MULLERIAN DUCT DYSGENESIS AND BILHARZIASIS: REPORT OF A CASE*

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SUMMARY

A case of Mullerian duct dysgenesis with selective anterior hypopituitarism and bilharziasis affecting the fallopian tubes, ovaries, vagina and rectum is reported.

The patient presented with primary amenorrhoea and poorly formed secondary sex characteristics. Laparotomy confirmed the absence of a normal uterus and its replacement by a fibrous cord. The ovaries were small and hypoplastic and follicle growth was retarded. Low gonadotrophic hormone, oestrogen and progesterone levels were demonstrated.

Bilharziasis as a cause of delayed puberty, primary amenorrhoea and menstrual disturbances is discussed. The patient was treated with a single injection of Etrenol. A rectal snip for presence of viable bilharzia ova 6 weeks after treatment was negative.

Bilharzia is an endemic disease in parts of South Africa. The rivers flowing into the Indian Ocean are infested or potentially infested and the intermediate host snails have also been found in the tributaries of the Vaal River in the south-western Transvaal. In some parts of these endemic areas, among the peoples of the northern and eastern Transvaal, Natal, and the Transkei, the incidence of infestation from an early age is high.

Several excellent papers dealing with gynaecological bilharziasis in South Africa have been published.[1-3] No section of the female genital tract is exempt from infection, although certain parts are more commonly affected than others.

Recently a case of diffuse pelvic bilharziasis associated with Mullerian duct dysgenesis was found in a Bantu female at Baragwanath hospital. It is worth while recording such a case, since a similar case has not been recorded in the literature to date.

CASE REPORT

A 20-year-old Swazi nullipara was seen in the Gynaecological Outpatient Department with the complaint that she had never menstruated. She was admitted for investigation of primary amenorrhoea on 21 July 1970. She was born near Sabie in the Eastern Transvaal in 1949. Seven years later her family moved to within 5 miles of the Numbi Gate of the Kruger National Park. Here she resided until November 1969 when she moved to Johannesburg. Medically, she had been well, never having been admitted to a hospital. She does, however, remember an episode of passing blood in her urine at the age of 10 years. This cleared up spontaneously in a few weeks without treatment. The patient was one of a family of 8 children. Most of her brothers and sisters have had bilharzia at some stage. However, none has had medical treatment.

On general examination, the patient was a well-nourished, intelligent, young Bantu female. There was no evidence of chronic disease. She was 168 cm tall and weighed 53·5 kg. The blood pressure was 110/70 mmHg. The temperature was normal. There was no evidence of anaemia. The cardiovascular, respiratory and central nervous systems were normal. No enlargement of the liver or spleen or any other abnormality was detected on examination of the abdomen. Evidence of a diminished oestrogen output was manifested clinically by poor breast development, and poorly developed external genitalia. The pubic and axillary hair growth was scanty.

A rectal examination was performed as the patient was *virgo intacta.* This revealed a small hard cervix, but no uterus could be palpated. Bilateral firm cords were palpated in the region of the ovaries. These were thought to represent streak ovaries.

At this stage, a diagnosis was made of primary amenorrhoea, with evidence of some Mullerian maldevelopment and oestrogen deficiency.

Investigation

Initially, she was investigated to determine the cause of her amenorrhoea. A full blood count on admission showed a haemoglobin level of 14·9 g/100 ml. The leucocyte count was 5 900/mm³ with 3% eosinophils. Urea and electrolyte estimations were normal. The Pregnosticon test for pregnancy was negative. Protein-bound iodine of 6·6 μg/100 ml and a total cholesterol of 198 mg/100 ml were within normal limits. Lateral vaginal wall smears showed completely atrophic material consisting entirely of parabasal cells. Well-marked inflammatory changes were noted and a few possible degenerate trichomonads were commented on by the cytologists. The cells were all chromatin positive. A buccal smear confirmed chromatin-

*Date received: 16 November 1970.

