Serologic profile of some sexually transmitted diseases in women with squamous intraepithelial lesions

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Summary

The purpose of this study consisted of the evaluation of some sexually transmitted diseases in patients with cervical pathology, namely squamous intraepithelial lesions. Methods: a prospective study was performed. Patients with an abnormal cervical smear were submitted to colposcopy, directed biopsy and an immunologic assay for Chlamydia, Herpes Simplex Virus (HSV) types 1 and 2, Cytomegalovirus, Treponema pallidum, Hepatitis B and Human Immunodeficiency Virus I and II. The same parameters were evaluated in women with normal cervical cytology in a matched control group. A comparative study was performed evaluating some epidemiological parameters and the referred immunologic assays. Results: 118 patients were separated into four groups. Statistically significant differences were observed in the personal history of fungi infections, as well as Chlamydia and HSV 2 IgM. Conclusion: immunologic assays may prove useful in identifying sexually-transmitted diseases, especially Chlamydia and HSV 2 infections, in Human Papillomavirus infected women.

Key words: Sexually transmitted diseases; Squamous intraepithelial lesions.

Introduction

Cancer of the cervix uteri is a common form of cancer in women, with an estimated rate of 500,000 new cases per year [1-3]. The global incidence and mortality have decreased in developed countries; paradoxically, in women under 40 years of age, levels of mortality have increased [2, 4, 5].

The etiopathogenic mechanisms responsible for this cancer are not completely understood, but various epidemiological studies reveal an association between cancer of the cervix and Human Papillomavirus (HPV) infection. When HPV-DNA is integrated in the human genome, a rupture at the E2 protein occurs, protein that limits the expression of the oncoproteins E6 and E7 [6-9]. The end products of transcription of oncoproteins E6 and E7 adhere to and cause degradation of the anti-oncogenes p53 and Rb. This is the mechanism that has been demonstrated as the oncogenic action of the HPV [5, 10]. Although HPV infection has been frequently implicated in neoplastic transformation, it is not an absolutely necessary or even a sufficient condition, as demonstrated by the existence of cervical carcinomas not associated with this virus, as well as HPV infections which spontaneously disappear [11, 12].

Therefore, the progression of the carcinogenic process appears to depend upon the action of promoting agents or co-factors which, acting in synergism with HPV, allow the evolution of the lesion and neoplastic transformation [10, 13].

The co-factors implicated are multiple and include sexually-associated factors, mainly sexually-transmitted diseases (STD).

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Materials and Methods

A prospective study was performed in the Gynecologic Department at University Hospital of Coimbra, from April 1995 to April 1996. Patients with an abnormal cytology were submitted to colposcopy, directed biopsy and an immunologic assay for Chlamydia, Herpes simplex virus type 1 and type 2 (HSV 1 and HSV 2), Cytomegalovirus (CMV), Treponema pallidum (VDRL), Hepatitis B (HBsAg), and Human Immunodeficiency Virus (HIV) I and II.

The same parameters were tested in women with normal cervical smears. This was considered the control group.

A comparative study was executed evaluating some epidemiological parameters and the referred infectious profile.

The data was processed in Statview and the statistic study was executed in Student T and Chi-square tests. p values <0.05 were considered significant.

Results

A total of 118 patients were separated into four groups, according to the cervical histological results: a control (CO) group with 27 patients; a cervicitis (CER) group with 16 patients, involving women with a cytologic squamous intraepithelial lesion (SIL) but histological cervicitis; a low grade SIL (LGSIL) group with 36 patients; a high grade SIL (HGSIL) group with 39 patients.

Table 1 shows the epidemiological parameters evaluated in this study.

The comparison of these parameters revealed no statistically significant differences.

Patient history of vulvar-vaginal symptoms, classified in fungal infections, offensive vaginal discharge (OVD), and unspecific pruritis (UNPRU) were evaluated. (See Table 2).

Patients with SIL were more likely to have fungal infections, with a statistically significant difference

Table 1. — *Comparison of epidemiologic parameters*

	CO(a)	CER(b)	LGSIL(c)	HGSIL(d)	p
Age	41.1±9.3	40.1±7.9	41.4±9.8	37.2±9.1	NS
Coitarche	22.3±5.1	20.9±2.3	20.3±2.7	20.2±3.4	NS
Parity	1.8±1.4	1.7±1.1	2.0±1.6	1.4±1.0	NS
Curettage	1.3±0.6	1.0±0	1.2±0.4	1.7±0.8	NS
Cervical electrocautery	1.0±0	1.0±0	1.0±0	1.2±0.4	NS

