Squamous cell carcinoma in the Afro-Caribbean community: an 11-year retrospective study

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Abstract

Background: Squamous cell carcinoma (SCC) is considered the most frequent skin cancer in black people. Its incidence is not known in the Afro-Caribbean population.

Objective: To assess the incidence of SCC in Guadeloupe, the largest island of the Lesser Antilles (405 000 inhabitants, mostly black people of African and European descent). The second objective was to characterize clinical and histological patterns of SCC occurring in the Afro-Caribbean community.

Methods: This retrospective study was conducted over an 11-year period (2000-2010). Data regarding 723 histological confirmed cases of SCC identified using the three Guadeloupean pathology laboratories computerized databases were retrieved from the records of 551 patients. Private practice dermatologists and general practitioners were contacted to obtain any missing data.

Results: The annual age-adjusted incidence of SCC was 15 per 100.000 residents in Guadeloupe. In the Afro-Caribbean community, SCC had a greater size (i.e.: 2.8±2.8 cm versus 1.5±1.0 cm, $p<0.001$), was more often located on the anogenital area (i.e. :48/79-60.8% versus 14/320-4.4%, $p<0.001$) in association with an underlying dermatosis due to HPV infection (15/71- 21.1% versus 3/366, 0.8%, $p<0.001$) and led more frequently to metastasis (13/84-15.5% versus 10/366-2.7%, $p<0.001$) and/or fatal evolution (11/83-13.3% versus 7/365-1.9%, $p<0.001$).

Conclusions: The results of this original study, which first estimated the incidence of SCC in West Indies, suggest that anogenital examination should be routinely performed in skin cancer screening of Afro-Caribbean people in order to detect the presence of SCC at an early stage.

Implication for practice

Squamous cell carcinoma is the most frequent skin cancer in black people. Its incidence is not known in the Afro-Caribbean population. In Guadeloupe, the largest island of the Lesser Antilles, the annual age-adjusted incidence of SCC was estimated to be 15.0 per 100,000 residents, 95% CI:[13.8; 16.2]. In the Guadeloupean Afro-Caribbean community, SCC seems to more frequently occur in the anogenital area, due to HPV infection. These results support to include a routine genital urinary examination in the skin cancer screening of people of Afro-Caribbean descent.

Abbreviations used:

POC: people of color

SCC: squamous cell carcinoma

HPV: human papilloma virus

UVR: ultraviolet rays

NMSC: non melanoma skin cancer

CF: common form (of SCC)

BD: Bowen disease or in situ SCC

KA: keratoacanthoma

VC: verrucous carcinoma

CI: confidence interval

PCR: polymerase chain reaction

Introduction

Although squamous cell carcinoma (SCC) is less common in people of color (POC) than in the white population it is the most frequent skin cancer in black persons, representing 30 to 65% of skin cancers in this population[1-10].

SCC (or epidermoid carcinoma) most commonly occurs on sun-exposed areas in white people [11] whereas it is frequently located on sun protected sites (i.e.: lower limbs or anogenital area) in black people[1-10, 12-15]. In fact additional factors other than UV radiation have been identified as major etiologic triggers in the development of SCC in the black population[1-6, 8,9,12]: i.e. chronic scarring caused by chemicals, thermal burns or skin ulcers as well as inflammatory processes such as lupus erythematosus and hydradenitis suppurativa. Moreover, high risk human papillomaviruses (HRHPV) have now been identified due to their implication in the development of anogenital SCC although specific studies focusing on POC have, to our knowledge, not yet been reported in the literature[16].

Though SCC is less common in Black rather than in Caucasian people, the mortality rate, in this population, is still high, ranging from 17% to 30% depending on the series[1,2,4,17].These data underline the need for prevention, early detection and treatment of SCC in the African American and Afro-Caribbean communities.

The current incidence of SCC among Afro-Caribbeans is difficult to estimate because non melanoma skin cancers (NMSC) are not consistently reported in most national or regional tumor registries. Moreover, cancer registries are not common in the Caribbean and only recently have become available for consultation in the French West Indies.

Therefore, we were prompted to retrospectively study SCC occurring in Guadeloupe, an overseas department of France which is the largest island of the Lesser Antilles within the

West Indies (405 000 inhabitants, mostly black people of African and European descent), over an 11-year period. Our aims were first to evaluate the incidence of skin and mucous SCC in residents of Guadeloupe and second to study the clinical and histological characteristics of SCC in Afro-Caribbeans.

