ACTA MEDICA LITUANICA. 2018. Vol. 25. No. 4. P. 197–205

Trends of basal cell carcinoma at the Centre of Dermatovenereology of Vilnius University

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Introduction and objectives. Basal cell carcinoma is the most common locally invasive malignant epidermal neoplasm in humans and its incidence has increased over the last decades worldwide, especially among the Caucasian population. Basal cell carcinoma accounts for about 75% of all skin cancers. Incidence data on basal cell carcinoma is sparse because traditional cancer registries often do not register these tumours. In Lithuania, patients with skin cancer and melanoma were traditionally treated in centralized oncological institutes. From 2006, the Centre of Dermatovenereology at Vilnius University Hospital Santaros Klinikos (Vilnius, Lithuania) provides modern diagnostic and treatment facilities to oncodermatological patients. The objective of the study was to evaluate epidemiological and clinical data of basal cell carcinoma at the Centre of Dermatovenereology during the last 15 years.

Materials and methods. Medical documentation of the cases of histologically-proven basal cell carcinoma diagnosed between 2000 and 2015 was analyzed. Epidemiological and clinical evaluation according to the patients' age, sex, and place of residence, as well as tumour localization, its histological type, and treatment options was performed.

Results. After the skin lesion biopsy and histopathological examination, a total of 847 basal cell carcinomas were confirmed to 782 patients. During the study period, the total annual number of newly diagnosed basal cell carcinomas rose steadily in our centre: 2.7% between 2000 and 2003, 6.5% between 2004 and 2006, 13.6% between 2007 and 2009, 27.6% between 2010 and 2012, and 49.6% between 2013 and 2015. The biggest part of patients (28.4%) were 70–79 years old, 4.6% – younger than 40, 7.3% – 40–49, 17.1% – 50–59, 27.2% – 60–69, 14.1% – 80–89, and 1.3% ≥90 years old. The average patient age was 66.0 (±13.6). Of these patients, 62.0% were female and 38.0% male; 63.6% were from the capital city, 18.3% from other cities, and 18.2% from rural areas. Basal cell carcinomas occurred most often in the face region 49.0%, followed by the trunk – 29.4%, the scalp and neck – 10.9%, arms and legs – 7.7%, in 2.9% location was not specified and the whole body – 0.1%. The predominant histological type of basal cell carcinomas was nodular (60.6%), other diagnosed types were superficial (22.9%), infiltrative/morpheaform (8.0%), mixed nodular and infiltrative (1.7%),

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pigmented (0.2%), rare types (micronodular, infundibulocystic, ductal and mixed) – 0.6%; the type was not specified in 6.0% of cases. Nodular, superficial, and infiltrative types were the most common morphological types in all body sites: respectively, in the face – 67.5%, 12.5%, 9.4%; in the scalp and neck region – 77.2%, 14.1%, 5.4%; in the trunk – 49.8%, 37.3%, 7.2%; in extremities – 41.5%, 43.1%, 7.7%. The nodular type was more common among the elderly and its incidence increased with age ($p = 0.009$), meanwhile, superficial basal cell carcinomas prevailed among younger patients (<40 years), and its incidence decreased with age ($p < 0.001$). Also, the nodular type was usually found in the areas of the face ($p < 0.001$) and the scalp and neck ($p = 0.045$), and the superficial type – in the areas of the trunk ($p < 0.001$) and extremities, specifically in the hand ($p = 0.022$). Basal cell carcinomas were mostly treated with surgical excision (79.6%), photodynamic therapy (5.5%; in our centre, this treatment option is available from 2007), and other/combined methods (14.9%).

Conclusions. The results showed that the number of newly diagnosed basal cell carcinomas increased continuously between 2000 and 2015. Basal cell carcinomas in our centre occurred most often among the patients aged 70–79 years. This tumour was more often diagnosed in female than male patients. Most of basal cell carcinomas were located on the chronically sun-exposed skin, such as the face region, and were of the nodular histological type, which is more common among the elderly, while the superficial type is more prevalent among younger patients. The most commonly used treatment option for basal cell carcinoma was surgical excision. Acknowledgment of the tendency of the rising number of basal cell carcinomas, healthcare resources, highlights the need for an effective skin cancer prevention strategy in Lithuania.

