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Original Research

Demodex folliculorum mite infestation in gynecological cancers: A case control study

Zeyneb Bakacak[1], Mustafa Kaplanoğlu[2], Murat Bakacak[3], Tuncay çelik[4]

[1] *Private Practice of Obstetrics and Gynecology, Kahramanmaraş, Turkey*

[2] *Cukurova University School of Medicine, Department of Obstetric and Gynecology, Adana Turkey*

[3] *Kahramanmaras Sutcu Imam University School of Medicine, Department of Obstetric and Gynecology, Kahramanmaras, Turkey*

[4] *Adiyaman University School of Medicine, Department of Parasitology, Adiyaman, Turkey*

Summary

Objective: To determine the frequency of Demodex (D.) folliculorum infestation in patients with gynecological cancer. *Materials and Methods:* This cross-sectional study was conducted between January 2015 and May 2015. Eighty-seven patients with gynecologic cancer and ninety control subjects were included and the patients characterics were recorded. Demodex was detected by standardized skin surface biopsy for skin lesions. *Results:* No statistically significant difference was found between the groups in terms of age, diabetes mellitus, body mass index (BMI), hypertension, and the use of radiotherapy and chemotherapy. D. folliculorum infestation was increased in the patient group (47.1%) when compared to the control group (8.9%) ($p < 0.001$). The frequency of D. folliculorum was higher in the cancer groups and particularly in ovarian cancer (58.7%). *Conclusions*: Patients with gynecological cancers are at risk for D. folliculorum mite infestation and this is explained by the immunosuppressed condition of the patients due to the cancer.

Key words: Gynecological cancer; Demodex folliculorum.

Introduction

The general prevalence of gynecological cancers is increasing every year [1]. Progress in surgical techniques and postoperative care in cancer patients and the new and effective anticancer drugs improve the quality of life that has deteriorated and increase survival. However, opportunistic infections remain a major health issue for these women and immunodeficiency plays an important role. Tumor progression and metastases secrete immunosuppressive cytokines from the regulator T-cells and antigen-presenting cells which leads to cancer-related immunosuppression. In addition, the immunosuppressive effect of many anticancer drugs often activates the parasites in the human microenvironment [2].

D. folliculorum is a permanent human ectoparasite with a size of 0.1-0.4 mm. The adult has a worm-like or cigar-like appearance. It is transmitted from person to person by close contact. The location of these mites play a significant role in the pathogenesis of rosacea, acne vulgaris, perioral dermatitis, seborrheic dermatitis and blepharitis, and are found in the hair follicles and sebaceous glands of the face. The mites live singly or in groups in the follicular openings. They are commonly found in the skin, forehead, cheeks, nose and nasolabial region where there is a significant number of sebaceous glands and sebum production [3]. Although infestation with this parasite is common, clinical symptoms are rarely observed. Clinically recognizable infestations are generally seen in local or systemic immunodeficiency states and linked to malignancy and chemotherapy [3-7]. Diabetes mellitus (especially in patients with uncontrolled blood sugar), elderly age and Acquired Immune Deficiency Syndrome (AIDS) are important risk factors [7].

We aimed to investigate the frequency of Demodex (D.) folliculorum infestation in patients with gynecological cancers who were diagnosed and treated in our clinic in this study.

Materials and methods

Approval for the study was granted by the Clinical Research Ethics Committee of Kahramanmaraş Sütçü Imam University (decision no: 01, session: 2015/8). The study was conducted in accordance with the principles of Helsinki Declaration. We included 87 gynecological cancer patients who were diagnosed, treated and followed-up at Adiyaman University Medical Faculty, Obstetrics and Gynecology Department and Kahramanmaraş Sütçü İmam University Faculty of Medicine Obstetrics and Gynecology Department between January 2010 and January 2015. The analysis of the patients' data was made between January 2015 and May 2015. The experimental design was a case-control and the control group was created by randomly selecting ninety patients from patients with no symptoms who had come for a routine annual gynecology examination.

