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Original article

Basal Cell Carcinoma: A Nationwide Clinicopathologic Study in an Israeli Population

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Abstract. *Background:* Basal cell carcinoma (BCC) is the most common malignancy worldwide, and its incidence is continually increasing. BCC occurs mostly on areas of the body subject to chronic sun exposure in older people. *Aim:* To characterize the anatomical distribution and properties of BCC in a nationwide sample in Israel. *Methods:* This retrospective study included histologically confirmed BCC samples obtained from surgeons throughout Israel during the first trimester of 2012. *Results:* A total of 1,716 BCC lesions were diagnosed during the study period. The head and neck had the highest density of BCC (65.9%). The mean lesion horizontal diameter was larger in males than in females (0.91 cm vs. 0.8 cm; P<0.001). The male sex and an older age were risk factors for lesion ulceration. *Conclusions:* According to our population-based study, males of older ages are at increased risk of developing larger and ulcerated BCC lesions. The head and neck are the areas most affected. With increasing age, the frequency of upper limb BCC increases in males and on the lower limbs in females. More frequent evaluations on the groups at risk, such as older males, with an emphasis on high-risk areas of the body are recommended.

Key words: Basal cell carcinoma, skin neoplasms, epidemiology, delivery of healthcare, risk factors

Introduction

Basal cell carcinoma (BCC) accounts for 30% of all human malignancies. It is the most common cancer, accounting for 75% of all non-melanoma skin cancers[1-4], and rates have tripled in the past 30 years[5]. Caucasians are at a greater risk to develop BCC, with a lifetime risk of approximately 30%[1,5,6]. BCC poses a substantial health concern with considerable healthcare burden and costs[1]. It rarely metastasizes or causes death; however, it leads to extensive morbidity, due to the invasion and destruction of local tissue[7-9]. Metastatic dissemination to lymph nodes, lungs, bones and the liver has been described, although it is a rare phenomenon (<0.1%)[10] and its mortality rates are low[9]. BCC mostly occurs on areas of the body which are chronically exposed to the sun, and about 70% of these cases occur on the head and neck areas[1,11-12].

The etiology of BCC is multifactorial. Ultraviolet radiation (UVR), specifically UVB, is a major risk-factor for developing BCC[13,14]. A latency period of 20 to 50 years is typically observed between the UV exposure period, especially during childhood and adolescence and the clinical diagnosis of BCC[13-15]. Therefore, BCC is mostly observed in adults over 50 years of age, with a male-to-female ratio of approximately 2:1[15,16]. This incidence varies geographically; the closer the population is to the equator, the greater the risk of developing skin cancer[3,4,16,17].

Data regarding the horizontal diameters of tumors and the proportions of ulcerated BCC lesions are limited. Ulceration rates of 32.6%–55.3% have been reported

by several studies[18-21] and a significant difference in the horizontal diameter of lesions, between males and females has also been reported[16,20,21].

Despite the high prevalence of BCC, data regarding tumor characteristics in the Israeli population are lacking. This is the first nationwide study intended to characterize the properties, anatomical distribution, and prevalence of BCC in Israel.

Materials and Methods

This retrospective, observational study included all histologically-confirmed BCC samples obtained during the first trimester of 2012. The data were collected from Patho-Lab Diagnostics, Ltd. (Rehovot, Israel), the largest provider of clinical histopathology and cytopathology laboratory services in Israel.

The age parameters were stratified into groups by decades. The different areas of the body were categorized as: head and neck, trunk, upper limbs and lower limbs, genitalia, and other. The tumors' horizontal diameter in centimeters and ulceration were recorded according to the official pathology report.

Ethics approval

The study was approved by the Institutional Review Board and was conducted in accordance with the principles set forth in the Helsinki Declaration of 2008. Informed consent was not required due to the retrospective study design.

