Ovarian Manson's Schistosomiasis: Rare Diagnosis or Underestimated Prevalence?

Esquistossomose mansônica no ovário: diagnóstico raro ou prevalência subestimada?

Elainne Christine de Souza Gomes[1] Ana Lúcia Coutinho Domingues[2]
Francisco Carlos Amanajás de Aguiar Júnior[3] Constança Simões Barbosa[1]

[1] Department of Parasitology, Laboratório e Serviço de Referência em Esquistossomose, Centro de Pesquisas Aggeu Magalhães, Fiocruz – Ministério da Saúde, Recife, Pernambuco, Brazil
[2] Hospital das Clínicas, Universidade Federal de Pernambuco, Recife, Pernambuco, Brazil
[3] Centro Acadêmico de Vitória, Universidade Federal de Pernambuco, Recife, Pernmbuco, Brazil

Address for correspondence Elainne Christine de Souza Gomes, PhD, Departamento de Parasitologia, Centro de Pesquisas Aggeu Magalhães, Fiocruz – Ministério da Saúde, Av. Professor Moraes Rego, s/n - Campus da UFPE - Cidade Universitária, Recife, PE, Brazil (e-mail: elainne.ca@gmail.com).

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Abstract

The occurrence of Manson's schistosomiasis in organs of the female reproductive tract is an uncommon event, given that the etiological agent for this disease is a blood parasite that inhabits the mesenteric veins. In this case report, a 45-year-old female patient reported that her first symptoms had been strong pain in the left iliac region around two years earlier. An endovaginal pelvic ultrasonography showed that the left ovary was enlarged, and the report suggested that this finding might be correlated with clinical data and tumor markers. After being examined at several healthcare services, the patient was referred to an oncology service due to suspected neoplasia, where she underwent a left ovariectomy. The result from the histopathological examination showed the presence of granulomatous inflammatory processes surrounding both viable and calcified eggs of *Schistosoma mansoni*. There was no evidence of any neoplastic tissue. The patient was medicated and followed-up as an outpatient.

Keywords

- ectopic schistosomiasis
- ovarian schistosomiasis
- schistosoma mansoni
- granuloma
- neoplasia

Resumo

A ocorrência da esquistossomose mansônica em órgãos do aparelho reprodutor feminino é um evento pouco comum, tendo em vista que o agente etiológico desta doença é um parasito sanguíneo que habita as veias mesentéricas. Neste relato de caso, uma paciente de 45 anos referiu como primeira sintomatologia fortes dores na região ilíaca esquerda há cerca de 2 anos. Uma ultrassonografia pélvica endovaginal identificou aumento do ovário esquerdo, e o laudo sugeriu correlacionar tal achado com dados clínicos e marcadores tumorais. Após passar por vários serviços de saúde, a paciente foi encaminhada para um serviço de oncologia por suspeita de neoplasia, sendo submetida a uma ovariectomia à esquerda. O resultado do exame histopatológico evidenciou a presença de processos inflamatórios granulomatosos em torno de ovos viáveis e calcificados de *Schistosoma mansoni*. Não houve qualquer evidência de tecido neoplásico. A paciente foi medicada, e seguiu em acompanhamento ambulatorial.

Palavras-chave

- esquistossomose ectópica
- esquistossomose de ovário
- schistosoma mansoni
- granuloma
- neoplasia

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Introduction

In Brazil, schistosomiasis continues to be a neglected disease. Despite the healthcare services' efforts to control and reduce its prevalence, it has persisted over the years, and continues to affect thousands of people who live in endemic areas.[1,2] In these areas, new epidemiological scenarios have emerged to challenge the healthcare services' strategies for diagnosing and controlling this disease.[3,4] Reports in the literature have drawn attention to the growing number of cases of ectopic forms of schistosomiasis.[5–8] Prominent among these is one of the severest presentations of this parasitosis: schistosomal myeloradiculopathy, caused by the formation of granulomas in the central nervous system that induce incapacitating lesions in the lower limbs of the individuals affected.[6,9,10]

