

## Squamous Cell Carcinoma and Bowen's Disease of the Skin in Singapore

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### Abstract

**Introduction:** Non-melanoma skin cancer is one of the commonest cancers in Singapore and worldwide. The aim of our study was to evaluate the demographic and clinicopathological patterns of squamous cell carcinoma (SCC) and Bowen's disease (BD) of the skin, in order to better understand the characteristics of these tumours in our population. **Materials and Methods:** Histologically proven cases of SCC and BD seen at our centre between 2002 and 2003 were retrospectively analysed according to age, sex, race, predisposing factors such as immunosuppression and ultraviolet therapy, site and size of tumour, histological differentiation and subtype, and treatment method. **Results:** A total of 161 patients were studied – 81 with SCC, 68 with BD, and 12 with both tumours. There were 199 tumours in total – 105 SCC and 94 BD. For both SCC and BD, males outnumbered females (ratio of 2.4:1 and 1.5:1 respectively); patient age averaged 72.9 years and 66.8 years respectively; and Chinese were the majority race. The mean duration to presentation was 21.2 months for SCC compared with 39.9 months for BD, and common symptoms were itch, pain and bleeding for both. The mean tumour size was 19.0 mm and 18.5 mm, and the commonest site was the head and neck for both. **Conclusions:** SCC and BD show rather similar patient characteristics, with a predominance among males, having a predilection for the head and neck region, and with a tendency towards slow growth. As incidences increase worldwide, it is important for healthcare providers to be adept at recognising and managing non-melanoma skin cancers.

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**Key words:** Arsenic, Skin cancer

### Introduction

Skin cancer is the seventh most common cancer in Singapore.<sup>1</sup> Koh et al<sup>2</sup> reported a total of 1407 squamous cell carcinomas (SCCs) occurring in the Asian population of Singapore using data obtained from the Singapore Cancer Registry over a 30-year period between 1968 and 1997. Tan et al<sup>3</sup> reported a total of 520 patients with skin cancer seen at the National Skin Centre (NSC) between 1980 and 1991, of which 36.5% were basal cell carcinomas (BCCs), 24.4% SCCs and 16.7% Bowen's disease (BD). Skin cancers represent a major public health problem worldwide, with increasing workload and cost in dealing with this problem, together with significant morbidity suffered by those affected. We sought to analyse retrospectively, data on histologically proven cases of SCC and BD seen over a 2-year period from 2002 to 2003, in order to develop a better understanding of the characteristics

of these skin cancers among the different races in Singapore. Previous studies have not characterised SCC or BD in our local context according to clinical subtype or histological differentiation.

### Materials and Methods

A retrospective study of patients with histologically proven SCC and BD seen at the NSC over 2 years (January 2002 to December 2003) was conducted by reviewing case records. The NSC is a tertiary referral centre in Singapore for dermatological diseases. Patients with more than one type of primary skin cancer were categorised under the respective types. A standard proforma was used for data entry. Examples of data items include occupation of patient, anatomic site of the lesion and histological differentiation. Statistical analysis was performed using SPSS version 11. Comparisons of differences between groups were done

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using Chi-square and 2-sample *t*-tests. A *P* value of <0.05 was considered statistically significant.

**Results**

*General*

There were a total of 161 patients studied in the 2-year period from 2002 to 2003. Of these, 81 patients had biopsy-proven SCC and 68 patients had biopsy-proven BD while 12 patients had lesions of both SCC and BD. Some patients had multiple tumours – 8 patients had >1 SCC and 10 patients had >1 BD documented over the 2-year period. In all, there were 199 biopsy-proven tumours, of which 105 were SCC and 94 were BD.

*Demographics (Figs. 1 and 2)*

*SCC (n = 93)*

Patient age averaged 72.9 years (range, 40 to 95). There was a higher proportion of males compared to females, with 66 males and 27 females. Ethnic distribution showed a predominance of Chinese, with 86.0% Chinese and 11.8% Caucasians. There were no Malays or Indians in our series, though they make up 14% and 8% of our population, respectively.<sup>4</sup>

*BD (n = 80)*

Patient age averaged 66.8 years (range, 32 to 95). There was a higher proportion of males compared to females, with 48 males and 32 females. Ethnic distribution was 85% Chinese, 5% Malays and 1.2% Indians.