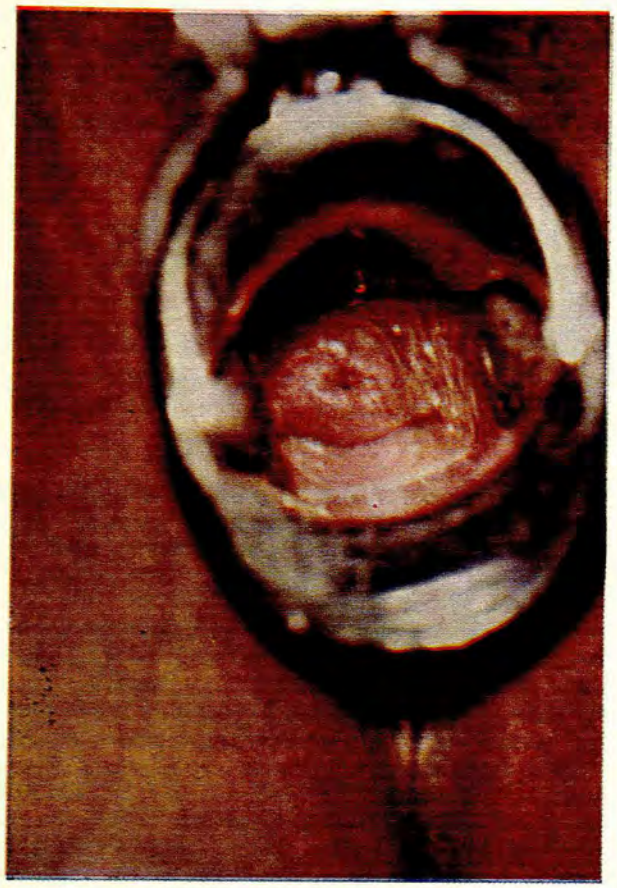

Fig. 1. Small rudimentary, non-patent cervix.

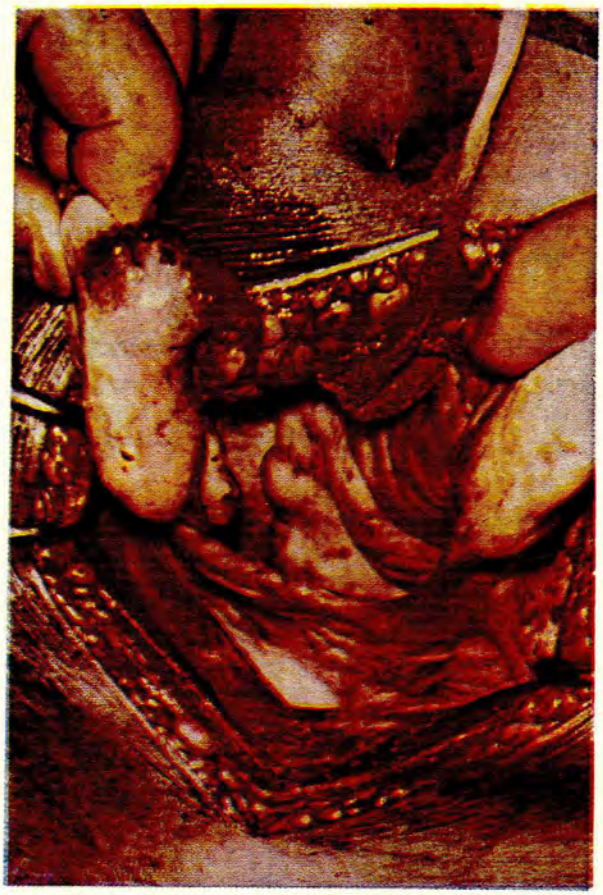

Fig. 2. Attenuated round ligament on the left side attached to the apex of the fibrous cord which replaced the uterus. The fibrosed cords comprising the proximal two-thirds of the fallopian tubes are shown. Note the distended distal third of the fallopian tubes on either side.

positive nuclei. Chromosome analysis of the peripheral blood showed a modal number of 46, karyotype 46XX. The 24-hour urine studies for follicle-stimulating hormone showed a level of less than 6 mouse units (normal female = 6 - 48 mouse units). This was confirmed by three further 24-hour urine specimens. Luteinizing hormone levels were below 25 IU/litre on three occasions (normal pre- and post-ovulation females have levels above 20 IU/litre). Low total oestrogen and low pregnanediol levels, of less than 1 μg/24 hours and 0·5 mg/24 hours respectively, were found in the urine on two different occasions. Total 17-hydroxycorticosteroid level of 5·0 mg and 17-ketosteroid level of 6·0 mg were normal for her age.

