ORIGINAL ARTICLE

Basal Cell Carcinoma in the Department of Dermatology, Hospital Kuala Lumpur

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Abstract

Introduction

Basal cell carcinoma (BCC) is the commonest skin cancer seen worldwide. This study aims to determine the clinical pattern of BCC in the Department of Dermatology, Hospital Kuala Lumpur, Malaysia

Methods

A retrospective review of 142 cases of BCC between January 2005 and December 2018 in the Department of Dermatology, Hospital Kuala Lumpur.

Results

Mean age at presentation was 66.0±11.7 years. There were 71 male and female patients. Chinese accounted for 49.3% of patients, followed by Malay (32.4%), Indian (5.6%) and other ethnic groups (12.7%). Our study found that 32.6% of the patients presented within 1 year after the lesion appeared, 43.9% between 1-5 years, and 23.5% of patients presented after 5 years. Most patients (81.6%) had BCC over the head and neck region, followed by trunk (14.9%), lower limbs (8.5%) and upper limbs (5.7%). Most patients required simple surgical excision (82.4%) while 7.0% of patients had more extensive excisions. Radiotherapy was given to 3% of patients. Staging was available for 75 of the patients, and majority (78.7%) were in Stage 1. Patient's outcome was available for 67 patients and 82.1% were in complete remission.

Conclusion

Our data showed that BCC tend to occur in older age groups (above 60) and in Chinese patients. Majority of the lesions occurred in the head and neck region. Simple surgical excision was the commonest treatment method, with very good outcome as evidenced by high percentage of complete remission.

Key words*: Basal cell carcinoma, non-melanoma skin cancer, national cancer resgistry*

Introduction

The World Health Organization (WHO) states that the global incidence of skin cancers has been steadily increasing since the past decade. It is now estimated that around 2-3 million non-melanoma skin cancers and 132,000 melanoma skin cancers occur globally each year.[1] Basal cell carcinoma (BCC) specifically, is estimated to affect 1-3% of the world's population.[2]

Malaysia, a country prominently known for its ethnic plurality, is a country located near the

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equator and is home to approximately 32.6 million people as of 2018. Its main ethnic constituents are Malay (54.7%), Chinese (24.3%), Indian (7.3%) and multiple other denominations (13.7%) and ethnicities. Malaysia, therefore, represents a study population that is unique in its heterogeneity of its people.[3] The latest available national data on skin cancer was taken from the Malaysian National Cancer Registry (MNCR) (2007-2011). It was reported that skin cancer is ranked 12th among the most common cancers in the Malaysian population, 10th most common cancer in males and 14th amongst females.[4] According to the registry, BCC alone accounted for 51.9% of all skin cancers in Malaysia from years 2007 to 2011, the highest amongst the different types of skin cancers.[4]

Once a disease occurring exclusively in the elderly, BCC are increasingly diagnosed in individuals under the age of 50, due to frequent exposure of known risk factors in susceptible patients and improvement in diagnostic modalities.[5,6] Classical risk factors include prolonged UV light exposure, family history of skin cancers and fairer Fitzpatrick skin subtypes.[7,8] Contrastingly, BCC can also appear on areas that are relatively sun protected as well such as the inner canthus of the eyes and the posterior aspect of the ears as it is estimated that a fifth of all BCC may occur on areas that are void of sun exposure.[9]

These statistics lead us to the overarching observation that both sun exposure and degree of skin pigmentation are notable risk factors in the development of skin cancers but skin cancer can still occur in patients who are seen as low risk as well. Hence, we are analyzing our BCC patients to identify clinical patterns and treatment outcomes to describe risk factors of acquiring BCC in our population of patients.

Materials and Methods

This was a 14-year retrospective review conducted at the Department of Dermatology, Hospital Kuala Lumpur (HKL), Malaysia. HKL serves as a tertiary referral center for various dermatological illnesses, including BCC. The data used for this study was retrieved from the Department of Dermatology Skin Cancer Registry. The source document for this registry was obtained from patient notes whom have clinically and histologically proven BCC. For the purpose of this study, we collected information from patients presenting to our department from January 2005 to December 2018.

Raw data regarding patient demographics, clinical attributes, symptoms, treatment modalities, outcomes and other clinical characteristics were among the information collected. The following data were then processed through Statistical Package for Social Sciences (SPSS) Version 20.0. Continuous variables were expressed as mean +/- standard deviation (SD), and categorical variables were described as frequencies/percentages. We excluded patients of whom clinical data was insufficient.

