

A clinicopathologic study of precancerous skin lesions

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Background: Precancerous lesions are disorders that are highly likely to become malignant. Early diagnosis of precancerous skin lesions helps to prevent skin cancers. The aim of this study was clinicopathological assessment of precancerous skin lesions in patients referred to the dermatology department of Imam Reza hospital.

Method: Two hundred and nine patients who were diagnosed with precancerous lesions and referred to the dermatology department of Imam Reza hospital from 1997 to 2007 were studied. Study parameters included participants' age, sex and occupation, type of precancerous skin lesion, clinicopathological type of the lesion and location. The data was collected from the patients' records in the dermatology department and their microscopic slides in the pathology department.

Result: The most common precancerous skin lesion was actinic keratosis (68.4%) followed by Bowen's disease (7.2%). About 67.5% of the patients were male with a mean age of 61.7 years. Moreover, 53.1% of the patients worked outdoors. The most common site of the lesions was head and neck (83.3%) and 18.7% of lesions were associated with malignancy. The most common pathological form of actinic keratosis was the proliferative type (28.9%).

Conclusion: The results of this study showed that precancerous skin lesions were more prevalent in men aged over 50 years, in sun-exposed areas and in occupations practiced outdoors. In addition to squamous cell carcinoma, these lesions could also be associated with basal cell carcinoma.

Keywords: actinic keratosis, bowen's disease, clinicopathology, precancerous skin lesions

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INTRODUCTION

Skin cancer is the most common human cancer. One of the useful measures to prevent skin cancer is early diagnosis of precancerous skin lesions. Some non neoplastic lesions such as solar keratosis of the skin are so clearly associated with cancer that are known as precancerous states. Although in the majority of these lesions no malignant neoplasm develops, the increased cancer risk is hereby focused on. Based on classification of William Dubreuilh,

precancerous skin lesions have been described as follows ¹: cutaneous horn, solar keratosis, xeroderma pigmentosum, keratosis in workers in contact with bitumen and paraffin, arsenical keratosis, leukokeratosis of mucous membranes, Darier's disease, Bowen disease, Paget disease and lentigo maligna.

Nowadays, precancerous skin lesions of keratinocyte origin are as follows ²: actinic keratosis, arsenical keratosis, thermal keratosis, hydrocarbon keratosis, keratosis due to chronic radiation, reactive

keratosis, PUVA keratosis, viral keratosis (bowenoid papulosis and epidermodysplasia verruciformis), Bowen's disease, erythroplasia of Queyrat, leukoplakia and erythroplakia. Porokeratosis, lentigo maligna, dysplastic mole, lichen sclerosis of vulva, intraepithelial neoplasia of vulva, Paget disease and Buschke-Lowenstein tumor are among other precancerous lesions of the skin³⁻⁷.

Iranians are at risk for skin cancer due to the geographical situation of the country in a sunny desert area. Therefore, we decided to evaluate precancerous skin lesions in patients who referred to dermatology clinic of Imam Reza hospital from 1997 to 2007 in terms of a clinicopathological review.

PATIENTS AND METHODS

This descriptive retrospective study was performed with the goal of evaluating the clinical and pathological aspects of precancerous skin lesions in patients of the dermatology department of Imam Reza hospital, with a diagnosis of precancerous skin lesions from 1997 to 2007. Referring to the records of the pathology department of Imam Reza hospital, all samples sent from the dermatology department with clinical or histopathological diagnosis of

precancerous skin lesions were retrieved and reviewed by a dermatopathologist. Demographic data of patients such as age, sex, occupation, site of lesion and its clinical morphology were obtained from the medical records and registered in the questionnaires prepared for this purpose. After collecting the data, they were analyzed using SPSS-11.5 statistical software. In all research steps, ethical guidelines and confidentiality of the patient data was observed.

