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Positivity of *Demodex* spp. in biopsy specimens of nevi

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Abstract. Melanocytic skin tumors are caused by nevus cells, epidermal melanocytes and dermal melanocytes. The aim of the study was to detect the positivity of *Demodex* spp. in biopsy specimens of skin diagnosed as nevus. In this retrospective study, the specimens obtained from 110 patients diagnosed with nevus and stained by hematoxylin & eosin (H&E) method were assessed for *Demodex*. Statistical analysis was done using independent sample t test, Pearson Chi-square and Yates' adjusted Chi-square test. For statistics, $p<0.05$ was considered significant. Consequently, 43 (39.1%) out of 110 specimens were detected to have *Demodex* spp. *Demodex* colonization augmented in nevi can be explained by the possible affinity of the parasite to the melanin pigment.

INTRODUCTION

Melanocytic skin tumors are caused mainly by nevus cells, epidermal melanocytes and dermal melanocytes. The benign melanocytic tumors composed of nevus cells are called melanocytic nevi (Nemlioglu & Or, 1994). While nevi are less in number in the newborn, they increase during childhood and adolescence and show regression after middle-age. The etiological factors in nevus development include genetic heritage, sunlight and UV light, hormones and immunsuppression. Exposure to sunlight in white race increases the number of nevus. This is an indicator of contact with sunlight and increased risk of malignant melanoma (Beral *et al*., 1983; Crickx, 1999; Lock-Andersen *et al*., 1999; Braun-Falco *et al*., 2000; Broberg & Augustsson, 2000).

Benign melanocytic nevi are classified under three main types: junctional nevus, compound nevus, and dermal (intradermal) nevus. Other nevi also included in this group are balloon-cell nevus, halo nevus, spitz nevus, pigmented spindle-cell nevus, congenital melanocytic nevus and dysplastic nevus (Nemlioglu & Or, 1994).

Junctional nevus in which nevus cells are solely located at the bottom of the epidermis are clinically characterized with flat lesions. In compound nevus, the nevus cells exist both in epidermis and dermis. They generally look like a symmetric papule or nodule, 0.5-1 cm in diameter, slightly or markedly swollen, brownish in colour, round or oval in shape. Intradermal type of nevus cells on the other hand are located only in dermis, clinically have lighter colour than other types and are characterized with papule and dome-like nodular lesions (Baykal, 2004).

Melanocytic nevi which exist during birth or appear during the first two years of life are classified as congenital type. In histopathological terms they generally have the characteristics of intradermal or compound nevus (Baykal, 2004).

There are different views regarding the pathology and clinical symptoms caused by the *Demodex folliculorum* and *Demodex brevis* parasites in human (Morsy *et al.*, 2000; Pena & Andrade Filho, 2000; Baima & Sticherling, 2002; Wesołowska *et al.*, 2005). Some researchers have reported that *Demodex* spp. is apathogenetic. There are researches, however, who reported that *D. folliculorum* may have a role in the etiopathogenesis of rosacea, acne vulgaris, blepharitis, perioral dermatitis, pustular folliculitis, papular-pustular lesions on hairy skin, and pustular lesions in acquired immune deficiency syndrome (Forton & Seys, 1993; Roihu & Kariniemi, 1998; Magro & Crowson, 2000; Mathieu & Wilson, 2000; Wesołowska *et al.*, 2005).

It was aimed in this study to detect the presence of *Demodex* spp. in the biopsy specimens of skin diagnosed with nevus.

MATERIALS AND METHODS

Ethical board approval was obtained from Inonu University, Faculty of Medicine. The specimens examined in this study were biopsies of skin diagnosed with nevus which were sent to the Pathology Laboratory in Faculty of Medicine at Inonu University during 2002-2005. This is a retrospective study and the specimens obtained from reported patients were examined for *Demodex*.