Keywords: skin, cancer, basal, cell, carcinoma, epidermal, neoplasm, oncodermatology, histopathology, epidemiology, Lithuania

INTRODUCTION AND OBJECTIVES

Basal cell carcinoma (BCC) is a locally invasive, slowly growing, and rarely metastasizing predominant form of skin cancer that accounts for nearly 25% of all malignancies and for about 75% of all skin cancers (1). The incidence of BCC alone is increasing by 10% per year worldwide, especially among the light-skinned population, suggesting that the prevalence of this tumour will soon equal that of all other cancers combined (2, 3). The average lifetime risk for Caucasians to develop BCC is approximately 30% (4).

Similar to other skin malignancies, ultraviolet radiation is thought to be the most important risk factor for the development of sporadic BCC (5). The other reasons for BCC incidence growth include the aging population, environmental changes,

migration patterns and increased prevalence of immunosuppressant use (6, 7). Moreover, a variety of hereditary syndromes can also result in an increased risk of developing BCC tumours, including nevoid BCC syndrome, Oley syndrome, Bazex–Dupre–Christol syndrome, Rombo syndrome, and xeroderma pigmentosum (8).

Based on the growing incidence of this usually non-life-threatening tumour, BCC appears to develop into an increasingly important public health problem. Incidence data on BCC is sparse because often traditional cancer registries do not register these tumours. Little was known about the trends of BCC in the Baltic countries until the recent study on BCC epidemiology in Lithuania, which showed that overall BCC incidence rates increased, the majority of BCC cases were reported in the urban population, the incidence of BCC among both sexes became almost equal in 2010, and the areas of chronic sun exposure – the head and the neck – were the most common sites of BCC for men and women (9).

Traditionally, patients with skin cancer and melanoma in Lithuania were treated in centralized oncological institutes. Since 2006, the Centre of Dermatovenereology at Vilnius University Hospital Santaros Klinikos (Vilnius, Lithuania) has been providing modern diagnostic and treatment facilities to oncodermatological patients.

The aim of this study was to evaluate epidemiological and clinical data of BCC at the Centre of Dermatovenereology during the last 15 years.

MATERIALS AND METHODS

A descriptive, cross-sectional, retrospective study was performed at the Centre of Dermatovenereology of Vilnius University Hospital Santaros Klinikos (Vilnius, Lithuania), which provides secondary and tertiary medical care levels for the residents of the city of Vilnius, Vilnius district, and people from all over Lithuania. The data were obtained from medical reports of histopathological examinations of patients with a confirmed diagnosis of BCC seen at the Dermatology Outpatient Clinic from 1 January 2000 to 31 December 2015. The material for histopathological examination was obtained through biopsy or total surgical excision of the suspicious skin lesion performed by the dermatologists of Santaros Klinikos. According to the International Classification of Diseases, BCC diagnoses were coded ICD-10 and defined as ICD-10 diagnosis C44. The histological type was obtained from anatomopathology reports issued by the National Centre of Pathology, which performs pathology tests both for major university hospitals and many other medical institutions in Vilnius and other countries and has more than ten years' experience of the College of American Pathologists Laboratory Accreditation.

Variables introduced in the current study were patient's sex, age at the date of diagnosis, place of residence (the capital city, other cities, rural areas), anatomical localization of BCC (face, scalp and neck, trunk, upper limbs, lower limbs, and unspecified), histological type (nodular, superficial, infiltrative, pigmented and unspecified), and treatment performed (surgical excision, photodynamic therapy, and other). The total number of BCC, rates for men and women were calculated separately. Numbers of BCC cases were subdivided by age into seven groups: five 10-year age groups (40–49, 50–59, 60–69, 70–79, and 80–89), the group of patients 40 years old or younger, and the group of patients 90 years old or older. The annual number of newly diagnosed BCC was calculated for 4-year moving means (2000–2003, 2004–2006, 2007–2009, 2010–2012, 2013–2015). Anonymity of the participants was maintained. The approval of the ethics committee was not required due to the observational design of the present study.

RESULTS

After the skin lesion biopsy and histopathological examination, a total number of 847 BCCs were newly diagnosed to 782 patients at the Centre of Dermatovenereology of Vilnius University Hospital Santaros Klinikos between 1 January 2000 and 31 December 2015. The number of patients with multiple (more than one) BCCs was 6.0% (n = 51), 58.8% (n = 30) of them were women, and 41.2% (n = 21) men. During the study period, the total annual number of newly diagnosed BCCs rose steadily: 2.7% (n = 23) between 2000 and 2003, 6.5% (n = 55) between 2004 and 2006, 13.6% (n = 115) between 2007 and 2009, 27.6% (n = 234) between 2010 and 2012, and 49.6% (n = 420) between 2013 and 2015 (Fig. 1).

