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Do We Need To Perform Cervical Colposcopy For Patients With VIN 2/3?

VIN 2/3 Hastalarinda Servikal Kolposkopi Gerekli Midir?

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ÖZET

Amaç: VIN insidansı özellikle genç, orta yaş bayanlarda giderek artmaktadır. Biz VIN 2/3 olan hastalarda servikal patolojileri değerlendirmek istedik.

Gereç ve Yöntemler: 2009-2014 yılları arasında Zekai Tahir Burak Kadın Sağlığı Eğitim ve Araştırma Hastanesi'nde cerrahi olarak tedavi edilen VIN 2/3 hastalarının kliniko-patolojik kayıtları bilgisayar tabanlı sistemden alınarak değerlendirilmiştir.

Bulgular: VIN 2/3 olan 12 hasta bulundu. Üç hasta post-menopozal idi. En sık görülen lezyon tipi bilateral ve multifokaldi. Tüm postmenopozal hastalar kaşıntı ve renk değişikliği şikayeti ile başvururken, premenopozal hastalar genellikle siğilimsi, yüzeyden kabarık lezyonla başvurdular. Hiçbir postmenopozal hastada HPV PCR pozitif bulunmazken, dokuz premenopozal hastanın yedisinde HPV testi pozitifti (77.7%) ($p<0.05$). Hiçbir postmenopozal hastada anormal bir kolposkopik bulgu izlenmezken; 5 premenopozal hastada anormal servikal smear ve kolposkopi sonucu (servikal intraepitelyal neoplazi 1/2) ($p<0.05$) izlendi.

Sonuç: VIN hastalarını premenopozal veya postmenopozal olarak analiz etmek, klinisyene bu durum ile ilişkili servikal patolojiler açısından yol gösterebilir. Premenopozal VIN 2/3 hastalarında HPV pozitifliği çok yüksek olduğundan biz tüm premenopozal VIN 2/3 hastalarına servikal smear sonucundan bağımsız olarak kolposkopi yapmayı öneriyoruz. Ek olarak postmenopozal hastalar için de kolposkopiyi smear sonucu ve diğer bulguların değerlendirilmesi ile yapmak uygun olacaktır.

Anahtar Kelimeler: VIN, CIN, smear, HPV

ABSTRACT

Aim: The incidence of VIN is tremendously increasing especially in young, mid-aged women. Our aim is to evaluate cervical pathologies in patients with VIN 2/3.

Material and Methods: Clinicopathological data of patients with VIN 2/3 who were surgically treated between 2009 and 2014 were retrieved from the computerized database of Zekai Tahir Burak Women's Health Education and Research Hospital.

Results: We identified 12 patients with VIN 2/3. Three patients were postmenopausal. The most common type of lesion was bilateral and multifocal. All the postmenopausal patients had a symptom of itching and discoloration whereas premenopausal patients came to the clinic generally with a globular-warty lesion. None of the postmenopausal patients were having a positive HPV PCR result. Nevertheless seven of nine premenopausal patients were having a positive HPV test (77,7%) ($p<0,05$). While none of the postmenopausal patients were having an abnormal colposcopic finding; five premenopausal patients (55,5%) had an abnormal cervical smear and colposcopic result as cervical intraepithelial neoplasia 1/2 ($p<0,05$).

Conclusion: Analysing VIN patients as premenopausal or postmenopausal may guide the clinician about the related cervical pathologies. For premenopausal patients, the risk of HPV is very high and we suggest performing colposcopy to all of the premenopausal patients with VIN 2/3 independent from the cervical smear result. Additionally for postmenopausal patients performing a colposcopy should be directed by other findings and cervical smear result.

Key Words: VIN, CIN, smear, HPV

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Introduction

Recently vulvar intraepithelial neoplasia (VIN) is frequently seen and the incidence of VIN is tremendously increasing especially in young, mid-aged women; 60-75% of cases (1). VIN is a pre-malignant condition and if not treated on time may progress to vulvar cancer (2). There are two types of VIN. Type 1 is associated with human papillomavirus infection and may progress to basaloid or warty type squamous cell carcinoma (SCC) (3). Type 2 VIN is asssociated with chronic inflammatory skin lesions without HPV infection and may progress to keratinizing SCC (4). Approximately 100% of cervical, 43% of vulvar and 70% of vaginal tumors are related to HPV infection (5). Vulvar Oncology Subcommittee in 2004 made a classification according to the morphologic criteria independent of HPV type; and declared that VIN should be named for high grade lesions not only for usual type by the high risk HPVs (VIN 2/3) but also for the differantiated type (VIN 3) which is seen notably in older women with lichen sclerosus and squamous cell hyperplasia (6). Anymore VIN 1 is classified in condyloma acuminata group. By the way, the debate on the issue of cervical pathologies in patients with VIN influenced us to retrospectively evaluate our patients with VIN 2/3.