The specimens stained using hematoxylin & eosin (H&E) were evaluated for positive *Demodex*. Within this study, 110 skin biopsies were examined for the presence of *Demodex* spp. regardless of the morphological distinction between *D. folliculorum* and *D. brevis*.

Statistical Analysis

The data were presented in terms of mean±standard deviation or number and percentages. Both normality and Shapiro-Wilk testes were conducted on the data. Independent samples t test, Pearson Chi-square and Yates' adjusted Chi-square tests were used for the statistical analyses. Analyses were done with SPSS 13.0 software program, with $p<0.05$ considered as statistically significant.

RESULTS

In the study, 43 (39.1%) out of 110 specimens diagnosed with nevus were detected to be infected with *Demodex* spp. The distribution of the results according to gender variable is shown in Table 1.

In this study no significant association was found between existence of *Demodex* spp. and gender (p=0.23). The distribution about the presence of *Demodex* spp. according to the location of specimen taken for biopsy is shown in Table 2.

An evaluation of the table reveals no significant association between the presence of *Demodex* spp. and the location of biopsy (p=0.76).

The distribution about the presence of *Demodex* spp. according to the types of nevus is shown in Table 3.

An evaluation of the table reveals a significant association between the presence of *Demodex* spp. and the types of nevus (p=0.004). Those diagnosed with dermal nevus in this study were found to have higher rates of parasite.

The distribution about the presence of *Demodex* spp. according to the age variable is shown in Table 4.

An evaluation of the table indicates a significant difference between positive and negative *Demodex* spp. according to age variable (p=0.021).

Table 1. The incidence of *Demodex* spp. according to gender

Gender	*Demodex* spp. Negative Number (%)	*Demodex* spp. Positive Number (%)	Total
Male	18 (51.4)	17 (48.6)	35 (100.0)
Female	49 (65.3)	26 (34.7)	75 (100.0)
Total	67 (60.9)	43 (39.1)	110 (100.0)

Table 2. The presence of *Demodex* spp. according to the location of the specimen taken for biopsy

Location	*Demodex* spp.		Total
	Negative Number (%)	Positive Number (%)	
Forehead	8 (72.7)	3 (27.3)	11 (100.0)
Nose	8 (53.3)	7 (46.7)	15 (100.0)
Chin	3 (75.0)	1 (25.0)	4 (100.0)
Hairy skin	7 (70.0)	3 (30.0)	10 (100.0)
Cheek	41 (58.6)	29 (41.4)	70 (100.0)
Total	67 (60.9)	43 (39.1)	110 (100.0)

Table 3. The presence of *Demodex* spp. according to the types of nevus

Types of nevus	*Demodex* spp.		Total
	Negative Number (%)	Positive Number (%)	
Dermal nevus	47 (54.0)	40 (46.0)	87 (100.0)
Compound nevus	2 (50.0)	2 (50.0)	4 (100.0)
Congenital nevus	18 (94.7)	1 (5.3)	19 (100.0)
Total	67 (60.9)	43 (39.1)	110 (100.0)

Table 4. The presence of *Demodex* spp. according to the age variable

Demodex	N	Mean	Sd	P
Negative	67	30.64	11.664	0.02
Positive	43	36.00	11.719	

DISCUSSION

It has been reported that the immunologic reactions developed against the parasite as a result of the proliferation of *D. folliculorum* due to immunological defects play a role in emergence of skin lesions (Dong & Duncan, 2006). It has also been reported that *D. folliculorum* can be associated with acne rosacea since it inhabits in hair follicles, hair roots and sebaceous glands in various locations including human cheek, chin, forehead, outer ear canal, back, hips, and penis (Morsy *et al.*, 2000; Wesołowska *et al.*, 2005).