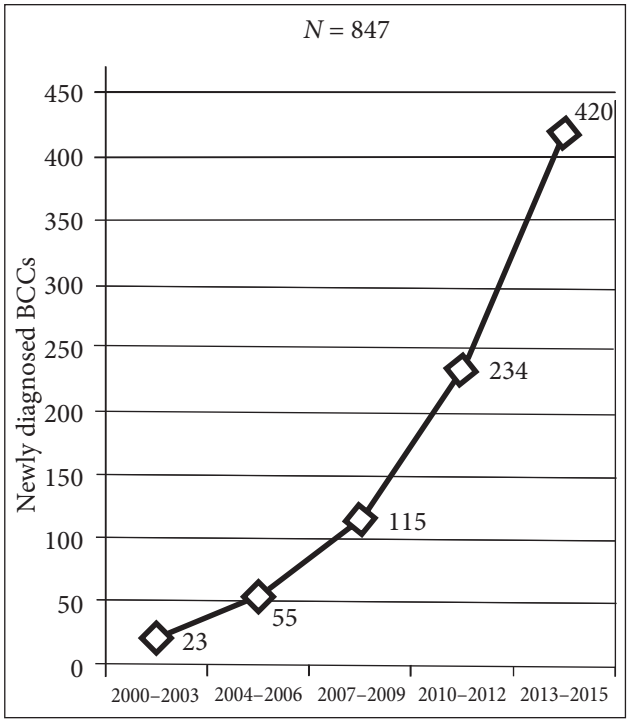

Fig. 1. Yearly distribution of newly diagnosed BCCs

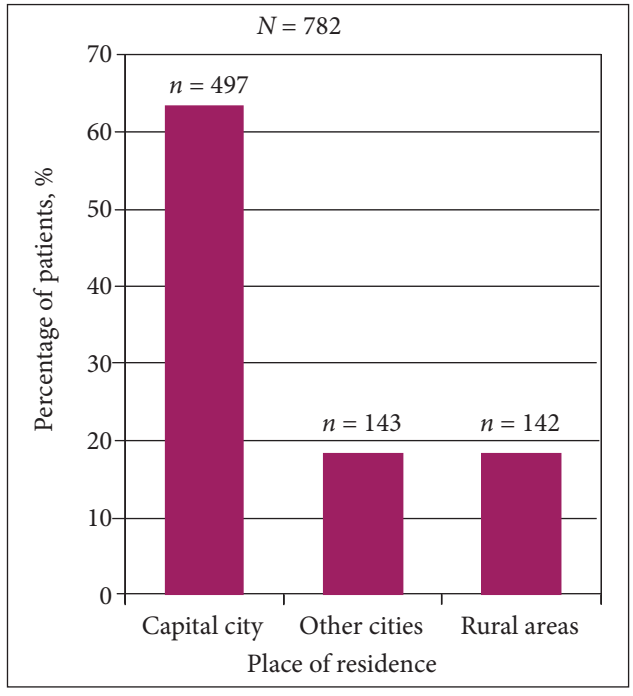

Fig. 2. Distribution of patients with BCC by place of residence, 2000–2015

Of these cases, 38.0% (n = 297) were men and 62.0% (n = 485) women. The age of the patients at the date of diagnosis ranged between 23 and 96 years, the mean age at which BCC was discovered was 66.0 (±13.6). An even distribution of the mean age among both women and men was observed, 65.5 years and 66.8 years, respectively. The biggest part of patients (28.4%) were 70–79 years old, 4.6% ≤ 40, 7.3% – 40–49, 17.1% – 50–59, 27.2% – 60–69, 14.1% – 80–89, and 1.3% ≥ 90 years old (Fig. 2).

More than half of the patients (63.6%) were from the capital city, 18.3% from other cities, and 18.2% from rural areas (Fig. 3).

BCCs most often occurred in the face region 49.0%, followed by the trunk – 29.4%, the scalp and neck – 10.9%, arms and legs – 7.7%. Location was not specified in 2.9% of the cases, whole body was affected in one case of Gorlin-Goltz syndrome – 0.1%.