On radiological examination, chest and skull X-rays were normal. The pituitary fossa was normal. An intravenous pyelogram, to detect possible associated renal abnormalities, was normal. A gynaecogram showed the absence of a uterus but showed two bi-

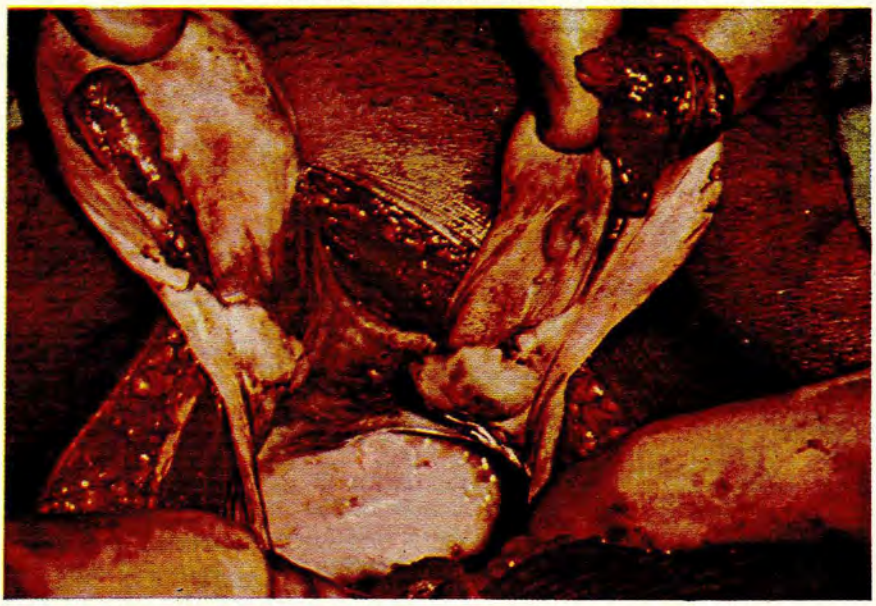

Fig. 3. Fibrous cord replacing the uterus in the centre. On either side of this one sees fibrous cords, which are the proximal two-thirds of the fallopian tubes. The dilated distal third of the fallopian tubes are well seen on either side. Note the fimbriae. Both infundibulo-pelvic ligaments are well shown inferolaterally. Note the two hypoplastic ovaries. Tiny, blue cysts can be seen in the right ovary.

lateral masses in the position of normal ovaries. These could not be felt on rectal examination. At this stage an examination under anaesthesia was performed. This confirmed the previous findings of poorly developed labia majora and minora, as well as a very small clitoris. Pubic hair was fine and scanty. The vagina was 5 cm long and an annular hymen was present. A small rudimentary cervix was palpated and later visualized with a small Cusco bivalve speculum (Fig. 1). Attempts to probe the external cervical os with a fine probe proved impossible. A punch biopsy specimen of the cervix was taken for histological examination. Neither the uterus nor the two masses which were shown on the gynaecogram could be palpated. However, two definite cords could be felt in the normal position of the fallopian tubes.