Patients and methods

Study design

This retrospective study was conducted from the 1st January 2000 to the 31th December 2010 within the French overseas department of Guadeloupe. Histological confirmed cases of skin and mucous SCC were retrieved from the computer database of the three Guadeloupean pathology laboratories, using DIAMIC software (Infologic Santé-Châteauneuf-sur-Isère-France).

Inclusion criteria were the following: i) histological diagnosis of SCC or Bowen disease ii) excision during the study period iii) residence within the department of Guadeloupe at the date of histological diagnosis. Albinism (phototype 0) was an exclusion criteria because it represents a genetic disorder as were pediatric cases.

Data collection

All pathological records were reviewed in order to retrieve demographic data of patients (i.e. age, gender) clinical features of SCC (i.e. site, size) and pathological characteristics (i.e. histological type, degree of cytological differentiation, associated dermatosis, node or systemic metastasis). Main SCC locations were distributed among 5 representative areas: face and neck, upper limbs, lower limbs, trunk and back, and anogenital

area. Histological types were divided as follows: common form of SCC (CF), SCC in situ or Bowen disease (BD), keratoacanthoma (KA) and verrucous carcinoma (VC). Associated dermatoses mentioned in the pathology records were divided into: HPV induced lesions (condyloma or morphological HPV infection with koilocytes), chronic leg ulcer, scar, lichen sclerosus and others. For SCC located on the anogenital area, HPV genotyping analysis was collected when available.

Clinical data of patients (i.e.: phototype, previous medical history of skin cancer and of HIV infection, intentional sun exposure, death in relationship with SCC) were obtain in medical records by contacting private practice dermatologists and general practitioners. HIV status of patients was also recorded from the HIV regional computer database.

Statistical analysis

Data were recorded using EPI INFO software. Results were presented as the mean ±standard deviation (SD) for continuous variables and as numbers and frequencies for categorical variables. Student's t-test and Chi-square or Fisher's exact tests were used, where appropriate, to compare continuous and categorical variables between patients with phototypes V or VI representing Afro-Caribbeans and patients with phototypes I to IV. Incidence rates were calculated with a confidence interval of 95%. Age-adjusted incidence rates were calculated using the references from IARC[18]. For all analyses, two-sided p-values of less than 0.05 were considered statistically significant. Data management and statistical analysis were performed using SPSS 21.0 software (IBM SPSS Statistics, Chicago, IL.).

The Ethics Committee for non-interventional research of Rouen University Hospital approved this retrospective study (Registration number: E 2015-41).

Results

Incidence of SCC in Guadeloupe

We identified 738 SCC that occurred in 566 patients during the study period. Of these, 15 patients living in the territorial collectivity of St Martin were excluded because this island is currently separated from the Guadeloupe administrative department. A total of 723 cutaneous and mucous SCC from 551 patients fulfilling the inclusion criteria were taken into account for incidence rates 'calculation. Crude and age-adjusted annual incidence rates were estimated to 16.5(95% CI: [12.5; 20.5]) and 15.0 per 100.000 (95% CI :[13.8 ; 16.2]) residents in Guadeloupe respectively. Age-adjusted and crude incidence rates according to gender and histological types of SCC are indicated in Table I.

Demographics data of the 551 patients

The main demographic characteristics are summarized in Table II. At the date of SCC histological diagnosis, the 551 patients had a mean age of 65 ± 15 years (range 15-99 years). Sex ratio was 1.1 (M: 287/F: 257, missing data for 7 patients). Intentional sun exposure and previous medical history of skin cancer were reported for 94/147 (64%) and 96/192 (50%) patients for whom information could have been collected, respectively. Fifteen patients (2.7%) had a positive HIV status. Death in relationship with SCC was reported for 13/538 (2.4%) patients. Finally, 327 phototypes were collected (i.e.: albinos: n=4, phototype I: n=4, phototype II: n=73, phototype III: n=127,phototype IV: n=39, phototype V: n=67, phototype VI: n=13).