The predominant histological type of BCCs was nodular – 60.6%. Other morphological types were superficial 22.9%, infiltrative/morpheaform – 8.0%, mixed nodular and infiltrative – 1.7%, pigmented – 0.2%, rare types (micronodular, infundibulocystic, ductal and mixed) – 0.6%, and the type was not specified in 6.0% of cases (Fig. 4).

Nodular, superficial, and infiltrative/morpheaform types were the most common morphological

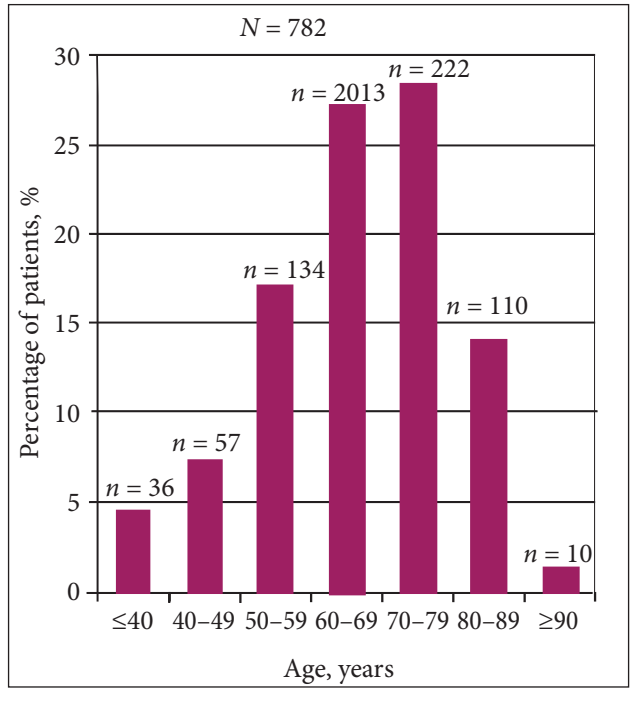

Fig. 3. Distribution of patients with BCC by age

types in all body sites: respectively, in the face – 67.5%, 12.5%, 9.4%, in the scalp and neck region – 77.2%, 14.1%, 5.4%, in the trunk – 49.8%, 37.3%, 7.2%, and in extremities – 41.5%, 43.1%, 7.7% (Fig. 4).

The relation between the histological type of BCC and patients' age was evident. The nodular type was more common among the elderly

