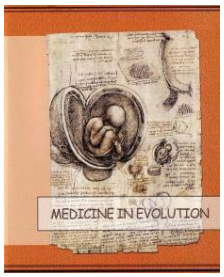
Microscopic and macroscopic features of 91 basal cell carcinoma patients, observed throughout a 2 year-period



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Abstract

Basal cell carcinoma (BCC) is the most frequent skin malignancy, which has been linked over time to multifactorial causes of which the most important is prolong solar exposure. The study aims to find a link between certain age groups, sex and basal cell carcinoma subtypes, both on a microscopic and macroscopic level. The present paper relies on a group of 91 patients diagnosed with basal cell carcinoma, whom were registered in the Bucharest University Emergency Hospital's Pathological Anatomy laboratory database between March 2016, through February 2018. Values were extrapolated using Microsoft Office Excel 2013. Within certain age groups, it has been observed that basal cell carcinoma, almost regardless of subtype and patient sex, has a tendency of appearing on sun-exposed areas in people with fair skin. The nodular and ulcerated subtypes are the most common. Basal cell carcinoma is an important source of morbidity with a major impact in modern society requiring a better pathological understanding and a new approach regarding screening opportunities.

Keywords: basal cell carcinoma, skin malignancy, solar exposure.

INTRODUCTION'

Basal cell carcinoma is a malignant tumor derived from the non-keratinized cells, whose origins lay in the basal layer of the epidermis and its annexes. Basal cell carcinoma is the most common type of cancer in humans – in most cases, its origin can be traced back to ultraviolet (UV) solar radiation exposure, and in some cases is associated with PTCH gene mutations. Also, basal cell carcinoma may occur in the context of genetic syndromes such as nevoid BCC syndrome (also known as Gorlin syndrome), Rombo or Bazex–Dupré–Christol syndromes (1).

The incidence of BCC is considered more than four times higher than that of squamous cell carcinoma and about 20 times higher than that of melanoma. The incidence of BCC has important regional variation. Many studies have shown relatively few cases in Northern Europe, compared to a considerably higher incidence in Australia. Also, some statistical analyses demonstrated that BCC occurs more frequently in men than in women and commonly affects caucasian people. In Oriental population, BCC is usually pigmented. The risk for caucasian men have a lifetime risk of up to 39% to develop BCC, while for women, the values are lower ranging between 23% to 28%. (2, 3).

Although basal cell carcinoma is considered by many to be a tumor of the epidermis, it is almost unanimously accepted in the medical world as being a tumor with a predominantly follicular differentiation (4). Thus, trichoblastic carcinoma, according to some authors, could be considered to be a more appropriate name to characterize basal cell carcinoma (5).

This type of tumor represents a frequently occurring subtype of cancer within medical practice, adding up to 80% of the total malignancies with an epidermal starting point. BCC is a locally aggressive tumor and usually affects elderly patients and has an extremely wide range of histological subtypes. The most common anatomical sites of its occurence consist of solar radiation exposed areas, generally, wherever pilous follicles are being found, but it can also appear in limited-exposure to solar radiation areas, even as far as none, whatsoever. Xeroderma pigmentosum patients, with limited repair possibilities regarding solar-induced mutations, tend to develop a large number of tumors, both basal cell, as well as spincolellular carcinomas, from a young age. If left untreated, this type of tumor will countinue to invade locally, which will lead to tissue damage, compromising the affected area at a functional, aswell as cosmetical level (6). Positive diagnosis is, usually, easy to obtain and relies on: patient history (age, profession, risk factors, preexisteng lesions, long-term evolution), location (frequently on solar exposed ares, especially on the upper two thirds of the face), clinical features (pointing out the typical translucent pearls) and the characteristic histopathological examination. However, given the very wide spectrum of clinical and histopathological subtypes, the diagnosis of basal cell carcinoma can be difficult.

Aim and objectives

The study aims to provide a new perspective regarding the distribution of patients afflicted with different histological basal cell carcinoma subtypes within a certain geographical distribution and how sex and age influence said variables.