RESULTS

A total of 142 patients were diagnosed with BCC in our department over the span of 14 years from year 2005 to year 2018. The mean age of diagnosis was 66.0 ± 11.7 years old. There were equal numbers of male and female patients at 71 patients each (Table 1). In terms of frequency of BCC amongst the Malaysian ethnicities, 70 patients (49.3%) were Chinese, 46 patients (32.4%) were Malay, 8 patients (5.6%) were Indian, and 18 patients (12.7%) were of other ethnicity. Regarding ethnicity and gender, our study showed that the incidence of BCC was slightly lower in Chinese females compared to Chinese males, with a male to female ratio of 1.15. Within the Malay community, the ratio of male to female was 0.57, whilst in the Indians the ratio was 0.33 (Table 2). Forty-six patients (32.6%) presented within 1 year of symptoms, while 95 patients (67.4%) presented 1 year after the manifestation of skin lesions. The vast majority of patients (118, 83.1%) had no history of previous malignancies. It was observed that 20 patients (14.1%) had prior history of skin malignancy and only 2 patients (1.4%) had a history solid organ malignancy.

Upon analyzing the location of BCC lesions, we found that 115 patients (81.6%) had BCC on the head and neck region. This was followed by trunk, seen in 21 patients (14.9%), lower limbs in 12 patients (8.5%), and upper limbs in 8 patients (5.7%). Three patients were found to have multiple BCC over different areas. The first patient was a 49-year-old Malay lady who was found to have lesions on her abdomen and feet. Following investigations, she was diagnosed with Gorlin Syndrome, also known as nevoid basal cell carcinoma syndrome, a hereditary condition that increases one's risk of developing multiple BCC. She still developed multiple, recurrence BCC to date. The second patient is a 43-year-old Iban male with underlying oculocutaneous albinism with a personal history of a previous BCC. He had multiple ulcerated plaques on his back and neck which required excision with

Table 1. Demography, Clinical Features, Staging and Mode of Treatments

Characteristics	n (%) or mean ± SD
Age, years	66.0 ± 11.7
Gender	
Male	71 (50%)
Female	71 (50%)
Ethnicity	
Malay	46 (32.4%)
Chinese	70 (49.3%)
Indian	8 (5.6%)
Others	18 (12.7%)
Duration of lesion prior to presentation	
< 1year	46 (32.6%)
1-5 years	62 (43.9%)
>5 years	33 (23.5%)
Previous History of Malignancy	
None	118 (83.1%)
Skin malignancy	20 (14.1%)
Solid organ malignancy	2 (1.4 %)
Not recorded	2 (1.4 %)
Staging	
Stage 1	59 (41.5%)
Stage 2	13 (9.2%)
Stage 3	2 (1.4%)
Stage 4	1 (0.7%)
Staging not available	67 (47.2%)
Mode of treatment	
Simple excision	117 (82.4%)
Excision+ graft/flap	10 (7%)
Radiotherapy	3 (2.1%)

Table 2. Total number and sites of BCCs according to Gender and Ethnicities

Sites of BCC	Malay (no. of patients)		Chinese (no. of patients)		Indian (no. of patients)		Others ethnicity (no. of patients)		Sites Total (% of sites)
	Male	Female	Male	Female	Male	Female	Male	Female	
Head and Neck	11	23	32	28	2	5	8	6	115 (81.6)
Upper Limb	1	-	4	1	-	-	1	1	8 (5.7)
Lower Limb	-	3	5	-	-	-	2	2	12 (8.5)
Trunk	5	4	5	1	-	1	3	2	21 (14.9)
Total BCC lesions	17	30	46	30	2	6	14	11	156 (100)

a graft for skin reconstruction. The third patient was an 83-year-old Chinese male with an underlying history of Bowen's disease, presented with lesions over his shoulders, trunk and calves. He was treated with a mixture of excision and cryotherapy which lead to only partial remission, and he later defaulted.

