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Vaginal Smear Findings in Our Kidney Transplant Recipients

Böbrek Nakli Hastalarımızda Vajinal Smear Bulguları

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ABSTRACT

Aim: The aim of this study was to evaluate the results of the smear tests in renal transplant recipients, determine the prevalence of abnormal outcomes and compare these patients with the general population in our center.

Material and Method: A total of 79 female patients who underwent renal transplantation at Pamukkale University were retrospectively evaluated. All patients were followed up during and after the surgical procedures by a gynecologist and the smear results were recorded periodically.

Results: The mean time of Pap smear results after transplantation in kidney transplant recipients was 36.7±4.5 months. There was a significant difference between the two groups in terms of atrophic cervicitis. In transplantation group, 7 patients (8.86%) had LG-SIL, 3 (3.79%) had ASC-US and 1 (1.26%) had HG-SIL. In control group, the numbers are 3 (3.79%), 2 (2.53%) and 0, respectively. The difference between the patient and control groups in terms of LG-SIL results (7 (8.86%) vs 3 (3.79%) was statistically significant (p<0.05).

Conclusion: We predict that kidney transplant recipients are at higher risk for precancerous cervical lesions and cervical cancer development due to immunosuppressive therapy. Smear screening and HPV testing should be repeated periodically to detect or prevent precancerous lesions and cervical cancer.

Keywords: Vaginal smear-HPV-kidney transplantation

ÖZ

Amaç: Bu çalışmanın amacı merkezimizde böbrek nakli alıcılarında yapılan smear testlerinin anormal sonuçlarını ve yaygınlığını belirlemek, bu sonuçları genel popülasyonla karşılaştırmaktır.

Gereç ve Yöntem: Pamukkale Üniversitesi'nde böbrek nakli yapılan 79 kadın hasta retrospektif olarak değerlendirildi. Tüm hastalar ameliyat öncesi ve sonrasında bir jinekolog tarafından takip edildi , yapılan işlemler ve smear sonuçları periyodik olarak kaydedildi.

Bulgular: Pap smear sonuçlarının ortalama takip süresi böbrek nakli alıcılarında 36,7±4,5 aydı. İki grup arasında atrofik servisit açısından önemli bir fark vardı. Transplantasyon grubunda 7 hastada (%8,86) LGSIL, 3 hastada (%3,79) AS-C-US ve 1 hastada (%1,26) HG-SIL vardı. Kontrol grubunda ise sırasıyla 3 (%3,79), 2 (%2,53) ve 0 olarak değerlendirildi. Hasta ve kontrol grupları arasındaki LG-SIL sonuçları sırasıyla 7 (%8,86) vs 3 (%3,79) olarak değerlendirildi ve istatistiksel olarak anlamlıydı (p<0,05).

Sonuç: Böbrek naklini alıcılarının immunsüpresif tedavi nedeni ile prekanseröz servikal lezyonlar ve rahim ağzı kanseri gelişimi açısından normal popülasyona göre daha yüksek risk altında olduklarını öngörmekteyiz. Smear taraması ve HPV testi ,prekanseröz lezyonların ve serviks kanserinin tespit edilmesi ve önlenmesi açısından periyodik olarak tekrarlanmalıdır.

Anahtar Kelimeler: Vajinal smear-HPV-böbrek nakli

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INTRODUCTION

Female organ transplant recipients are at risk for many cancers including cervical cancer of viral origin, autoimmune diseases and infections, due to long-term immunosuppressive therapy when compared to the women in general population (1). Papanicolaou (Pap) smear test remains as the primary method for screening cervical pathology, including preinvasive and invasive lesions. The results of this screening method have been associated with decreased incidence and mortality of cervical cancer. It is well known that persistent high-risk Human Papilloma Virus (HPV) infections increase the risk of cervical cancer development (2). In female renal transplant recipients, high-risk HPV prevalence has been reported to be between 5-63%. The number of studies showing the distribution and prevalence of HPV genotypes in renal transplant recipients are limited in the literature. While the risk of developing cervical intraepithelial neoplasia (CIN) due to immunosuppressive therapy is higher in female transplant population, a close follow-up with smear tests is quite important in early detection of these lesions (3). The immunosuppressive therapy can increase the risk of malignancy through various mechanisms increased rates of infection with oncogenic viruses such as HPV. The abnormal outcomes include atypical squamous cells of undetermined significance (ASC-US), low-grade squamous intraepithelial lesion (LGSIL or LSIL), high-grade squamous intraepithelial lesion (HGSIL or HSIL), and atypical squamous cells. The progression of cellular abnormalities and preinvasive diseases can lead to development of cervical cancer (4). The aim of this study was to evaluate the results of the smear tests in renal transplant recipients, determine the prevalence of abnormal cytologic diagnosis and compare these patients with the general population in our center.