MATERIAL AND METHODS

Given the implications that the basal cell carcinoma brings with it, the purpose of this paper is to clear a pathway towards understanding which age groups are more likely to be the victims of onset and which particular subtypes can be associated with a higher incidence regarding age and sex.

The present paper is a cohort retrospective sudy that relies on a group of 91 randomly selected patients diagnosed with basal cell carcinoma, whom were registered in the Bucharest

University Emergency Hospital's Pathological Anatomy laboratory database between March 2016, through Fabruary 2018. Values were extrapolated using Microsoft Office Excel 2013. After surgical excision, the specimen samples were fixated with 10% buffered formalin and were processed by conventional histopathological methods using paraffin embedding, sectioning and Hematoxylin–Eosin (HE) staining. The final diagnosis was performed in accordance with the latest criteria of the World Health Organization concerning the histopathological evaluation and diagnosis of skin tumors.

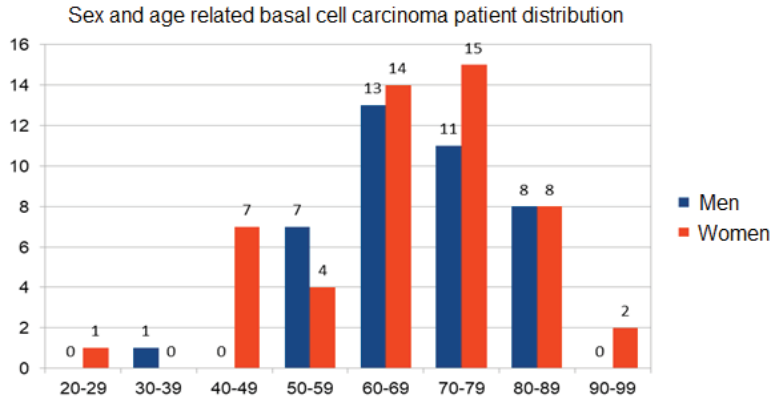

Figure 1. Distribution of basal cell carcinoma patients according to age groups and sex (n=91)

Fig. 1 Age wise, the 6th and 7th decade of life were found to be associated with the most number of BCC cases, both in men and women, alike, followed by the 8th for both sexes and the 5th and 4th. During the first 40 years and after 90 years of age, only 4 cases were registered for both genders. Women lead men in the total number of cases between 60 and 79 years of age, as well as having the only registered BCC presence in the 2nd, 4th and 9th dacade of life. Meanwhile, men lead during the 5th and 3rd decade, the 8th being tied between the sexes.

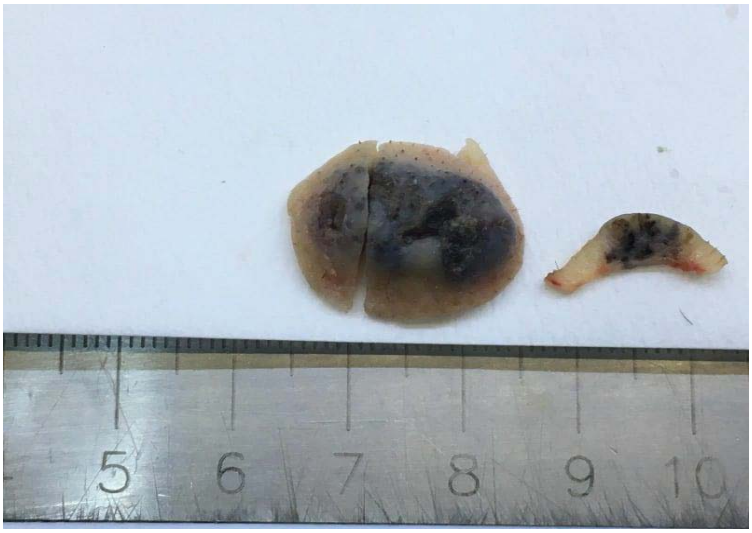

Figure 2. Gross aspect of a pigmented basal cell carcinoma after fixation with 10% buffered formalin, Emergency University Hospital of Bucharest, Pathology Department