Demographic data (age, BMI, gravidity and parity), cancer-related data and the presence of additional medical and surgical pathology were recorded at the time of patient

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Table 1. — *Baseline clinical characteristics of study population*

	Cancer group n (%)	Control group n (%)	*p* value
	N = 87	N = 90	
Age (years) (mean ± SD)	54,8 ± 5,5	53,1 ± 5,8	0.052
Gravidity (mean ± SD)	2.6 ± 0.8	2.8 ± 0.9	0.093
Parity (mean ± SD)	2.4 ± 0.5	2.3 ± 0.7	0.394
DM			0.487
Positive	24 (27,5%)	20 (22,2%)	
Negative	63 (72,4%)	70 (77,7,59	
HT			0,457
Positive	20 (23%)	16 (17,7%)	
Negative	67 (77%)	74 (82,2%)	
BMI (mean ± SD)	26,1 ± 2,9	25,7 ± 3,1	0.438

DM: Diabetes Mellitus, BMI: Body Mass Index, HT: Hypertansion

Table 2. — *Distribution of D. folliculorum according to cancer type*

Type of Cancer	DF positive patients n (%)
Ovarian Ca	27/46 (58,7)
Endometrium Ca	10/24 (41,6)
Cervix Ca	4/15 (26,6)
Vulva-vaginal Ca	0/2 (0)

DF: Demodex Folliculorum

admission. The presence of diabetes mellitus (DM) and hypertension (HT) was also recorded. The patients were divided into groups defined by the origin of their cancer: cancer of the ovary, endometrium, cervix, or vulvovagina. Data were obtained by directly asking patients and from hospital records.

Study inclusion criteria

The inclusion criteria consisted of patients who attended for reviews and their clinical information being complete; an absence of other disease causing immunosuppression; not having taken any hormonal therapy within the previous 12 months; absence of an allergic condition; chemotherapy and radiotherapy was completed at least 6 months prior to the study); absence of a diagnosis of skin disease (rosacea and facial seborrheic dermatitis, blepharitis, allergic disease); and not having taken anti-biotherapy for a minimum of one month prior to the study.

Sampling

With the patients' consent, samples for Demodex sp. were taken from the forehead, cheeks, nose and chin area with standard superficial skin biopsy (SSSB) using a cyanoacrylate adhesive. An area of 1 cm^2 was drawn with a ruler on one side of the slide. The unmarked side of the slide was wiped with ether to clean it of artifacts and the target skin region was wiped with alcohol to remove excess sebum which can prevent the adhesion of the glass slide. One drop of cyanoacrylate was placed on the marked area on the ether-wiped slide surface. The slide was then placed on the patient's forehead, cheeks, nose and chin and the slide was gently removed after one minute. The material obtained was examined within 1 hour. Two to three drops of immersion oil or glycerin were dropped on the slide where the material was obtained and shielded with a coverslip for examination. A field survey was performed with the 4x magnification of the microscope (Olympus CH20; Olympus Optical, Tokyo, Japan) and the marked area was then scanned with the diaphragm slightly closed at 10x and 40x magnification. The Demodex sp. density per cm^2 was evaluated by a parasitologist. A positive diagnostic result was defined as 5 or more Demodex sp. per cm^2.

The statistical analysis was performed using the Statistical Package for Social Sciences version 15 for Windows (SPSS Inc., Chicago, IL, USA). A Pearson Chi-square test was used to compare the prevalence of Demodex positivity in patient and control groups and a Student's t test was used to measure the distribution of the ages of the patients. Statistical significance was determined as a p value less than 0.05 for all parameters.

Results

No statistically significant difference was found between the patient and control groups in terms of the mean age (54.8 ± 5.5 years and 53.1 ± 5.8 years respectively) (p=0.052). Similarly, no statistically significant difference was found between the patient groups in terms of BMI, DM and HT (p=0.438, p=0.487, p=0.457 respectively). Table 1 outlines these findings.

The frequency of D. Folliculorum infestation was statistically significantly higher in the cancer patient group (47.1% and 8.9% respectively) ($p<0.001$). The prevalence was 58.7% (27/46) in the ovarian cancer group, 41.6% (10/24) in the endometrial cancer group, 26.6% (4/15) in the cervical cancer group, while no D. folliculorum positive patient was found in the vulvovaginal cancer group (p=0,07). (See Table 2) Similarly, no statistically significant difference was found between the cancer groups in terms of BMI, and DM and HT presence (p= 0.939, p = 0.854 and p= 0.963, respectively).