Statistical analysis

Patient characteristics and data were recorded on an Excel spreadsheet (Microsoft Corp., Redmond, WA, USA). A descriptive analysis was performed for all study parameters. Spearman's correlation was used to evaluate the relation between sex and anatomical location. Binominal proportion tests were used to compare between the sexes. Descriptive and univariate statistical analyses were performed using SPSS-21 (Statistical Package for the Social Sciences, IBM Corp, Armonk, NY). Two-sided P-values <0.05 were considered significant.

Results

During the study period, 1,716 samples were diagnosed through histopathology as BCC. Out of these, 1,011 (59%) were excised from males and 705 (41%) from females (P<0.001). The mean age ± standard deviation (SD) of the cohort was 70.0 ± 13.0 years, 70.9 ± 16.0 for males and 68.7 ± 21.7 years for females, (P<0.001). Table 1 describes the characteristics of the study cohort.

Anatomical distribution

The absolute tumor distribution was highest on the head and neck, with a total of 1,132 (66%) lesions (65.8% in males vs. 66.2% in females), followed by 280 (16.3%) lesions on the trunk (17.1% in males vs. 15.1% in females). There were 187 (10.9%) upper

Table 1. Study cohort characteristics, lesion location and ulceration rates.

Characteristic	**Males** 1011 (59%)	**Females** 705 (41%)	**Total** N =1716	**P-value**
Mean age, y (SD)	70.9±16	68.7±21.7	70±13	<0.001
Location, n (%)				<0.001
Head and Neck	665 (65.8)	467 (66.2)	1132 (66.0)	
Trunk	173 (17.1)	107 (15.1)	280 (16.3)	
Upper limb	105 (10.3)	82 (11.6)	187 (10.9)	
Lower limb	68 (6.7)	49 (6.9)	117 (6.8)	
Total	1011 (59)	705 (41)	1716 (100)	
Lesion Diameter, cm [range]	0.91 [0.1-3.8]	0.8 [0.1-2.5]	0.86 [0.1-3.8]	<0.001
Ulceration	100 (72)	39 (28)	139 (8.1)	0.011
N, number of cases; y, years; SD, standard deviation				

limb lesions (10.3% in males vs. 11.6% in females), and 117 (6.8%) on the lower limbs (6.7% in males vs. 6.9% in females).

Correlation between body site distribution and age

The highest number of lesions were excised from people in their sixth decade (504 lesions), followed by the seventh (460) and eighth (446). The frequencies of the various lesions were calculated according to age in decades and body site distribution. The correlation analysis between body site distribution and age groups found that with increasing age, the frequency of BCC on the upper limbs increased for the entire cohort (Rs=0.904, P=0.002) and for both males and females (Rs=0.934, P<0.001 and Rs=0.89, P=0.002).

Tumor horizontal diameter – lesion size

The mean horizontal diameter of the lesions for the entire cohort was 0.86 cm (range 0.1–3.8); 0.91 cm (range 0.1–3.8) among males and 0.8 cm (range 0.1–2.5) among females (P<0.001).

Ulceration

Lesion ulceration was present in a total of 139 (8.1%) cases, 100 (72%) males and 39 (28%) females (P=0.011). The distribution of age-specific lesion ulcerations is illustrated in Figure 1. The correlation analysis between lesion ulceration and age groups by decades, showed a positive trend with increasing age (Rs=0.9, P<0.001). The risk of developing an ulcerated lesion was 1.78 times greater among males than females (RR 1.78, 95%CI 1.25–2.55, P=0.0014). No significant differences were found between lesion ulceration and anatomical distribution.

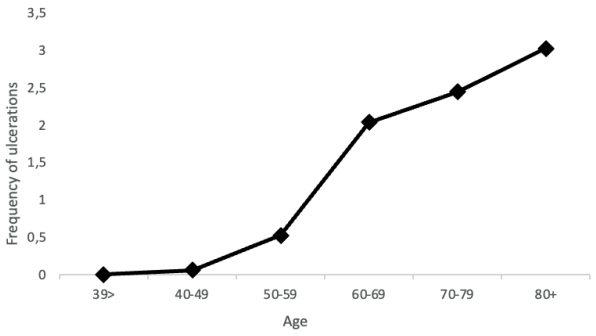

Figure 1. Frequency of basal cell carcinoma ulceration by age in the entire cohort.