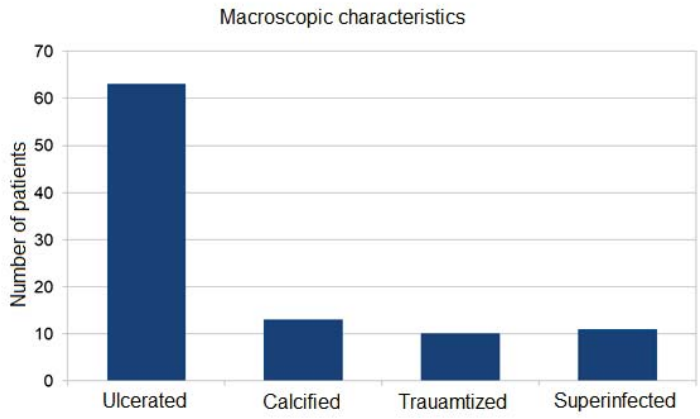

Figure 3. Macroscopic characteristics of analyzed group (number of patients); as revealed, the most common subtype of basal cell carcinoma is the ulcerated type, accounting for no less than 63 out of the total of 91 analyzed patients, followed by the calcified type with 13, superinfected, with 11 and traumatized, with 10 cases, respectively.

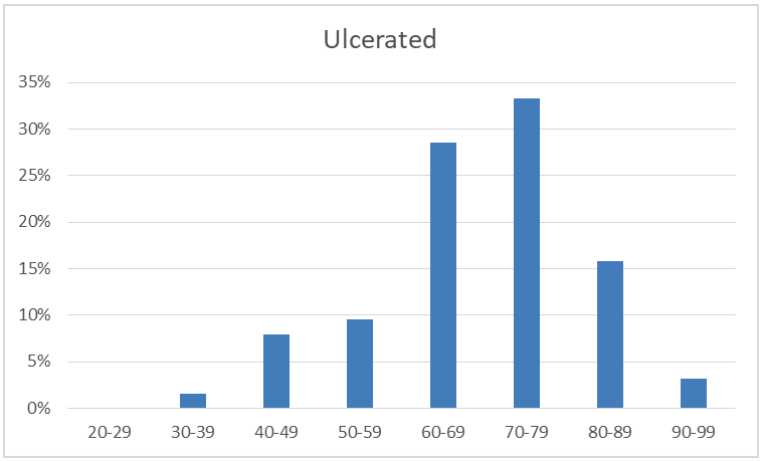

Figure 4. Frequency of ulcerated subtype of basal cell carcinoma patients related to peak age groups; it has been noticed that over 50% of the total analyzed cases were found to be associated with higher age group, the 7th decade, alone, making up over 30%, followed by the 6th and 8th. The least common finds were in the first 4 decades and during the 9th, making up less than 10% of the total number of patients.

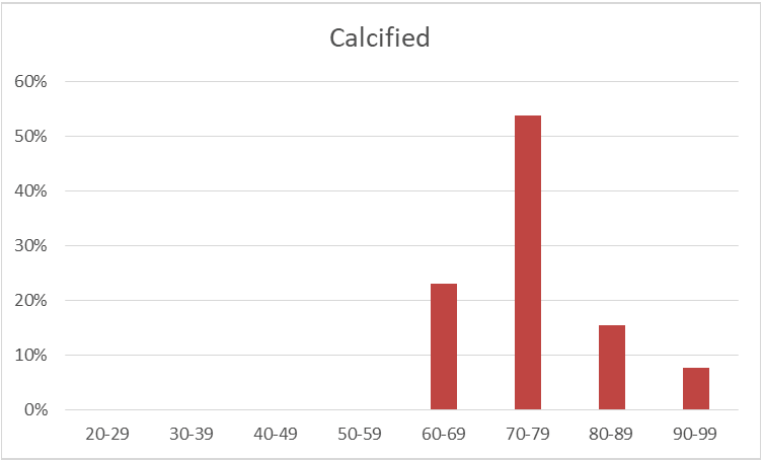

Figure 5. Frequency of calcified subtype of basal cell carcinoma patients related to peak age groups; as observed, the 7th decade registered over 50% of the cases, followed up by the 6th and the 8th decades, while the 9th took up less than 10%. Between 20 and 59 years of age, not a single case was noted in our research