Pathological data of SCC

Table III shows the main pathological features of the 723 SCC representing the entire series. "Face and neck" was the most reported location of SCC with a mean size of 1.8 ± 1.9

centimeters (cm). The most frequent types of SCC were KA (43.3%)(fig 1) and CF (42.9%) with a high degree of differentiation in most cases (94.5%). An underlying skin dermatosis was associated to 59/704 informed SCC (8.4%) including HPV induced lesions (n=21), chronic leg ulcers (n=6), scars (n=5), lichen sclerosus (n=5) and other dermatoses (n=22) (i.e.: ichthyosis, radiodermatitis, chronic inflammation, missing data n=6). Squamous cell carcinoma led to complications in 27 cases of node or systemic metastases (27/712: 3.8%).

SCC in the Afro Caribbean community

Eighty-four SCC occurred in 80 patients, 38 men, 41 women (missing data for one patient) with phototype V or VI, representing Afro-Caribbeans. The most frequent type of SCC in the Afro-Caribbean population was the CF (45.2%) and mean size of the tumor was 2.8± 2.8 cm. Location of the tumor was well-informed in 79 cases: i.e.: anogenital area (n=48), face and neck (n=10), trunk (n=9), upper limbs (n=4), lower limbs (n=8). HIV status was positive for 7/15 Afro-Caribbean patients. Interestingly, HIV seropositive patients had more often a SCC located on the anogenital area than patients with a negative HIV status (i.e.: 7/39 versus 0/29, p=0.039). An underlying dermatosis was reported in 21/71 informed SCC (29.6%), mostly condyloma or morphological HPV infection (n=15, 71.4%). Data on HPV genotyping analysis were available for 10 anogenital SCC from 9 Afro-Caribbean patients. The high risk HPV type distribution was as follows: HPV 16 (n=4), HPV18 (n=2), HPV 31 (n=1), HPV 33 (n=1), HPV 35 (n=1), HPV 51 (n=1). Finally, 11/79 (13.9%) Afro-Caribbean patients for whom this information was available had a fatal evolution.

Comparison between Afro-Caribbean patients and patients with phototypes I to IV is shown in table IV. In the Afro-Caribbean's group, SCC had a greater size (i.e.: 2.8±2.8 cm versus 1.5±1.0 cm, $p<0.001$),was more often located on the anogenital area (ie:48/79-60.8% versus 14/320-4.4%, $p<0.001$) in association with an underlying dermatosis due to HPV (15/71-

21.1% versus 3/366, 0.8%, p<0.001), led more frequently to metastasis (13/84-15.5% versus 10/366-2.7%, p<0.001) and/or a fatal evolution (11/83-13.3% versus 7/365-1.9%, p<0.001).

A lower frequency of intentional sun exposure (8/26-30.8% versus 86/117-73.5%, p<0.001) and of past history of skin cancer (2/27-7.4% versus 67/136- 49.3%, p<0.001) also characterized Afro-Caribbean patients.

Discussion

To our knowledge, this11-year population-based study, conducted on Guadeloupe Island with focus on the Afro-Caribbean community, is the first epidemiological study on SCC in the Caribbean.

The study shows a high SCC annual age-adjusted incidence rate of 15.0 per 100 000 residents (men: 16.9/women:12.5). The exhaustiveness of these results is assured by current practice of Guadeloupean dermatologists and surgeons who routinely direct all suspected cases of SCC samples to the three pathology laboratories of the island. This incidence rate is considerably higher than that of 3 per 100 000 inhabitants currently reported in black people [19,20]. Nonetheless it is similar to SCC annual age-standardized incidence rate previously reported in South Africa (i.e.: men: 20.8/women: 8.5) whose population is as intermixed as that of Guadeloupe island [21]. As expected the SCC incidence rate calculated in our study is still lower than that of SCC in Caucasians reported to be 100 to 300 per 100 000 in white Americans, and about 30 per 100 000 in Northern Europe [11,19-27].

As regards the demographic characteristics of our series, sex ratio and mean age of patients are similar to that previously reported in the largest series of SCC in black

people[28]from Africa due to the composition of the Guadeloupean population (i.e.: 90% of African descent [29]).

