Gynecol Surg (2009) 6:177–179
DOI 10.1007/s10397-008-0412-z

COMMUNICATION

An unusual association: vulval schistosomiasis, microinvasive vulval squamous cell carcinoma and high-grade vulval intraepithelial neoplasia in HIV patient

A. O. Alalade · S. C. Leeson · U. Andrady

Received: 29 March 2008 / Accepted: 21 May 2008 / Published online: 19 July 2008

Abstract This case describes the unusual association between vulval schistosomiasis, microinvasive squamous cell carcinoma of vulva and high-grade vulval intraepithelial neoplasia in a human immunodeficiency virus-positive patient and response to treatment with imiquimod and praziquantel.

Keywords Vulval intraepithelial neoplasia · Vulval schistosomiasis · Imiquimod · Praziquantel

Case report

Mrs LA, a 39-year-old Zimbabwean who was first diagnosed human immunodeficiency virus (HIV) 1-positive in 1989, was referred to the gynaecological clinic with symptoms of vulval soreness, multiple warty lesions on vulva with surrounding areas of leukoplakia and ulceration. She has been a resident in Europe for the past 18 years. She had previously been referred to the colposcopy clinic for management of severe dyskaryosis 2 years earlier. At that time, she was diagnosed with cervical intra-epithelial neoplasia (CIN) 3 and subsequently had a large loop excision of transformation zone. She was on highly active antiretroviral therapy (HAART)—lamivudine, saquinavir and lopinavir/ritonavir—and had a CD4 count of 80 cells per cubic millimeter and a detectable HIV viral load of 32,000 copies per millilitre. Her antiretroviral drug compliance has been poor in the past, and it was thought she had developed HIV drug resistance due to non-adherence. She was also a heavy smoker. On examination, she had pigmented areas at the vulval introitus (Fig. 1).

Colposcopy revealed widespread low-grade changes involving the ectocervix, upper vagina, vulvo-vaginal introitus and perineum with human papilloma virus (HPV) changes. Biopsies were taken. Histology revealed extensive high-grade vulval dysplasia (VIN 3) and multiple calcified eggs of *Schistosoma haematobium* (Fig. 2) There was also a small area of early microinvasive squamous cell carcinoma of vulva. Subsequently, she was tested for Schistosoma serology (enzyme-linked immunosorbent assay) and microscopy on first-catch early-morning urine for schistosoma eggs, and both these investigations were negative. She did not undergo cysto-urethroscopy. This case was reviewed at a gynaecological cancer the multidisciplinary meeting in March 2007. Invasive disease confirmed stage 1a squamous cell carcinoma. A wide local excision was considered adequate treatment.

She commenced a treatment course of topical imiquimod for her VIN 3 and two doses of oral praziquantel for schistosomiasis. In view of her failing HAART regimen, she was started on a new combination with zidovudine/lamivudine (Combivir), tenofovir, darunavir, ritonavir and etravirine. These reflected a rise in her CD4 count (Fig. 3) as well a steep fall in her HIV viral load. Clinic follow-up showed good response to treatment with imiquimod and clinical resolution of her symptoms. Imiquimod was stopped in December 2007. Colposcopic follow-up is planned.

A. O. Alalade (✉) · S. C. Leeson · U. Andrady
Department of Obstetrics and Gynaecology,
Ysbyty Gwynedd,
Bangor, Wales LL57 2PW, UK
e-mail: drlaolu@yahoo.co.uk

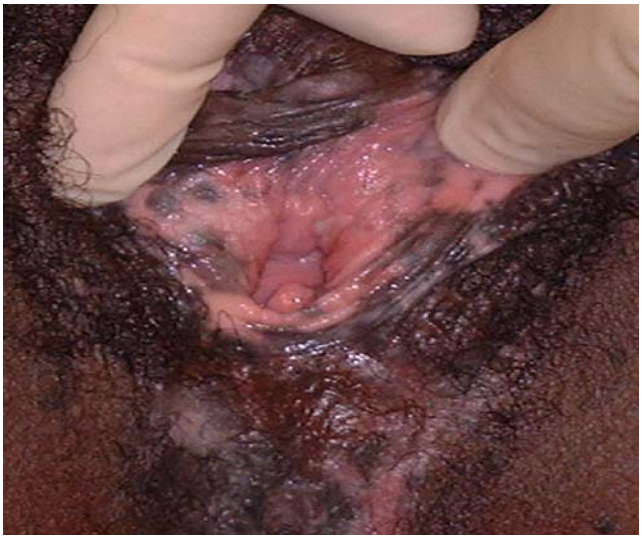

Fig. 1 Appearance at colposcopy. Pigmented and acetowhite areas at the vaginal introitus

Discussion

Schistosomiasis is a chronic trematode infection affecting over 200 million people worldwide. It is endemic in Africa, East Asia, Middle East and South America. Female genital schistomiasis is a well-recognised presentation affecting about 13 million people worldwide [1]. Sequelae include ectopic pregnancy, infertility, abortion and cervical lesions. Pongggensee et al. in their study established the presence of female genital schistosomiasis (FGS) in patients with negative urine samples for *S. haematobium* [2]. The occurrence of FGS is thought to increase the susceptibility of HIV infection [3].

