BASAL CELL CARCINOMA - INCREASING INCIDENCE LEADS TO GLOBAL HEALTH BURDEN

CARCINOMUL BAZOCELULAR – CREȘTEREA INCIDENȚEI ȘI IMPACT ASUPRA SĂNĂTĂȚII PUBLICE

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Abstract

Basal cell carcinoma is the most common form of skin cancer with a slow growing rate and extremely rare metastasis, but with an important susceptibility of local recurrences. In recent years its incidence has increased significantly, putting an important strain on global health systems. This higher rate of new cases may be explained by excessive UV exposure, in the form of outdoor or indoor tanning (especially at a young age), air pollutants, chemical carcinogens, and immunosuppression. BCCs arises frequently on sun exposed areas, most commonly on the head and neck, followed by the trunk and extremities. There is no standardized approach to BCC treatment. Physicians can offer patients a few surgical and non-surgical treatment options depending on the size, location, number of lesions and clinical form of BCC, that take up an important amount of medical and financial resources. Prevention strategies are the key for lowering BCC incidence in the long term, whether it is de novo tumor development or tumor recurrence, and restricting the overuse of health system resources. These strategies should include limitation of UV exposure, correct sunscreen use, restriction of tanning bed use and regular skin cancer screenings.

Keywords:

basal cell carcinoma, growing incidence, excessive UV exposure, health system burden, prevention strategies

Rezumat

Carcinomul bazocelular reprezintă cea mai frecventă formă de neoplazie cutanată, având o creștere lentă și metastazare extreme de rară, dar cu risc crescut de recidive locale. În ultimii ani incidența sa a crescut substanțial, cu impact major asupra sistemelor medicale din întreaga lume. Rata crescută de cazuri nou-apărute poate fi explicată prin expunerea excesivă la radiațiile UV, la poluanții aerogeni și carcinogenii chimici, prin bronzarea atât în exterior cât și în saloanele de bronzare (în special la tineri), imunsupresie. CBC apare frecvent pe zone fotoexpuse, cel mai frecvent la nivelul capului și gâtului, dar și pe trunchi și extremități. Nu există o abordare terapeutică standardizată a CBC. Medicii pot oferi pacienților numeroase metode terapuetice atât chirurgicale cât și medicale, în funcție de mărimea, localizarea, numărul și tipul tumorilor, metode terapeutice costisitoare. Cheia diminuării incidenței CBC pe termen lung o reprezintă strategiile de prevenție, fie că este vorba despre tumori apărute de novo, fie recidive tumorale, acestea limitând și suprasolicitarea resurselor sistemelor de sănătate publică. Aceste strategii ar trebui să includă limitarea expunerii la radiațiile UV, utilizarea corectă a fotoprotecției, restricții asupra dispozitivelor de bronzare artificială și campanii de screening

Cuvinte-cheie:

epiteliom bazocelular, incidența în creștere, expunere excesivă la UV, impact asupra sistemelor de sănătate, strategii de prevenție

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Introduction

Basal cell carcinoma (BCC) is the most common form of skin cancer, with a growing incidence in recent years. There is evidence that the number of patients that present with multiple BCC (mBCC) is also on the rise. The exact incidence of BCC is difficult to estimate, and for mBCC even more so, due to the lack of a national skin cancer registry. Patients developing another BCC after the first one are a common occurrence[1]. One possible explanation for this growing incidence is higher UV exposure, in the form of outdoor sun exposure or the use of tanning beds. A 5-year prospective study reported that 36% of patients that had one treated BCC developed a second one[2]. The rising incidence puts a strain on global health systems in terms of diagnosis, treatment and follow-up, as it takes up a considerable amount of medical and financial resources. Data considering the ideal approach of patients who present with BCC or who are at risk of developing other BCCs in the future is scarce. Furthermore, there are no strict guidelines for patients with BCCs regarding follow-up regimens that could lower the global burden on health care systems.

1. Epidemiology

Basal cell carcinoma incidence rates are rising worldwide, carrying an increasingly important public health burden because of the large number of patients presenting with single or multiple BCCs, high cost of treatment and follow-up [5]. The major difficulty in assessing the true incidence of BCC comes from poor registration practices or, in most countries, lack thereof. The causes of this sustained rise are the effects of increasing UV exposure, ozone depletion, population aging, growing popularity of tanning beds, but also increased surveillance[5,10]. Genetic defects causing basal cell carcinoma syndromes will not be discussed here. Increased longevity probably plays a major part in the growing incidence of BCC owing to cumulative sun exposure and photodamage over time[10,11].

