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STUDY OF THE GRAVITY PROFILE OF BASAL CELL CARCINOMA CASES IN A TERTIARY REFERRAL CENTER

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Basal cell carcinoma (BCC) is the most common skin malignancy and its incidence is increasing worldwide. It rarely metastasizes, but can lead to significant morbidity due to its local invasion and tissue destruction. The objective of this study was to assess the clinical and histopathological characteristics of BCCs diagnosed in a Dermatology center during January 2011 - December 2014. Based on the medical records of patients diagnosed with BCC, we assessed variables like age, sex, anatomic location, clinical subtype and histologic features. 381 patients were diagnosed with BCC in our clinic during the mentioned time period. The mean age at diagnosis was 68.20 ± 13.01 years. Gender ratio was 1.12. The head and neck area was the most common anatomic location. The diameter of the tumors ranged from 0.2 to 5.5 cm (mean diameter 1.42 ± 0.86 cm). Nodulo-ulcerative BCC was the most frequent subtype in our patients (75.6%), followed by the superficial subtype (16.8%) and morfeiform subtype (7.06%). 82.3% of BCC extended into the deep dermis, 16.9% into the hypodermis, and 10% of BCC invaded the subjacent musculature. Patients often present with BCC in late stages, characterized by large tumor diameter and deep invasion.

Key words: basal cell carcinoma, histopathology, late diagnosis

INTRODUCTION

Basal cell carcinoma (BCC) is a nonmelanocytic cutaneous neoplasm arising from the epidermal basal layer or from the basal cells of follicular structures. It is the most common malignancy in the Caucasian population, accounting for 65–75% of all skin cancers[1]. Its incidence is rising worldwide[2,3]. BCC usually occurs after the age of 50[4-6] on sun exposed areas, 80% of cases involving the head and neck area [(1,6-9)]. Although sun exposure is the most important risk factor for the development of BCC[1,4-6,10], other predisposing factors such as fair skin, a series of genetic disorders (albinism, xeroderma pigmentosum, Gorlin syndrome, basal cell nevus syndrome, Rombo syndrome, Bazex syndrome, nevus sebaceous, epidermodysplasia verruciformis), arsenic, X-ray and Grenz ray exposure and immunosuppression also predispose to its occurence[11].
BCC is a low-grade malignancy with a slow growing rate, extremely low metastatic potential and a low mortality rate[1,5]. Nevertheless, it can cause significant morbidity due to its potential for local invasion and tissue destruction. Tumors arising in the proximity of or infiltrating vital structures (brain, eyes, nose, ear, lips) are often difficult to treat without considerable morbidity and can lead to disfigurement, disability and may become locally advanced or metastasize[12]. Moreover, recurrences are frequent (reported 5-year recurrence rates are 2–3 %[13] and can pose treatment problems[14]. In addition, patients diagnosed with BCC are at significantly increased risk for the development of both new BCC (the 5-year cumulative risk was estimated at 41-45%, compared to the risk of 5% in the general Caucasian population)[15,16] and melanoma (relative risk of 17% compared to the general Caucasian population) [(17)]. Therefore, despite their favorable prognosis, BCCs represent an expensive and serious public health issue. As early detection and treatment are essential for the reduction of morbidity and costs[5,18,19], education on BCC epidemiological and clinical characteristics is of major importance.
Generally, official cancer registries do not include data on BCCs or only collect data on histologically confirmed tumors, not taking into account clinically diagnosed BCCs. Thus, the true prevalence and incidence of this cutaneous neoplasm is difficult to estimate[20]. Since existing data on BCC in Romania is scant, the aim of this study was to assess the clinical and histopathological characteristics of BCCs, as well as the severity profile of BCCs diagnosed in a tertiary referral Dermatology center in Bucharest between January 2011 and December 2014

and to identify the profile of severity of the disease in our patient population.

MATERIAL AND METHODS

We performed a retrospective study in the Dermatology Department of Elias Emergency University Hospital, in Bucharest. The medical records of patients with histologically confirmed BCCs admitted to our clinic between January 2011 and December 2014 were examined. Variables like age, sex, anatomic location, clinical subtype and histopathologic features were assessed, as well as information on size, treatment modalities and recurrences.

Statistical analyses was performed using SPSS V17, STATA V10. The relation between the presence of BCC and continuous variables was analyzed using Student t-test, while the relation with categorial variables was assessed by Fisher exact test. Two-sided *P* values less than 0.05 were considered statistically significant.

RESULTS AND DISCUSSIONS

A total of 381 patients were diagnosed with BCC and treated in our clinic during the mentioned time period, representing 4.8% of all hospitalized patients and 71.08% of all patients diagnosed with skin cancer in our department. Of these 381 patients, 202 were men (53%) and 179 were women (47%). The gender ratio (M/F) was 1.12.