Material and Methods

Clinicopathological data of patients with VIN 2/3 who were surgically treated between 2009 and 2014 were retrieved from the computerized database of Gynecologic Oncology Department at Zekai Tahir Burak Women's Health Education and Research Hospital which is a tertiary referral center in Turkey. Medical records were reviewed for demographic information, symptoms, lesion type, pre-operative biopsy results, treatment type, permanent pathology result, concurrent cervical smear, HPV PCR and colposcopy result.

Statistical analyses were performed with SPSS for Windows version 17.0 statistical package (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean±SD, discrete variables as median (range), and categorical variables as number (percentage). Univariate analysis was performed to reveal the risk factors. A *p* value <0.05 was set for statistical significance.

Results

We identified 12 patients with a pre-operative biopsy result of VIN 2/3. The minimum age was 23 and the maximum age was 69; with a mean age of 42±15,9. Four of the patients (33,3%) were older than the age of 50. And three patients (25%) were postmenopausal.

Half of the lesions were VIN 2 and the other half was VIN 3. While four out of six (66,6%) VIN 3 patients had a bilateral lesion, three out of six (50%) VIN 2 patients had a bilateral lesion. Therefore the most common type of lesion was bilateral and multifocal. For postmenopausal patients, 2 (of 3) lesions were bilateral and for premenopausal patients 5 (of 9) lesions were bilateral. Excisional surgical procedures were performed for the treatment of all patients. Only one postmenopausal patient with a biopsy result of VIN 3 had a permanent pathology result of SCC. Additionally we found an anal intraepithelial neoplasia (AIN) 3 with one patient who was HPV 16 positive.

All the postmenopausal patients had a symptom of itching and discoloration (100%), however premenopausal patients (7 of 9) came to the clinic generally with a globular lesion especially in warty type (77,7%). None of the postmenopausal patients were having a positive HPV PCR result. Nevertheless seven of the nine premenopausal patients were having a positive HPV test result (77,7%) (p<0,05). The most common HPV type was HPV 16.

Only one postmenopausal patient had an abnormal cervical smear result as atypical squamous cells of undetermined significance (ASCUS); however for premenopausal patients; 2 patients had ASCUS result, 2 patients had low grade squamous intraepithelial lesion (LSIL) result and one patient had high grade squamous intraepithelial lesion (HSIL) result. We performed cervical colposcopy±biopsy to all of our patients. While none of the postmenopausal patients were having an abnormal colposcopic finding; totally five premenopausal patients (55,5%) were having cervical intraepithelial neoplasia (CIN) 1 or 2 as an abnormal finding (p<0,05) (Table 1).

Discussion

Vulvar cancer is a mortal disease that the precursor lesion VIN needs to be treated urgently. Vulvar cancer is not seen often; it constitutes approximately 4% of all genital cancers and SCC is the most seen counterpart (>90%) of vulvar cancers (7). Vulvar cancer commonly occurs in women older than 60 (>60%), one of our patients had a permanent pathology result of vulvar cancer that she was 69 years old.

VIN, a premalignant lesion of vulva, if not treated on time could easily progress to a cancer (8), and also 3% of women who had a surgery for VIN concurrently may have an occult invasive cancer (9). The regression of VIN 2/3 is controversial; pregnancy may have a role in the regression (9). Additionally Jones et al. (10) retrospectively evaluated 14 women who had a spontaneous regression of VIN 2/3 and stated being young or having a multifocal pigmented lesion as a role player in the regression of VIN2/3. We performed an excisional surgical procedure to all of our patients that one of them had a SCC result. In that manner all patients with a result of VIN 2/3 need to have a local wide excisional procedure.

In our study the most common clinical symptom for premenopausal patients was a warty-globular mass on the vulva (77,7%). Maniar et al. (11) stated coexistence of condylomatous lesions with high grade VINs. Nevertheless in postmenopausal patients itching and discoloration was the most common symptom(100%). Previously pruritus and pain had been stated as the most frequent symptom and also a long history of itching and chronic vulvar lesions occupy the foremost suspicious conditions (12).