BCCs usually occur in populations over 50 years of age, usually men, but studies show increasing rates among people younger than 40 years, with patients likely being women[10,12]. Contrasting with most countries, Denmark has an extensive registration of non-melanoma skin cancers (NMSC) in two nation-wide population registries: the Danish Cancer Registry and the Danish Cancer Registry of Pathology, facilitating the analysis of NMSC over time. Using data from these two registries, one study has shown that women showed a higher average incidence for BCC compared to men[15.] Another observation was that the average annual increase in BCC among people aged between 20-40 years was significantly higher compared to older people for (both) men and especially for women. The explanation could reside in the fact that younger people pay more attention to public awareness campaigns, women being more likely to seek medical attention because they are more mindful of their physical appearance. One US-based study evaluated BCC incidence trends over a span of 20 years and found that age-adjusted BCC incidence rates increased from 519 cases per 100,000 person-years to 1,019 cases per 100,000 person-years for women and increased from 606 cases per 100,000 person-years to 1,488 cases per 100,000 person-years for men[14].

While it is rarely life-threatening, it causes important functional and cosmetical morbidity, since most lesions are located on the head and neck[6]. However, many patients present with multiple lesions located on the trunk and extremities. One study[6] predicted that by 2020 incidence rates for primaries on the arms in men will increase 3.5-fold and 2.3-fold on the trunk in women. A recent prospective population-based study in a population over 55 years of age showed that one third of BCC patients developed multiple BCC lesions over an average period of follow-up of 10 years, of whom 18.1% developed two and 12.9% three or more BCCs[13].

2. Risk factors

Although the precise etiology of BCC remains unclear, it encompasses a plethora of risk factors. Exposure to ultraviolet radiation has long been considered as *the* most important risk factor for BCC development, responsible for most of the skin damage, especially UVB radiation with a wavelength between 290-320 nm[16,17]. Recent studies have shown that intermittent or "recreational" sun exposure as a child or teenager plays a major role in the occurrence of adulthood BCCs[18]. Sunburns, especially in non-tanners, are the result of intermittent high-dose UV exposure and have a positive correlation with BCCs in terms of number and intensity [16] . In this regard, several researchers have suggested that BCC and melanoma might share some risk factors [18]. Also, there is evidence that the increasing number of truncal lesions and in particular superficial tumors in young patients are the result of intense intermittent sun exposure and skin damage, rather than the accumulation of long term UV exposure[10]. However, increasing incidence with age most likely reflects cumulative sun exposure and photodamage over time. A study from 2013[14] found a strong and consistent association between BCC risk and cumulative UVB exposure in both men and women, with a relative risk for cumulative UVB exposure being

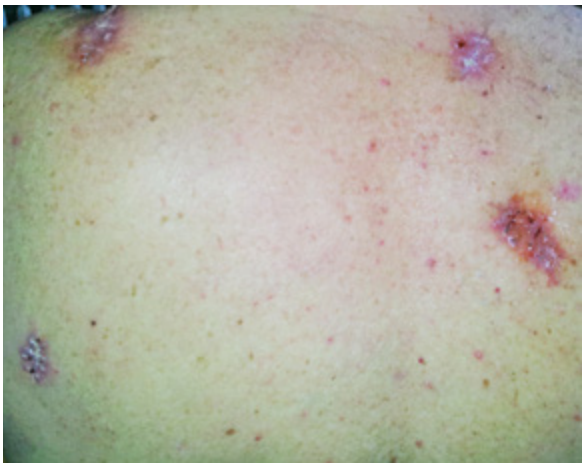

Figure 1. Carcinoame bazocelulare multiple. (Photo library of Prof. Dr. Călin Giurcăneanu)