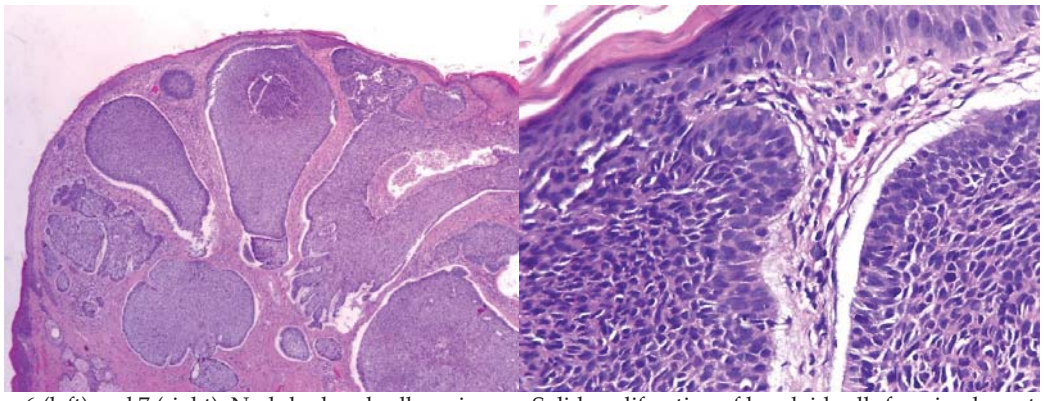

Figure 6 (left) and 7 (right). Nodular basal cell carcinoma. Solid proliferation of basaloid cells forming large tumor nodules infiltrating the superficial and deep dermis. Note the classic artefactual clefting around nodules and the characteristic peripheral palisading at the interface between the basaloid cell lobules and the stroma. Hematoxylin and eosin staining, 40x magnification (right) and 400x magnification (left).

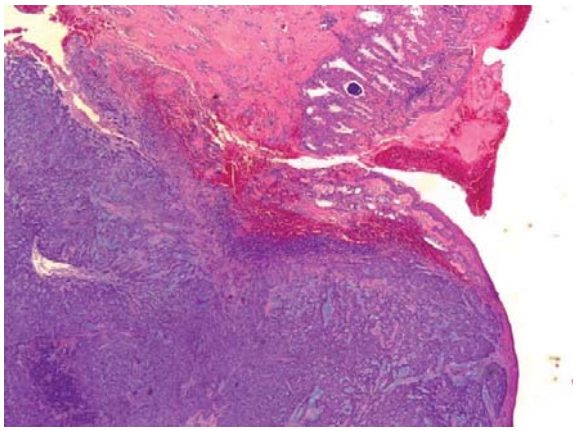

Figure 8 (left). Microscopic appearance of an ulcerated and infected basal cell carcinoma. Haematoxylin and eosin 40x magnification

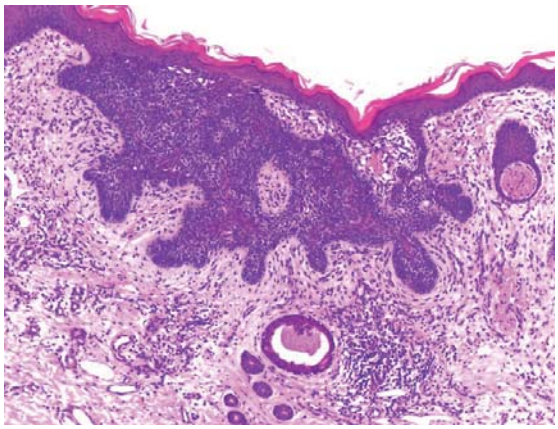

Figure 9. Superficial basal cell carcinoma: tumor nests attached in the basal leyer of the epidermis. Hematoxylin and eosin, 10x magnification

DISCUSSIONS

Regarding the peak age group for both sexes, the 6th and 7th decade of life have been observed to be the most common when it comes to basal cell carcinoma onsets, women registering slightly higher numbers than men, in accordance with the entire group split, women consisting of 56% of the entire number of studied patients. The data obtained are discordant with similar studies that have shown a higher prevalence of these tumors in women (7). The high incidence among elderly population might be explained by ithe boost of life-expectancy, the addition of cell mutations, combined with a poor education concerning solar skin damage.

