

A Correlative Analysis of Cervical Lesions in Patients with Vulva Condyloma Acuminatum

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OBJECTIVE To analyze the relation ship among vulva condyloma acuminatum, high-risk human papillomavirus (HPV) infections and cervical epithelium lesions.

METHODS From May 2002 to April 2004 patients with vulva condyloma acuminatum were examined employing vulva biopsy, colposcopy, high-risk HPV-DNA test and cervical bioscopy.

RESULTS In 418 cases of vulva condyloma acuminatum, verified by pathologic analysis, high-risk HPV (+) infections were detected in 68.7% (287/418) of the cases. Among those patients, 20.6% (59/287) had concurrent subclinical cervical intraepithelial neoplastic (CIN) lesions. Among the high-risk HPV(-) 31.3 % (131), patients 7.6% (10/131) had concurrent subclinical CIN lesions. Pathological examination results: cervicitis, 167 (40.0%); cervical HPV infection, 182 (43.5%); CIN-I, 51(12.2%); CIN-II, 16 (3.83%); CIN-III, 2 (0.5%); cervical cancer, none. Another patient had vulva condyloma acuminatum with valva intraepithelial neoplasia (VIN) II~III.

CONCLUSION It was concluded that simultaneous cervical HPV infection of many types was rather common in patients with vulva condyloma acuminatum. Vulva condyloma acuminatum is the chief clinical symptom which hints at a high possibility of infection with high-risk HPV. The patients are at high-risk for CIN and cervical cancer. We must pay more attention to the cervix in cases with vulva condyloma acuminatum.

KEYWORDS: condyloma acuminatum, human papillomavirus (HPV), cervical intraepithelial neoplasia (CIN), external genital warts.

There are at least 40 subtypes of human papillomavirus (HPV) related to infections and diseases of the female lower genital tract, including 13 definitely high-risk subtypes and 5 low-risk subtypes. Infections by high-risk subtypes are associated with cervical intraepithelial neoplasia and cervical cancer; while infections by low-risk subtypes cause development of symptoms such as as wart-like lesions of the vulva, vagina and cervix, but usually do not lead to cervical cancer.^[1] Most infections by HPV are subclinical without developing apparent symptoms. Many of the patients with cervical intraepithelial neoplasia, are first diagnosed because of vulvar warts. In this study, we evaluated the combined incidence of infections by high-risk HPV subtypes and the occurrence of cervical diseases in patients first diagnosed as condyloma acuminatum.

MATERIALS AND METHODS

General information

All patient data were derived from the Diagnosis and Treatment Cen-

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ter of Cervical Diseases in our hospital from May 2002 to April 2004. Of the 8,802 patients who underwent colposcopy, 519 were diagnosed as condyloma acuminatum (5.9%). Information on 101 of these 519 patients was not complete, leaving 418 patients for analysis. The ages of patients ranged between 18 to 69 years (MOM 30), with 286 (68.4%) younger than 30 years and 105 (25.1%) between 21 and 25. Thirty-three patients were pregnant.

Diagnostic criterion

Diagnostic criteria for vulvar condyloma acuminatum

① Macroscopy: diagnosis of cauliflower-like, papuloid, platypapuloid genital warty lesions^[2] occurring in the uerthral orifice, vaginal vestibule, vulva and anus. ② Colposcopy: Papillose, cauliflower-like, crest-like neoplasms, surrounding the vulva, urethral orifice and anus. After an acetic acid test, the neoplasms became white, papillae appeared upright, with a fused base that remained without subsiding for long time. ③ Pathological diagnosis: condyloma acuminatum grow outword as small, thick hyperplastic papillae. In the upper layer cellular parakeratosis and hyperkeratosis are present; the stratum basal and stratum spinosum are hyperplastic, and there are characteristic focal koilocytes with perinuclear halos in the superficial or superficial-middle layer of epithelium^[3] associated with excessive hyperplasia and allotypic cells. These changes involve the middle and upper thirds of the epithelium which is called vulvar intraepithelial neoplasia II~III (VIN II~III).