RESULTS

Among 47, 810 biopsy cases, 209 were precancerous skin lesions. The most frequent of which was actinic keratosis with 156 cases (74.6%). The male to female ratio was 2.07: 1 (male=141, female=68). Information on age was available for 206 patients. The patients ranged from 7-107 years in age (mean \pm SD: 61.7 \pm 16.7 years) with 64 cases (31%) belonging to the most common age group of 61-70 years. The patient's occupation was recorded in 162 cases with the most common jobs being farmer and worker, each with 43 cases (26.5%). The occupations were practiced indoors in 76 cases (46.9%) and outdoors in 86 cases (53.1%).

Table 1. Clinicopathological features of precancerous lesions of keratinocyte origin

Characteristics	Precancerous lesions			
	Actinic keratosis	Actinic cheilitis	Bowen disease	leukoplakia
Frequency	156 (74.6%)	14 (6.7%)	15 (7.2%)	1 (0.4%)
Sex				
Male	109 (69.8%)	10 (71.4)	10 (66.7%)	
Female	47 (30.2%)	4 (28.6%)	5 (33.3%)	1 (100%)
M/F	2.3/1	2.5/1	2/1	
Age				
Commonest age group	61-70 y	61-70 y	61-70 y	
Max	107	83	79	19
Min	14	14	17	
X \pm SD	65.5 \pm 12.5	60.7 \pm 10.2	65.1 \pm 15.9	
Job				
The most common	Farmer (31.8%)			
In-door	59 (56.7%)	Worker (38.4%)	Worker (30.7%)	
Out-door	45 (43.3%)			
Location	Head and neck (97.2%)	Nose (27%) Scalp (15.1%) Forehead (9.3%) Cheek (25.8%)	Lower lip (92.8%)	Lower limb (66.7%)
Morphology	Plaque (38.5%)		Ulcer (50%)	Plaque (60%)
Associated malignancy				
Yes	37 (23.7%)	BCC (11.5%) SCC (12.1%)	0	BCC 1 (6.7%)
No	119 (76.2%)		14 (100%)	14 (93.3%)

The most common clinical site of the lesions was the head and neck in 174 cases (83.3%); in the head and neck region, the most common site was the nose in 43 cases (24.7%) followed by the cheek in 40 cases (23%) and the scalp in 27 cases (15.5%). The most common clinical form of the lesions was plaque (70 cases 33.5%). Thirteen cases of actinic keratosis manifested their lesion as cutaneous horn. Among 209 cases, 170 cases (81.3%) had no associated malignancy while 39 cases (18.7%) were associated with malignancy; 20 cases (9.6%) had basal cell carcinoma and 19 cases (9.1%) had squamous cell carcinoma. Clinicopathological features of precancerous skin lesions of keratinocyte origin are shown in table 1 according to lesion type, and other precancerous skin lesions are presented in table 2. Histopathologic types of actinic keratosis and Bowen's disease are shown in table 3.

DISCUSSION

In this study, 209 precancerous skin lesions were evaluated over a 10-year period and it was noted that the most common lesions were actinic keratosis with 156 cases (74.6%) and Bowen's disease with 15 cases (7.2%). Stojanovic et al, studied 411 cases of precancerous skin lesions in more than 10 years study and reported that the most common lesion was actinic keratosis with 335 cases (81.5%)⁸. In terms of gender, our study included 141 (67.5%) men and 68 women (32.5%) with a male to female ratio of approximately 2 to 1 but in the study performed by Stojanovic et al, there were 166 men and 245 women with a male to female ratio of 1 to 1.5. This difference may be due to the more frequent exposure of men to sun than women in Iran. The mean age of our participants