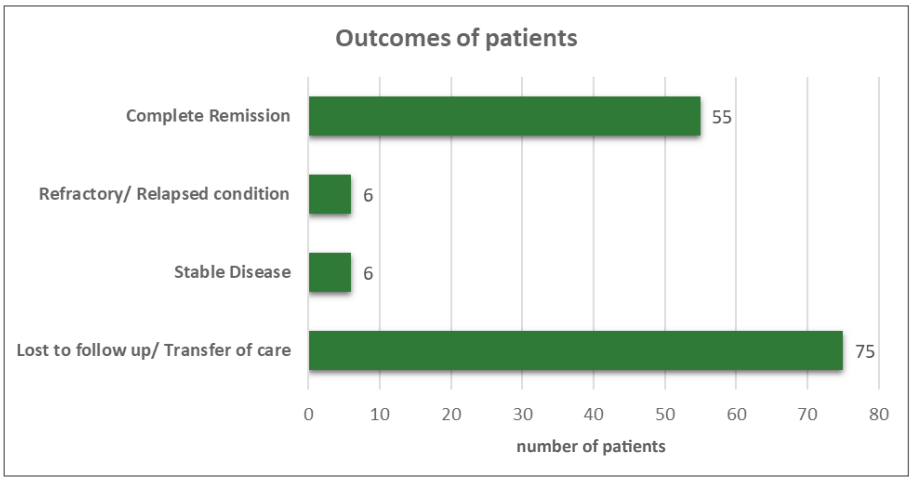
Data on staging was available for 75 out of 142 patients (52.8%). It revealed that a majority of 59 (41.5%) patients were diagnosed at Stage 1, 13 patients (9.2%) Stage 2, two patients (1.4%) Stage 3 and 1 patient (0.7%) Stage 4. A Majority of patients of 117 (82.4%) required simple excision of BCC as the treatment of choice. Ten patients (7%) had wide excisions with graft or flap closure and 3 patients (2.1%) received radiotherapy. Unfortunately, outcome data was available for only 67 out of 142 patients. On analyzing the outcomes to the previously mentioned treatments, 55 patients (38.7%) achieved complete remission. Asides from that, 6 patients (4.2%) had stable disease, another 6 patients (4.2%) had a relapse in condition. Our study also found that 64 patients (45.1%) was transferred to other departments (namely Plastic Surgery) for further follow up and management and 10 patients (7%) were lost to follow up (Figure 1).

Discussion

Age and Sex

This study serves to provide better insight into the pattern of occurrence of BCC in Malaysia in

Figure 1. Outcomes of patients with BCC



arguably the largest tertiary center for Dermatology in the country. Firstly, our study identified that there was a predilection for the malignancy to occur in the elderly population with no gender predominance. The average age of our population for BCC was 65 years in males and 66 years in female. Similarly, other studies confirmed this finding, as evidenced by Ch'ng et al in another study conducted in University Malaya, who found that the average age for BCC was 68 years of age.[10] A retrospective study done in 2006 in our neighbouring country Singapore by Sng et al looked into various skin cancers from years 1968 to 2006.[11] The study found that BCC had a particularly alarming incidence in those aged 60 and above, with an average of 4.5/100,000 person years in 2003-2006.[11] Globally, this range of age group is fairly consistent with studies carried out in other countries such as Poland and Turkey.[12,13]

However, when age and gender were taken into account, the data in many other studies around the world is conflicted. While many studies found that men were more likely to develop BCC in their lifetime, women were seemingly diagnosed at younger ages comparatively.[5,14,15] Studies from countries such as Taiwan, Turkey and Poland demonstrated that women with BCC presented at a slightly younger age compared to men.[12,13,15] The study done in Taiwan specifically, showed that median age in years for BCC was 67 in females and 71 in males, a noticeably older overall cohort as well.[15] This could be due to the fact that women are often more concerned by their appearance and sought treatment earlier compared men who may not seek treatment until the lesion worsens. However, a large study carried out in Strasbourg, France in 2002 revealed a slightly higher female ratio to male ratio instead (52% vs 48%).[14] This study which included 10,245 patients with histologically proven BCC identified that women with BCC presented at an older age and that older female preponderance could be in part due to women living to an older age in regions of the world where mortality to cardiovascular diseases and internal cancers were higher in the male population.[14]

Ethnicity

Ethnicity is a major determinant of one's risk of developing BCC. Malaysia is a multiracial country with different Fitzpatrick skin phototypes. It is purported that the Malaysian population has a wide range of skin phototype from III to V.[15] Our study showed that the ethnicity associated with the lowest Fitzpatrick skin tone, Chinese ethnicity, were diagnosed with more BCC, followed by Malay and the Indian ethnicity. We also found that females in both Malay and Indian races outnumbered their male counterparts, differing from the Chinese race which showed male to be more affected than female. Our findings of a majority Chinese ethnicity were consistent with a study by Yap FBB in Sarawak with the Chinese population representing 44% of the 43 BCC patients.[17] A Singaporean study published in 1995 investigated skin cancers in 2 tertiary referral skin hospitals in Singapore, namely the Middle Road Hospital and National Skin Centre. In 190 biopsy proven BCC patients, 68.9% were Chinese, 22.6% were Caucasians with Malay and Indians forming a small minority.[18] Even when expanding these observations to include other skin cancers such as Bowen's disease or SCC, Chinese ethnicity was still heavily afflicted at rates of 90.8% and 83.5% respectively.[18] In many western reviews, BCC occurs more frequently in individuals with fair skin, red haired and those with light eye colors.[16,19] Conversely, dark skinned individuals are estimated

to be 19 times less at risk of developing BCC due to the protective role of skin pigmentations against the mutagenic nature of UV light.[9,19]