Discussion

Demodex species were first reported by Berger in 1841 and Simon identified in 1842 that Demodex microorganisms were located in pilosebaceous follicles. Two morphologically and biologically different species of D. folliculorum and D. brevis were found in humans. The normal presence and intensity of D. folliculorum in the follicles is determined by several control mechanisms, however, the exact control mechanism is not known [7-9].

The co-existence of the Demodex mite and cancer has been evaluated in numerous studies and such co-existence has been reported with various cancers and skin disorders. High rates of co-existence have been reported for eyelid basal cell cancer and Demodex mites by Erbagci et al. [10]. It has also been suggested that Demodex mites can be a triggering factor for such cancer types. Sun et al. similarly found a high prevalence of D. folliculorum infestation in facial basal cell carcinoma and squamous cell carcinoma samples [11]. However, some studies report contrasting data. Talghini et al reported an association of D. folliculorum with malignant melanoma but not with basal cell or squamous cell carcinoma [12]. This difference between the studies is possibly due to methodology differences and patient sampling diversity.

Hematologic malignancies have also been studied. Seyhan et al found a high Demodex frequency in hematologic malignancies [13]. The highest rate was with acute myeloid leukemia. Similarly, a high density of Demodex infestation was found in childhood leukemia by Damian et al., possibly due to cancer-related immunosuppression [6]. A high frequency of D. folliculorum was also found in breast and urologic cancers [14, 15]. The essential mechanism of increased Demodex folliculorum infestation is thought to be local and systemic immune deficiency in all these studies.

Regardless of the type of cancer, an immunodeficiency that may result in a Demodex infestation in the patients through various mediators (TGF-β and IL-10) that are involved in immunosuppression in the circulation. A reduction in the local immune response and selective suppression of T lymphocytes are held responsible for this infestation [16]. The immunosuppressive effect of varying degrees caused by the drugs used in cancer treatment can also cause an increase in the frequency of Demodex infestations. However, it has been suggested that immunosuppression and/or immune disturbance does not occur with anticancer therapy, that no increase in Demodex prevalence can occur in relation to this treatment, and that the skin infection increase during the cancer treatment period is due to the host immunodeficiency related to cancer [17]. Similarly, a coincidental co-existence of cancer and Demodex spp. has been suggested [17]. Similarly, a high frequency of Demodex presence was found in patients who were immunodeficient due to reasons such as renal transplantation [18]. The relationship between Demodex presence and endometriosis in adolescent patients with severe acne was evaluated by Xie et al. A 20% increased risk of endometriosis was found in patients with severe acne in 4382 patients with and without endometriosis as confirmed by laparoscopy. In conclusion, severe teenage acne was suggested to be a potential non-invasive indicator of endometriosis presence [19].

Women with gynecologic cancer have increased D. folliculorum infestation when compared to the healthy control subjects. The highest co-existence rate was found in ovarian cancer cases. Ovarian cancer causes the highest immunosuppression rates among gynecologic cancers [20, 21]. This may explain why this group has the highest D. folliculorum prevalence. There was no statistically significant difference found between the groups regarding DM or HT presence and BMI which could have affected the results.

The relatively low number of cases and the very low number of vulvovaginal and tubal cancers and our cases are not chosen randomly are major limitations in this case control study.

Conclusion

Patients with gynecological cancers are at risk of D. folliculorum infestation due to immune suppression. The most significant risk increase was found in women with ovarian cancer. We believe that the skin Demodex density increase could be a marker in the early diagnosis of gynecological cancer such as reported with severe teenage acne.

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Conflicts of interest:

The authors declare that there is no conflict of interest regarding the publication of this manuscript.

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Corresponding Author:
MUSTAFA KAPLANOGLU, M.D.
Cukurova University School of Medicine, Department of Obstetric and Gynecology, Adana (Turkey)
e-mail: mustafakaplanoglu@hotmail.com