*Predisposing Factors*

*SCC (n = 93)*

Three patients had previous radiotherapy (DXT) – one to the neck for lymphoma, another to the pelvic region for

bladder malignancy and the third had total skin electron-beam therapy for mycosis fungoides (MF) a few months prior to tumour development on the thigh. This patient had also had previous psoralen ultraviolet A (PUVA) therapy for MF in the 1980s. Tumours from the first 2 patients were not at sites of DXT but were found on the scalp and cheek respectively. Six patients (6.5% of total) had a history of exposure to arsenic. Three of them had taken traditional Chinese medication containing arsenic for asthma in their youth, and 1 had drunk well-water from rural Singapore in the past. The two remaining patients had characteristic clinical manifestations of arsenic poisoning but the source of arsenic exposure could not be determined. None of our patients had a positive family history of skin cancer. Among the patients, 12.9% had a previous history of SCC, 8.6% had previous BCC, 5.4% had previous BD and 1 patient had melanoma previously. Seventy-two per cent had no prior history of cancers. Five patients had a history of previous phototherapy for psoriasis but duration of treatment could not be determined. Four patients were on immunosuppressive therapy – 2 patients had previous renal transplants and 1 was on cyclophosphamide and prednisolone whilst the other patient’s medications could not be determined; 1 patient was on chemotherapy for thyroid carcinoma; and 1 patient was on chemotherapy for chronic lymphocytic leukaemia (CLL). Finally, 15 patients (16.1%) were documented to have had heavy sun exposure in the past.

*BD (n = 80)*

One patient (1.3% of the total) had previous DXT for cervical cancer, but the site of the skin tumour was the cheek. Ten patients (12.5% of the total) had a history of arsenic exposure – 6 from TCM, 2 from well water locally, and 2 undeterminable. Smoking history was not taken in 96% of cases and none of these patients had a positive family history of skin cancer. Ten per cent had a previous history of BD, 3.8% had SCC history, 5.0% had BCC history whilst 77.5% had no prior history of cancers. Six patients had had previous phototherapy for psoriasis, 1 patient was on methotrexate for psoriasis and 1 patient was on chemotherapy for CLL. Eight patients (10%) were documented to have had heavy sun exposure in the past.

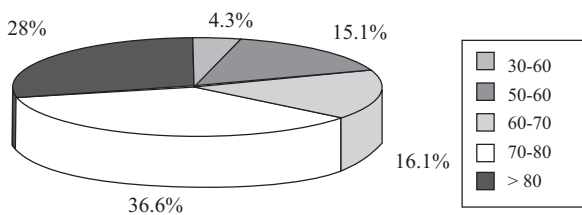


Fig. 1. Patient distribution by age group in squamous cell carcinoma.

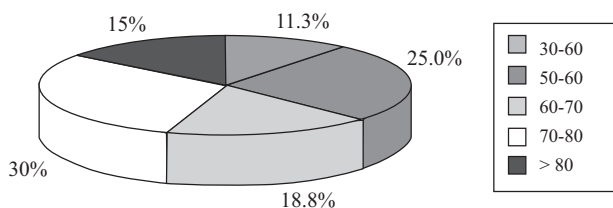


Fig. 2. Patient distribution by age group in Bowen's disease.

*Tumour Characteristics*

*SCC (n = 105)*

The mean duration of tumour before presentation to our centre was 21.2 months (range, 0.1 to 360). Among these patients, 58.1% had no symptoms recorded, whilst 21.9% had itch, 15.2% had pain and 16.2% complained of bleeding from the tumour (Table 1). The mean size of the tumour was 19 mm (range, 4 to 60) for 68 cases, whilst size was not documented in the history taking in 37 cases. The majority

were primary tumours (98 cases), whilst 5 cases were recurrences and 2 had arisen from existing skin lesions (actinic cheilitis and chronic ulcer). The commonest site (Table 2) was the head and neck, with 41% of tumours represented. Other sites in descending order of frequency were the upper limbs (23.8%), lower limbs (17.1%), trunk (14.3%) and genitalia (3.8%). Histologically, well-differentiated tumours comprised the majority (89.5%), 6.7% were moderately-differentiated, and 1.9% or 2 cases were poorly-differentiated tumours. Two cases (1.9%) were reported as being of the acantholytic subtype, whilst there were none reported as undifferentiated or anaplastic. No other subtypes of SCC were reported. None of the 105 SCCs had metastasised, which was determined by clinical examination for lymphadenopathy. Pearson's correlation coefficient between size of tumour and duration of symptoms was 0.431, which was significant ( $P = 0.001$ ).