Late Presentation

We recorded that only 32.6% of our histologically confirmed BCC patients presented to our department within 1 year of skin lesion onset while an alarming 67.4% presented after 1 year. These findings may reflect the indolent but insidious nature of BCCs, causing almost no symptoms that would trigger a visit to a doctor for many years until its later stages.[6,14] This effect is further compounded by the fact that Malaysian elderly may not seek medical consultation if they deem the skin lesion to be of a "cosmetic issue". In addition, many benign skin lesions that are related to photo-ageing such as solar lentigo can be difficult to distinguish between the more malignant BCC in its early stages.[6,14] Mabula et al conducted a retrospective study in 2012 among 64 Albinos in Northwestern Tanzania and found that most of their patients presented late with a median presentation time of 24 months.[20] Many of these skin cancers were SCC, BCC and malignant melanoma that were already ulcerating or fungating upon presentation. Furthermore, 42% of their patients had defaulted treatment after initial excision or during courses of radiotherapy. The authors reported that due to inadequate facilities, patients often needed to spend heavily on time and resources to travel far for radiotherapy.[20] Delays in diagnosis, and therefore treatment, will lend itself to the rapid emergence of locally invasive tumours and metastatic BCC. [21] However the healthcare in Malaysia is of a single-payer system that is heavily subsidized and most defaulter rates can be attributed inadequate education or access to healthcare in some rural areas.

Location of Lesions

This study found that the vast majority of BCCs have a site specific occurrence. This study was able to reproduce similar findings to other studies. In this study, most BCC occur on areas of the head and neck (81.6%) followed by trunk (14.9%), lower limb (8.5%) and upper limb (5.7%). Rates of BCC on the head and neck have been similarly high in many places of the world.[7,8,10,13,17,18,22,24] The head and neck are areas typically exposed to sunlight over the years. Prolonged sunlight exposure causes photo-damaged skin which increases the likelihood of accruing not just BCC but other skin cancers as well.[2,25] In recent years, artificial UV radiation has been designated as a human carcinogen. The International Agency for Research on Cancer, an affiliate of the WHO has included UV tanning devices in the same group as smoking, plutonium and solar UV radiation as cancer causing to humans.[26] The literature is clear; skin cancers such as BCC have become increasingly more common in women under 40 primary due to increased exposure to UV radiation either from the sun or artificial sources. It is reported that having 5 or more sunburns doubles risk for skin cancers such as BCC and melanoma while any history of indoor tanning increases the risk of developing BCC before the age of 40 by 69%.[15, 25, 27, 28]

Multiple BCC

While many BCCs occur solitarily in each patient, multiple lesions can occur in the same patient. In our three patients with multiple BCC, many of these lesions occured over the abdomen, feet, shoulders, and back. Interestingly, these areas are not commonly associated with chronic UV light exposure. In an Iranian study published in 2013 by Zargaran et al, the authors found that they had identified 804 BCC in 746 patients.[22] Similar findings were found from various studies. Hakverdi et al study in Turkey identified 197 BCC in 181 patients with 12 patients having 2 or more tumours.[12] A UK case control study in 1997 of 827 histologically proven BCC found 278 patients with multiple BCC. That study in particular found that patients with multiple lesions were more likely to have truncal tumour at first presentation (p=0.002, OR 4.03, 95% CI 1.64 - 9.89).[23] Conferring from the breadth of information regarding multiple BCC in a single patient, it was found that those with BCC of the trunk, impaired immune responses, previous arsenic treatment in psoriatic patients, possessing high risk immunogenentics (i.e. HLA-DR4), history of radiation exposure, and the presence of the CYP2D6 genetic polymorphism were known risk factors of having multiple or recurrence BCC.[2,5,19,22,25,29]

Modes of Treatment

Most of our patients underwent simple excisions (82.4%), followed by excision and skin graft/ flap and radiotherapy. This is in keeping with the vast majority of our patients who presented earlier at Stage 1 and Stage 2, allowing for relatively localized therapy. Our study identified a relatively low relapse rate of 0.04% (only 6 patients) in which further therapy was mandated. Most simple excisions carried out in our center included a margin of clinically normal skin. Evidence from a large retrospective study of 3957 patients in 2014 by