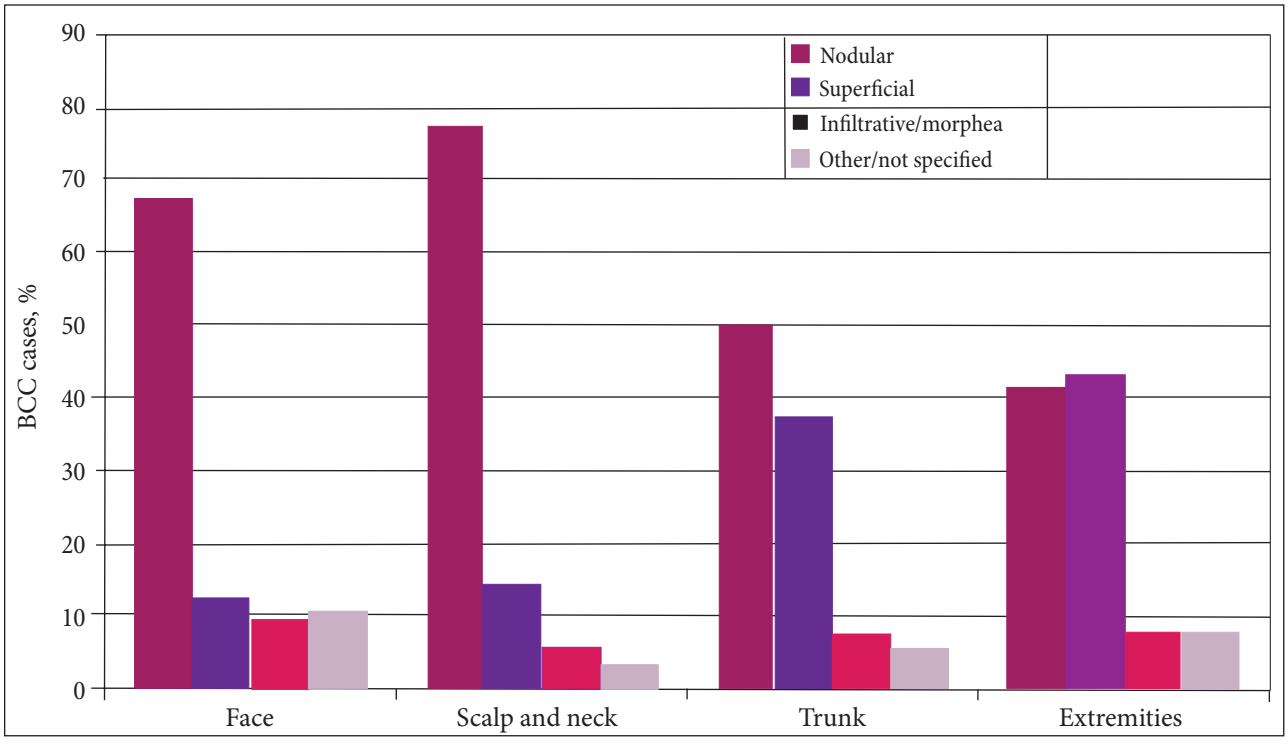

Fig. 4. Morphological types of BCC by localization

and its incidence increased with age ($p = 0.009$); meanwhile, the superficial BCCs prevailed among younger patients (<40 years) and its incidence decreased with age ($p < 0.001$).

Some significant correlations among the histological type of BCC and its localization in the body were observed in this study: the nodular type was usually found in the areas of the face ($p < 0.001$) and of the scalp and neck ($p = 0.045$); superficial type in the areas of trunk ($p < 0.001$) and extremities, specifically in the hand ($p = 0.022$).

The vast majority of BCCs – 79.6% – were treated surgically, 5.5% with photodynamic therapy, and 14.9% with other/combined methods (Fig. 5). Additional treatment options included such methods as electrodessication and curettage, cryotherapy (liquid nitrogen), topical imiquimod, and CO_2 laser therapy.

Before 2009, the majority of patients diagnosed with nodular BCC were referred to the Lithuanian Oncological Centre (the present National Cancer Institute) for surgical treatment. At the end of 2009, the operating theatre was established at the Day Care Unit of the Centre of Dermatovenereology and surgical treatment was performed in this unit. At the Centre of Dermatovenereology,