Diagnostic criteria for cervical diseases

① Colposcopy: All patients underwent colposcopy and fixed-point cervical biopsy under colposcopy; for those without apparent cervical diseases, a cervical biopsy was performed at 6 and 12 o'clock of the cervix in order to produced a pathologic diagnosis. Cervical exfoliated cells in pregnant patients were collected for cytological examinations to exclude high-grade squamous intraepithelial lesions (HSIL), and a cervical biopsy was only performed if it was necessary (the patient and her relatives agreed). ② Pathological diagnosis: ① Cases of chronic cervicitis, and for those cases without morphological changes due to HPV infection in the cervical squamous epithelium, were considered to be a general infection, diagnoses which showed no occurrence of HPV infection. ② Benign hyperplasias included condyloma lata, condyloma endogenesis and condyloma acuminatum occurring in the cervical squa-

mous epithelium, which was diagnosed as HPV infection. ③ Cervical intraepithelial neoplasia were mild, moderate and severe, and were diagnosed as CIN I, II, III, respectively.

Cervical high-risk type HPV-DNA detection

Specimens from the cervical os were collected to detect high-risk type HPV-DNA. Hybrid Capture 2 (HC2, Digene) was used to detect the 13 types of high-risk HPV including HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68. Results ≥ 1 pg were regarded as positive.

RESULTS

Results of high-risk type HPV detection

Among these 418 patients, 287 were high-risk type HPV positive (68.7%) and 131 were negative (31.3%). In the 385 non-pregnant patients, 275 were high-risk type HPV positive, with an incidence of infection of 71.4%. In the 33 pregnant patients, 12 were high-risk type HPV positive, with an infection incidence of 36.4%.

Combined cervical diseases

For the incidence of combined vulvar condyloma acuminatum and cervical and/or vaginal condyloma acuminatum (Table 1).

Table 1. Combined vulvar condyloma acuminatum and cervical and/or vaginal condyloma acuminatum

	Cases	Percentage (%)
Vulva	226	50.07
Vulva & cervix	82	19.61
Vulva & vagina	79	18.90
Vulva & cervix & vagina	31	7.42
Total	418	100

In Table 2 it can be seen that the pregnant patients with vulvar condyloma acuminatum were more susceptible to combined cervical and/or vaginal condyloma acuminatum when compared with non-pregnant patients.

Results of cervical pathological examinations

There were 167 patients who had no HPV infection (40.0%) and 251 patients who had a pathologically confirmed cervical HPV infection and/or combined CIN (60.1%). Of these cases a cervical HPV infection was detected in 182 (43.5%). There were 51 cases

(12.2%) of CIN-I, 16 (3.8%) of CIN-II and 2 (0.5%) of CIN-III, but there was no evidence of cervical cancer. In the group with pathologically confirmed HPV infections, the incidence of CIN was 27.5% (69/251). There was only 1 case of vulvar condyloma acuminata complicated by CIN II-III.

Table 2. Incidence of lower genital tract condyloma acuminatum in pregnant and non-pregnant patients

	Non-pregnant patients		Pregnant patients	
	Cases	%	Cases	%
Vulva	214	55.58	12	36.36
Vulva & cervix	72	18.70	10	30.30
Vulva & vagina	77	20.00	2	6.06
Vulva & cervix & vagina	22	5.72	9	27.28
Total	385		33	

High-risk type HPV and cervical diseases

Table 3 shows the incidences of cervical disease in patients with vulvar condyloma acuminatum who were infected and those not infected with high-risk type HPV.

The ages of patients between positive and negative high-risk HPV groups were not different. The incidence of CIN in the positive high-risk HPV group was 20.6%, which was higher than the high-risk HPV negative group (7.6%), the difference being significant. In the group of negative high-risk HPV patients, cases without cervical disease dominated (64.9%), and only 10 cases of CIN-I were found but no CIN II-III (Table 3).

DISCUSSION

The combined mixed infection and multiple sites of le-

sions in the patients with vulvar condyloma are known to acuminata. Patients with a lower genital tract HPV infection are susceptible to a simultaneous infection with high and low-risk types of virus, so it is necessary to perform a complete total lower genital tract examination.^[2] Also, infection with HPV can produce symptoms of warts in the genitalia, vulva, vagina, cervix and anus, or intraepithelial neoplasms or invasive squamous cell carcinomas at these sites.^[5] The results of our study of 418 patients with vulvar condyloma acuminatum showed that the percentage of complicated cervical condyloma acuminatum cases was 19.6%, complicated vaginal condyloma acuminatum cases were 18.9% and that there was 7.4% of doubly complicated cases. So mixed infection often existed in patients with macroscopically visible genital warts, i.e. different subtypes of HPV, multiple lesions and potentially different types of infection can exist simultaneously. The problem of mixed infection is that no obvious symptoms or similar symptoms existed. Some patients with other types of infection could not be detected, which not only delays treatment but also leads to serious outcomes (e.g. cervical cancer) and permits the infection to be continuously transmitted in the population. So it is necessary for clinicians to completely examine the total lower genital tract and draw up a detailed plan of treatment and follow-up that correlates with the extent of infection.

