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Schistosomiasis with Cervical Cancer: About 2 Cases and Literature Review

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Abstract

Schistosomiasis is a chronic disease, and remains a major public health problem. It holds second place among parasitic endemics in the world. Schistosoma can infect various organs through the blood vessels. The genital form affects at least 16 million women in endemic areas, and the uterine cervix is the most common site. Two cases of cervical cancer associated with schistosomiasis of the cervix are presented. The aim of this study is to discuss the epidemiological, clinical and histopathological features. Both of the patients lived in Mahanjaga, aged respectively 57 and 43 years old. They complained of uterine bleeding disorder and presented cauliflower lesions with ulceration of the uterine cervix that extended to the vagina in one case. They were undergone cervical biopsies. The diagnosis was, in both cases, invasive, well-differentiated squamous cell carcinoma with cervical schistosomiasis.

Keywords

Cervical Cancer, Schistosomiasis, *Schistosoma haematobium,* Madagascar

1. Introduction

Schistosomiasis, also known as bilharzia, is a parasitic disease caused by trematode flukes of the genus, Schistosoma. Five species are pathogenic and cause human infection. *Schistosoma haematobium* is responsible for urinary and genital schistosomiasis. It is a major parasitic endemic and ranks second of parasitic disease, after malaria by the World Health Organization (WHO) [1].

Schistosoma can affect several organs through the human blood vessels. One

of the main consequences is tissue infiltration of Schistosoma ova. It induces persistent chronic inflammation which is responsible for the production of a carcinogenic enzyme: beta-glucuronidase [1] [2]. The association of schistosomiasis and cancer of the cervix is little reported, at least in Madagascar.

Two cases of cervical cancer associated with schistosomiasis are presented. The aim of this study is to discuss the epidemiological, clinical and histopathological features.

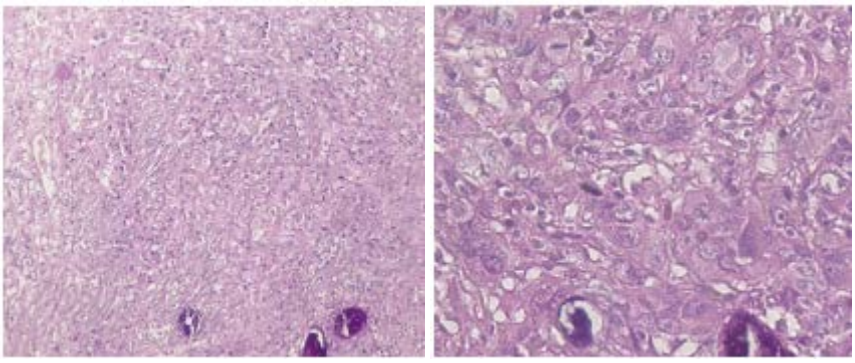
2. Observation

Case No. 1

A 57-year-old Malagasy woman, lived in Mahanjaga (a region in the western part of Madagascar), Betsirebaka ethnic group. She had been postmenopausal for 4 years. She was examined because of uterine bleeding disorder. She presented a necrotic lesion with erosion in the uterine cervix, extending to the vagina and was undergone for cervical biopsy. Samples (four fragments) were firm; the diameter varies from 0.3 to 0.5 cm. Histological examination revealed an invasive carcinomatous proliferation in a cervical mucosa. The cells presented a moderate cyto-nuclear atypia, organized in clusters, with squamous differentiation without keratinization. The stroma was fibrous with numerous calcified Schistosoma ova. The diagnosis was well-differentiated, invasive squamous cell carcinoma with cervical schistosomiasis (**Figure 1**). Praziquantel was given at 40 mg/kg body weight. The patient was undergone for hysterectomy and radiation therapy.

Case No. 2

She was 43-year-old, lived in Mahanjaga (Sakalava ethnic group). She was undergone for a gynaecological examination at the hospital in the region because of a dysmenorrhea. The patient presented an ulceration of uterine cervix. Cervical biopsies were performed and the samples were sent to Antananarivo, at JRA University Hospital. There were multiple fragments, with 2.2 × 1.6 × 0.5 cm



(a) (b)

Figure 1. Uterine cervix. Well-differentiated, invasive squamous cell carcinoma with numerous calcified schistosome eggs (arrow). HE ×40 (a) ×400 (b). Source: Department of Pathology, Joseph Ravoahangy Andrianavalona University Hospital, Antananarivo, Madagascar.

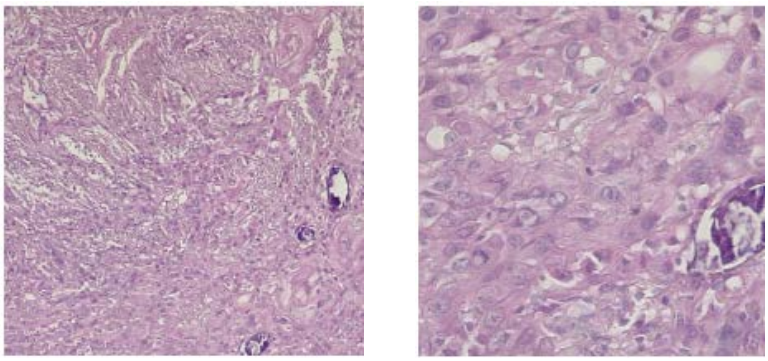
diameter in clusters. The histological features were an infiltrating tumor proliferation, with squamous differentiation and keratinization. Calcified schistosome eggs surrounded by inflammatory granulomas with multinucleated giant cells were found in the stroma. The diagnosis was a well-differentiated, invasive squamous cell carcinoma with schistosomiasis (**Figure 2**). Praziquantel was given at 40 mg/kg body weight and she was undergone for hysterectomy.

