of schistosomal appendicitis, each with distinct clinicopathological features and different pathogenetic mechanisms. They could be called obstructive and granulomatous schistosomal acute appendicitis, respectively.

Schistosomiasis of the appendix is a recognised phenomenon, the appendix being regarded as one of the ectopic sites for haematobium species. In a necropsy study of 96 patients Lima¹ found appendiceal disease in four with "ectopic lesions" due to *Schistosoma mansoni* infestation. As far as we know there has been no previous detailed study on the role of schistosomiasis in the pathogenesis of acute appendicitis, even from endemic areas. In another necropsy study Smith² reported that *Schistosoma haematobium* eggs prefer the appendix, but the problem was not addressed by Abdel Wahab in his work on schistosomiasis in Egypt.³ In this paper we examine the role of schistosomes in the pathogenesis of acute appendicitis.

Material and methods

The material for this study was retrieved from the files of the pathology department of King Fahd Hospital, Al-Khobar, during 1982-1985. Of all the cases of acute appendicitis coming to surgery in that period, those showing schistosomal ova in the appendiceal wall were included in this study. Without prior knowledge of their clinical data or diagnoses, a detailed histopathological evaluation was performed on stained paraffin sections. Where necessary, sections were recut from retrieved paraffin blocks and stained with haematoxylin and eosin to investigate any correlation between presence of the ova and clinical presentation.

Histopathological criteria recorded included the presence or absence of the following: active granu-

lomatous inflammation with eosinophilic necrosis around ova; tissue eosinophilia; purulent exudate in lumen, or wall, or both; fibrosis without a purulent exudate or active granulomas; and faecoliths. We considered that the appendix showed pathological evidence of recent symptomatic inflammation if there were active granulomas with tissue necrosis (fig 1) or a purulent exudate in lumen or wall, or both. The first group were called schistosomal granulomatous acute appendicitis and the second, schistosomal obstructive acute appendicitis. Appendices that showed neither active granulomas nor a purulent exudate, but only schistosomal ova occasionally accompanied by fibrosis and calcification (fig 2), were considered to show no pathological evidence of recent symptomatic inflammation.

The patients' charts were reviewed for information on age, sex, symptoms and duration, signs, clinical diagnosis, operative findings and the white cell counts, including the neutrophil and eosinophil counts.

Results

Of 16000 surgical specimens, 1600 were appendicectomies. On histopathological review, 1400 (87%) showed transmural acute appendicitis. In all, 26 cases of appendiceal schistosomiasis were found. Of these, 19 showed pathological evidence of recent symptomatic inflammation. Eleven of these qualified for inclusion in the group with schistosomal obstructive acute appendicitis and eight for inclusion in the group with schistosomal granulomatous acute appendicitis. The remaining seven did not show pathological evidence of recent symptomatic inflammation. Severe fibrosis

Fig 1 Appendix with active granulomatous reaction and tissue necrosis. (Haematoxylin and eosin.) $\times 375$.

Fig 2 Appendix with schistosomal ova and fibrosis in wall. Note absence of granulomas and purulent exudation. (Haematoxylin and eosin.) $\times 125$.

of the wall with numerous calcified ova was the pathological hall mark of this group. Interestingly, fibrosis and calcification of ova were consistently present in the wall of appendices that showed purulent exudation (fig 3), which was not a conspicuous feature of appendices with active granulomas and eosinophils in the wall.

Table 1 summarises the clinicopathological correlation between these patients. Of the 21 patients with clinically diagnosed acute appendicitis, 19 had histopathological evidence of recent symptomatic inflammation, accounting for the symptoms and signs. The remaining two showed no pathological evidence of recent symptomatic inflammation. The three patients with clinically diagnosed chronic appendicitis showed no pathological evidence of recent symptomatic inflammation. In one of these three patients the appendix had been removed during cholecystectomy because of chronic cholecystitis. Two patients had clinically diagnosed ureteric obstruction, and their appendices were removed. No pathological evidence of recent symptomatic inflammation was found in either case.

Table 2 shows the information on age, sex, and

white cell counts of patients with schistosomal obstructive appendicitis. Table 3 shows that pertaining to patients with schistosomal granulomatous acute appendicitis, and table 4 that of patients with appendices without pathological evidence of recent symptomatic inflammation.