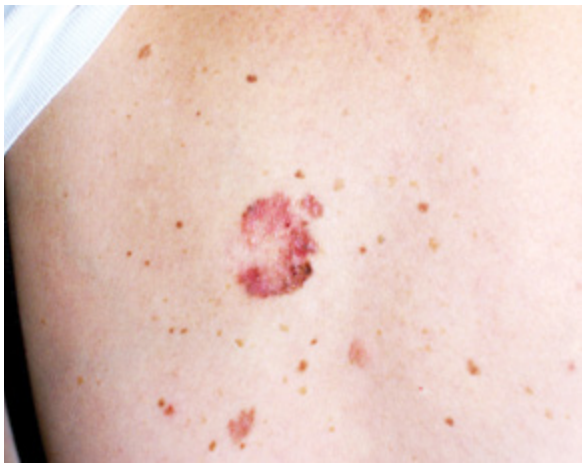

Figure 2. Carcinom bazocelular superficial. (Photo library of Prof. Dr. Călin Giurcăneanu)

much higher in women than in men. This in turn shows that, over time, women may be more susceptible to cumulative UV radiation than men. The last few decades have witnessed a change in sun exposure habits: families tend to work most of the year and go on vacation over the weekend, thus not permitting the skin to develop and preserve photo-protective systems[19].

Furthermore, tanning beds have become an integrative part of western culture, mainly targeting the young population. One 2002 study reported that ever-use of tanning beds increased BCC risk by 50% and young age at first use was associated with a higher risk [20]. Tanning beds can produce 10-15 times as much radiation as sun exposure during noon hours, resulting in a reaction similar to sunburn[23]. There is extensive evidence that there is a dose-response relation between tanning bed use and the risk of developing a BCC at a young age, especially in individuals who used tanning beds in highschool or college or between ages 25 and 35. Classically, light hair color (especially red and blond), fair skin and freckling are regarded as independent risk factors for BCC development[3], with brown eyes being a protective factor[25]. However one study showed that there is no significant difference for the risk of BCC development among women with low pigment score and those with high pigmentation that use indoor tanning, similarly affecting all phototypes [21]. One measure adopted in a growing number of countries is age restriction from tanning salons. Brazil has banned indoor tanning for cosmetic purposes and, as of the beginning of 2015, Australia has banned indoor tanning in five out of six states, according to the Centers for Disease Control and Prevention. European countries have taken action as well, adopting an 18-year old age restriction for tanning bed use: Austria, Belgium, Finland, France, Germany, Iceland, Italy, Norway, Portugal, Spain, and the United Kingdom. The YRBSS (Youth Risk Behavior Surveillance System), that monitors health-risk behaviors that contribute to the leading causes of death and disability among youth and adults in the USA, noted in the 2013 surveillance summary that nationwide 12.8% of students had used an indoor tanning device, such as a sunlamp, sunbed, or tanning booth one or more times during the 12 months before the survey, the prevalence being higher among female students[22]. A study analyzing the risk of early-onset basal cell carcinoma in relation to indoor tanning reported that 95% of individuals started tanning at 25 years of age or younger and, even more alarming, half reported first use of a tanning bed at 17 years or less [24].

A higher educational level and socioeconomic status have also been associated with basal cell carcinoma, probably because of lifestyle habits, frequent UV exposure in sunny vacations and longer life expectancy[13,24].

Other exposure risk factors frequently linked to basal cell carcinoma are ionizing radiation, chemical carcinogens, such as arsenic and air pollutants, and polycyclic aromatic hydrocarbons[3,14].

Lastly, immunosuppression plays an important role in BCC pathogenesis, mainly in solid-organ transplant recipients. Together with squamous cell carcinomas, they account for the majority of skin cancers in these individuals. Compared to the general population, organ transplant patients are 10-16 times more likely to develop a BCC than the general population[26]. Factors that influence the development of NMSC in such patients are: history of BCC, patient sun exposure history, geographic location, intensity and duration of immunosuppressive therapy, type of transplant and age at transplantation[27].

3. Clinical features

BCCs arises on sun exposed areas, most commonly on the head and neck (in 80% of cases),

followed by the trunk and extremities[3]. Less common sites include the axillae, groin, breasts, palms and soles, which lends to a more difficult positive diagnosis. Some authors observed a change in the anatomical tumor distribution, with only 60% of BCCs occurring on the head and neck, and a growing number developing on the trunk in younger patients, probably explained by excessive UV exposure, whether it is indoors or outdoors[10]. Regarding clinical subtypes, between 56% to 78.9% are nodular tumors, followed by the superficial subtype found in between 9% and 17.5% of cases, and the morpheaform subtype in 0.5-16.6% of cases[28,29]. Uncommon variants such as basosquamous, keratotic, micronodular, granular-cell, adamantinoid and clear-cell BCCs are found in fewer cases[3]. Metastases rarely occur, and are correlated with tumor size and depth and, to a lesser extent with tumor subtype[30].