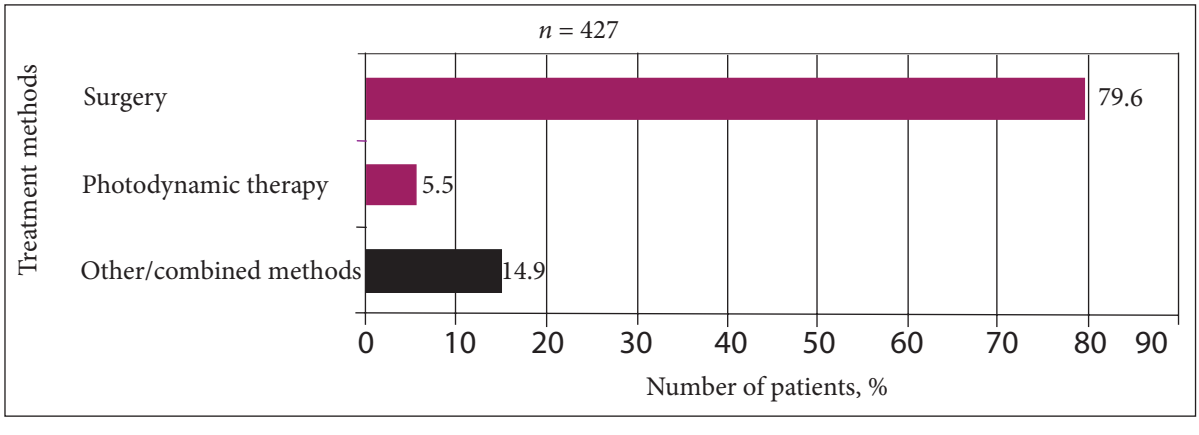

Fig. 5. Treatment of BCC, 2000–2015

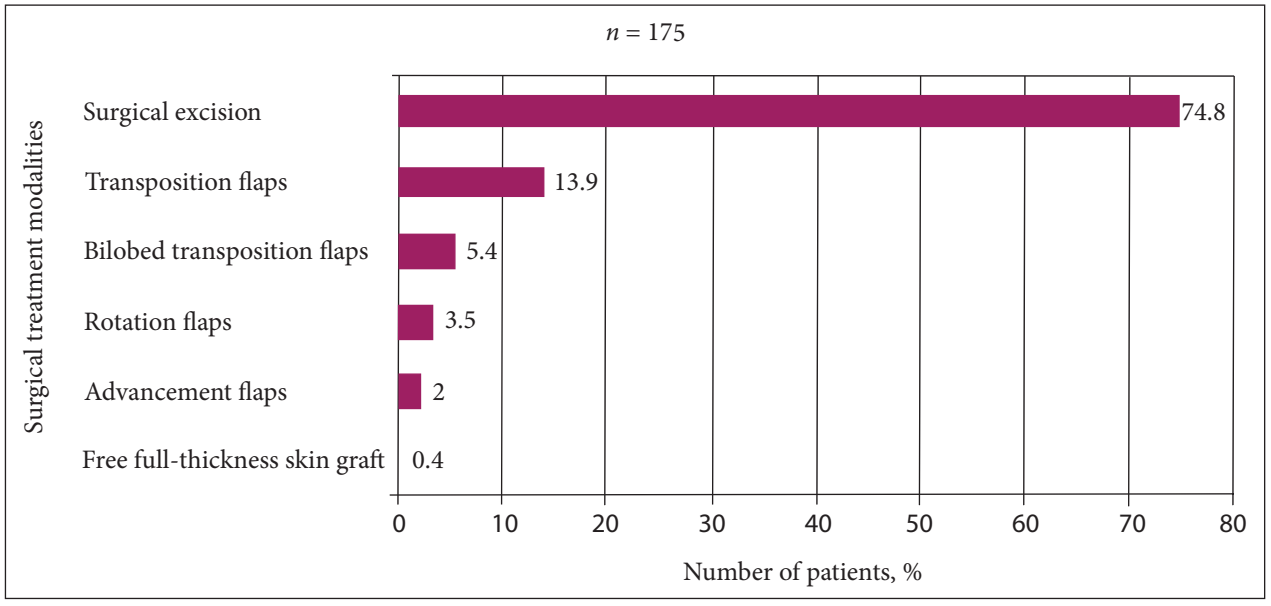

Fig. 6. Surgical treatment modalities of BCC, 2009–2012

photodynamic therapy has been available since 2007. From October 2009, 460 BCCs were treated surgically at the Day Care Unit. Of these, 255 BCCs (55.4%) involved the head and neck region and the remaining 205 (44.6%) were located in other anatomic regions. Primary surgical excision, which is a highly effective and historically the most common treatment option for primary BCC, was performed in 344 cases (74.8%). In addition to surgical excision, other surgical reconstruction modalities based on local flaps were applied: 64 transposition flaps (13.9%), 25 bilobed transposition flaps (5.4%), 16 rotation flaps (3.5%), nine advancement flaps (2.0%), and two free full-thickness skin grafts (0.4%) (Fig. 6).

DISCUSSION

BCC is the most common type of skin cancer among white individuals (4).Worldwide, the incidence of BCC varies widely, with the highest rates in Australia (>800 per 100 000 person years for BCC) and the lowest rates in parts of Africa (<1 per 100 000 person years for BCC) (10, 23). It is very uncommon in black and other dark-skinned populations. In the United States, the incidence of BCC has been rising by more than 10% annually, and the lifetime risk of developing a BCC is 30% (11). An increasing incidence over time has also been observed in such other countries as Canada, Finland, and Australia (12–14).

From 1996 to 2010, the overall increase of BCC incidence rates in Lithuania was from 27.4 to 46.0 cases per 100,000. In 1996, the incidence of BCC was higher among females than among males (28.2 and 27.6 per 100,000, respectively), but the incidence of BCC rose faster among males than among females (by 3.3% and 2.6% per year, respectively) (9).

Although most studies report the predominance of male sex (15, 16), the opposite was observed in our patients. In our study, like in others (17), BCC was more common among older patients, both among males and females, and presented on the chronically exposed skin, such as the face area. Other common localizations of BCCs were the trunk, the scalp, and the neck. The sub-site distribution of BCC observed in our study is broadly consistent with reports of the previous studies from a variety of countries across the world. The increasing number of diagnosed tumours seems to be clearly connected to the changing habits of sun-exposure occurring in the past decades (18). The high number of BCCs diagnosed on sun-exposed skin, particularly on the face and the neck, corroborates the widely accepted association between these neoplasms and long-term UV-radiation (18, 19). It is interesting to observe in the literature that male sex was clearly predominant for BCCs located in the torso, possibly revealing a higher level of UV-exposure of this skin area among males than among females imposed by the

differences in gender-specific clothing habits (18). This male predominance has also been verified for scalp BCC, and is probably justified by the difference in the average hair length in both sexes, and eventually related to the higher incidence of alopecia androgenetica in men (19). In other studies, remarkable expected increases were found for BCCs on the trunk and legs (20, 21), especially in females, probably due to the popularity of sunbathing and bikini wearing that has been rising since the 1960s.