In cases of infection by *Schistosoma haematobium*, which affects the reproductive and urinary systems of both men and women, findings of granulomas in these tissues are common.[11–14] However, there are few records regarding *Schistosoma mansoni*, and the infections caused by this parasite are considered to be ectopic presentations of the disease, given that the habitat of this species is the mesenteric veins that irrigate the digestive tract.[15,16]

Over the last two decades, there have been several reports from around the world of cases of Manson's schistosomiasis associated with the female reproductive system.[17,18] Brazil is prominent in this regard, with more than ten scientific papers presenting cases affecting these organs, which include the ovaries, the uterine tubes and the endocervix.[7,19,20] Some authors have drawn attention to the underreporting of the ectopic forms of the disease, which would be directly associated with the difficulty in diagnosing them and with the lack of proper investigation for the confirmation of such diagnostic hypotheses.

The aim of this study was to present a case of ovarian schistosomiasis and to raise a discussion on the underreporting of the cases involving the female reproductive system. Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

Case Report

A 45-year-old female patient reported that in the middle of 2014 she began to feel a strong pain in her left iliac region. After going to several emergency services, she underwent an endovaginal pelvic ultrasonography (in September 2014), which showed enlargement of the left ovary (image of the cyst: 2.84 cm; total volume of the ovary: 16.82 cm^3; normal range: 3.0–9.0 cm^3). The report suggested that there might be a correlation between this finding and clinical data and tumor markers. In October 2014, the patient underwent tumor marker tests, which showed that they were within the normal range (cancer antigen [CA] 125: 11.1 IU/mL; CA 19–9: 13.6 IU/mL). However, magnetic resonance imaging showed that the left ovary was enlarged, and that ovarian neoplasia could not be ruled out. The patient underwent new blood tests in the beginning of 2015, to investigate cancer markers (carcinoembryonic antigen: 3.0 ng/mL; CA 125: 8.7 IU/mL), and the results found were also within the normal range.

The patient was then referred to the oncological service of Hospital das Clínicas de Pernambuco, because of suspected neoplasia. A left ovariectomy was performed as surgical treatment to remove the possible tumor tissue. However, the histopathological examination of the material extracted identified ovarian schistosomiasis caused by the presence of granulomatous inflammatory processes surrounding both viable and calcified eggs of *S. mansoni*. There was no evidence of any neoplastic tissue (in April 2015).

The patient was then referred to the specialized schistosomiasis outpatient service of the same hospital for evaluation, treatment and follow-up, but was only able to get her first consultation with the doctor one year after the surgery (in April 2016). This patient was born in the municipality of Cabo de Santo Agostinho, and was living in the municipality of Jaboatão dos Guararapes, which are both endemic localities for schistosomiasis in Pernambuco. At the time that her history was being taken, she said that she did not have any upper digestive tract hemorrhage or symptoms of pulmonary arterial hypertension. She reported that around ten years earlier, she had habitually been bathing in rivers.

Upon physical examination, the patient was in good general condition. She was eupneic, had normal coloration, and did not present jaundice. Her weight was 52.4 kg, and her height was 1.48 m; therefore, her body mass index (BMI) was normal (23.9). An ultrasound examination of her abdomen did not show any abnormalities of the liver, spleen, portal vein, gallbladder or kidneys. Three parasitological feces examinations were performed using the Kato-Katz method, at the schistosomiasis reference center of Centro de Pesquisas Aggeu Magalhães, Fiocruz, Pernambuco. The examinations revealed a residual *S. mansoni* infection with the following parasite loads: 60, 192 and 156 eggs per gram of feces respectively.

The results from these examinations and the histopathological material from the left ovary were sent to the clinical pathology service of Hospital das Clínicas. The macroscopic examination showed an irregular elastic yellow-brown tissue formation measuring 5.0 × 4.0 × 2.5 cm. The cut surface was compact and greyish-brown, with a brownish area measuring ~ 1.5 × 1.2 cm. Under a microscope, the observed surface was coated with simple squamous epithelium. In the cortical region, under the tunica albuginea, there were no ovarian follicles, but a large quantity of corpus albicans. In the medullary region, several foci of chronic granulomatous inflammation in the stroma of loose connective tissue that was richly vascularized and innervated were identified (►**Fig. 1**).