Discussion

This is the first nationwide study conducted in Israel to characterize the properties and anatomical distribution of BCC in its population. Traditionally, BCC was diagnosed more often amongst older patients, usually males, and presented mostly on the areas of the body which are chronically exposed to the sun, such as the head and neck. These patient characteristics reflect the effects of accumulating UVR damage and age-related changes in one's immune function, with a latency period of 20–50 years[1,11,13,17,22]. Accordingly, our findings demonstrate that older age, the male sex, and the head and neck are significant risk-factors for developing BCC. Most of the BCC lesions (66%) in our cohort occurred in the head and neck area. Nevertheless, this is lower than the 70% rate described by Nguyen and Ho[1] and the 91% noted by Tiftikcioglu et al.[23]. These statistical differences might be explained by the different geographic and ethnic characteristics and patterns of dress in Israel. Israel lies north of the equator and has a Mediterranean climate, with a long, hot, dry summer. Consequently, clothing is less concealing than in European climates; hence, increased UV exposure leads to a higher incidence of lesions in other body areas, such as the trunk and limbs. Studies have suggested that lesions on different body sites may predict their clinical behavior and that their etiologies may differ[21,24-26].

Anatomic distribution according to an analysis based on sex revealed higher rates of lesions on the upper limbs among the entire cohort for both males and females. This rise in frequency of lesions on the upper limbs with increasing age might be explained by various molecular and genetic factors of these subsets of lesions that have yet to be described.

The upper limbs showed a positive trend for the number of lesions with increasing age among males and females. This trend is in accordance with the theory of cumulative UVR damage and latency. The neg-

ative trend for the trunk area is in contrast with this theory yet is compatible with the notion that truncal BCC is a subset of lesions associated with distinct exposure patterns and susceptibility genes[26].

The average horizontal diameter of the lesions was larger in males (0.91 cm) compared to females (0.80 cm), and older males were found to have slightly more than 1.5 times the risk of developing an ulcerated lesion. Sex differences influencing the presentation of BCC lesions at diagnosis might be attributed to behavioral factors, similar to differences found among melanoma patients[27]. Some studies on melanoma suggest that women have higher levels of medical awareness: as they evaluate themselves more often and seek medical attention earlier, whereas men tend to ignore or delay the changes they notice in their skin[27-29]. We can infer a similar situation when it comes to the diagnosis of BCC: men delay medical check-ups and inspect themselves less often, which in turn results in lesions that are larger and more ulcerated upon presentation and diagnosis. Further research should be conducted regarding the etiology of differences between the sexes.

Israel has a Mediterranean climate along with a diverse population and as such, many of the results described here may apply to the inhabitants of other Mediterranean countries.

Limitations of this study are related to its retrospective nature, although missing data were minimal. Data were collected from the largest provider of pathology services in Israel and may not include ethnicities with limited representation in the study population (Hispanic, African-American and Asian). An advantage of this study is that all lesion diagnostics and characteristics are based on histopathological reports.

To our knowledge, this is the first analysis performed that describes the relationship between anatomic distribution of BCC according to age groups and sex in a large, population-based study.

Conclusions

According to this population-based study, older males are at increased risk of developing larger and ulcerated BCC lesions. The head and neck areas are the most affected. With increasing age, the frequency of BCC in the upper limbs increases in males, and in the lower limbs in females.

The increased frequency of evaluations of at-risk groups, such as older males, with an emphasis on high-risk areas of the body, is recommended.

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Author Contributions
Avshalom Shalom, Ariel Berl, Ofir Shir-az: study conception and design: Ariel Berl, Ofir Shir-az: Data curation and analysis: Ariel Berl, Ofir Shir-az: Writing original draft. Avshalom Shalom, Ariel Berl, Ofir Shir-az, Manar Kawar, Gilad Winder: Writing – review & editing. All authors read and approved the final manuscript.

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