Discussion

Acute appendicitis is a common clinical problem. Surgically removed appendices comprise 10% of material coming to our surgical pathology labora-

Table 1 Summary of clinicopathological correlation of patients with appendiceal schistosomiasis

Clinical diagnosis	No of patients	Pathological diagnosis	
		Recent symptomatic inflammation	Not inflamed
Acute appendicitis	21	19	2
Chronic appendicitis	3		3
Incidental removal at ureteric exploration	2		2

Fig 3 Appendix with fibrosis and calcification in wall in presence of purulent exudation. (Haematoxylin and eosin.) $\times 320$.

tory. About 87% of these appendices showed evidence of transmural acute appendicitis. Obstruction followed by infection from faecal contaminants is thought to be an important pathogenetic mechanism in acute appendicitis.⁴ Objective evidence of such an obstruction, however, is found only in a proportion of cases, further emphasising the existence of the non-obstructive form of acute appendicitis.

Of the 19 appendices with schistosomal and histopathological evidence of recent symptomatic inflammation, 11 showed suppuration in addition to severe fibrosis of a portion of the wall, induced by the numerous calcified ova inside it. No active granulomas or tissue eosinophilia were noted. As no faecoliths were found, the schistosomal fibrosis was probably the cause of the obstruction that led to bacterial infection from faecal contaminants: we suggest that this be termed schistosomal obstructive acute appendicitis.

These appendices were all from male patients, with an age range between 25 and 45 years and a median of 39 years. Leucocytosis with an absolute neutrophilia was a notable feature, in keeping with bacterial infection. Blood eosinophilia was occasionally noted. All of these 11 patients had the typical symptoms and signs of acute appendicitis.

The remaining eight appendices with schistosomiasis showed active granulomatous inflammation around viable ova, with tissue necrosis and a tissue eosinophilia. No obstruction was noted, and neutrophil exudation was not a feature. All of these patients presented with typical symptoms and signs of

Table 2 Schistosomal obstructive acute appendicitis

Case No	Age	Sex	White cell count $\times 10^9/l$	Neutrophil %	Absolute neutrophils $\times 10^9/l$	Eosinophil %
1	43	M	12.5	91	11.4	0
2	38	M	8.9	57	5.1	10
3	42	M	11.8	70	8.3	4
4	39	M	13	75	9.8	3
5	45	M	9.3	64	6.0	2
6	29	M	11.3	65	7.4	3
7	40	M	13.4	50	6.7	5
8	34	M	12.8	77	9.9	6
9	36	M	11.3	88	9.9	0
10	25	M	6.4	60	3.8	17
11	40	M	8.7	73	6.4	1

Table 3 Schistosomal granulomatous acute appendicitis

Case No	Age	Sex	White cell count $\times 10^9/l$	Neutrophil %	Absolute neutrophils $\times 10^9/l$	Eosinophil %
1	27	M	6.8	52	3.5	7
2	30	M	9.3	70	6.5	3
3	23	M	4.7	29	1.4	2
4	25	M	7.0	45	3.2	2
5	17	M	12.2	65	7.9	1
6	30	M	8.6	59	5.1	3
7	18	M	6.5	55	3.6	10
8	19	M	7.1	68	4.8	13

Table 4 Appendices without pathological evidence of recent symptomatic acute inflammation

Case No	Age	Sex	Clinical diagnosis	White cell count $\times 10^9/l$	Neutrophil %	Absolute neutrophils $\times 10^9/l$
1	35	M	Acute appendicitis	6.8	65	4.4
2	18	M	Acute appendicitis	5.6	54	3.0
3	40	M	Chronic appendicitis	6.6	50	3.3
4	30	M	Chronic appendicitis	3.3	48	1.6
5	45	M	Cholecystectomy	5.3	63	3.3
6	26	M	Ureteric obstruction	6.3	64	4.0
7	25	M	Ureteric obstruction	7.2	64	4.6

Table 5 Two disease states of schistosomal acute appendicitis

Feature	Granulomatous	Obstructive
Sex	Male	Male
Age range (years)	17-30	25-45
Median	23	39
Total white cells	Normal or mild leucocytosis	Leucocytosis
Neutrophils (blood)	Normal	Increased
Granulomas with tissue necrosis	Present	Absent
Tissue eosinophils	Numerous	Relatively few
Purulent exudate	Absent	Present
Fibrosis and calcification of wall	Absent	Present
Faecolith	Absent	Absent
Pathogenesis	Immunological	Bacterial: follows fibrotic obstruction
Time of occurrence after infestation	Early (weeks)	Late (months to years)

acute appendicitis; we suggest that this be termed schistosomal granulomatous acute appendicitis. These patients were all men, but of a relatively younger age, 17 to 30 years and a median of 23 years. Their total white cell counts were either normal or low-high in contrast to patients in the group with obstructive appendicitis who, except one, had total white cell counts above $8.7 \times 10^9/l$. Absolute neutrophilia was noted in most of the patients with schistosomal obstructive acute appendicitis. Blood eosinophilia was noted in some cases, and was not an important differentiating feature between the two disease states.

