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An interesting finding in the uterine cervix: *Schistosoma hematobium* calcified eggs

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ABSTRACT

Schistosoma hematobium infection is an endemic parasitic disease in Africa, which is frequently associated with urinary schistosomiasis. The parasite infection causes epithelial changes and disruption, facilitating the infection by the human papilloma virus and human immunodeficiency virus (HIV). The authors report the case of a 44-year-old African HIV-positive woman who presented an abnormal routine Pap smear. Colposcopy examination revealed dense acetowhite micropapillary epithelium covering the ectocervix, iodine-negative, an erosion area in endocervical canal, and atypical vessels. Histologic examination of the surgical specimens showed numerous calcified schistosome eggs (probably *S. hematobium*) and a high-grade cervical intraepithelial neoplasia. The relation between *S. hematobium* infection and bladder cancer is well known; however, this relationship with cervical cancer remains controversial. The symptoms of schistosomiasis of the female genital tract are rather non-specific, and are often misdiagnosed with other pelvic diseases. The familiarity of health professionals with schistosomiasis of the female genital tract is less than expected, even in endemic regions. Therefore, great awareness of this differential diagnosis in routine gynecological practice is of paramount importance.

Keywords
Schistosoma hematobium; Genital Diseases, Female; Schistosomiasis hematobia; HIV.

INTRODUCTION

Schistosomiasis hematobia is a common disease in many parts of the world, especially in developing countries with inadequate sanitation, and in many African regions (mainly southern and sub-Saharan Africa) where the risk of infection by freshwater contact is significant. Transmission also occurs in the Egyptian Nile River valley, in the Maghreb region of North Africa, and in regions of the Middle East.[1] Schistosomiasis is a chronic infection caused by blood flukes of the genus Schistosoma. The life cycle of the schistosome involves humans as the final host, and snails as the intermediate host. Urogenital schistosomiasis is considered a risk factor for human immunodeficiency virus (HIV) infection, especially among women.[2] Lesions are caused by the host response to either dead or live schistosome eggs.[3] The cervix, fallopian

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tubes, and vagina are the most common sites involved in S. *hematobium* infection. Female genital tract schistosomiasis usually does not present a single lesion, but with several coexisting lesions surrounded by an altered epithelium, which loses the physical barrier to some viral infections.[4]

S. hematobium has a known relationship with the development of bladder cancer; however, its association with cervical cancer remains controversial.[4] Recent studies argue that the parasite can act as a potential cofactor in cervical carcinogenesis. The female genital tract schistosomiasis occurs mostly during puberty. Therefore, the egg-induced cervical lesions (ulcer and erosion) present at the beginning of sexual activity, and facilitate the transmission and acquisition of the human papillomavirus (HPV) infection.[5] In the prospective study conducted by Van Bogaert[6], HIV-positive women with evidence of schistosome infection and cervical cancer were, at the time of diagnosis, approximately 15 years younger than those with invasive cervical carcinoma but who were HIV negative and free of schistosome infection.

Thus, treatment of genital schistosomiasis in women infected by HIV may prevent HPV infection. Eradication of schistosomiasis in endemic regions may contribute to controlling the spread of HIV.[4]

CASE REPORT

A 44-year-old Angolan woman was diagnosed with a high-grade intraepithelial lesion on Pap smear, which was confirmed by histology of the cervix biopsy that revealed high-grade cervical intraepithelial neoplasia (CIN 3). Her past medical history included obesity, hypertension, multiparity, and HIV infection diagnosed 8 years before. She was on antiretroviral therapy (lamivudine/nevirapine/zidovudine); the CD_4 count was 484/mm^3 and the viral load was 5970 copies/mL.

Colposcopic examination (Figure 1) revealed completely visible squamous-columnar junction, dense micropapillary acetowhite epithelium occupying all the ectocervix, iodine-negative, extending to the posterior fornix and erosion area in the endocervical canal. The classic conization was proposed because of the atypical vascularization involving the endocervix and the posterior lip, which is consistent with invasive disease.

Histologic examination of the conization specimen showed multiple calcified, degenerated, oval-shaped structures, some of them exhibiting a characteristic terminal polar spine, consistent with *S. hematobium* eggs, in a fibrotic stroma with neither granulomatous reaction nor apparent inflammatory cellular infiltration (Figure 2).

The overlying epithelium exhibited high-grade cervical squamous intraepithelial neoplasia with extension into endocervical crypts. Because of this finding, praziquantel therapy was proposed, and a total abdominal hysterectomy was undertaken because of the endocervical CIN 3 involvement, and a potential troublesome follow-up.

The surgical specimen revealed a CIN 3 extending to endocervical crypts in the residual cervix, with no evidence of schistosomiasis in the analyzed genital structures.