Interestingly, the most frequent form of SCC found in our study was KA (43%) with an incidence rate that was almost equal to that of CF (i.e.: 6.6 per 100,000 population and 6.3 per 100,000 population respectively) whereas the commonly reported KA versus SCC incidence ration is 1/3. Chuang et al. previously published adjusted age incidence rates of KA and SCC with a ratio similar to our (i.e.:104 cases per 100,000 persons per year for KA and 118 cases per 100,000 persons per year for SCC)[30,31]in white residents of Hawaii. In the light of this Caucasians focused study, we found that KA was the most common form in patients with phototypes II and III (i.e.: 143/179:80%), the largest group of patients with informed phototypes of our series (i.e.:200/327: 61%). It is likely that the KA/SCC ratio found in our study was in related to this unequal distribution.

The main result of our study is the description of a SCC Afro-Caribbean pattern. In the present series as in previously reported studies on black patients, SCC rarely occurred in relationship with intentional sun exposure or located in sun exposed areas. Moreover, we found that the most affected site was the anogenital area representing 48/79: 61% of the SCC locations in black patients of our series whereas the current prevalence of the anogenital area damage in black people is 10% to 23%[2,6]. It is likely that this high prevalence of anogenital area location was due to HPV infection which was identified in 21% of SCC in Afro-Caribbeans versus 0.8% in other patients of our series. In fact, HPV designated as "high risk" (HR) types are implicated in approximately 30 to 90 % of anogenital cancers other than cervix[16] and are highly prevalent in Caribbeans (i.e.:36% in Guadeloupe to 57% in English speaking islands in healthy individuals)[32,33]. Interestingly HR HPV type distribution of our samples was not exclusively focused on current types 16 and 18 but implicated other HR HPV

types (i.e.: 31,33,35,51) according to recent reports from the African Caribbean Cancer Consortium[32, 34-35]. As reported in the literature, positive HIV status was significantly associated with HRHPV infections since all HIV seropositive Afro-Caribbean patients had a SCC located on the anogenital area [36].

A high mortality rate of 13.9% was recorded in Afro-Caribbeans with SCC of our series whereas it was estimated to be 0.8% for the other patients ($p<0.001$). These results are in accordance with the literature data where the mortality rate ranges from 17% to 29% depending on the series. As this higher mortality rate was associated with a higher prevalence of metastasis (15.5% versus 2.7% , $p<0.001$) and a greater tumor size (2.8±2.8 cm versus 1.5±1.0 cm, $p<0.001$), this may be relative not only to more natural aggressiveness of SCC in Black people but may also reflect a later diagnosis and consecutive more advanced disease[37]. These data underline the role of prevention, early detection and treatment of SCC in the African American and Afro-Caribbean communities and emphasizes the need for physicians to be more familiar with SCC in Black people [6].

The limitations of our study are primarily due to its retrospective design. Patients and physicians were contacted to collect clinical data such as phototype, intentional sun exposure, past history of skin cancer, etc.. Unfortunately, as the histological diagnosis of SCC went back 11 years ago in some cases, missing clinical data were numerous except for HIV status of the series that could be retrieved from the regional computer database.

Overall the present study showed the occurrence of a high frequency of anogenital area location of SCC in Afro-Caribbean people, probably related to the high prevalence of HPV

infection in Caribbeans. Moreover, this study confirmed the high mortality rate of SCC previously reported in people of African ancestry from other countries. These findings suggest that a genital urinary examination in the skin cancer screening of black people of Afro-Caribbean descent should be routinely performed in order to detect the possible presence of SCC at an early stage, particularly in cases of a positive HIV status.

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Figures legend

Fig 1. Penile squamous cell carcinoma in an Afro-Caribbean patient.

SCC of the foreskin discovered during a routine examination for skin cancer screening in an Afro-Caribbean patient.

Fig 2. Keratoacanthoma in an Afro-Caribbean patient referred for this nasal lesion to the private practice dermatologist.

Table I. Incidence of SCC in Guadeloupe from 2000 to 2010 according to gender and histological types.