The treatment modalities applied in our centre reflect worldwide trends in BCC treatment, complete surgical excision being the treatment of choice (23).

The vast gap between the urban vs. rural population observed in Lithuania could be explained by behavioural differences. This pattern may reflect socioeconomic variations in health-seeking behaviour, access to healthcare services, and differences in the exposure to risk factors.

Over the last decade, the situation concerning professional and public education about skin cancer has changed in Lithuania. If ten years ago only oncologists diagnosed and treated skin cancers, nowadays well-trained dermatologists play an important role in the management of non-melanoma skin cancer and melanoma patients. Various skin cancer awareness campaigns, including Euromelanoma campaign (since 2008), provide a free public screening action with an intense, mass-media-supported public skin cancer education initiative (22).

CONCLUSIONS

The results showed that the number of newly diagnosed BCCs was steadily rising between 2000 and 2015. In our Centre, BCCs occurred most often among the patients of 70–79 years of age. BCC was more often diagnosed in women than in men. Most of BCCs were located on the chronically exposed skin, such as the face region, and were of the nodular histological type, which is more common among the elderly, with the superficial type being prevalent among younger patients. The most commonly used treatment option for BCC was surgical excision. Acknowledging the trend of the rising number of BCCs, which demands considerable AMOUNT of healthcare resources, highlights the need for effective skin cancer prevention strategy in Lithuania.

Received 9 December 2018
Accepted 18 February 2019

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BAZALINIŲ LĄSTELIŲ KARCINOMOS GYDYMO POKYČIAI VILNIAUS UNIVERSITETO DERMATOVENEROLOGIJOS CENTRE

Santrauka

Įvadas ir tikslai. Bazalinių ląstelių karcinoma – dažniausiai diagnozuojama lokaliai invazyvi piktybinė epiderminė neoplazija. Pastaraisiais dešimtmečiais stebimas didėjantis sergamumas bazalinių ląstelių karcinoma, ypač europidų populiacijoje. Šis navikas sudaro beveik 75 % visų diagnozuojamų odos vėžio atvejų. Vis dėlto duomenys apie bazalinių ląstelių karcinomos paplitimą yra nepakankami, nes šis navikas dažnai nėra įtraukiamas į įprastinius vėžio ligos registrus. Lietuvoje pacientai, sergantys odos vėžiu, ilgą laiką buvo gydomi centralizuotose onkologijos institucijose. Nuo 2006 m. onkodermatologiniams pacientams Vilniaus universiteto Santaros klinikų Dermatovenerologijos centre yra teikiamos šiuolaikiškos diagnostinės ir gydymo paslaugos. Šio tyrimo tikslas buvo įvertinti bazalinių ląstelių karcinomos epidemiologinius ir klinikinius duomenis, surinktus Dermatovenerologijos centre 2000–2015 metais.

Metodika. Analizuota 2000–2015 m. diagnozuotų histologiškai patvirtintų bazalinių ląstelių karcinomos atvejų medicininė dokumentacija. Atliktas epidemiologinis ir klinikinis duomenų, apimančių pacientų amžių, lytį, gyvenamąją vietą bei naviko lokalizaciją, histologinį tipą ir gydymą, vertinimas.