In a worldwide study, the mean age for usual VIN and differentiated VIN was 48.5 and 60 respectively. We found similar results in our study. HPV DNA was identified in the majority of VIN cases (>80%), whereas HPV was positive only 40% of invasive squamous cell carcinomas. The most common type of HPV was HPV 16 (3).

Table 1: Demographic findings of the patients

	Premenopausal	Postmenopausal
Age (mean)	34.4±9.3	64.6±5.1
Patient number	9 (75%)	3 (25%)
Symptom	Warty lesion (77.7%)	Itching, discoloration (100%)
Bilaterality	5 (55.5%)	2 (66.6%)
Abnormal smear	5 (55.5%)	1 (33.3%)
HPV DNA	7 (77.7%)	0
Positive colposcopic finding	5 (55.5%)	0

VIN is a high grade lesion and VIN 1 is no longer classified as a premalignant lesion, just a self-limited HPV infection (6). There are two distinct types of VIN, usual type is associated with carcinogenic genotypes of HPV additionally smoking and being immune-compromised are risk factors for persistence. Whereas the other type, differentiated VIN is generally associated with chronic vulvar lesions like lichen sclerosus (13). The etiological difference; role of HPV infection worry gynecologic oncologs about the risk of concurrent cervical pathology; CIN or an invasive carcinoma.

CIN is a premalignant lesion of uterine cervix that CIN 1/2/3 is named according to the severity of dysplastic changes. CIN 2 and 3 are high grade lesions and women with this pathology have an increased risk of cervical cancer in the future or synchronously (14). HPV constitutes nearly 100% of the etiological database of CIN cases and invasive cervical cancer. Especially HPV 16 and 18, the high risk oncogenic HPVs are seen in the 70% of invasive cervical cancers (15). HPV 16 is the most common type for usual VIN; HPV 31, 33 and 45 are the other identified genotypes (16).

Usual VIN is often multifocal and multi-centric; a relationship between CIN, vaginal intraepithelial neoplasia (VaIN) and AIN could be seen and suggests a multifocal disease originating from the same area in lower genital tract (17). Multicentric lesions are commonly seen in young women and decreases in women over 50 years of age (18). In our study we found predominantly multifocal disease. It was over 50% both for premenopausal and postmenopausal patients.

CIN and VIN are the frequent problems of young adult ages and share the same etiological pathology 'HPV' to some extent. Baser et al. (19) reviewed risk factors for persistence of HPV after high risk lesions and found young patient age is an important determinant of persistence. HPV 16 was not found to be significant at that study. Maniar et al. (11) found prior or concurrent abnormal cervical cytology with VIN in 13 of 14 patients that all of them were having an immune-compromised condition. Median age of these patients was 39.

In this study, we performed colposcopy to all of our patients. Only one postmenopausal patient had an abnormal cervical smear result; ASCUS, nevertheless during colposcopy we did not find any lesion or pathologic area so any biopsy was not taken. HPV PCR was also negative for all postmenopausal patients. For premenopausal patients, 2 patients were ASCUS, 2 patients were LSIL and 1 patient was HSIL as an abnormal cervical smear result. Five of 9 premenopausal patients with an abnormal cytology were also positive for HPV PCR especially positive for HPV 16. Two patients who were positive for HPV did not have an abnormal cervical cytology. Colposcopic findings of 5 patients suggested CIN 1 or CIN 2 as a result.

Ribeiro et al. (20) evaluated 29 VIN patients and found previous or concomittant CIN lesion in 10 (34%) of them. In that study 41,4% of lesions were multifocal, mean age was 51 and 13 (44,8) patients were younger than 50 years old.

In conclusion, the incidence of vulvar squamous cell carcinoma is increasing. The different types of VIN and associated lesions lead us to prevent women from other pathologies of lower genital tract. Analyzing VIN patients as premenopausal or postmenopausal like HPV positive or negative respectively may guide the clinician about the related cervical pathologies. For postmenopausal patients, the detection rate of HPV is very low and probability of a negative colposcopy is high. However for premenopausal patients the risk of HPV notably HPV 16 is very high and we suggest performing colposcopy to all of the premenopausal patients with VIN 2/3 independent from the cervical smear result. Additionally for postmenopausal patients performing a colposcopy should be directed by other findings and cervical smear result. Alternatively it should not be forgotten that all patients with CIN 2/3 need a good inspection to the vulvar and anogenital region.