Type of SCC	Number of cases	Crude Incidence	95 CI%	Age-adjusted Incidence	95 CI%
All forms	**723**	**16.5**	**[12.5 ; 20.5]**	**15.0**	**[13.8 ;16.2]**
Male	409	19.8	[13.5 ; 26.2]	16.9	[15.0 ; 18.8]
Female	305	13.2	[8.3 ; 18.1]	12.5	[11.0 ; 14.0]
Common Form (CF)	**310**	**7.1**	**[4.5 ; 9.7]**	**6.3**	**[5.5 ; 7.1]**
Male	198	9.6	[5.2 ; 14.0]	8.0	[6.6 ; 9.3]
Female	108	4.7	[1.7 ; 7.6]	4.4	[3.6 ; 5.3]
Keratoacanthoma (KA)	**313**	**7.2**	**[4.5 ; 9.8]**	**6.6**	**[5.8 ; 7.4]**
Male	159	7.7	[3.7 ; 11.7]	6.8	[5.6 ; 8.0]
Female	149	6.5	[3.0 ; 9.9]	6.1	[5.1 ; 7.1]
In situ-BD	**76**	**1.7**	**[0.4 ; 3.0]**	**1.6**	**[1.2 ; 2.0]**
Male	32	1.5	[0.0; 3.3]	1.3	[0.8 ; 1.8]
Female	44	1.9	[0.0 ; 3.8]	1.8	[1.3 ; 2.4]

Table II. Demographic data of the 551 patients of the series

Age		65 years ± 15
Sex ratio (Male/Female)		1.1 (287/257)
Intentional sun exposure		94/147 (64%)
Previous medical history of skin cancer		96/192 (50%)
Phototype (n=327)	0	4 (1.2%)
	I	4 (1.2%)
	II	73 (22.3%)
	III	127 (38.9%)
	IV	39 (11.9%)
	V-VI	80 (24.5%)
HIV positive status		15 (2.7%)
Death in relationship with SCC		13/538 (2.4%)

Table III: Pathological data of the 723 SCC of the series

Type of SCC	Common form	310 (42.9%)
	Keratoacanthoma	313 (43.3%)
	In situ-BD	76 (10.5%)
	Verrucous SCC	18 (2.5%)
	Others	6 (0.8%)
Size of SCC (cm)		1.8 +/- 1.9
Site of SCC (n=648)	Face and neck	248 (38.3%)
	Upper limbs	130 (20.1%)
	Trunk	98 (15.1%)
	Lower extremities	93 (14.3%)
	Anogenital area	79 (12.2%)
Associated skin disease (59/704 : 8.4%)		
	HPV induced lesions	21
	Chronic ulcer	6
	Scars	5
	Lichen sclerosus	5
	Other	16
Cytological differentiation (n=703)	high	664 (94.5%)
	Medium	25 (3.6%)
	Low	14 (2.0%)
Perinervous invasion		1/705 (0.1%)

Local recurrence	15/711 (2.1%)
Node or systemic invasion	27/712 (3.8%)

Table IV: Comparison of SCC clinical and histological data between patients with phototypes V-VI representing Afro-Caribbeans and patients with phototype I to IV.

		phototypes V/VI	phototypes I/II/III/IV	p
Patients / SCC : **N**/n		**80**/84	**243**/368	
mean age (years)		**64.7±16.1**	**66.1±14.8**	**p=0.470**
sex ratio (M/F)		**0.93 (38/41)**	**1.08 (126/117)**	**p=0.562**
previous medical history of skin cancer		**2/27 (7.4%)**	**67/136 (49.3%)**	**p<0.001**
intentional sun exposure		**8/26 (30.8%)**	**86/117 (73.5%)**	**p<0.001**
SSC histological type	CF	38 (45.2%)	164 (44.6%)	p=0.911
	KA	17 (20.2%)	161 (43.8%)	p<0.001
	BD	17 (20.2%)	36 (9.8%)	p=0.007
	VC	8 (9.5%)	6 (1.6%)	p<0.001
SSC mean size (cm)		2.8± 2.8	1.5± 1.0	p<0.001
SSC site		n=79	n=320	
head and neck		10 (12.7%)	139 (43.4%)	p<0.001
trunk		9 (11.4%)	48 (15.0%)	p=0.412
upper limbs		4 (5.1%)	74 (23.1%)	p<0.001
lower limb		8 (10.1%)	45 (14.1%)	p=0.356
anogenital area		48 (60.8%)	14 (4.4%)	p<0.001
HPV underlying dermatosis		15/71 (21.1%)	3/366 (0.8%)	P<0.001

high degree of cytological differentiation	73/79 (92.4%)	343/358 (95.8%)	P=0.240
metastasis	13/84 (15.5%)	10/366 (2.7%)	p<0.001
SCC with fatal evolution	11/83 (13.3%)	7/365 (1.9%)	p<0.001