Codazzi et al support the notion of having negative margins during excision of BCC. The paper found that recurrent rates following histologically positive margins was 26.8% compared to 5.9% in histologically negative margins.[30] Indeed, other studies support that an excision of non-aggressive subtypes of BCC with 3-4mm margins in low risk anatomic regions translated to a 2-4% recurrence rate after a 3-5 year period.[21] However, apart from good margin clearance, subtype of BCC and anatomical sites are the predictor factors for recurrence rate, in which our study did not collect the data. Hakverdi et al found that the most common site for margin positivity included the eyes (34.4%), nose (25%) and ears (15.6%).[13] These tumors are difficult to treat due to the potential unwanted facial disfigurement hence are liable to recurrence.[21,25]

Tumours in areas that are difficult to treat such as the ears and periocular regions are routinely referred to the plastic surgeons in our institution for optimal multidisciplinary care as surgical defects in these areas require their expertise for reconstruction. Infiltrative BCC tumours, are believed to have an aggressive nature and also relate to a high histopathological positivity after excision.[31] Mohs Micrographic surgery (MMS) has been touted as a method to remove difficult or recurrent cutaneous tumours since its inception in the 1940s. A RCT comparing Surgical Excision (SE) and MMS with 10 year follow up had shown that for primary facial BCC, the cumulative risk for recurrence was 4.4% in the MMS group compared to 12.2% in the SE group.[32] Furthermore, the 10 year probability for recurrence in patients treated for recurrent BCC were 3.9% in MMS but 13.5% in SE group thus confirming the clinical superiority of MMS over SE in cutaneous tumours arising in inconvenient areas.[32] A study by Greywal et al in 2019 looked into factors that would lead to BCC requiring large subclinical extensions during MMS and found that being male, Fitzpatrick skin type 1 and having prior history of BCC were predictors of requiring more extensive tissue removal.[33]

Table 3. Comparison of our study with other published studies

Clinical features	Current study 2005-2018	Yap BB et al[3] 2000-2008	Yeh YW et al[4] 1985- 2011	Hakverdi S et al[5] 2005-2010	Ciążyńska M et al[6] 1999-2015
Population	HKL, Malaysia (n=142)	Sarawak GH (n=43)	Taiwan (n=103)	Turkey (n=181)	Poland (n=890)
Mean age (years)					
Male	65	62	71	64	66
Female	66	60	67	59	66
Gender					
Male	71(50%)	22 (52%)	59 (57%)	101 (56%)	386 (43%)
Female	71(50%)	21 (48%)	44 (43%)	80 (44%)	504 (57%)
Ethnicities	Chinese : 49% Malay: 32% Indians : 5% Others : 12%	Chinese : 44% Malay: 32% Bidayuh : 14% Iban : 7%	Taiwanese	Fair Turkish	Polish
Commonest site of BCC	Head & neck - 115 (81%)	Head & neck - 36 (83%)	Head & neck - 91 (83%)	Head & neck - 166 (92%)	Head & neck - 409 (46%)

Limitations of study

This study is limited by its retrospective nature and small number of cases. This study collected data from a single tertiary center, the Dermatology Department of Hospital Kuala Lumpur. As a result, this number of cases only allowed us to perform a univariate analysis in this study as we did not have the required sample size to proceed with a multivariate analysis. We had selected proven BCC patients to look for clinical parameters to tie correlations to the development of BCC, possibly opening our study to selection bias. We did not include categories into the different subtypes of BCC as some other studies cited may have as this was not collected in the 14 years' time frame chosen for the study. Studies that sampled patients in multiple centers and prospective study designs may resolve some of the limitations pertaining to this study.

Conclusion

Our study confirmed the long held beliefs that BCC is commonly found in older age groups (above 60), Chinese patients, over the head & neck area and mostly have good prognosis if managed early. The results of our study concur with other studies in the South East Asian region that the Chinese ethnicity was the most implicated ethnic group, followed by

Malay and Indian. Simple surgical excision was the commonest treatment method and deemed to be adequately effective. This study is limited by its retrospective nature, single-centre data, and lack of histology analysis on the types of BCC. These findings may serve as a useful guide in screening patients at primary care in early detection of BCC. Public awareness on risk exposure are crucial to reduce morbidity of BCC by early presentation to a certified Dermatologist.

Conflict of Interest Declaration

The authors have no conflict of interest to declare.

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