The importance of classifying tumors by subtype and location resides in the fact that some variants tend to be more aggressive (micronodular, infiltrative, basosquamous, morpheaform types), while in most cases tumors take a less aggressive clinical course (nodular and superficial types)[31]. Clear assessment of tumor characteristics dictates treatment choice. Moreover, early diagnosis results in lowering patient morbidity and treatment costs. Another important issue in BCC patients is that a noteworthy percentage return with multiple new lesions a few years after treatment of the first one. One study reported that almost half of patients studied over a 10-year period returned with multiple BCCs[32], similar to another 2005 study that observed that 43% of patients developed a second BCC within a 4 and half year time frame[33]. Patients with multiple lesions tend to have been diagnosed with a first BCC before the age of 65, have red hair, and a higher educational level[13]. The consequence of this high number of patients with mBCCs is a substantial strain on health care systems consuming a great amount of resources on treatment.

4. Treatment options

There is no standardized approach to BCC treatment, since there are few randomized trials, prospective or comparative studies available. Therefore, physicians can offer patients a few options depending on the size, location, number of lesions and clinical form of BCC. Treatment should focus on local control, maximal conservation of function and cosmesis[3]. Another important goal is prevention of recurrence, because recurrent tumors are more difficult to treat [7]. Treatment options can be surgical and non-surgical. Surgical options are electrodessication and curettage, cryosurgery, surgical excision and

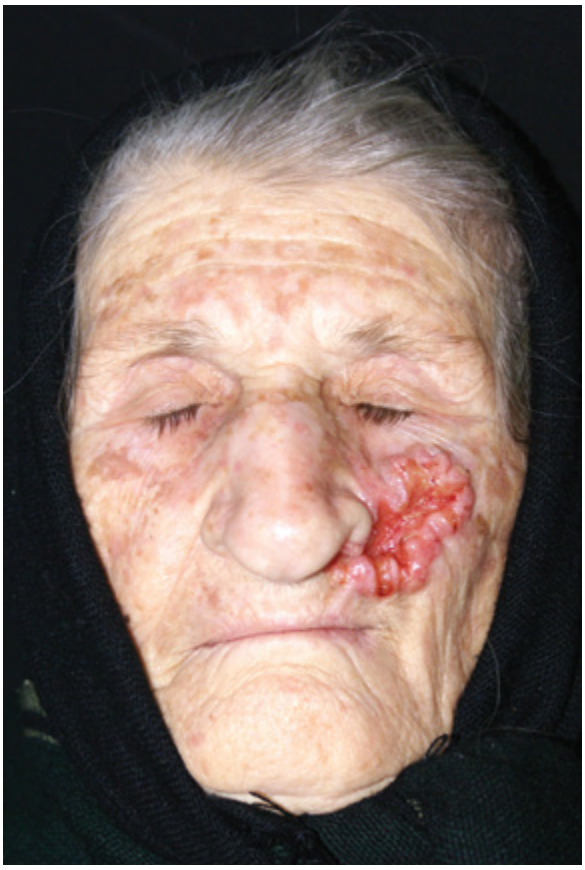

Figure 3. Carcinom bazocelular nodular. (Photo library of Prof. Dr. Călin Giurcăneanu)

Mohs micrographic surgery (MMS). Non-surgical treatments include topical therapies (5-Fluorouracil, Imiquimod), photodynamic therapy (PDT), intralesional therapy (interferons, 5-Fluorouracil or bleomycin) and radiation therapy. Radiotherapy is recommended for lesions in difficult to treat locations and for patients that cannot be subjected to surgical excision[8].