Granulomatous tissue destruction is probably the direct cause of symptoms and signs in patients with schistosomal granulomatous acute appendicitis. The granuloma formation is most likely a host immunological reaction to a product of the ova, the so called soluble egg antigen (SEA).⁵ It has been speculated that granuloma formation reaches its maximal size several weeks after onset of egg laying and thereafter decreases around eggs newly deposited in tissues. This phenomenon was originally called endogenous desensitisation.^{6,7} In support of this theory of an immunological reaction to recently deposited eggs, one of the appendices with active granulomatous inflammation that we studied showed a viable schistosomal worm in a venous channel of the appendiceal wall, probably indicating recent ova laying (fig 4). The relatively younger age of patients with schistosomal granulomatous acute appendicitis further supports this theory, indicating a probably recent infection with schistosomes.

Granulomatous inflammation of the appendix has been reported to be the direct cause of symptoms and signs of acute appendicitis. Fourteen of 19 patients with isolated Crohn's disease of the appendix had a history of less than 72 hours and a clinical diagnosis of acute appendicitis.⁸ In another series⁹ 22 of the reviewed 31 cases with primary Crohn's disease of the appendix had a preoperative diagnosis of acute appendicitis. In a third series¹⁰ six of 12 patients with Crohn's disease of the appendix had a disease history of one to three days. Vague right lower abdominal pain due to granulomatous appendicitis, presumably secondary to yersinia infection was reported in three cases.¹¹ Tuberculosis¹²⁻¹⁴ and sarcoidosis¹⁵ were also reported to offset the appendix and produce symptoms and signs of acute appendicitis. In all of these cases and in schistosomal granulomatous acute appendicitis it was the granulomatous destruction of tissue that was the direct cause of pain in the absence of purulent exudation.

The data presented suggest that schistosomes could cause acute appendicitis via either one of two pathogenetic pathways. The recently deposited ova might induce an immunological granulomatous reaction leading to tissue destruction and thus directly leading to acute appendicitis (schistosomal granulomatous acute appendicitis). This occurs in younger patients during the early phase of egg laying in the appendix. Neutrophil leucocytosis is not a characteristic feature. Schistosomes could also result in acute appendicitis via an indirect pathway. Excessive fibrosis, the result of long standing inflammation and calcified ova in the

wall, could lead to obstruction followed by bacterial infection, which occurs in other forms of obstructive acute appendicitis.

The presence of schistosomal ova in the wall of the appendix is not always symptomatic. Appendices with schistosomal ova but without pathological evidence of recent symptomatic inflammation were removed in seven instances (table 4). In three patients this occurred during either exploration for ureteric obstruction (two patients) or cholecystectomy (one patient). There were no symptoms or signs referable to the appendix. In two instances the indication for removal was vague symptoms referred to as chronic appendicitis. Two other patients had a clinical diagnosis of probable acute appendicitis, which was not confirmed at operation or histologically. In all seven patients the total white cell counts were normal, with a normal neutrophil count but an occasional eosinophilia. They were all men with an age range of 18 to 45 years and a median of 30 years. These fibrotic appendices containing the calcified schistosomal ova were asymptomatic. If left alone, they are probably the precursor lesion of schistosomal obstructive acute appendicitis, which occurred in an older age group (median 39 years).

Fig 4 Appendix with viable schistosomal worm in venous channel in wall. (Haematoxylin and eosin.) $\times 125$.

In conclusion, we believe that schistosomal acute appendicitis is a definite clinicopathological entity. It occurs in about 1-5% of all cases of an appendicitis like syndrome presenting to surgeons practising in endemic areas. The mere presence of schistosomal ova in the appendix without a purulent or granulomatous inflammatory reaction is, on the whole, asymptomatic, but the resulting fibrosis may later produce the obstructive form of schistosomal acute appendicitis. Schistosomal acute appendicitis exists as two disease states that differ in some of their clinical and histopathological features, as well as in their pathogenic mechanisms (table 5).

We thank Mr Andrew Archibald for his help with the half tones, and Mrs Lolita Galdones-Santos for her secretarial help.

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