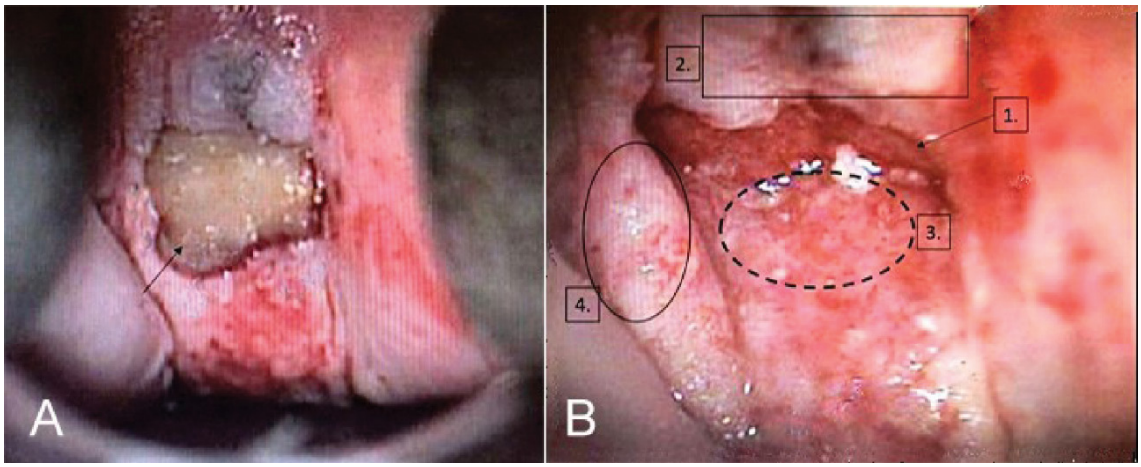

Figure 1. A – Colposcopic examination (× 10): cotton in cervical os (arrow). **B** – Colposcopy examination (× 16): 1. = Cervical os; 2. = Dense acetowhite epithelium; 3. = Atypical vessels; 4. = Sandy patches.

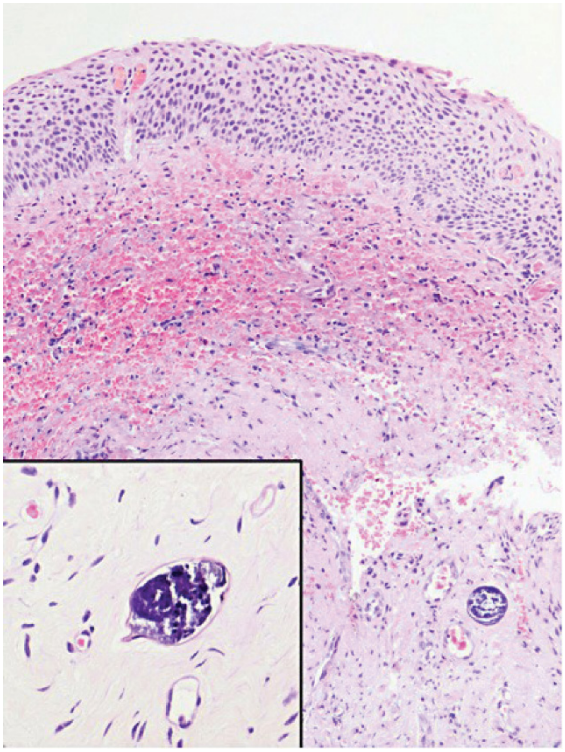

Figure 2. Photomicrography of a cervical conization specimen showing high-grade squamous intraepithelial neoplasia and calcified eggs of *S. hematobium* in the stroma. Note the poverty of inflammatory infiltration and the lack of granulomatous reaction (H&E, 100X; inset: H&E, 400X).

DISCUSSION

Genitourinary schistosomiasis, caused by an infection due to S. hematobium, can result in infertility and increased risk for HIV transmission. Eggs are excreted in the urine causing micro or macroscopic hematuria in early infection. In chronic infection, eggs cause granulomatous inflammation and ulceration, which leads to bladder wall fibrosis and calcification. In the female genitalia, one can find hypertrophic and ulcerative lesions in the vulva, vagina, and cervix. Infertility may be due to the involvement of the ovaries and fallopian tubes.[7]

A consensus meeting on female genital schistosomiasis held in October 2010 in Copenhagen[8] concluded that in women originating from *S. hematobium* endemic areas, one of three following gynecological examination findings is adequate to confirm the diagnosis: (I) grainy sandy patches; (II) homogenous yellow sandy patches; or (III) rubbery tubercles Before this meeting's statement, the genital tissue biopsy was considered the gold standard for the parasitological diagnosis of genital schistosomiasis.[3] The so-called sandy patches can appear grainy or homogenous and are often associated with abnormal blood vessels and easy bleeding due to the mucosal fragility.[9]

The cervix is thought to be the most frequent site for finding trapped eggs; however, it is believed that misdiagnosis may occur since eggs are found to be equally distributed in other pelvic sites in autopsy specimens.[3] A broad spectrum of histopathological features may be found, which range from a marked cellular infiltration wrapping the eggs to the formation of scar tissue apparently without inflammatory infiltration.[10,11] Histologically, viable and non-viable eggs of *S. hematobium* are surrounded by neo vascularization and high-density inflammatory cells infiltration. Calcified eggs may also induce vascular proliferations as well as an influx of immune cells, edema, and hemorrhage.

This agent should be investigated mainly in endemic regions, especially in HIV women. Schistosoma treatment would reduce the risk of neoplasia.

Kallestrup et al.,[12] in a randomized controlled trial with both HIV-positive and HIV-negative persons, found that the treatment of schistosomiasis with praziquantel was associated with a slight increase in the CD_4 cell count in HIV-positive women.

In terms of public health impact, schistosomiasis remains the second most frequent parasitic infection.[3] In addition, concerning the involvement of the female genital tract, it is also known to increase susceptibility to HIV and HPV co-infection. Therefore, this parasitic infection should be remembered when attending women from endemic regions. Our case illustrates the close association between HIV, HPV, and *S. hematobium.*

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