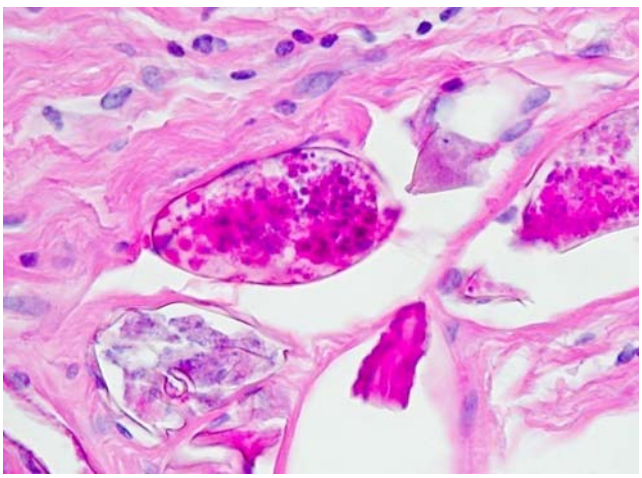

Fig. 2 *S. haematobium* (calcified eggs)

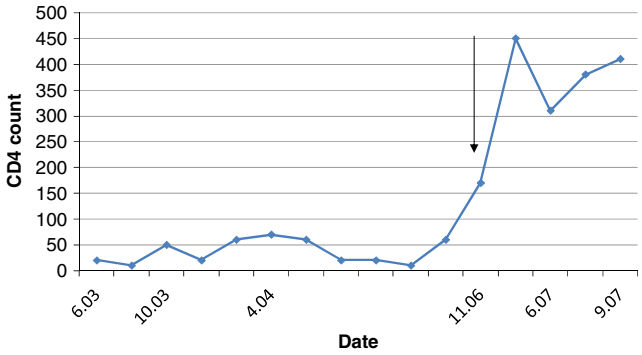

Fig. 3 Graph illustrating changes in CD4 count. The *arrow* indicates the point of commencement of new retroviral medications

Vulval schistomiasis is a cutaneous manifestation commonly caused by *S. haematobium*. Skin involvement may occur at site of penetration of cercariae and may present as itchy papular eruption (swimmer's itch). An uticarial reaction may occur 4–8weeks after exposure due to an immune mediated response. This may manifest as fever, athralgia, purpura and abdominal pain [4]. Cercariae pass via lungs and portal system with the adult flukes lodging in the venous plexuses. These spread by direct retrograde spread flow to the plexus supplying vulva with deposition of ova in vulval skin. Presentation takes months to years after primary infection as pruritic papules, papillomata, ulcers, granulomata and vulval warts [5]. Careful history and awareness helps in early diagnosis of disease.

Vulva intraepithelial neoplasia (VIN) is a pre-malignant disease of vulva with malignant potential of about up to 80% in untreated cases [6]. It affects mainly the labia minora and perineum. Human papilloma virus infection is a recognised aetiological factor; subtypes 16 and 33 most commonly associated. Low-grade lesions are commonly observed; high-grade ones require treatment with laser, excision or imiquimod. Imiquimod is a topical immunomodulatory agent formulated as a 5% cream. It stimulates the production of interferon-alpha and other local cytokines with good clinical response [7].

Mrs LA represents a case of multicentric intraepithelial neoplasia. Its aetiology is a combination of HPV infection and immunosuppression of varying degrees. It has been described in cases of cell-mediated immunosuppression. HIV patients currently undergo annual cervical screening in view of increased risk of high-grade CIN and cervical cancer. Cervical cancer remains an acquired immune deficiency syndrome-defining illness. Data suggests that women with normal CD4 count respond better to treatment than those with low counts. The improvement of her CD4 count, decrease in viral load with a change of course of her HIV medications as well as good compliance is reflected in her rapid

response to treatment of VIN with imiquimod. The association of bladder carcinoma and *S. haematobium* is well-established [8], but to our knowledge, there has been no association with vulval dysplasia or malignancy. In our patient, discovery of calcified schistosoma eggs may be a coincidental finding, but it could also be a co-factor for development of lower genital tract premalignancy and malignancy with or without high-grade HPV.

References

1. Poggensee G, Feldmeier H (2001) Female genital schistosomiasis: facts and hypothesis. Acta Tropica 22:193–210
2. Poggensee G, Kiwelu I, Saria M et al (1998) Schistosomiasis of the lower reproductive tract without egg excretion in urine. Am J Trop Med Hyg 59(5):782–783
3. Feldmeier H, Krantz I, Poggensee G (1994) Female genital schistosomiasis as a risk factor for transmission of HIV. Int J STD AIDS 5:368–372
4. Leslie TA, Goldsmith PC, Dowd PM (1993) Vulval schistosomiasis. J R Soc Med 86:51
5. Mckee PH et al (1983) Vulva schistosomiasis. Clin Exp Dermatol 8:189–194
6. Jones RW, Rowan DM (1994) Vulval intraepithelial neoplasia 3: a clinical study of the outcome in 113 relation to the development of invasive vulval cancer. Obstect Gynaecol 5:741–745
7. Todd RW, Etherington IJ, Luesley DM (2002) The effects of 5% imiquimod cream on high-grade vulval intraepithelial neoplasia. Gynaecol Oncol 85(1):67–70(4)
8. El-Mawla NG, el-Bolkainy MN, Khaled HM (2001) Bladder cancer in Africa: update. Semin Oncol 28:174–178