Vulvar condyloma acuminatum can be regarded as a characteristic condition, that suggests the possibility of cervical high-risk HPV infection complicated by CIN.^[9] The results of our study showed that the detection rate of cervical high-risk HPV-DNA was 68.7% in the 418 patients with vulvar condyloma acuminatum. This rate was 3 times higher than that found in a population

Table 3. Incidence of high-risk type HPV infections and cervical diseases in 418 patients with vulvar condyloma acuminatum

	High-risk type HPV (+) group		High-risk type HPV (-) group	
	Cases	%	Cases	%
No occurrence of cervical diseases	82	28.57	85	64.89
HPV infection	146	50.87	36	27.48
CIN-I	41	14.29	10	7.63
CIN-II	16	5.57	0	0
CIN-III	2	0.70	0	0
Total	287		131	

After χ^2 test, the differences between the 2 groups were significant ($P \leq 0.05$).

in Xiangyuan (19.2%),^[4] Shanxi province, where these is a high-incidence region of cervical cancer. At the same time, the incidence of CIN in the high-risk HPV positive group was 20.6%, also higher than that in the population of Xiangyuan.^[4] In the pathologically confirmed group, 27.5% of the patients with HPV infection showed complications with CIN, while the rate outside China was as high as 77.78%.^[9] In American adolescent girls, genital warts are the most common clinical manifestation of HPV infection.^[7] Infection of HPV is very prevalent in females with external genital warts.^[9] Vulvar condyloma acuminatum is a characteristic condition suggesting the most possible cervical high-risk HPV infection, so these patients should be regarded as part of a high-risk population and optimal follow-up be administrated. Those patents with a history of condyloma acuminatum in the lower genital tract also should be considered to be a high-risk population for cervical cancer, because the characteristic condition of condyloma acuminatum can disappear after various therapy. However the infection of high-risk HPV can remain and later develop into abnormal intraepithelial hyperplasia and squamous carcinoma.

In the same situation, the susceptibility of pregnant women to HPV infection is increased. The epidemiology of HPV in pregnant and non-pregnant women is very different. Some older studies have suggested that the physiological changes in pregnancy affect the host's immune function and increase the risk of cervical high-risk types of HPV infection, but future effects to the cervix are not definite.^[10] The results of our study showed that, in the 33 cases of vulvar condyloma acuminatum complicated by pregnancy, there were 12 cases of positive high-risk HPV with an incidence of infection of 36.4%. A Mexican study reported that the incidence of high-risk HPV infection in pregnant women was 37.2%, i.e. it was much higher than non-pregnant women (14.2%). Although our study was limited in the number of pregnant women with vulvar condyloma acuminatum, the results basically coincided with the data from outside China.

In patients with immunodeficiency, pregnancy or their use of immunosuppressants, the growth of warts is more significant.^[6] Among the 418 patients with vulvar condyloma acuminatum in our study, 33 were complicated by pregnancy (7.9%). In these patients, 63.6% had combined vaginal, cervical condyloma acuminatum or had lesions at all three sites and the in-

cidence was higher than that in non-pregnant (44.4%) women. High-risk HPV can be transmitted from the mother to a baby through the birth canal or by postpartum contact. However, in a recent study researchers collected amnion fluid, umbilical cords and placentas during the 3rd stage of labor in order to detect HPV in pregnant women with a cervical high-risk HPV infection. For 36.6% of these patients, high-risk HPV could not be detected in the amnion fluid or umbilical cord, but from the placenta, 5.2% of these cases were found to be high-risk HPV positive. These results suggested that maternal-fetal vertical transmission may not be common.^[8]

Under the same economic conditions, age, gynecologic and obstetric state, pregnant women are more susceptible to HPV infection. The prognosis of condyloma acuminatum complicated by pregnancy has a profound effect on future cervical diseases, which require further evaluation and evidence-based studies.

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