The age at the time of diagnosis varied between 30 and 95 years. The mean age was 68.20 ± 13.01 years. The mean age at diagnosis did not differ significantly between men (69.17± 13 years) and women (67.11± 13 years) diagnosed with BCC (data analyzed using *t*-test, p= 0.1235). Regarding the age range distribution of BCCs, the highest frequency was observed among patients aged 70-79 (30%). No case was diagnosed under the age of 30 (Figure 1). When analyzing the age distribution of BCCs according to gender, we noted that men developed BCC most frequently during the seventh decade of life (27.5%), while for women the highest frequency was among 70-79 years olds (34.7%) (Figure1).

The head and neck area was the most common anatomic location (71% of cases), followed by the trunk (20% of cases), lower limbs (5% of cases) and upper limbs (4% of cases). No significant difference was observed between male and female patients regarding the distribution of BCCs based on their anatomic location. The head and neck area was by far the most frequent location in all age groups, except for the 40-49 years age group, in which most of the tumors were located on the trunk.

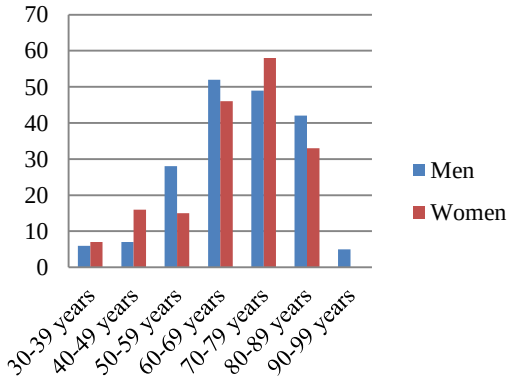

Figure 1. Age distribution of BCCs according to gender

The diameter of the tumors ranged from 0.2 to 5.5 cm, the mean diameter being 1.42 ± 0.86 cm (Figure 2). The mean size of BCCs occurring in women was 1.35 ± 0.78 cm, while the mean diameter of BCCs in male patients was 1.48 ± 0.91cm, showing no significant difference between male and female groups (data analyzed by *t*-Test, p= 0.1396).

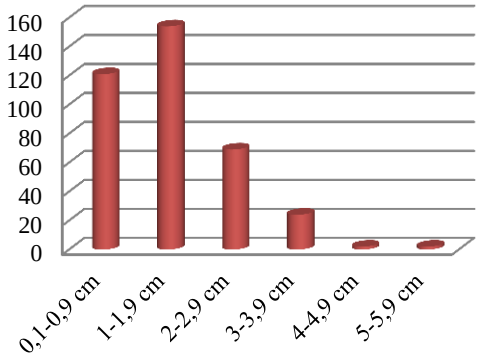

Figure 2. Distribution of BCCs based on tumor diameter

Nodulo-ulcerative BCC was the most frequent subtype in our patients (75.6%), followed by the superficial subtype (16.8%) and the morpheaform subtype (7.06%). In the 30-39 years and 40-49 years age groups the nodulo-ulcerative and superficial subtypes of BCC appeared with similar frequency (60% vs. 40%, 52% vs.48% respectively) and no morpheaform or infiltrative BCC were registered. With older age, the nodulo-ulcerative subtype presented with a significantly higher frequency compared to the superficial and the morpheaform subtypes (Figure 3).

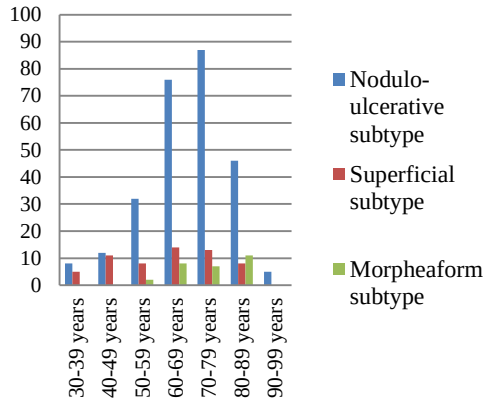

Figure 3. Age distribution of the histopathologic subtypes of BCC

The distribution of the histopathologic subtypes of BCCs according to the anatomic location did not differ significantly between male and female patients.

The histopathologic examination showed that 82.3% of BCCs extended into the deep dermis, 16.9% into the hypodermis, and 10% of BCCs invaded the subjacent musculature. Perineural invasion was uncommon and was identified in 1.83% of cases. Invasion of the hypodermis and musculature varied between age groups and according to gender. The majority of invasive BCCs were observed after the age of 60 as illustrated in Figure 4.

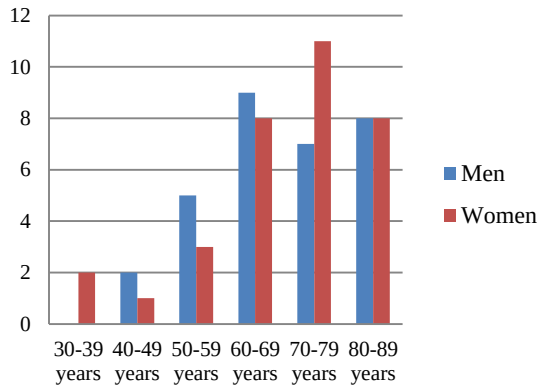

Figure 4. Invasion of the hypodermis and musculature according to age and gender

The mean tumor diameter of BCCs invasive in the hypodermis or deeper structures was significantly larger than that of tumors limited to the dermis (1.77 ± 0.95 cm vs. 1.28 ± 0.77 cm) (data analyzed using t-test, $p<0.0001$).