MATEERIAL AND METHOD

The study was carried out with the permission of Pamukkale University Medical Ethics Committee (Date: 19/09/2023, Decision No:15).All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

A total of 79 female patients who underwent renal transplantation at Pamukkale University between January 2006 and December 2018 were retrospectively evaluated. The patient group was compared with a control group consisting of same number of healthy adults of similar age group. The screening procedures before and after the surgery were performed following the standard protocols. All patients were followed-up during and after the surgical procedures by a gynecologist and the smear results were recorded periodically. In our clinic, we perform an immunosuppressive therapy protocol including basiliximab, tacrolimus, mycophenolate mofetil and corticosteroid. All smear examinations were evaluated following the Bethesda 2001 criteria.

Statistical analysis

All data analysis was performed using a statistical software (SPSS, version 15.0, IBM Corporation, SPSS Inc., Armonk, NY, USA). Chi-square test was used to compare the variables. $P<0.05$ was accepted as statistical significance.

RESULTS

The mean age of renal transplant patients was 38.1 years. The mean time of available Pap smear results after transplantation in kidney transplant recipients was 36.7±4.5 months. Candida infection was detected in 14 (17.72%) kidney transplant recipients and 5 (6.32%) control subjects. One (1.26%) patient and two (2.53%) control subjects had Trichomonas vaginalis infection. Even though there was a statistically significant difference in renal transplant recipients in terms of candida infection, there was no significant difference with regard to other infections. Chlamydia infection, reactive changes caused by intrauterine devices and radiation-related changes were not detected in either group. There was a significant difference between the two groups in terms of atrophic cervicitis. Based on Bethesda 2001 classification, chronic cervicitis and atrophic cervicitis was observed in 10 (12.65%) and 9 (11.39%) patients, respectively. However, there was no significant difference compared to the control group. In transplantation group, 7 patients (8.86%) had LG-SIL, 3 (3.79%) had ASC-US and 1 (1.26%) had HG-SIL. In control group, the numbers are 3 (3.79%), 2 (2.53%) and 0, respectively. The difference between the patient and control groups in terms of LG-SIL results (7 (8.86%) vs 3 (3.79%) was statistically significant ($p<0.05$) (**Table 1**).

Table 1. Pap Smear Results of Study and Control Patients

Variables	Transplant Group (n:79) %	Control Group (n:79) %	P value
Mean Age(y)	38.1	38.3	
Infections			
Trichomonas Vaginalis	1(1.26)	2(2.53)	NS
Candida	14(17.72)	5(6.32)	.0001
Bacterial Vaginosis	11(13.92)	7(8.86)	NS
Bethesda(2001) Findings			
Chronic Cervicitis	10(12.65)	14(17.72)	NS
Atrophic Cervicitis	9(11.39)	5(6.3)	.0001
LG-SIL	7(8.86)	3(3.79)	.05
ASC-US	3(3.79)	2(2.53)	NS
HG-SIL	1(1.26)	0(0)	NS

Y:year,NS: Not Significant , LG-SIL: Low-grade squamous intraepithelial lesion, ASC-US: Atypical squamous cells of undetermined significance ,HG-SIL: High grade squamous intraepithelial lesion .A p-value < 0,05 was considered significant.

DISCUSSION

Immunosuppressed renal transplant recipients are at risk in terms of HPV and associated malignancies (especially uterine cervical intraepithelial neoplasia) and some types of infections. These lesions can be investigated by screening methods such as Pap smear, HPV tests and colposcopy before and after the transplantation surgery. The rate of incidence in these patients is 11% (5). They have a 3-times higher risk of in-situ cancer incidence compared to the general population (6). In our study, we did not detect any patients with cervical cancer. Routine cervical screening with Pap smear has shown that there is no increase in in invasive cervical cancer incidence. This screening method is easy, low-cost, highly sensitive and specific. This cytological screening test is recommended for all females.