Table 2. Clinicopathological features of other precancerous lesions

Characteristics	Precancerous lesions			
	Epidermodysplasia verruciformis	Porokeratosis	Dysplastic nevus	Lentigo maligna
Frequency	5 (2.4%)	7 (3.3%)	7 (3.3%)	4 (1.9%)
Sex				
Male	1 (20%)	4 (57.1%)	6 (85.7%)	1 (25%)
Female	4 (80%)	3 (42.9%)	1 (14.3%)	3 (75%)
M/F	1/4	1.33/1	6/1	1/3
Age				
Commonest age group	11-20	11-20,41-50	21-30	61-70
Max	27	67	46	71
Min	7	19	11	54
X ± SD	15.8 ± 7.1	38.8 ± 19.5	30.2 ± 11.1	66 ± 0.8
Job	Employee 3 (75%)	Employee 5 (83.3%)	Employee 6 (85.7%) Farmer 1 (14.3%)	Housewife (66.7%)
Location	Trunk 2 (40%)	Upper limb 6 (85.7%)	Upper limb 4 (57.1%)	Head and neck (100%) Cheek (50%)
Morphology	Papule and plaque 4 (40%)	Plaque 6 (85.7%)	Nodule 3 (42.9%)	Patch/macule (100%)
Associated malignancy				
Yes	0	0	0	0
No	5 (100%)	7 (100%)	7 (100%)	4 (100%)

Table 3. Pathologic types of actinic keratosis and Bowen disease

Histopathologic subtypes	lesion	
	Actinic keratosis	Bowen disease
Pigmented	9 (5.76%)	Verruco Hyperkeratotic 1 (6.6%)
Proliferative	50 (32.05%)	
Hyperkeratotic hyperplastic	28 (17.9%)	
Atrophic	24 (15.38%)	Clear cell 1 (6.6%)
Bowenoid	17 (10.9%)	
Clear cell	1 (0.64%)	
Hypertrophic	13 (8.33%)	Psoriasiform 13 (86.6%)
Acantholytic	7 (4.48%)	
Lichenoid	7 (4.48%)	

was 61.7 years with the maximum incidence of lesions in the seventh decade of life. In the study performed by Stojanovic et al, the mean age of the participants was higher (68.4 years) with the maximum incidence of precancerous skin lesions in the eighth decade of life ⁸.

In this study, among 156 cases of actinic keratosis, 109 (69.8%) were male and 47 (30.2%) were female with a male to female ratio of approximately 2.3:1. Actinic keratosis was also more prevalent in men in studies conducted by Naldi et al and McBride et al ^{9,10}, but according to other, actinic keratosis was more frequent in women ^{8,11,12}. The average age of the individuals diagnosed with actinic keratosis was 65.5 years in our study, and actinic keratosis was more common in the seventh decade of life. McBride et al, reported that age was the strongest predictive factor for actinic keratosis, and in their study actinic keratosis was more prevalent in participants above 60 years of age ¹⁰. In our study, associated malignancy was observed in 37 cases (23.7%) of actinic keratosis; 19 cases (12.1%) had squamous cell carcinoma and 18 cases (11.5%) had basal cell carcinoma. Actinic keratosis is regarded a precancerous lesion with the ability to transform to squamous cell carcinoma. In a study conducted by Criscion et al, 65% of squamous cell carcinomas and 36% of basal cell carcinomas originated from lesions initially clinically diagnosed as actinic keratosis. Criscion et al, concluded that actinic keratoses had the capacity of malignant transformation to both types of squamous and basal cell carcinomas ¹³. There are three probable reasons for simultaneous presence of actinic keratosis and basal cell carcinoma. One reason involves the role of ultraviolet radiation as a common factor that can induce actinic keratosis lesions and basal cell carcinoma. Another possible reason is the role of local effects of one of these pathological processes on creating the other one. The third reason could be the presence of pluripotential stem cells in the epidermis capable of differentiation into different directions during malignancy, resulting in both actinic keratosis lesions and basal cell carcinoma. Research has indicated that the proliferative type of actinic keratosis has a high tendency to progress to skin malignancy of both types of squamous and basal cell carcinomas ¹⁴.