A laparotomy was performed on 11 August 1970. The abdomen was entered through a left paramedian incision. The absence of the uterus was confirmed. However, this was replaced by a fibrous cord about 5 mm in diameter. Poorly developed round ligaments were identified on either side attached to the apex of this fibrous cord (Fig. 2). The fallopian tubes were grossly abnormal. The outer two-thirds of both tubes were dilated and measured 5·5 × 2·5 cm. Fimbriae could be seen on both sides. These tapered down suddenly and the medial one-third of the tube on either side consisted of a firm fibrous cord which was not patent. Small hypoplastic ovaries were present on both sides (Fig. 3). Macroscopically, the ovaries were white but had numerous tiny blue cysts on the surface. Right-sided salpingo-oophorectomy was performed and a biopsy specimen was taken from the ovary on the other side. No adhesions were noted in the abdomen. She had an uneventful postoperative course. The temperature did not rise above 99·5°F. The abdominal wound had healed well by the 8th postoperative day.

Histopathological Report

The specimen consisted of a fallopian tube 5·3 cm in length with an ovary attached and a 2-cm diameter area of fibrosis between the tube and the ovary. A separate contralateral ovarian biopsy was also submitted. Cut section of the larger specimen showed the fallopian tube to be thickened and the fibrosis to extend almost the entire length of the tube. The ovaries contained tiny cysts (Fig. 4).

Microscopic examination showed the lumen of the tube to be within normal limits. The mucosa and the peritubal fibrosis showed the presence of innumerable ova of *Schistosoma haematobium* (Fig. 5). The area of fibrosis showed, in addition to ova, both adult male and female schistosomes (Fig 6).

The ovaries both showed similar features. Ova of schistosoma were present in abundance and there were numerous primordial follicles, one or two early Graaffian follicles and the occasional simple follicle cyst. No evidence was noted of corpus luteum, corpus fibrosum or corpora albicantia in any section studied (Fig. 7).

Section of the cervix uteri showed no evidence of parasitic invasion. The endocervical mucosa appeared low and the glands immature. A rectal biopsy also showed the presence of schistosomal ova. A repeat vaginal smear detected the presence of *Schistosoma haematobium* ova and a vaginal biopsy showed evidence of marked non-specific chronic inflammation and haematoidin pigment. The bilharzial complement-fixation test was positive and cystoscopy showed mild haemorrhagic cystitis. Bilharzia ova, however, were not found on terminal and 24-hour urine studies.

Treatment

A single dose of Etrenol (hycanthone) 150 mg was given by deep intramuscular injection. No adverse reaction was observed in the patient. Liver-function tests before the injection were within normal limits, and repeat tests 24 hours later showed no change. A rectal biopsy performed 6 weeks after treatment showed a few degenerated bilharzial ova.

DISCUSSION

A case of Mullerian duct dysgenesis and coincidental bilharziasis of the pelvic organs presenting with primary amenorrhoea is reported. We believe this to be a rare occurrence. No reference to a similar case could be found in the literature. Bilharzia constitutes, after malaria, the second most important epidemiological problem facing the world today.[4] It is well known that the male worm carries the female in its gynaecophoric canal. They migrate against the host's blood stream until they reach the terminal venules of the vesical and haemorrhoidal plexus. The female then leaves the male and passes along terminal venules of the vesical and rectal vessels and deposits its ova. Some of these ova pass through the rectal and vesical mucosa to the exterior, causing open lesions; others fail to reach the exterior and remain entrapped in the tissues, causing closed lesions. The reaction of the host tissue varies, but usually it is mild in open lesions and severe in closed ones. The nature of the reaction may be proliferative, simulating a neoplasm, or fibrous and granulomatous, leading to bilharziomatous masses, stenosis or calcification in the affected tissues.[5]

In this case, the male and female worms were found in the stenosed, fibrous proximal portion of the fallopian tube and the distended distal portion of the fallopian tube showed marked fibrous tissue response. The amenorrhoea in this case was due to end-organ maldevelopment, in that the uterus was only a vestige, comprising a fibrous cord 5 mm in diameter. This is most likely due to failure of canalization of the Mullerian system. In addition a reduction in stimulatory hormone levels, as evidenced by below-normal-for-age levels of follicle-stimulating hormone, luteinizing hormone and total oestrogen and progesterone, was found.