3. Discussion

Worldwide, bilharzia affects at least 200 million people, the equivalent of one among 30 people [3] [4] and 80% are in Africa [5]. Madagascar is one of the endemic African countries, it occurs especially in the western part [6]. Both of our patients lived in this coast of the island. Lesions are caused by host responses to dead or viable schistosomiasis eggs into different organs and lead for different forms of the pathology: urinary, genital, ... Concerning the genital schistosomiasis, it can affect the different part of the female genital tract, but uterine cervix is the most common site to harbor *Schistosoma haematobium* [7] [8].

Cervical schistosomiasis can be asymptomatic for a long time [9]. Concerning the symptomatic form, symptomatology is unspecific and the patients may present leucorrhoea, dyspareunia or dysmenorrhea. Clinical appearance may take one of three different forms: endocervical polypoid excrescences; indurated area with zones of ulceration or erosion; cauliflower mass which bleeds on touch, thus simulating cervical carcinoma. Ulceration is the most characteristic pathological finding [10]. Both of our patients presented dysmenorrhea with ulceration zones, and underwent a biopsy for histological examination.

The diagnosis of bilharzia was confirmed by the presence of schistosome granuloma or schistosome eggs. The lesions are located in the mucosa, the submucosa and sometimes in the muscularis mucosae [11]. Several cases of cervical schistosomiasis have been reported and some are associated with cancer. In Senegal, Abdou Magib Gaye *et al.* [12] reported 6 cases, which represent 33.3% of cervical schistosomiasis and 0.2% of all cases of cervical cancer. Malagasy studies



(a) (b)

Figure 2. Well-differentiated, invasive squamous cell carcinoma with keratinization (arrow) with cervical schistosomiasis. HE ×40 (a) ×400 (b). Source: Department of Pathology, Joseph Ravoahangy Andrianavalona University Hospital, Antananarivo, Madagascar.

by Rajaonarison JJC *et al.* [5] and Randrianasolo BS *et al.* [13] concerning genital schistosomiasis, have not reported any association with cervical cancer. However, HT Andrianjafitrimo *et al.* [14] identified one case of cancer developed on bilharzia among the 10 cases of cervical bilharzia. Squamous cell carcinoma is the most histological type in association with cervical schistosomiasis, as reported by Abdou Magib Gaye *et al.* [11] and HT Andrianjafitrimo *et al.* [14]. Our cases had the same histological type. G El Tabbakh *et al.* reported a case of adenocarcinoma with cervical schistosomiasis [10].

Regarding risk factors for developing cancer, urinary schistosomiasis is a known predisposing factor for bladder cancer. Human papillomavirus (HPV) infection is well established as a necessary cause of cervical cancer [15]. But the relationship of cervical schistosomiasis to cervical cancer is controversial. Szela *et al.* [14], for example, carried out a comparative study in 2 different regions, non-endemic and endemic for bilharzia. In the endemic area, 46% of patients presented cervical schistosomiasis, one of which with CIN2, and 33% are HPV positive. In the non-endemic area, no morphological feature of schistosomiasis was observed after cervical biopsy, none of the patients presented a pre-cancerous lesion whereas 48% of them are HPV positive. They conclude that there is no causal relationship between cervical schistosomiasis and CIN or cervical cancer [16].

In the United States, on the other hand, KL Fachinan *et al.* [10] reported two cases, one of CIN3 and another of invasive cancer, with cervical schistosomiasis and no evidence of a high risk HPV of cervical cancer has been identified. They concluded that cervical schistosomiasis appears to be a possible risk factor for the development of CIN and cancer [11] [17]. Menye *et al.* [18] shared this same observation. The presence of Schistosoma ova lead to persistent chronic inflammation and ulceration of the cervix with formation of schistosoma granuloma [1] [2]. Cervicitis with ulceration can make or increase the virulence of a Human Papillomavirus infection. The majority of HPV infections are transient and not sufficient to induce carcinogenesis. Only persistent infections with high-risk HPV types will eventually result in progression towards invasive cervical cancer. Schistosomiasis may be a probable cofactor of uterine cervix cancer [12]. Kjetland *et al.* [4] found that the development of high-grade intraepithelial neoplasia was significantly associated with cervical schistosomiasis that has progressed for at least 5 years [4] [8].

Moubayed *et al.* [19] [20] found no association between cervical cancer and schistosomiasis. However, they observed that women with both schistosomiasis and cervical cancer are significantly younger than those affected only with cervical cancer. This could be matched with the hypothesis that bilharzia could increase the carcinogenic effect of HPV infection on the cervix. It can promote the persistence of HPV infection [19] [20].

4. Conclusion

The association of cervical cancer and schistosomiasis is still little reported in

Madagascar. The evidence of the relationship between schistosomiasis and cervical cancer is not yet well defines. It is possible that chronic cervical infestation is a factor for a persistent HPV infection and subsequent development of cervical intraepithelial neoplasia. As Madagascar is an endemic country of schistosomiasis, through this study, it is important to keep in mind that patients with cervical schistosomiasis should be performed for regular screening for possible precancerous lesions.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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