In our study, of 15 patients (7.2%) with Bowen's disease, 10 (66.7%) were male and 5 (33.3%) were female with a male to female ratio of 2:1. In the study performed by Stojanovic et al, there were 14 cases (3.4%) of Bowen disease including 11 men and 3 women ⁸. Other studies also demonstrated that Bowen's disease was more common in men as compared to women ¹⁵⁻¹⁷ while Eedy et al and Kovacs et al reported that Bowen's disease was more common in women ^{18,19}. In our study, the average age of those with the diagnosis of Bowen's disease was 65.1 years, and the most common age group was the seventh decade of life with 12 cases (85.7%) over 50 years and 11 cases (78.6%) over 60 years of age. In studies conducted by Rienzer et al, Stojanovic et al and Kovacs et al, the average age was almost the same as ours ^{8,15,18}. In our study, the most common clinical site of the lesions in Bowen disease was the extremities similar to studies conducted by Riezner et al and Hansen et al ^{15,17}. The most common clinical site of the lesion was the trunk in the study conducted by Stojanovic et al and the head and neck in studies performed by Sun et al and Eedy et al ^{8,16,19}. Their studies are different from our study because we reported lesions similar to Bowen's disease in sun exposed areas as actinic keratosis of the Bowenoid type so that 11.1% of our cases of actinic keratosis in the head and neck region were the Bowenoid type. In our study, there was one case (6.7%) of Bowen's disease associated with malignant invasive carcinoma of the keratinocyte type. In a study performed by Cowax et al, eight (10.8%) cases of invasive carcinoma were reported ¹⁸. In our study, out of five cases of epidermodysplasia verruciformis, 1 (20%) was male and four (80%) were female but in a study undertaken by Gul et al, there were 7 patients with a male to female ratio of 4:3 ²⁰. This difference could be due to the limited number of participants in both studies. There was no case of associated malignancy among the 5 cases of epidermodysplasia verruciformis in our study while in the study performed by Gul et al, 6 of 7 cases were associated with squamous cell carcinoma ²⁰.

In our study, one case (0.5%) of leukoplakia was detected in a 19-year-old male worker with a plaque on the tongue that was pathologically reported as a benign lesion. Perhaps scarcity of leukoplakia sample may be due to the fact that the

majority of oral precancerous lesion samples are sent to pathology department of Dentistry College. In the study conducted by Stojanvik et al, there were 3 cases (0.7%) of leukoplakia including one man and two women with an average age of 64.3 years. The clinical site of the lesion was on the lower lip in all cases⁸. Moreover, of the 7 cases of Prokeratosis, 4 (57.1%) were males and 3 (42.9%) were females with a male to female ratio of 1.3:1. In a study performed by Trabelsi et al, 2 patients (33.3%) were male and four (66.6%) were female with a male to female ratio of 1:2²¹. The most common clinical site of the lesion was the upper extremity with six cases (85.7%) and 14.3 percent of the cases were located in the head and neck. In the study by Leow et al, all cases were in sun exposed areas²². In this study, the most common clinical form of the lesion was plaque similar to the report of the Trabelsi et al²¹. All cases of porokeratosis in our study had porokeratosis mibelli. In the Trabelsi study, 50 percent of the cases had porokeratosis mibelli and 50 percent had disseminated superficial actinic porokeratosis²¹. In Leow study, 41.9 percent of the cases had disseminated superficial actinic porokeratosis and 35.5 percent had porokeratosis mibelli²². There was no associated malignancy in porokeratosis cases in this study.

In our study, among the seven cases of dysplastic mole, male to female ratio was 6:1. In a study conducted by Hussein et al, dysplastic mole was also more common in men with a male to female ratio of 2:1²³. In our study, all cases of lentigo maligna had their lesions in the head and neck region. In a study performed by Madan et al, 90.9 percent of the cases of lentigo maligna were located in the head and neck region²⁴. In our study, the most common location in the head and neck was the cheek with two cases (50%), and lower eyelids and nose each comprised 25 percent of the cases. In a study performed by Al-Niaimi, cheeks were the most common site of lesion in 66 percent of the cases followed by the nose with 25 percent²⁵.

Based on our findings, the most common precancerous lesion was actinic keratosis with a frequency of 74.6%. This lesion was associated with keratinocyte malignancy of squamous or basal cell carcinoma in 27.3% of the cases. The most common pathologic type of actinic keratosis in cases with or without associated malignancy was the proliferative type.

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