The granulomas presented degenerated eggs of *S. mansoni* at their centers, surrounded by lymphoplasmacytic and eosinophilic inflammatory infiltrates, occasional multinucleated giant cells and epithelioid macrophages that were organized into palisades. Slight hyperplasia of the fibroblasts and incipient fibroplasia were observed. (►**Fig. 2**).

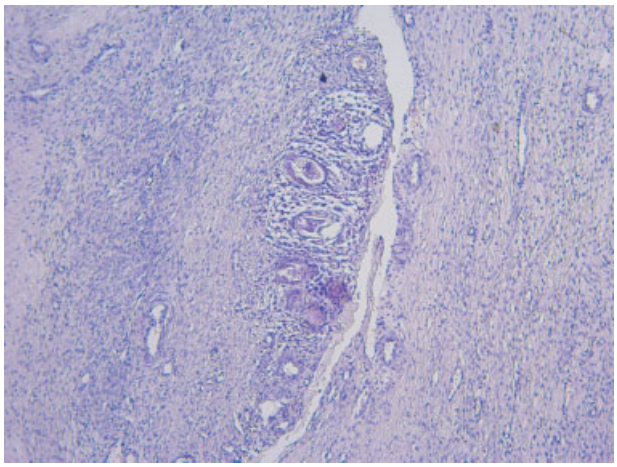

Fig. 1 Granuloma characteristic of schistosomiasis in ovary tissue. Histological section through the ovary in the medullary region, with hematoxylin-eosin staining, at final magnification of 100x, showing the presence of multiple small schistosomal granulomas arranged concentrically around degenerated eggs of *S. mansoni*.

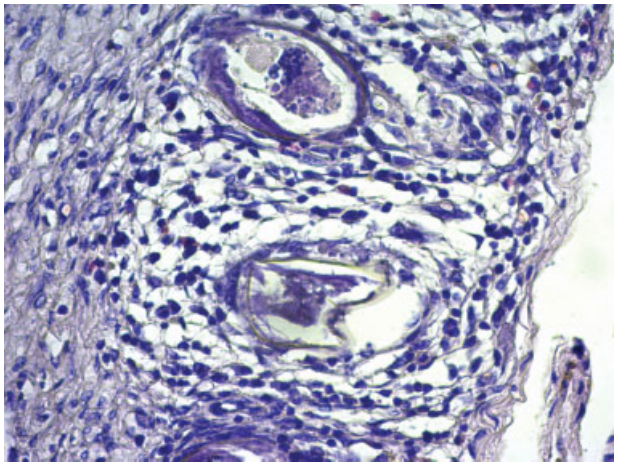

Fig. 2 *Schistosoma mansoni* egg in ovary tissue. Histological section through the ovary, with hematoxylin-eosin staining, at final magnification of 400x, showing eggs of *S. mansoni* surrounded by lymphoplasmacytic and eosinophilic infiltrates, epithelioid macrophages and slight fibroplasia.

Treatment consisting of praziquantel 50 mg/kg (600 mg/tablet; 4.5 tablets) was administered. Because the disease was in one of its ectopic forms, a two additional treatments with the same dose, at two-month intervals, were performed. The patient was followed-up as an outpatient.

Discussion

The histopathological findings from this case, consisting of the presence of schistosomal granulomas surrounding eggs of *S. mansoni*, along with the formation of inflammatory infiltrate and the presence of multinucleated giant cells, are expected in cases of chronic *S. mansoni* infection.[8,21,22] These findings have already been described in many other cases of ovarian schistosomiasis.[20,23–25] This is an immune-cellular response to the presence of a foreign body in the tissue stroma. Schistosomal granulomas can be characterized as compact and organized collections of migrant cells that, together with cells of the affected organ, become arranged as components of a heterogeneous extracellular matrix that forms a spherical structure surrounding each egg individually.[22] Schistosomal granulomas are the best example in the literature of granulomatous reactions caused by extracellular agents.[26]

According to the data in the literature, the ovaries are the most affected organ in cases of female genital schistosomiasis, followed by the cervix, the fallopian tubes, the uterus and the vulvae.[11,27,28] This is due to the migration of the adult parasites through a complex vascular network. Initially, the parasites leave the portal vein and migrate against the venous flow until reaching the anorectal plexus. After overcoming this obstacle, the worms have easy access to the perivesicular and uterovaginal plexuses via the rectovaginal septum or through vascular networks between the bladder and the reproductive organs. In this manner, these parasites can migrate to any genital organ,[11,29] thus causing the characteristic tissue lesions and a variety of signs and symptoms.

