Cervical cancer screening in HIV positive patients. A new face for an old tragedy?

Abstract

Objective. *In the late 1980s Romania was confronted with one of the most painful public health problems of the time, but the drama was not publicly disclosed earlier than 1989s: children who had been infected with human immunodeficiency virus (HIV) in hospitals during medical procedures. About 21 years after this event, this generation has reached reproductive age and a new tragedy is about to occur on the foundations of the old one. The purpose of our work was to assess the prevalence of dysplastic lesions of the cervix in HIV positive patients in order to propose a coherent and evidence based strategy of early detection, treatment and follow-up in this particular group of patients.* ***Methods.*** *We enrolled a total of 37 HIV positive patients who were investigated by performing Pap cytological examination.* ***Results.*** *All the patients in the study were iatrogenic infected with HIV during childhood. The results were then compared with those of 237 healthy patients of the same age group (control group) undergoing smear examinations at the same time and same cytology laboratory. There was no statistical significant difference between HIV positive patients and normal control group regarding abnormal Pap test in the same age group.* ***Conclusions.*** *Our data showed no differences regarding abnormal Pap smears between the two analyzed groups, although many other studies suggested that women living with HIV infection have a much higher risk of precancerous dysplastic lesions of the cervix than do HIV-uninfected women. These findings could open new open questions for many other further debate studies.*

Keywords: *dysplastic, cervix, cytology, human immunodeficiency virus.*

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Acknowledgments: This manuscript was financially supported by the Sectorial Operational Program Human Resources Development, financed from the European Social Fund and by the Romanian Government under the POSDRU/89/1.5/S/64109 grant.

Introduction

In the late 1980s Romania was confronted with one of the most painful public health problems of the time, but the drama was not publicly disclosed earlier than 1989s: children who had been infected with human immunodeficiency virus (HIV) in hospitals during medical procedures.

Having in the view that invasive cancer of the cervix and its precursor lesions are the most important genital pathological manifestations in HIV positive patients[1,2], after 21 years this generation has reached reproductive age, a new tragedy was about to occur on the foundations of the old one.

On the other hand, Romania has the highest incidence of cervical cancer mortality in Europe, 13/100.000, a rate 6.3 times higher than other European countries. Furthermore, the mortality rate increased 15% since 1990 till 2000[3,4].

The objective of our study is to found a risk of precancerous dysplastic lesions of the cervix (atypical squamous cells of undetermined significance, ASCUS), low-grade squamous intraepithelial lesions (LSIL), atypical squamous cells of undetermined significance, a high-grade squamous intraepithelial lesion is not excluded as a possibility (ASCH), and high-grade squamous intraepithelial lesions (HSIL) in HIV positive patients, taking into account the epidemic characteristics which are particular in Romania, first by the higher rate of infection and then its implications.

Methods

Between January 1st, 2010 and March 31st, 2012, HIV positive patients from the Regional Center Mures, Clinic for Infectious Diseases I, from Târgu-Mureș, were enrolled in this study.

The control group consisted of 237 healthy patients in the same age group, having the annual screening for Pap test. Every woman had a Pap test done in the same cytology laboratory by the same cytologist who was unaware of the HIV status of the patients. The Bethesda 2001 system was used for the Pap test report[4].

The Regional Center Mureș is in charge of 359 HIV positive patients and out of those, 305 are receiving antiviral treatment, from which 148 are women.

All of the patients were informed and signed an informed consent document. The study was approved by the University of Medicine and Pharmacy Târgu-Mureș Ethics Committee.

From the total of 148 HIV positive patients investigated by us, 5 of them were older than 25 and these 5 had been sexually infected with HIV. Therefore, we decided to investigate HIV positive women aged between 20 till 24, with HIV infection acquired during childhood hospitalization only, a representative cohort for our country.

Furthermore, only 37 agreed to participate in our study. The results were reported by odds ratio (OR) and 95% confidence interval (CI). Proportions were compared using Fischer's test. Among the risk factors associated with HPV infection we analyzed the early onset of sexual activity,

Received: *18th July 2012*
Revised: *2nd September 2012*
Accepted: *14th October 2012*

the number of sexual partners, the number of pregnancies (multiparity), and the immune suppression.

Results

In the group of HIV positive patients we found 5.4% abnormal results (n=2, both LSIL) while in the control group, the number of abnormal results was 16.1% (n=38, 26 cases ASCUS, 4 cases LSIL, and 8 cases ASCH) (see Figure 1).

We did not found any significant differences between the groups (p=0.130) in terms of Fisher's test. The calculated OR was 0.297 with 95% CI between 0.068 and 1.292. The median age at diagnosis of HIV in the study group was 10.1 years (5 and 21 years old range). The median age of onset of sexual activity in the study group was 18.5 years (between 16 to 21 years range). About 75% of our study patients reported only one sexual partner.

The total number of pregnancies in our study group was 24 (between 0 to 3 range). This relatively high number of pregnancies should draw attention to the inevitable epidemiological changes in this particular group of HIV positive patients which now reach reproductive age.