Consistent with the available literature data, BCC represented the most common type of skin cancer diagnosed in our department during the mentioned time period, accounting for approximately 70% of all cutaneous malignancies.

In our study, we observed a slight male predominance, the gender ratio (M/F) being 1.12. A series of previous studies reported higher frequencies of BCC in men compared to women and attributed this gender predilection to greater occupational and recreational exposure to ultraviolet radiation[5,21-25]. On the other hand, Flohil et al.[26], Custódio et al.[1], Omari et al.[27], and Bariani et al.[28] reported more cases of BCCs in female patients than in male patients. Nowadays, in many societies, women and men have equal job opportunities, which partly explains the increase in the frequency of BCC among women. Moreover, apart from ultraviolet radiation exposure, other risk factors such as genetic factors, fair complexion, exposure to chemicals, ionizing radiation, immunosuppression, chronic irritation, chronic inflammation play important roles in the development of this type of skin cancer[5].

Although it can occur at any age, BCC usually affects the elderly, the majority of cases appearing after the age of 50[4-6]. This is mostly due to the cumulative effects of sun exposure which lead to DNA damage [5,29] and to the reduced immune surveillance and DNA regeneration capacity with older age[28].

The occurrence of BCC in children and adolescents is rare and is generally associated with genetic disorders such as albinism, xeroderma pigmentosum, Gorlin syndrome, basal cell nevus syndrome, Rombo syndrome, Bazex syndrome, nevus sebaceous, epidermodysplasia verruciformis or radiotherapy. In our study, no case was diagnosed under the age of 30. Compared to the findings of other studies[1,5,19,30,31] the mean age at diagnosis was higher (68.20 ± 13.01 years), the highest frequency being observed among patients aged 70-79 (30%). Although not statistically significant, the mean age at diagnosis was higher in men (69.17± 13 years) compared to women (67.11± 13 years).

Sun exposed areas are most frequently affected by skin cancer[1]. Closely resembling the results of other studies [1,5,28], the head and neck area was the most common anatomic location in our patients (71% of cases), followed by the trunk (20% of cases), lower limbs (5% of cases) and upper limbs (4% of cases). The distribution of BCCs according to their anatomic location was similar in both sexes.

The diameter of the tumors ranged from 0.2 to 5.5 cm, the mean diameter being larger in men (1.48 ± 0.91cm) compared to women (1.35 ± 0.78 cm). This difference might be explained by women's increased attention to skin problems, particularly in the head and neck region, seeking medical advice sooner than men.

The histopathologic characterization of BCCs is crucial for establishing prognosis and treatment planning. As

expected, the nodulo-ulcerative BCC was the most frequent subtype in our patients (75.6%), followed by the superficial subtype (16.8%) and the morpheaform subtype (7.06%). Morpheaform and infiltrative BCCs were only seen in older patients. The frequency of the histopathologic subtypes of BCCs did not differ significantly between male and female patients.

Regarding the invasive potential of BCCs, most of the tumors in our study (82.3%) extended into the deep dermis, while 16.9% extended into the hypodermis, and 10% of BCCs invaded the subjacent musculature. Perineural invasion was only observed in 1.83% of cases. The majority of invasive BCCs occurred in patients older than 60. No metastatic BCC was diagnosed in the mentioned time period in our department.

Of note, BCCs invasive into the hypodermis or deeper structures were significantly larger than tumors limited to the dermis (1.77 ± 0.95 cm vs. 1.28 ± 0.77 cm). This is an important finding considering that the size of the tumor represents a risk factor for metastasis occurrence. The incidence of metastatic BCC was reported to be 0.0028–0.5%[32]. Nevertheless, the probability of metastasis increases with tumor diameter, being estimated at 1-2% for tumors larger than 3cm, 20-25% for BCCs larger than 5cm, and more than 50% for tumors larger than 10cm[5]. Other risk factors for metastasization are involvement of the head and neck area, long duration of the disease, multiple primary BCCs and recurrences, prior radiation therapy, increased tumor depth, perineural and blood vessels invasion, fair skin, male gender, and immunosuppression[33].

Therefore, although the majority of BCCs are slow-growing, nonaggressive tumors, they can become, if left untreated, locally distructive and can metastasize, leading to significant morbidity and mortality.

CONCLUSIONS

Although BCCs are more common in elderly individuals, they are becoming increasingly frequent in people younger than 50 years of age and tend to affect women as frequently as men. BCC usually develops on sun-exposed skin, but the incidence of tumors occurring on the trunk is increasing. Patients often present with BCC in late stages, characterized by large tumor diameter and deep invasion, features which are associated with therapeutic difficulties, higher recurrence rates and greater metastatic potential.

Screening for skin cancer at national level, improving public awareness on cutaneous malignancies and implementing efficient strategies for the prevention and early diagnosis and treatment are urgently needed in order to decrease morbidity and costs.

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