There are various studies carried out on the epidemiology and pathogenesis of *D. folliculorum*. *Demodex folliculorum* has been detected in immunocompromised children with acute lymphoblastic leukemia. It was reported that this parasite caused rosacea and perioral dermatitis in these children (Gutierrez, 2000). Though *Demodex* spp. is seen less among children, it was reported to have a more intensive incidence in AIDS and lymphoproliferative disorders (Morras *et al.*, 2003). Similarly, it was reported that the infection can progress severely among patients whose immune systems are suppressed and who use immunosuppressive drugs and among middle-aged and elderly people with poor immunologic reactivity (Patrizi *et al.*, 1997).

In another study on diabetic patients the intensity of the *D. folliculorum* was found to be significantly higher compared to the control group especially in specimens taken from cheek (Akdeniz *et al.*, 2002). Still in another study on 47 patients with chronic renal failure, 12.76% of the patients were found to have the parasite (Ozcelik *et al.*, 2007). Karıncaoglu *et. al.* (2005) found in their research on 67

dialysis patients and 67 healthy people that the former had a parasite intensity of 6.12/cm^2 while the latter had that of 0.31/cm^2.

In another study, specimens taken using skin surface biopsy technique from three different locations on the face (forehead, cheek and chin) of 78 patients with acne were examined for *D. folliculorum* and 12 of them (15.4%) were found positive (Polat *et al*., 2003). In another research looking for the incidence of *D. folliculorum* in the eyelashes of patients diagnosed with blepharitis and healthy people, *D. folliculorum* was detected among a total of 68 subjects (34%), 28 (37.7%) out of 75 patients diagnosed with blepharitis and 40 (32%) out of 125 people in control group. It was reported that the parasite can exist asymptomatically among normal people to a considerable extent as well as among patients with blepharitis (Arici *et al*., 2002). Degerli *et al*. (1998) found *D. folliculorum* among 13 (59%) out of 22 patients diagnosed with acne rosacea aged 14-60. Yereli *et al*. (1997) examined the skin biopsy materials of 36 patients aged 15-75 diagnosed as acne rosacea, and found *D. folliculorum* among 12 (33.3%) of them. A significant association was found between age and *Demodex* spp. positivity in the study. Based on this finding it can be interpreted that as the age increases the positivity of *Demodex* spp. also increases.

Marufi *et al*. (1996) found *D. folliculorum* in the outer ear canal skin of two patients and reported that it is controversial to attribute the pruritus on the outer ear to the presence of *D. folliculorum*.

Tanyuksel *et al*. (1995) found 43 *D. folliculorum* cases in the histopathological examination of the biopsy materials. They reported that 9 of these cases were sebaceous nevus, 12 were folliculate, 7 were basal cell carcinoma and 15 were invasive ductile carcinoma. The fact that *D. folliculorum* was detected in invasive ductile carcinoma, sebaceous nevus and folliculates, it led to the assumption that the parasite can be the possible agent in some of the cases. In the present study 110 biopsy specimens which were diagnosed as nevus were examined and 39.1% of them were found to be *Demodex* spp. positive. The evaluation of the positive specimens revealed no significant association between the presence of *Demodex* spp. and the variables of gender and biopsy location. Based on this finding it can be interpreted that the parasite can settle in any location where it finds convenient habitat in the hair roots, as suggested by the findings of the other researches. It was found that they could be present in any human regardless of gender.

In the present study a significant association was found between the presence of *Demodex* spp. and types of nevus. The patients diagnosed as dermal nevus were detected to have higher rate of parasites. Based on this finding it can be interpreted that the augmented colonization of *Demodex* in nevi can be attributed to possible affinity of the parasite to melanin pigment. Since the biopsy specimens were evaluated retrospectively, the patients couldn't be accessed. Therefore, it was not possible to provide the patients with parasite treatment. The mite intensity per cm^2 was not able to be detected. In conclusion, the parasite is highly seen in patients diagnosed with nevus. Experimental studies with control group are needed. Future researches can analyze comprehensibly the relationship between the presence of *Demodex* spp. and nevus by evaluating, treating and tracing such patients in a collaborative project by the departments of pathology, parasitology, and dermatology.

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