Attia[6] reported on a case of complete suppression of menstruation due to bilharzial endometritis and Mouktar[5] reports a case of a patient with bilharzial endometritis presenting with primary amenorrhoea, who failed to menstruate despite priming with oestrogen and progestogen. Both these cases had normal uteri.

It has also been reported that bilharzial infestation of the ovaries is capable of causing a disturbance in the endocrine control of the menstrual cycle, either by direct destruction of ovarian tissue or by a varying degree of

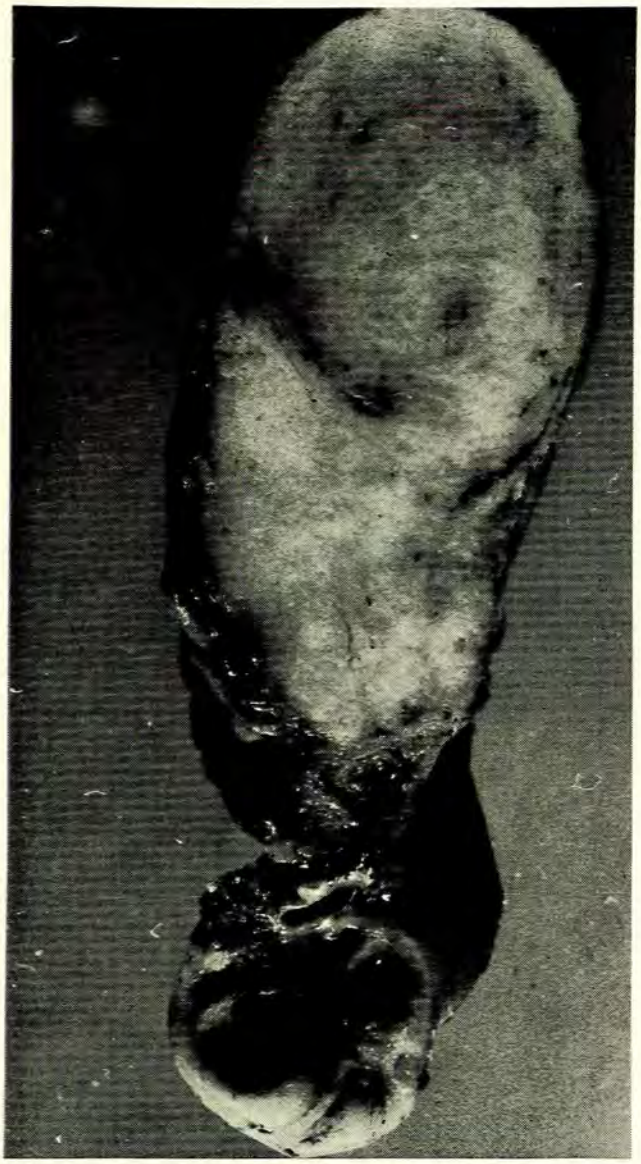

Fig. 4. The macroscopic pathological specimen showing a thickened and fibrosed fallopian tube and the ovaries, which contained tiny cysts.