Rezultatai. Atlikus ištirtų odos darinių biopsijas ir histopatologinius tyrimus, 782 pacientams patvirtinti 847 bazalinių ląstelių karcinomos atvejai. Tyrimo laikotarpiu Dermatovenerologijos centre naujai diagnozuojamų bazalinių ląstelių karcinomų skaičius kasmet augo: 2000–2003 m. sudarė 2,7 % visų atvejų, 2004–2006 m. – 6,5 %, 2007–2009 m. – 13,6 %, 2010–2012 m. – 27,6 %, 2013–2015 m. – 49,6 %. Didžiąją dalį pacientų (28,4 %) sudarė 70–79 metų sulaukę asmenys, 4,6 % – jaunesni negu 40 metų, 7,3 % – 40–49 metų, 17,1 % – 50–59 metų, 27,2 % – 60–69 metų, 14,1 % – 80–89 metų ir

1,3 % – vyresni negu 90 metų asmenys. Nustatytas vidutinis pacientų amžius – 66,0 (±13,6) metai. 62,0 % pacientų sudarė moterys, 38,0 % – vyrai. 63,6 % buvo atvykę iš sostinės, 18,3 % – iš kitų miestų, 18,2 % – iš provincijos. Dažniausios bazalinių ląstelių karcinomos pasireiškimo lokalizacijos buvo: veidas – 49,0 %, liemens sritis – 29,4 %, skalpo ir kaklo sritis – 10,9 %, galūnės – 7,7 %, 2,9 % atvejų lokalizacija buvo nepatikslinta, 0,1 % sudarė visame kūne pasireiškusios bazalinių ląstelių karcinomos. Nustatytas vyraujantis mazginis bazalinių ląstelių karcinomos tipas sudarė 60,6 % atvejų, paviršinis – 22,9 %, infiltracinis / sklerozuojantis (morphea) – 8,0 %, mišrus mazginis infiltracinis – 1,7 %, pigmentinis – 0,2 %, kiti retesni tipai (mikronodulinis, infundibulocistinis, duktalinis (latakinis) ir mišrus) – 0,6 %, nepatikslintas tipas – 6,0 % atvejų. Mazginis, paviršinis ir infiltracinis buvo dažniausi morfologiniai bazalinių ląstelių karcinomos tipai, nustatomi visose kūno lokalizacijose: veido srityje siekė atitinkamai 67,5 %, 12,5 %, 9,4 % nustatytų atvejų, skalpo ir kaklo srityse – 77,2 %, 14,1 %, 5,4 %, liemens srityje – 49,8 %, 37,3 %, 7,2 %, galūnėse – 41,5 %, 43,1 %, 7,7 %. Mazginis tipas dažniau diagnozuotas senyvo amžiaus pacientams, nustatytas ryšys tarp mazginės bazalinių ląstelių karcinomos išsivystymo ir vyresnio amžiaus (p = 0,009). Paviršinė bazalinių ląstelių karcinoma dažniau diagnozuota jauniems pacientams (iki 40 metų), o kuo žmogus vyresnis, tuo šios ligos atvejų nustatoma mažiau (p < 0,001). Mazginis tipas dažniausiai nustatytas veido (p < 0,001) bei skalpo ir kaklo (p = 0,045) srityse, paviršinis tipas – liemens (p < 0,001) ir galūnių srityse, dažniau rankų odoje (p = 0,022). Daugiausia nustatytų bazalinių ląstelių karcinomos atvejų buvo taikomas chirurginis šalinimas (79,6 %), fotodinaminė terapija (centre šis gydymo metodas taikomas nuo 2007 m.) – 5,5 % atvejų ir kiti gydymo metodai – 14,9 % atvejų.

Išvados. Tyrimo rezultatai parodė, kad naujai diagnozuotų bazalinių ląstelių karcinomų skaičius 2000–2015 m. nuolat augo. Vilniaus universiteto Santaros klinikų Dermatovenerologijos centre dažniausiai diagnozuojamos bazalinių ląstelių karcinomos buvo 70–79 metų pacientams. Šis navikas dažniau nustatytas moterims negu vyrams. Dauguma bazalinių ląstelių karcinomų nustatytos ilgalaikį saulės poveikį patiriančiose kūno srityse, tokiose kaip veidas. Mazginis tipas yra dažnesnis tarp senyvo amžiaus pacientų, o paviršinis – būdingas jaunesnio amžiaus asmenims. Dažniausiai taikomas bazalinių ląstelių karcinomos gydymas buvo chirurginis naviko šalinimas. Tyrimu patvirtinamas augantis nustatomų bazalinių ląstelių karcinomų skaičius. Ši tendencija reikalauja didelių sveikatos apsaugos sistemos išteklių, atskleidžiamas augantis veiksmingos odos vėžio prevencijos strategijos poreikis Lietuvoje.

Raktažodžiai: odos, vėžys, bazalinių, ląstelių, karcinoma, epiderminė, neoplazija, onkodermatologija, histopatologija, epidemiologija, Lietuva