Review

Ethical and legal issues of HIV screening in anal condylomatosis: an overview

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Abstract: Although the strong evidence of the prevalence of condylomata in the HIV-positive population, literature on HIV prevalence and regulation of HIV screening in HIV-unscreened population which is diagnosed with condylomata is unconclusive. Our aim is to review literature about HIV screening and diagnosis of anal condylomata in order to evaluate medical aspects, ethical and legal issues concerning the management of this disease. We undertook an online search on Pubmed for the keywords "HIV", "screening" and "anal condylomata" and 21 papers were analysed, 2 being randomized controlled trial, 9 comparative studies and 10 reviews. A total of 1211 patients were reviewed. All authors strongly recommend HIV testing in patients with clinical evidence of anal condylomata. In undeveloped countries with high prevalence of HIV, a proctological evaluation could be a good opportunity to have a "targeted" screening in a high risk population. In conclusion, two HPV vaccines now available could represent an unexpected therapeutic option for HIV infected male patients to prevent anal cancer. Clinical trials and prospective studies are necessary to validate this interesting hypothesis.

Keywords: Anal condylomatosis; HIV screening; Papilloma virus.

INTRODUCTION

HIV infection is a true plague and a major health concern worldwide. It is estimated that 33.4 millions people globally have been infected to date. HIV transmission is by sexual contact, intravenous drug abuse, maternal to fetal route or rarely through transfusion of infected blood or blood products. HIV infection is a dynamic process with pathological features that vary with the chronology of the disease[1]. Nowadays, though most countries have ready access to screening centers and retroviral treatment, factors such as extreme poverty, social stigma and lack of education can be obstacles to proper management of the disease. Despite tremendous efforts by organizations worldwide, personal, political, social and economic barriers compromise treatment and prevention. Chronic immunosuppression for various reasons is an important risk factor for persistent infections with human papillomavirus (HPV) and, consequently, HPV-associated disease[2]. Most genital warts (condylomata lesions) will spontaneously resolve in the immunocompetent population[3], but immunocompromised patients with condylomata (especially HIV-infected patients) generally require an expensive therapy, carrying a high risk of recurrence. There seems to be a complex interaction between HIV, HPV and local mucosal immune mechanisms[4]. HIV enhances the HPV transcription and upregulates HPV E7 which influences the cellular differentiation leading to the higher amounts of HPV DNA in the tissue[5]. Furthermore, HPV causes a decrease in the number of the local macrophages, Langerhans and CD4 cells and the impairment of the local cytokine production resulting in impaired local immune control of HPV infection[6]. Many studies have now documented that people living with human immunodeficiency virus (HIV)/AIDS, mainly men who have sex with men (MSM), but also heterosexual men and women, have an increased risk for anal cancer[7,8]. In HIV-infected women, the risk for anal cancer is approximately 14 times higher than among HIV-positive women diagnosed with AIDS, with the anal cancer rate estimated at 30-36 per 100 000 person-years[9]. Although there is strong evidence of the prevalence of condylomata in the HIV-positive population, literature on HIV prevalence and regulation of HIV screening in HIV-unscreened population who is diagnosed with condylomata is unconclusive[10,11]. Because of the intimate nature of questions on sexual behaviors and sexually-transmitted infection risks, detailed and accurate data to assess HIV risk are challenging to collect. Anogenital warts can be considered a visible marker of HIV risk and could help clinicians treating non-gay-identified MSM who may be reluctant to disclose some sex behaviors. Particularly for these non-gay-identified MSM (but for all MSM as well as transgenders), failure to screen for HIV during any health-related encounter represents a missed opportunity to detect incidental infections. Our aim is to review the literature about HIV screening and diagnosis of anal condylomata in order to evaluate medical aspects, ethical and legal issues concerning the management of this disease.

MATERIALS AND METHODS

We undertook an online search on Pubmed for the keywords "HIV", "screening" and "anal condylomata" and we found 83 papers, which have been published during the last 30 years. We included in our review all the original articles and reviews in order to evaluate the state of art in terms of HIV screening and diagnosis of anal condylomatosis. We excluded papers which were not written in English and single case report. Our analysis considered several clinical characteristics, HPV genotypes, coexisting HIV infection and related therapeutic options.

RESULTS

21 papers were analysed, 2 being randomized controlled trials, 9 comparative studies and 10 reviews. A total of 1211 patients were reviewed. Some studies investigated HPV genotypes , others compared results after surgical treatment versus no surgery but topical cream, in several papers authors evaluated the efficacy of several HPV detection tests. 2 studies did not include HIV patients.