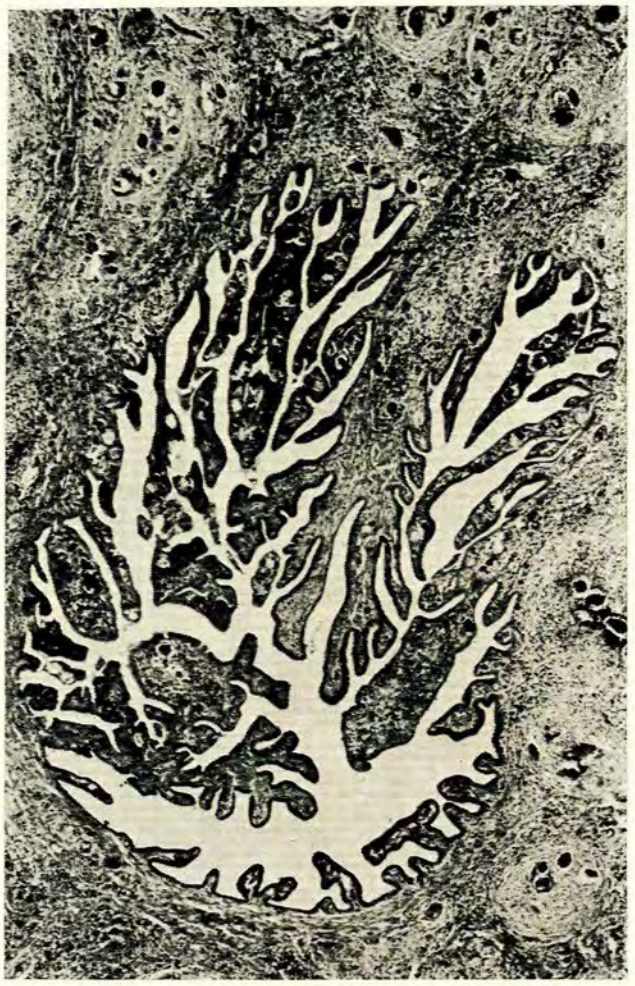

Fig. 5. Patent lumen of the right fallopian tube and innumerable ova of *Schistosoma haematobium*.

thecal proliferation in the ovary. Ferguson[7] reported that in young married Egyptian women, the ovaries might be so altered by a chronic oophoritis that this form of infection persisting from infancy might be a cause of sterility.

Gilbert[8] and Afifi[9] report that the primary amenorrhoea so often seen in bilharziasis is due to ovarian fibrosis. Charlewood *et al.*[2] felt that this might sometimes be the case in the very severe disease seen in Egypt, but felt that it was unlikely that the ovarian tissue was sufficiently destroyed in Rhodesian or South African cases to cause amenorrhoea.

Girges[10] said the following about *Schistosoma haematobium* infections in Egypt: 'In girls, the normal establishment of puberty and menstruation (11 - 13 years), may be delayed up to as late as 17 - 22 years. The periods may be suspended for 2, 4, 5 and 8 months, in some cases altogether, the latter taking place . . . at about 30 - 40 years.' According to Nabawy *et al.*[11] sexual underdevelopment may be seen in Egyptian children suffering from bilharziasis. Some children manifested stunting of growth; however, sexual underdevelopment did not always occur in these children.

Prates[12] suggested that bilharziasis could be a congenitally acquired disease. Narabayashi[3] has observed ova of *S. japonicum* in the stools of 3 newly born infants whose mothers had been working during their pregnancy in contaminated rice fields. Cases of placental bilharziasis have been reported.[13]

One could postulate that this patient, who lived in an endemic area all her life, could have acquired bilharziasis congenitally and that this predisposed to the maldevelopment of her sexual apparatus. However, we do not feel this to be likely. Toxaemia and debility have been suggested as a cause of the primary amenorrhoea.[14] These patients may be ill-nourished, stunted in growth and scholastically retarded.[15] Our patient was intelligent, in good general condition, and was certainly not stunted.

