An Unusual Cervical Finding

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A 41-year-old African woman who was positive for human immunodeficiency virus (HIV) presented to the outpatient acquired immunodeficiency syndrome clinic for a regularly scheduled follow-up visit, with no new complaints. A Papanicolaou smear showed multiple syncytial-like aggregates of keratinocytes with dense eosinophilic cytoplasm, enlarged hyperchromatic nuclei, and coarse chromatin (Figure 1). A gynecologic examination 6 months later revealed flat cervical lesions with coarse punctuations at the 5-o’clock and 8-o’clock positions, and a cervical biopsy was performed.

Histologic sections showed that the squamous epithelium was composed predominantly of atypical keratinocytes with hyperchromatic nuclei, high nuclear-cytoplasmic ratio, pleomorphism, and readily identified mitotic figures in the upper one third of the epithelium (Figure 2). Some of the endocervical glands were replaced by similar atypical squamous epithelium. In the underlying fibrotic stroma at the ectoendocervical junction, multiple 110- to 170-μm elliptical, purple, calcified structures were seen (Figure 3). Many of these elliptical structures contained internal structures, and a rare terminal spine was identified (Figure 4, arrow).

What is your diagnosis?
Pathologic Diagnosis: Female Genital Schistosomiasis With Associated Cervical Severe Squamous Dysplasia (Cervical Intraepithelial Neoplasia Grade III)

Abstract

Up to 40 million people in Africa may be infected with schistosomiasis, with a prevalence rate of female genital schistosomiasis (FGS) ranging from 30% to 75%. The cervix is the most commonly infected organ, leading to a variety of symptoms and clinical findings. We present a case of FGS with associated cervical severe squamous dysplasia (cervical intraepithelial neoplasia grade III) in a 41-year-old human immunodeficiency virus–positive African woman. Histologic sections demonstrated multiple 110- to 170-µm calcified shell fragments within a fibrotic stroma. Many of these elliptical structures contained internal structures, and a rare terminal spine was identified. In addition, full-thickness squamous dysplasia was noted in the overlying squamous epithelium. Although it is unclear if FGS alone or lead to cervical carcinoma, investigators have recently proposed that schistosomiasis may alter the mucosal barrier, increase viral propagation, and decrease viral clearance, leading to an increased risk of human papillomavirus and human immunodeficiency virus infection and an accelerated rate of progression to cervical carcinoma.

Three species of Schistosoma, a trematode, can infect humans, causing schistosomiasis in a variety of organs. Schistosoma mansoni is common in the Caribbean islands and in northeastern South America, Schistosoma japonicum is found in eastern Asia, and Schistosoma haematobium is common in the Middle East and in Africa. Part of the life cycle of schistosomes takes place in water snails, and these release the cercariae. These cercariae then enter the circulation through the skin of human hosts who come in contact with contaminated water. Once in the circulation, they can migrate to the portal venous system, where they develop into adult flukes and deposit ova in the venules. Depending on the species, the schistosome adults may be located in the portal veins of the small intestine for S japonicum, in the large intestine for S mansoni, and in the veins of the pelvis and urinary bladder for S haematobium. The ova are released into the urine or feces, where they hatch and release miracidia that enter the snail host. The ova that are not excreted die in the host tissue and elicit a granulomatous and subsequent fibrotic response.

Although schistosomiasis is uncommon in the United States, up to 40 million people in Africa may be infected. A 2001 review article cited 4 population-based studies that have demonstrated that female genital schistosomiasis (FGS) is a common manifestation of S haematobium, with a prevalence rate ranging from 30% to 75%. The cervix is the most commonly infected organ, followed by the vagina, vulva, and fallopian tube. Therefore, it is important to consider schistosomiasis in patients from endemic areas and in patients who have visited endemic areas and came into contact with fresh water.

The clinical manifestations of FGS include dysmenorrhea, menorrhagia, leukorrhea, lower abdominal pain, postcoital bleeding, metrorrhagia, dyspareunia, spontaneous abortion, and infertility. The cervical findings on colposcopy vary from normal, with no visualized lesion, to cauliflower-like growths, ulcerations, and pathognomonic sandy patches. The diagnosis of schistosomiasis of the reproductive tract is usually made incidentally by observation of the following histologic features: (1) a granulomatous and chronic inflammatory infiltrate with eosinophils around viable eggs or (2) a fibrous tissue reaction with minimal inflammation around nonviable eggs or calcified shell fragments. In both types, the ova are located mainly at the ectoendocervical junction. The S haematobium eggs are roughly 150 × 50 µm in their greatest dimensions, with a terminal spine and a basophilic internal structure seen on hematoxylin-eosin–stained sections. In contrast, the spine of S mansoni ova is on the lateral aspect, and S japonicum ova have no spine.

The potential oncogenic effects of schistosomiasis of the cervix have been debated for many years. Although the association between schistosomiasis and bladder cancer is well documented, there is no consensus on the relationship between cervical schistosomiasis and cervical carcinoma. Initially, studies documenting an association between the 2 entities did not control for coinfection with human papillomavirus (HPV), and recent large studies have failed to document cervical carcinoma in patients with FGS without HPV. However, a recent case report documented high-grade cervical intraepithelial neoplasia and invasive cervical cancer in 2 women with schistosomiasis who tested negative for high-risk HPV. In our patient, there was a coexistence of Schistosoma, HIV, HPV, and cervical dysplasia. Although it is unclear if FGS alone can lead to cervical carcinoma, investigators have recently proposed an association between schistosomiasis and increased risk of coinfection with HPV and HIV.

Schistosomiasis alters the cervical mucosa barrier, facilitating the transmission of other viruses, including HPV and HIV. Mechanisms for increased viral propagation and decreased viral clearance have also been proposed.

Therefore, cervical schistosomiasis may increase patients' risk of HPV and HIV infection and their viral load without directly causing cervical carcinoma. As in the patient described herein, patients who are coinfected with schistosomiasis, HPV, and HIV may have an accelerated rate of progression to cervical carcinoma.

References