The rise of BCC incidence as well as greater exposure to risk factors translate in many different aspects with direct impact on treatment. From treatment costs that burden health systems, to quality of life related issues, all must be taken into account when choosing the appropriate form of treatment. There is insufficient literature considering exact treatment costs per procedure. According to one study[34] BCC is one of the more expensive cancers to treat. Another study shows that surgical excision is similar in cost to MMS[35], however MMS is not readily available in all physician-office settings. Therefore, resorting to traditional surgical excision is widely accepted as an adequate option, with good results and a low recurrence rate. M-M Chren et. al. noted that there was no significant difference regarding quality of life for patients receiving either classical surgical excision or MMS[41], but both therapies had better outcomes than electrodessicaton and cautery. Some authors suggest that curettage and cryotherapy may(be)

be an option for minimally invasive BCC[9]. In the majority of cases alternatives as curettage and electrocautery, PDT, laser, topical imiquimod and cryosurgery should not be regarded as first line due to recurrence risk[36]which in turn results in additional healthcare costs.

The main goal of treatment is not only prevention of tumor recurrence but also increasing/ raising quality of life in the form of years of potential life and productivity conservation. Given that most BCCs develop on the head and neck, areas with high psycho-social impact, treatment choice in this particular areas should have as end points total tumor removal, adequate cosmesis and function conservation. Moreover, physicians must take into account the social, familial and individual impact that a skin tumor diagnosis and treatment generate.

Data regarding such issues are scarce. In 2009 Baker et al. studied the impact of NMSC overall and observed that NMSC patients were concerned about the public's lack of understanding and recognition of skin cancer and about possible scarring and disfigurement[37].Another study on data recorded from discussion groups with patients regarding BCC knowledge and treatment processes, found that patients were unsatisfied with the amount of information offered by their physician about their treatment options, side-effects and possible pain and scarring. Therefore the psychosocial impact of NMSC must not be underestimated or minimized and more effort should be put into informing patients and raising public awareness.

5. Prevention

Prevention strategies are the key for lowering BCC incidence in the long term, whether it is de novo tumor development or tumor recurrence. Primary prevention focuses on modifiable risk factors like excessive UV exposure. Active campaigns promoting sunscreen use should be initiated, all the more so as studies have shown that the use of broad spectrum sunscreens offers a good protection against UV-related tumors[39]. Importantly, it was shown that sun-protective behaviours increased after treatment for NMSC[42].

There is a particular need for public campaigns aiming at young adults, especially young women and individuals who are susceptible to sun burns, in order to decrease indoor and outdoor sun exposure[16]. Most authors suggest, based on extensive data, that indoor tanning must be restricted[6,15,21,40] especially for minors. The Netherlands have not only established an age restriction to tanning bed use for 18 years of age, but have also placed a UV exposure limit according to skin type[6].

Public education in the lines of parents, teachers and children in terms of photoaging, sunscreen use and sun-related behavior could lead to a decrease in disease incidence and health system burden. Simple measures including regular use of sunblocking agents, avoiding sun exposure during midday hours, staying in the shade and wearing UV-protective clothes[43] are easily implementable. Healthcare providers should encourage regular skin examinations, particularly in men aged 50-60 years and women aged 55-65 years, in the effort for lowering future encumbrance of health systems[14].

Secondary prevention encompasses skin cancer screening methods, having as end point detecting BCCs when tumors are small enough for treatment to result in satisfactory functional and cosmetical outcomes. In 2008 Germany has introduced statutory skin cancer screening every two years for individuals older than 35 years[43]. Secondary prevention strategies should be combined with patient education on sun-related behaviour. Patients should be encouraged and informed about the benefits of skin cancer screening and the risks of delaying a dermatological consult.

Finally, tertiary prevention targets individuals that have had a BCC diagnosis and aims at early detection of tumor recurrence or de novo tumor development. Stricter follow-up regimens must be implemented since such patients are susceptible to developing subsequent skin tumors in following years[13]. Even though BCC has a 30% recurrence rate[43], studies have demonstrated that destructive methods (electrodessication and curretage) are much more susceptible to tumor recurrence than surgical excision and MMS [7]. Therefore, patients that opt for such alternatives must be examined at shorter interval[43]. Self examination could be an easy method to reducing follow-up and long-term health system costs.

In summary, the growing incidence of basal cell carcinoma, although curable when early diagnosis is made, represents an important financial burden on health care systems. In order to plan public health strategies against aggressive intermittent sun exposure, especially in children and young adults, in addition to regular sunscreen use, it is important to understand basal cell carcinoma risk factors and incidence. Awareness campaigns may represent an important weapon in public education that could lead to lowering skin cancer incidence in general, as well as overuse of health-related resources.

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