8 papers reported ethical and legal issues about the management of HPV-HIV coexisting disease and HIV screen-

ing in patients affected by anogenital warts. All authors strongly recommend HIV testing in patients with clinical evidence of anal condylomata. Prior to testing, the patient should be consented with a thorough explanation of the rationale, risks, and benefits of testing[12]. Consequently, the discussion of ethical and legal issues about HIV testing is the key to obtain a voluntary informed consent[13]. In case of positive result, the patient must be directly sent to the proper treatment. Taking care of the positive patients as soon as possible is an ethically fundamental step to ensure patients to benefit from knowing their HIV condition. An unconsented HIV testing is forbidden. As regard as HIV-tested patients, all standard measures to ensure strict confidentiality should be applied, consistently with applicable law. These include storing HIV test results in a secure medical record, protection of the legal proceeding if applicable, and establishing security protections to prevent unauthorized disclosure of test results to third parties[14,15]. The incidence of anal cancer in HIV-positive MSM is comparable with that of cervical cancer before the introduction of screening programme[16] and the question is whether such a screening would also be an effective strategy to decrease the incidence of anal malignancy. According to cost-benefit model, anal cytological screening in HIV-positive MSM should be cost-effective for preventing anal cancer.

DISCUSSION

HIV has become a more and more frequent condition all over the world, nevertheless many questions about screening guidelines remain unanswered. Anal condylomatosis is a disease which is frequently associated to HIV sero-positivity and could be a marker of concomitant infection. However the intimate nature of the disease and the common patient reticence about sexual habits together with the strict policy regulating HIV diagnosis make the management of this condition very difficult form the medical, ethical and legal views. To date, literature about this topic provides unclair results[17,18].

Youngs and Hooper[19] found no strong ethical objections to self-testing being made widely available in the UK. Pretest counselling for an HIV test is not an ethical necessity, and self-testing has the potential to increase early diagnosis of HIV infection, thus improving prognosis and reducing ongoing transmission. Self-testing kits might also empower people and promote autonomy by allowing people to dictate the terms on which they test their HIV status. Admittedly, there are some potential areas of concern. These include the possibility of user error with the tests, and the concern that individuals may not present to health services after a positive result. False negatives have the potential to cause harm if the 'window period' is not understood, and false positives might produce psychological distress. There is, however, little evidence to suggest that self-testing kits will cause widespread harm, and we argue that the only way to properly evaluate whether they might cause significant harm is to carefully evaluate their use, now that they are available on the market.

Maybe it can be a good solution in undeveloped countries with high prevalence of HIV, where a proctological evaluation could be a good opportunity to have a "targeted" screening in a high risk population.

Limitations of the study are poor quality data and the fact that the majority of included studies are retrospective analyses, but in our opinion it represents a pragmatic overview about an interesting and overdiscussed aspect of a diffuse pathological condition.

CONCLUSION

Improved medical therapy of HIV infection have made individuals with advanced immunosuppression live longer, so the incidence of HPV-associated tumors and other cancers within this population shows an increasing trend[20,21]. Although it is clear that HIV patients have higher incidence of anal intraepithelial neoplasia, the correct approach to the treatment of this pre-carcinogenic condition is not well established[22]. For this reason, HIV screening in patients affected by HPV genotype 16 and 18 might be a valid tool to study the histological and immunohistochemical features of the interaction between these viruses and lesions deriving from their co-infection[23]. Moreover, two HPV vaccines now available[24] could represent an unexpected therapeutic option for HIV infected male patients to prevent anal cancer. Clinical trials and prospective studies are necessary to validate this interesting hypothesis.