In the present case report, the symptoms presented by the patient were in line with what has been described in the scientific literature. Pain in the pelvic region has, by far, been the symptom most frequently mentioned, followed by bleeding, discharges, changes to the menstrual cycle and pain and bleeding during coitus.[17]

Although ovarian schistosomiasis is not a common clinical finding for infections caused by *S. mansoni*, several cases have been described in the Brazilian literature.[20,23–25,30] However, it is noteworthy that in most of these cases, neoplasia was not a diagnostic hypothesis at any moment of the clinical investigation.[20,23–25,30] In most cases of ectopic forms of Manson's schistosomiasis, a single parasitological examination may have the capacity to prove the presence of parasitosis and open the way to better directed history-taking and investigation, thus enabling faster diagnoses with less harm to the patients' health.

We should emphasize that the time spent on reaching a precise diagnosis and the therapeutic path followed by the patient until the diagnosis was obtained and the adequate treatment was instituted are unacceptable, given the simplicity of the parasitological diagnosis for this parasitosis. In fact, in most cases, the diagnosis was only made after an exploratory surgical intervention, by means of a histopathological examination of the material extracted.[17,19,20,24,25,28,31] Furthermore, some patients were discharged without the adequate treatment of the parasitosis,[8] and had to seek specialized hospital outpatient services to obtain a simple drug treatment consisting of the administration of praziquantel in a single or fractioned dose.[32] It is important to mention that the use of three doses of praziquantel to treat ectopic forms of the disease is a clinical

practice among specialists to ensure parasitological cure. This is done firstly because the cure rate with only one dose is around 75%;[30] and secondly, in the ectopic forms of the disease, the worm eggs are encysted (encapsulated by granulomas), thus hindering drug access.

A certain degree of neglect on the part of healthcare services in Brazil regarding proper treatment and referral for individuals diagnosed with ectopic forms of schistosomiasis has been observed.[8] This goes against the guiding principle of the Brazilian National Health System, which is that healthcare actions should be comprehensive, aiming to meet all of the individuals' needs, going from health promotion to health recovery.[33] Thus, we can presume that many ectopic cases of this disease are underreported. Accidental diagnoses that are reached through investigating other diagnostic hypotheses are less likely to be recorded in the healthcare information systems.

The Brazilian Ministry of Health currently categorizes schistosomiasis as a disease that is "on the way to eradication." Nevertheless, it persists as a neglected disease because of the lack of knowledge and regard among healthcare professionals and services, which is reflected in maintenance of the prevalence and incidence rates for this disease.

Although uncommon, occurrences of cases of Manson's schistosomiasis associated with the female reproductive system are a reality that needs to be taken into consideration, given the existence of patients coming from endemic areas. According to the data in the literature, between 6 and 27% of women with intestinal schistosomiasis temporarily suffer from pathological conditions induced by the accidental presence of eggs of this parasite in their genital organs.[11] A study in an endemic area for schistosomiasis that used biopsies and cervical smears did not identify any cases, but the authors raised the hypothesis that these results might have been related to the low parasite load of the population of their study.[34]

The data in the literature on occurrences and cases of schistosomiasis associated with the female reproductive tract are divergent. However, a recent bibliographic review on this topic drew attention to the lack of population-based studies in areas that are endemic for Manson's schistosomiasis, taking into account the reports from Brazil regarding the ectopic form of the disease in the female reproductive tract.[18]

Taking into consideration the current estimate of four to six million individuals in Brazil infected by S. mansoni,[2] we hope that healthcare professionals and services will direct their attention to the present study, especially the professionals who act directly in the specialty of obstetrics and gynecology, so that cases like the one described here do not go unnoticed. We should emphasize that reporting these cases is essential in order to gain greater comprehension of the pathophysiology of this ectopic form of the disease.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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