On a macroscopic level, over 60 out of the 92 patients were observed presenting the ulcerated form, overwhelming the calcified, traumatized and superinfected types. All types of basal cell carcinoma can present ulceration. In some neglected cases, the ulcerations can have a destructive appearance with irregular margins, thus beeing called ulcus rodens. If left untreated it can evolve into a mordid form called "ulcus terebrans", destroying adjacent tissue structures such as soft tissue, cartilage, even bone.

Regarding the histological aspects, in hematoxylin-eosin staining, BCC has a characteristic appearance: a proliferation of medium-large basaloid cells (round or cubic cells, with a large nucleus, and basophilic cytoplasm and with a somehow monomorphous appearance), with a marginal palisadation of individual tumor cells and sometimes with an artefactual clefting between tumor nests and adjacent stroma. Mitosis are frequent. The tumor

nests are surrounded by a fibrous or mucin rich stroma. Sometimes the tumor nest can undergo cystic degeneration, calcification and necrosis. Amiloid deposition is another commonly found feature. No proliferations of melanocytes are present, but there is a pigmented subtype of basal cell carcinoma wich can contain melanin within dendritic melanocytes located inside or around tumor nests.

In our study the pigmented, superinfected, cystic, ulcerated and calcified subtypes respected the peak age groups, while the nodular type reached its peak value in the 8th decade of life, followed by the traumatized subtype, whose values were focused on the 5th and 6th decade, respectively.

There are numerous studies concerning risk factors linked with the development of BCC, the most plausible evidence being related to sun exposure (skin type, hair color, solar keratosis, sunburns in childhood, occupational hazard, high altitude, indoor tanning, high levels of serum vitamin D and photosensitizing medication) (8, 9, 10). Immunosuppression and impaired DNA repair are also linked to increased BCC incidence in elderly patients (11). The relation between HPV infection and development of basal cell carcinoma is not yet well defined (12).

Treatment options for BCC depends on a number of circumstances including the size, site and histopathological subtype, comorbidities, previous treatment history, immunological status, life expectancy and patient options. It is also crucial to acknowledge whether the intention of treatment is curative or palliative. Therapeutical options include: Mohs surgical excision, electrodessication and curettage, cryosurgery, imiquimod, photodynamic therapy, local chemotherapy (5-fluorouracil, imiquimid), radiation therapy, combination therapy and observation (13,14). Therapeutical agents tend to follow in the footprints of the progresses made in understanding the pathogenesis of BCC; as such, Hh inhibitors (hedgehog pathway inhibitors) are also a novel approach for treating BCCs, as this biochemical signaling pathway is employed in the develompent of the basal cell carcinoma; to date, two Hh inhibitors have been approved for BCC therapy, namely sonidegib and vismodegib (15). Consequently, the armorarium for BBC therapy is constantly developping.

CONCLUSIONS

Even though modern approaches have greatly increased the life quality and survival of basal cell carcinoma patients, we must pursue our search for better treatments, especially since the most likely ones to suffer from this affliction are having to face the cons of an aging immune system. Given these facts, non-melanoma skin cancers are a common pathology in current clinical practice, with large socio-economic implications, whose etiopathogenesis has not, yet, been completely understood. Therapeutical agents tend to follow in the footprints of the progresses made in understanding the pathogenesis of BCC; therefore, further research in this domain is always warranted and welcome.

Conflict of interests: The authors declare that they have no conflict of interests.

Compliance with ethical standards: We undersign, certificate that the procedures and the experiments we have done respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2000 (5), as well as the national law.

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