REFERENCES

1. Wieland U, Kreuter A, Pfister H. Human papillomavirus and immunosuppression. Curr Probl Dermatol. 2014; 45: 154-65. doi: 10.1159/000357907. Epub 2014 Mar 13.
2. Nadal SR, Horta SH, Calore EE, Nadal LR, Manzione CR. How far into the anal canal should the brush be introduced for more efficient cytological evaluation? Rev Assoc Med Bras. 2009; 55 (6): 749-51.
3. Lee PK, Wilkins KB. Condyloma and other infections including human immunodeficiency virus. Surg Clin North Am. 2010 Feb; 90 (1): 99-112.
4. Mistrangelo M, Cornaglia S, Pizzio M et Al. Immunostimulation to reduce recurrence after surgery for anal condyloma acuminata: a prospective randomized controlled trial. Colorectal Dis. 2010; 12 (8): 799-803. doi: 10.1111/j.1463-1318.2009.01960.x. Epub 2009 Jun 22.
5. Sarzo G, Del Mistro A, Finco C et al. Extensive anal condylomatosis: prognosis in relation to viral and host factors. Colorectal Dis. 2010; 12:e128-34. doi: 10.1111/j.1463-1318.2009.01902.x. Epub 2009
6. Rapose A. Human papillomavirus and genital cancer. Indian J Dermatol Venereol Leprol. 2009; 75 (3): 236-43; quiz 243-4. doi: 10.4103/0378-6323.48429.
7. Pereira AC, Lacerda HR, Barros RC. Diagnostic methods for prevention of anal cancer and characteristics of anal lesions caused by HPV in men with HIV/AIDS. Braz J Infect Dis. 2008; 12 (4): 293-9.
8. Klaristenfeld D, Israelit S, Beart RW et Al. Surgical excision of extensive anal condylomata not associated with risk of anal stenosis. Int J Colorectal Dis. 2008; 23 (9): 853-6. doi: 10.1007/s00384-008-0494-0. Epub 2008 Jun 12.
9. Chaturvedi AK, Madeleine MM, Biggar RJ et Al. Risk of human papillomavirus-associated cancers among persons with AIDS. J Natl Cancer Inst 2009; 101:1120-30.
10. Viazis N, Vlachogiannakos J, Vasiliadis K et Al. Earlier eradication of intra-anal warts with argon plasma coagulator combined with imiquimod cream compared with argon plasma coagulator alone: a prospective, randomized trial. Dis Colon Rectum. 2007; 50 (12): 2173-9.
11. Sanclemente G, Herrera S, Tyring SK et al. Human papillomavirus (HPV) viral load and HPV type in the clinical outcome of HIV-positive patients treated with imiquimod for anogenital warts and anal intraepithelial neoplasia. J Eur Acad Dermatol Venereol. 2007; 21 (8): 1054-60.
12. Palefsky JM. HPV infection in men. Dis Markers. 2007; 23 (4): 261-72.
13. Anderson CA, Boller AM, Richardson CJ et Al. Anal condyloma: a comparison between HIV positive and negative patients. Am Surg. 2004; 70 (11): 1014-8.
14. Hagensee ME, Cameron JE, Leigh JE, Clark RA. Human papillomavirus infection and disease in HIV-infected individuals. Am J Med Sci. 2004; 328 (1): 57-63.
15. Vukasin P. Anal condyloma and HIV-associated anal disease. Surg Clin North Am. 2002; 82 (6): 1199-211.

16. Sobhani I, Walker F, Aparicio T et Al. Effect of anal epidermoid cancer-related viruses on the dendritic (Langerhans') cells of the human anal mucosa. Clin Cancer Res. 2002; 8: 2862-9.
17. El-Attar SM, Evans DV. Anal warts, sexually transmitted diseases, and anorectal conditions associated with human immunodeficiency virus. Prim Care. 1999; 26 (1): 81-100.
18. Aynaud O, Piron D, Barrasso R, Poveda JD. Comparison of clinical, histological, and virological symptoms of HPV in HIV-1 infected men and immunocompetent subjects. Sex Transm Infect. 1998; 74 (1): 32-4.
19. Youngs J, Hooper C. Ethical implications of HIV self-testing. J Med Ethics. 2015; 41 (10): 809-13.
20. Metcalf AM, Dean T. Risk of dysplasia in anal condyloma. Surgery. 1995; 118 (4): 724-6.
21. Palefsky JM. Human papillomavirus-associated anogenital neoplasia and other solid tumors in human immunodeficiency virus-infected individuals. Curr Opin Oncol. 1991; 3 (5): 881-5.
22. Sonnex C, Scholefield JH, Kocjan G et Al. Anal human papillomavirus infection: a comparative study of cytology, colposcopy and DNA hybridisation as methods of detection. Genitourin Med. 1991; 67 (1): 21-5.
23. Cestaro G, De Rosa M, Gentile M, Massa S.A case of HPV and acquired genital lymphangioma: over-lapping clinical features. Ann Ital Chir. 2015 25; 86 (ePub).
24. Kanduc D, Shoenfeld Y. From HBV to HPV: Designing vaccines for extensive and intensive vaccination campaigns worldwide. See comment in PubMed Commons below Autoimmun Rev. 2016; 15: 1054-1061.

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