Table 2. — *Patient history of genital infections*

	CO(a)	CER(b)	LGSIL(c)	HGSIL(d)	p
Fungal	3.7%	6.3%	8.3%	17.9%	a – d
O V D	18.5%	25.0%	16.7%	23.1%	NS
UNPRU	14.8%	18.8%	8.3%	12.8%	NS

Table 3. — *Serologic positivity in the different groups*

STD	CO(a)	CER(b)	LGSIL(c)	HGSIL(d)	p
Chlamydia	14.8%	37.5%	16.7%	35.9%	a – d
HSV 1	92.6%	100 %	86.1%	92.3%	NS
HSV2 IgG	51.9%	50 %	55.6%	53.8%	NS
IgM	14.8%	25 %	11.1%	18.4%	NS
CMV IgG	92.6%	100 %	100 %	82.9%	NS
IgM	0 %	0 %	0 %	0 %	—
VDRL	0 %	0 %	0 %	0 %	—
HIV I	0 %	0 %	0 %	0 %	—
HIV II	0 %	0 %	0 %	0 %	—
HBsAg	0 %	0 %	5.6%	2.6%	NS

Table 4. — *Serologic profile in patients with SIL*

	LGSIL HPV		HGSIL HPV		p
	Positive (a)	Negative (b)	Positive (a)	Negative (b)	
Chlamydia	18.2%	14.3%	42.9%	9.1%	c – d
HSV 1	81.8%	92.9%	92.9%	90.9%	NS
HSV2 IgG	50.0%	64.3%	60.7%	36.4%	NS
IgM	9.1%	14.3%	28.6%	0 %	c – d

($p<0.05$) observed when groups CO and HGSIL were compared.

The immunologic assays of the different groups for the different STDs are shown in Table 3.

A statistically significant difference was observed concerning Chlamydia infection between the control group and high grade SIL group.

Only three patients were HBsAg positive, and all had SIL: two patients had LGSIL and were HSV 1 positive and HSV 2 IgG positive; one patient had HGSIL and was Chlamydia positive.

Patients with SIL were separated into two groups according to histologically-detected HPV. We then performed a comparative analysis between HPV-positive and HPV-negative patients. The results are shown in Table 4.

Although some differences were observed in patients with LGSIL, none of them were statistically significant. However, in patients with HGSIL, the difference in Chlamydia and HSV 2 infections was statistically significant.

Discussion

From an epidemiological point of view, we can stress the homogeneity of the patients' history in the different groups, except for fungal infections (CO vs HGSIL) where the HGSIL group had a greater percentage of these infections, this difference being statistically significant. However, we were not able to find in the literature consulted an association between fungi-SIL as was observed in our study.

When we consider the different sexually transmitted diseases individually, we can observe that none of them have a significant association with squamous intraepithelial lesions, except Chlamydia infection; in this case a significant association with high grade SIL was observed, in agreement with some authors who have demonstrated the apparent importance of Chlamydia in the etiopathogeny of cancer of the cervix uteri [10, 15-18].

None of the patients was VDRL or HIV positive. We were not able to find an association between syphilis-SIL in the literature consulted [15, 17]; as for HIV, this association appears to be demonstrated and, although the number of false negatives in the cervical smears are considerable, histological evaluation has demonstrated organic lesions when cytology was negative [18-19]. Since we had no HIV-positive patients in this study, we are unable to draw any conclusions.

Three patients were HBsAg positive, all with histological lesions. Due to an insufficiency of patients with hepatitis B in this study we are unable to draw conclusions, but it is expected that patients with chronic hepatitis should present alterations that resemble those observed in patients with chronic infectious diseases, including HIV [10].

Various studies demonstrate a lack of association between HSV I and SIL. This study was no exception, as shown by the high prevalence of positive serology in all groups. The prevalence of HSV 2 was lower (about 50%) and we were also unable to establish a relationship between HSV 2-SIL. In fact, multiple studies are contradictory, some referring to the importance of HSV 2 in the oncological transforming cascade, others denying an association [10, 15, 17, 21, 22].

A consensus exists today about the importance of HPV in the etiopathogeny of carcinoma of the cervix and it is concurred that its action alone is not sufficient and needs other co-factors in order for the neoplastic cascade to evolve. When we associated HPV and STD, we noted that in patients with LGSIL no difference was observed between HPV-positive and HPV-negative patients. However, in patients with HGSIL a significant association was observed between HPV-Chlamydia and HPV-HSV 2 (particularly IgM).

Conclusion

In conclusion we can state that it is of interest to know the immunologic assay for Chlamydia and HSV 2. These two infections acquire some importance when we study patients with LGSIL, especially when associated with HPV, and profess to know the probability of these lesions evolving to HGSIL or carcinoma of the cervix.

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