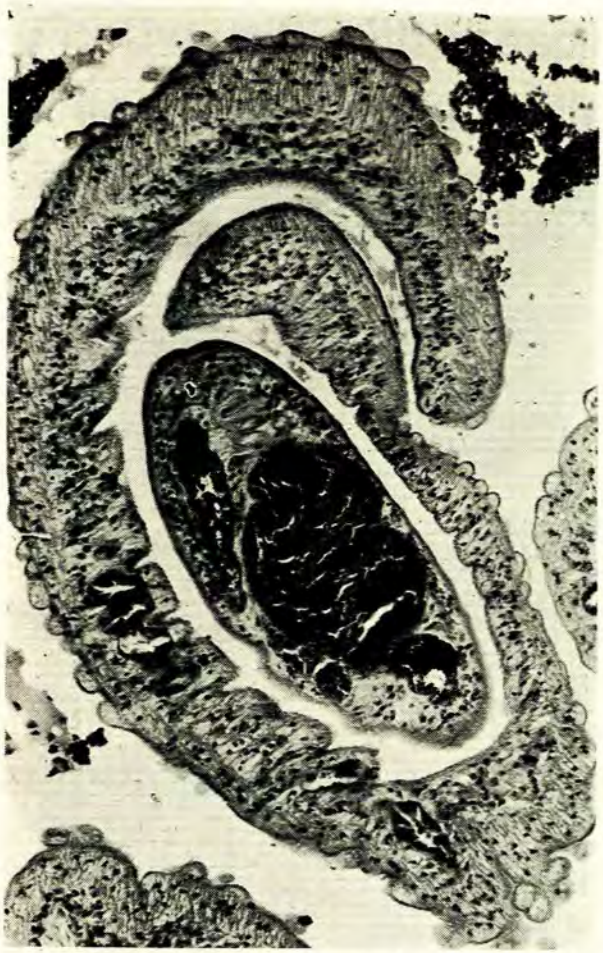

Fig. 6. Male and female worms, the female lying in the gynaecophoric canal of the male.

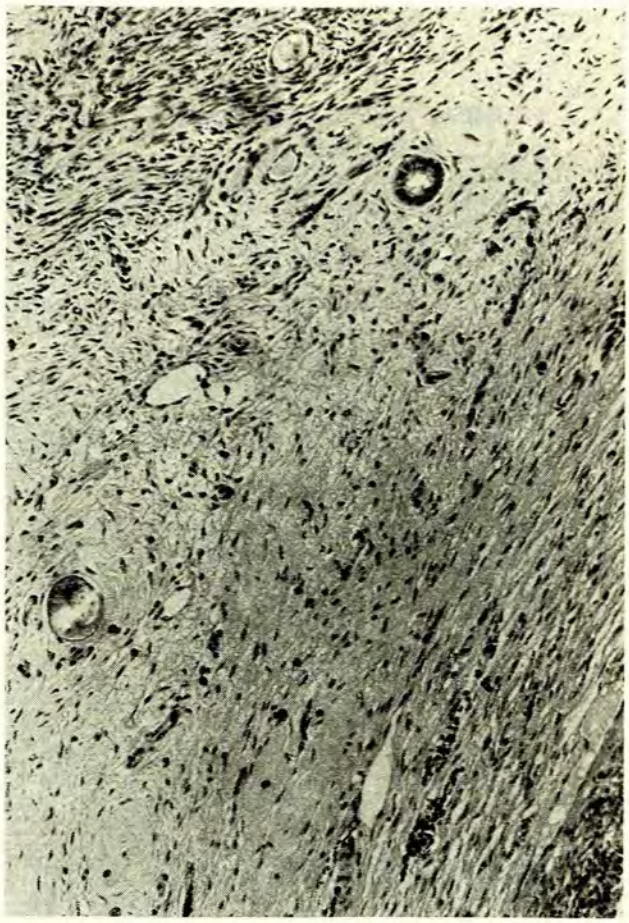

Fig. 7. Ovary showing ova of *Schistosoma haematobium* and a few immature follicles.

Badawy[16] makes the statement that *Schistosoma mansoni* tends to affect mainly the tubes and ovaries, whereas *S. haematobium* usually involves the vulva, vagina and cervix. Our patient had *S. haematobium* involvement of the fallopian tubes and ovaries and it seems that the site involved depends on the parasite prevalent in the area. Fallopian tube bilharziasis in South Africa, according to Charlewood *et al.*[2] and Friedberg and Schneider,[3] causes a fibrous tissue response in the muscular and serosal layers but does not so affect the mucosa. Such tubes are thickened and heavy, but are characteristically patent. In this case, the proximal third of the tube was stenosed and the dilated distal two-thirds were patent.

A striking feature in this case was the complete absence of adhesions in the peritoneal cavity. Authors stress the difficulty of pelvic surgery in bilharziasis due to the extensive fibrosis and adhesions which are encountered.[5] Charlewood *et al.* felt that these only occur when secondary infection is present as well.[2]

A further unusual feature is the almost complete non-development of the corpus uteri associated with a hypoplastic, non-canalized cervix uteri and short, but patent, vagina.

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