Immune suppression was followed by monitoring CD4 (or T-cells) cell count and viral load (VL) and the results showed that the immune status of patients in our study group was relatively good, with <250 cells/μL CD4 cell count in 19% of patients. We found CD4 cell count between 250 and 500 cells/μL in 35% of patients and CD4 cell count >500 cells/μL in 46% of patients. VL was detected in 40% of patients being less than 20 (see Table 1).

Discussion

Our results are in contrast with some other studies founded in current literature which reports a five times higher risk of precancer cervical lesions among HIV positive patients than in uninfected women[5-10].

Accordingly, the prevalence of cervical dysplasia among HIV positive patients was reported between 11 and 60% according to immunosupression[6,11-23].

In a cohort study with a large number of patients enrolled, abnormal cytology results were 38% of the 1680 HIV positive patients[24], also much higher than the 5.4% resulting from the analysis of our group.

The recurrence rate of cervical neoplasia may be more than 50% in HIV positive patients, compared with only 10% in HIV negative patients[25-27].

In addition, Chiasson and colleagues founded a frequency of invasive cervical cancer three times higher in HIV positive patients in comparison with HIV negatives[10]. Furthermore, another study showed that both African and American patients and young Hispanic HIV positive patients, could have a 4 till 7 times higher risk of invasive cervical cancer in comparison with control[10].

Altogether, causality in the association of HIV infection and increased risk for cervical cancer has remained obscure, highlighting prospective studies to define the importance of HIV as a risk factor for cervical intraepithelial lesions and invasive cervical cancer[6,11-14].

We believe that our data are in response to the epidemiological features of HIV infection which started in 1988-1989s period in Romania. Our results indicate that iatrogenic, nosocomial transmission of the HIV infection, different from the sexually transmission makes our study one of the few defined other published studied regarding Human Papillomavirus (HPV) risk factors.

Our study founded sexual behavior risk only sporadically, which have also raised awareness about sexual contamination risk.

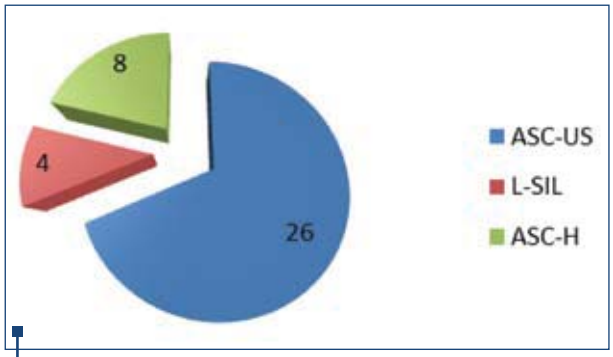

Figure 1. Abnormal cytology results in control group

Table 1 Demographics and HIV control

	Range	
Median age at diagnosis 10,1 years	5-21	
Median age of sexual activitity 18,5 years	16-21	
Total number of pregnancies 24	0- 3	
CD4	< 250 cells/μl	19% of pacients
	250-500 cells/μl	35% of pacients
	>500 cells/μl	46% of pacients
VL	<20	40% of pacients
	20 - 5000	34% of patients
	> 5000	16% of patients

Since 1993 U.S. Centers for Disease Control and Prevention (CDC) included cervical cancer among AIDS defining conditions[28]. CDC issued recommendations stipulating that initial screening examination to be composed of two Pap examinations at six months intervals, followed by annual Pap test if the initial results of both tests were normal[29].

Other recommendations stipulated Pap test twice a year, colposcopy annually or even colposcopy twice a year[30,31]. These recommendations were subsequently the subject of numerous reviews and changes[32-34].

We consider that adopting in our HIV positive population these international guidelines regarding the monitoring of cervical dysplasia in HIV positive patients should be precautions made.

We also believe that the HIV epidemic in our country has features that make it epidemiologically different, mainly because of the demonstrated lack of risk factors for the HPV infection in this particular population with nosocomial childhood HIV infection.

These patients were early included in national surveillance and treatment programs that led to a good immune status.

The justified our patients number of 20-24 years old taken into the study is supported by the fact that this represent the largest age group of HIV positive women in Romania, as far as we know.

Interestingly, our results may have the same trend as the results of a recent large prospective study which suggested that HIV infected women undergoing long-term clinical follow-up who are cytologically normal and oncogenic HPV negative have a higher risk of cervical precancer similar to that in HIV uninfected women through 5 years of follow-up[35].

Conclusions

We consider in this context that the screening of cervical cancer in HIV positive patients with good adherence to antiretroviral therapy can be done by Pap examination performed annually. Nowadays, with these individuals reaching reproductive age, this group of HIV positive patients could become sources of HIV spread by both sexual and mother-to-child infection.

Our data showed no differences regarding abnormal Pap test between the two analyzed groups, although many other studies suggested that women living with HIV infection have a much higher risk of precancerous dysplastic lesions of the cervix than do HIV-uninfected women. Our findings could catalogue HIV one of the most serious of the illnesses and infections on the same scale with AIDS, which could open new questions for further ongoing studies. ■

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