Calcineurin inhibitors (cyclosporine and tacrolimus) potentially induce carcinogenesis through the production of cytokines that regulate TGF-β, metastasis and angiogenesis. All immunosuppressive agents affect the immunological system, reduce the immunological tolerance of neoplastic cells and increase the incidence of infections related to oncogenic viruses (HPV, etc.) that cause DNA damage (7). Oncogenic HPV types such as HPV-16 are less common in LG-SIL (CIN 1) lesions compared to HG-SIL (CIN 3) lesions. Non-oncogenic HPV types are more common in CIN 1 lesions. The average time necessary for the lesion to progress from ASC-US to LG-SIL or worse and from LG-SIL to HG-SIL or worse is shorter in patients with oncogenic HPV types than those without HPV infection (8). Randomized trials have shown that detection of high-risk HPV is more sensitive than conventional cytology in screening of cervical intraepithelial neoplasia (9). A limitation of our study was that the HPV status could not be determined in patient group. We believe that HPV vaccination before the transplantation and an HPV test are mandatory in renal transplant patients to avoid HPV-associated malignancies. In our study, a statistically significant association between the increase in LG-SIL risk and renal transplantation was detected. In another study by Paternoster et al., HG-SIL has been detected in 5 patients and LG-SIL has been detected in another 5 patients in renal transplant recipients (10).

Another important effect of immunosuppression on cervical cytology is on fungal infections. In our study, 14 of 19 patients with candida infection were kidney transplant recipients. There was a significant difference between the two groups in terms of candida infection. However, there was no statistically significant difference between the two groups with regard to Trichomonas vaginalis and bacterial vaginosis infections. It is possible to see the association between renal transplantation and immunosuppression in terms of cervical atrophy. Thinning of squamous epithelium and decrease in mucus production and the use of long-term immunosuppressive drugs lead to atrophy. There was a significant difference between the two groups in terms of atrophy. The presence of this condition and the presence of a shift suggesting bacterial vaginosis in the flora may be due to disturbances in the estrogen cycle.

CONCLUSION

Our results predict that kidney transplant recipients are at higher risk for precancerous cervical lesions and cervical cancer development due to immunosuppressive therapy. Our study has also shown significantly increased LG-SIL incidence compared to normal population. Therefore, smear test screening and HPV vaccination should be performed before renal transplantation. Smear screening and HPV testing should be repeated periodically to detect or prevent precancerous lesions and cervical cancer.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Pamukkale University Medical Ethics Committee (Date: 19/09/2023, Decision No:15).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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REFERENCES

1. Kim JH, Kim SO, Han DJ, Park SK. Post-transplant malignancy: a burdensome complication in renal allograft recipients in Korea. Clin Transplant. 2014;28(4):434-42.
2. Ho GY, Bierman R, Beardsley L, Chang CJ, Burk RD. Natural history of cervicovaginal papillomavirus infection in young women. N Engl J Med. 1998;338(7):423-8.
3. Courtney AE, Leonard N, O'Neill CJ, McNamee PT, Maxwell AP. The uptake of cervical cancer screening by renal transplant recipients. Nephrol Dial Transplant. 2009;24(2):647-52.
4. Solomon D, Davey D, Kurman R, et al. The 2001 Bethesda System: terminology for reporting results of cervical cytology. JAMA. 2002;287(16):2114-9.
5. Ghazizadeh S, Lessan-Pezeshki M, Nahayati MA. Human papilloma virus infection in female kidney transplant recipients. Saudi J Kidney Dis Transpl. 2011;22(3):433-6.
6. Madeleine MM, Finch JL, Lynch CF, Goodman MT, Engels EA. HPV-related cancers after solid organ transplantation in the United States. Am J Transplant. 2013;13(12):3202-09.
7. Freiberger D, Lewis L, Helfand L. Human papillomavirus-related high-grade squamous intraepithelial lesions of the esophagus, skin, and cervix in an adolescent lung transplant recipient: a case report and literature review. Transpl Infect Dis. 2015;17(1):98-102.

8. Schlecht NF, Platt RW, Duarte-Franco E, et al. Human papillomavirus infection and time to progression and regression of cervical intraepithelial neoplasia. J Natl Cancer Inst. 2003;95(17):1336-43.
9. Veijalainen O, Kares S, Kujala P, et al. Human papillomavirus test with cytology triage in organized screening for cervical cancer. Acta Obstet Gynecol Scand. 2016;95(11):1220-7.
10. Paternoster DM, Cester M, Resente C, et al. Human papilloma virus infection and cervical intraepithelial neoplasia in transplanted patients. Transplant Proc. 2008;40(6):1877-80.