References

1. Wallbillich J.J., Rhodes H.E., Milbourne A.M., Munsell M.F., Frumovitz M, Brown J, Trimble C.L., Schmeler K.M.; Vulvar intraepithelial neoplasia (VIN 2/3): comparing clinical outcomes and evaluating risk factors for recurrence, Gynecol Oncol 2012; 127: 312-5.
2. Kaushik S, Pepas L, Nordin A, Bryant A, Dickinson H.O.; Surgical interventions for high grade vulval intraepithelial neoplasia, Cochrane Database Syst Rev, 2014; 3: p. CD007928.
3. De Sanjose S, Alemany L, Ordi J, Tous S, Alejo M, Bigby S.M., Joura E.A., Maldonado P. et al.; Worldwide human papillomavirus genotype attribution in over 2000 cases of intraepithelial and invasive lesions of the vulva, Eur J Cancer, 2013; 49: 3450-61.
4. Reyes M.C. and K. Cooper; An update on vulvar intraepithelial neoplasia: terminology and a practical approach to diagnosis, J Clin Pathol, 2014; 67: 290-4
5. Lowy D.R. and J.T. Schiller; Reducing HPV-associated cancer globally, Cancer Prev Res (Phila), 2012; 5: 18-23.
6. Sideri M, Jones R.W., Wilkinson E.J., Preti M, Heller D.S., Scurry J, Haefner H, Neill S; Squamous vulvar intraepithelial neoplasia: 2004 modified terminology, ISSVD Vulvar Oncology Subcommittee, J Reprod Med, 2005; 50: 807-10.
7. Judson P.L., Habermann E.B., Baxter N.N., Durham S.B., Virnig B.A.; Trends in the incidence of invasive and in situ vulvar carcinoma, Obstet Gynecol, 2006; 107: 1018-22.
8. Jones R.W., D.M. Rowan, and A.W. Stewart; Vulvar intraepithelial neoplasia: aspects of the natural history and outcome in 405 women, Obstet Gynecol, 2005; 106: 1319-26.
9. Van Seters M, M. van Beurden, and A.J. de Craen; Is the assumed natural history of vulvar intraepithelial neoplasia III based on enough evidence?, A systematic review of 3322 published patients, Gynecol Oncol, 2005; 97: 645-51.
10. Jones R.W. and D.M. Rowan; Spontaneous regression of vulvar intraepithelial neoplasia 2-3, Obstet Gynecol, 2000; 96: 470-2.
11. Maniar K.P., Ronnett B.M., Vang R, Yemelyanova A; Coexisting high-grade vulvar intraepithelial neoplasia (VIN) and condyloma acuminatum: independent lesions due to different HPV types occurring in immunocompromised patients, Am J Surg Pathol, 2013; 37: 53-60.
12. McNally O.M., Mulvany N.J., Pagano R, Quinn M.A., Rome R.M.; VIN 3: a clinicopathologic review, Int J Gynecol Cancer, 2002; 12: 490-5.
13. Committee on Gynecologic Practice of the American College of et al.; Management of vulvar intraepithelial neoplasia, J Low Genit Tract Dis, 2012; 16: 1-3.
14. Montz F.J.; Management of high-grade cervical intraepithelial neoplasia and low-grade squamous intraepithelial lesion and potential complications, Clin Obstet Gynecol, 2000; 43: 394-409.
15. De Sanjose S, Quint W.G., Alemany L, Geraets D.T., Klaustermeier J.E., Loveras B, Tous S, Felix A; Human papillomavirus genotype attribution in invasive cervical cancer: a retrospective cross-sectional worldwide study, Lancet Oncol, 2010; 11: 1048-56.

16. Riethdorf S, Neffen E.F., Cviko A, Loning T, Crum C.P., Riethdorf L; p16INK4A expression as biomarker for HPV 16-related vulvar neoplasias, Hum Pathol, 2004; 35: 1477-83.

17. McCluggage W.G.; Premalignant lesions of the lower female genital tract: cervix, vagina and vulva, Pathology, 2013; 45: 214-28.

18. Preti M, Van Seters M, Sideri M, Van Beurden M; Squamous vulvar intraepithelial neoplasia, Clin Obstet Gynecol, 2005; 48: 845-61.

19. Baser E, Ozgu E, Erkilinc S, Togrul C, Caglar M, Gungor T; Risk factors for human papillomavirus persistence among women undergoing cold-knife conization for treatment of high-grade cervical intraepithelial neoplasia, Int J Gynecol Obstet, 2014; 125: 275 - 8

20. Ribeiro F, Figueiredo A, Paula T, Borrego J; Vulvar intraepithelial neoplasia: evaluation of treatment modalities, J Low Genit Tract Dis, 2012; 16: 313-7.