Table 1. Reported Symptoms

Symptoms	SCC (%)	BD (%)
Itch	23 (21.9)	15 (16)
Pain	16 (15.2)	11 (11.7)
Bleeding	17 (16.2)	9 (9.6)
Others	4 (3.8)	0 (0)
Nil	61 (58.1)	68 (72.3)

BD: Bowen's disease; SCC: squamous cell carcinoma

Table 2. Sites of Involvement of Squamous Cell Carcinoma (SCC) and Bowen's Disease (BD)

Site	SCC (%) n = 105	BD (%) n = 94
Head and neck	43 (41.0)	27 (28.7)
- scalp	8 (7.6)	1 (1.1)
- forehead	4 (3.8)	6 (6.4)
- temple	3 (2.9)	7 (7.4)
- periorbital	1 (1.0)	0
- ear	5 (4.8)	1 (1.1)
- cheek	13 (12.4)	10 (10.6)
- nose	1 (1.0)	2 (2.1)
- philtrum/lips	4 (3.8)	0
- jaw	3 (2.9)	0
- neck	1 (1.0)	0
Trunk	15 (14.3)	18 (19.1)
Upper limbs	25 (23.8)	24 (25.5)
Lower limbs	18 (17.1)	23 (24.5)
Genitalia	4 (3.8)	2 (2.1)

### BD (n = 94)

The mean duration of lesions before presentation to our centre was 39.9 months (range, 0.5 to 360). Of the patients, 72.3% had no symptoms recorded, whilst 16% had itch, 11.7% had pain and 9.6% complained of bleeding from the lesion (Table 1). The mean size of the lesions was 18.5 mm (range, 3 to 50) for 49 cases, whilst size was not documented in the remaining 45 cases. The majority were primary tumours (91 cases), whilst 3 cases were recurrences. The commonest site (Table 2) was the head and neck region (27 cases, 28.7%). Other sites, in descending order of frequency, were the upper limbs in 25.5%, lower limbs in 24.5%, the trunk in 19.1% and genitalia in 2.1%. None of the 94 tumours had metastasised. Pearson's correlation coefficient between size of tumour and duration of symptoms was 0.273, which was not significant ( $P = 0.066$ ).

### Management

#### SCC (n = 105)

Of the 105 tumours, 57 (54.3%) were diagnosed by punch biopsy, 36 (34.3%) by excisional biopsy, 1 (1.0%) by incisional biopsy and 10 (9.5%) by shave biopsy. One patient, who had a 60-mm tumour on the dorsum of the hand, was referred directly to the plastic surgery department in a different hospital following biopsy for further management before waiting for histological confirmation as the tumour was very clinically suggestive of SCC. Twenty-two cases (21.0%) were initially not diagnosed as SCC till histological confirmation was made. Examples of clinical diagnoses made prior to histological confirmation were basal cell carcinoma (Figs. 3 and 4), actinic keratosis, melanoma, keratoacanthoma and viral wart. The treatment in the majority of cases was by excision (88 cases, 83.8%). Other treatment modalities included DXT (1 case) and curettage (1 case). One patient had SCC on the big toe, which was amputated. Thirteen patients were referred to surgical departments for excision therefore further details on their management were unavailable. One patient refused any treatment and defaulted. Of the 88 who had excisions done at our centre, clearance of margins was achieved in 79 cases (89.8%). In 4 cases (4.6%), margins were not clear, and in 5 cases (5.7%), margin clearance was not indicated but the patients were closely followed up subsequently. In 13 cases (12.4%), SCC was clinically diagnosed as actinic keratosis or seborrhoeic keratosis initially, and treated with cryotherapy. Biopsies done at a later stage, upon failed treatment or recurrence of the lesion, subsequently revealed SCC.

#### BD (n = 94)

Of the 94 tumours, 70 (74.5%) were diagnosed by punch biopsy, 17 (18.1%) by excisional biopsy and 7 (7.5%) by



Figs. 3 and 4. A 92-year-old Chinese lady with squamous cell carcinoma on philtrum.

shave biopsy. Thirteen cases (13.9%) were initially not diagnosed as BD till histological confirmation was made. Examples of clinical diagnoses made prior to histological confirmation were basal cell carcinoma, actinic keratosis and keratoacanthoma. The treatment in the majority of cases was by excision (58, 61.7%). Other treatment modalities included cryotherapy (14, 14.9%), topical 5-fluorouracil (5-FU) (6, 6.4%), imiquimod (5, 5.3%), curettage followed by CO<sub>2</sub> laser ablation (2, 2.1%), curettage alone (1, 1.1%), CO<sub>2</sub> ablation alone (1, 1.1%) and shave excision (1, 1.1%). One patient had a labia majora lesion and was referred to the gynaecology department in another hospital for management. Four patients defaulted and were lost to follow-up. Of note were 3 patients who failed treatment with cryotherapy – 2 of them eventually had surgical excision whilst 1 had treatment with 5-FU. Of the 58 who had excisions done at our centre, clearance of margins was achieved in 53 cases (91.4%), whilst in 2 cases (3.5%) margins were not clear, and in 3 cases (5.2%), margin clearance was not indicated but the patients were followed up closely subsequently.

## Discussion

BD or SCC-in-situ is a cutaneous malignancy first described by Bowen in 1912.<sup>5</sup> The normal presentation is that of an asymptomatic, slowly growing, sharply defined erythematous scaly plaque. It typically occurs in the sun-exposed areas of fair-skinned patients older than 60 years. Three to eight per cent of untreated cases may progress to invasive carcinoma although controversy still exists about its true malignant potential. Various modalities for treatment of BD have been described, including cryotherapy, curettage and cautery, surgical excision, laser ablation, photodynamic therapy (PDT), topical 5-FU and topical imiquimod.<sup>6</sup> Its invasive counterpart, SCC, is a malignant tumour arising from the keratinocytes of the epidermis. It is the second most common skin cancer worldwide after BCC. However,

due to its greater tendency to recur and metastasise, SCC causes the majority of deaths among non-melanoma skin cancers (NMSCs).<sup>7</sup> Sun exposure has been established as a significant risk factor for SCC (as well as BCC and melanoma), and it has been proposed that simple use of sunscreen during childhood could decrease the lifetime incidence of NMSCs by 78%.<sup>8</sup> Additionally, models for SCC risk demonstrate that a 1% increase in ultraviolet light exposure increases risk by about 2%.<sup>9</sup> The management of invasive SCC in node negative patients is usually surgery. DXT is a non-surgical modality that can be considered for patients who are poor surgical candidates, or for inoperable tumours. In addition, Mohs micrographic surgery is fast becoming the standard of care for high-risk node negative SCC.<sup>7</sup>

The data from this retrospective study on SCC and BD reveal an under-representation of affected Malays and Indians as compared to census studies on the population of Singapore.<sup>4</sup> Differences in skin type and sociocultural differences leading to varying environmental exposure to UV radiation may account for this. The profile of patients with SCC was largely similar to those with BD, a key difference being an older average age (mean of 72.9 years compared with 66.8 years). The demographic data of BD and SCC show that both tumours occur most frequently on the head and neck region of elderly men and both have a tendency towards slow growth. Most patients are asymptomatic, but others complain of itch as their primary symptom, followed by bleeding and pain.

Arsenic exposure is an established risk factor for the development of SCC and BD. This is of particular relevance in our local context given that there were 6.5% (6 of 93) and 12.5% (10 of 80) of patients with SCC and BD, respectively, with a history of arsenic ingestion. These patients tended to have multiple tumours which had developed at a younger age than the mean for the whole cohort. In particular, the

youngest patient in our study was a 32-year-old Chinese female who had taken traditional Chinese medication for asthma in childhood and had multiple Bowen's tumours on her arms. Drinking water from wells was a practice of the past when kampongs (native settlements) existed in Singapore.

An alarming statistic is the long delay in consulting a physician shown by patients in the study, with a mean of 21 months and 40 months for SCC and BD, respectively. Possible explanations could be the lack of symptoms in these tumours, the slow-growing nature of the tumours, as well as the possible aversion seen in elderly patients in Singapore towards consulting a physician. An additional reason is public ignorance of the significance of the tumour. This highlights the need for greater public education to increase awareness of these skin cancers and to stress the importance of early treatment to prevent spread and increased morbidity. The limitation of our study was the short analysis period of 2 years, which did not allow us to look at recurrence rates after treatment.

From a clinical standpoint, these cancers may be mistaken for benign neoplasms such as seborrhoeic keratoses and viral warts, thus highlighting the need for clinicians to have a high index of suspicion in the elderly patient and to be especially vigilant to the presence of risk factors such as excessive sun exposure and arsenic exposure. As incidences of SCC and BD increase worldwide, it is important for

healthcare providers to be adept at recognising these NMSCs and managing them.

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