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Cutaneous Squamous Cell Carcinoma: A 7-year Review

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Abstract

Introduction: Cutaneous squamous cell carcinoma (SCC) is rare in sub-Saharan Africa. In Senegal, its prevalence was estimated at 0.09% in 2004. It occurs most frequently in pre-neoplastic acquired or genetic dermatoses. The aims of this study were to describe the epidemiological, clinical and therapeutic aspects of SCC, and to identify associated risk factors.
Methodology: This was a descriptive cross-sectional study in the Oncology Department at the Joliot Curie Institute of the Aristide Le Dantec Hospital over a 7-year period (January 2015 to December 2021). We included all patients hospitalized and followed up for SCC. The diagnosis was confirmed by histopathology. Data entry and analysis were performed using epi-info software version 7.2.5.0 and Excel 365.
Results: We recorded 189 cases of SCC, representing an incidence of 24 cases per year and a hospital frequency of 0.77%. The mean age was 51 and the sex ratio 1.28. The ulcero-budding form was predominant in 67.2% of cases. The majority of lesions were located on the lower limbs (30.6%) and 28.4% on the cephalic extremity. Squamous cell carcinoma was well-differentiated in 49.2%. Metastases were present in 40.2%. Pre-neoplastic dermatoses were noted in 28.6%. These were burn scars in 43%, chronic ulcer in 23.39%, discoid lupus in 2%, Buschke Lowenstein tumor in 4%. Geno dermatoses included albinism in 6 cases and xeroderma pigmentosum in one. Voluntary use of depigmenting cosmetics was noted in 11 cases. Patients underwent surgery in 32.3%, radiotherapy in 8.5% and chemotherapy in 32.8%. Favorable progression was in 20.6%. Recurrence was noted in 2 cases, metastasis in 3 and death in 5.
Conclusion: Squamous cell carcinoma remains a serious tumor in Africa. There is a delay in diagnosis, with some tumors being very advanced. Early surgical management is the main factor in curing the cancer.

Keywords: epidemiology; cutaneous squamous cell carcinoma; senegal

Introduction

Cutaneous squamous cell carcinoma (SCC) is a malignant tumoral proliferation of keratinocytes in the spinous layer of the epidermis [1]. Epidemiologically, it is characterized by its rarity in people with a pigmented phototype (phototype V and VI). In 2001, studies carried out in Senegal over a 20-year period estimated the prevalence of SCC at 0.09% [2]. This rarity is explained by the protective effect of melanin against the sun's ultraviolet (UV) rays. SCC occurs most frequently in acquired or congenital pre-neoplastic dermatoses [2]. In people with a light phototype (phototype I and II), SCC occurs almost exclusively on photo-exposed areas, and most often develops on actinic keratoses [3,4]. The incidence of SCC varies worldwide, accounting for 20% of all skin cancers [1]. On white skin, its incidence is estimated at 150 to 360 per 100,000, while on black skin it is 3 cases per 100,000 in the United States [5,6]. In sub-Saharan Africa, the occurrence of squamous cell carcinoma in women undergoing voluntary cosmetic depigmentation is often reported in the literature [7,8]. SCC has an aggressive local course, with a high metastatic potential due to its lymphophilic nature [9]. Several series have reported the worse prognosis of squamous cell carcinoma in subjects with pigmented skin, with a metastatic risk of 20 to 40% compared to the light phototypes of the order of 1 to 5% [10]. The aims of this study were to describe the epidemiological, clinical and therapeutic aspects of cutaneous squamous cell carcinoma, and to identify associated risk factors.

Patients and Method

This was a retrospective cross-sectional study carried out over a 7-year period from January 1er 2015 to December 31, 2021 in the oncology department of the Joliot Curie Institute at Aristide Le Dantec

Hospital. This department is the reference center for cancer care in Senegal. We included all patients hospitalized and followed up as outpatients for cutaneous squamous cell carcinoma. The diagnosis of cutaneous squamous cell carcinoma was confirmed by histopathology. A questionnaire was used to collect epidemiological, clinical, therapeutic and evolutionary information. Data entry and analysis were performed using epi-info software version 7.2.5.0 and Microsoft Excel 365.

Results

We collected 189 cases of cutaneous squamous cell carcinoma, representing an incidence of 27 cases per year. The hospital incidence rate was 0.77%. Figure 1 shows the annual distribution of cutaneous squamous cell carcinomas. The mean age was 51 years, range: 7–92 years. Figure 2 shows the age distribution of patients. Patients were female in 106 cases (56.1%) and male in 83 cases (43.9%), i.e., a sex ratio of 1.28. The geographical origin of the patients was Senegal in 184 cases, Gambia in 2 cases, Guinea Conakry in 2 cases and Cape Verde in one case. Table 1 shows the distribution of cases by geographical origin in Senegal. The average consultation time was 20 months, with extremes of 1 month and 20 years. Patients received initial care in 46 cases (23.8%), with a general practitioner in 35 cases and a nurse in 11 cases. The squamous cell carcinoma was ulcero-budding (Figure 3) in 127 cases (67.2%), ulcerated (Figure 4) in 40 cases (21.2%), vegetating in 11 cases (5.8%) and nodular in 11cases (5.8%). Lesions were localized to the lower limbs (Figure 5) in 58 cases (30.6%). Table 2 shows the topography of cutaneous squamous cell carcinomas. Histopathology confirmed all cases of SCC. Squamous cell carcinomas were well-differentiated in 137 cases (72.4%) and invasive in 179 cases (94.7%). Table 3 shows the histopathological characteristics of cutaneous squamous cell carcinomas. Patients had a metastasis at the time of diagnosis in 71 cases (40.2%). These included bone metastases in 28 cases (36.8%), visceral metastases in 24 cases (31.6%), lymph node metastases in 18 cases (23.7%) and brain metastases in one case (1.4%). Pre-neoplastic lesions were noted in 54 cases (28.6%). The majority were burn scars and leg ulcers. Table 4 shows the various pre-neoplastic dermatoses. There was also voluntary use of depigmenting cosmetics in 11 cases (5.8%). Hydroquinone was most frequently used, with an average duration of use of 20 years. Smoking was noted in 50 cases (26.5%) and HIV infection in 6 cases. Surgery was performed in 61 cases (32.3%), with amputation in 22 cases (36.1%), wide excision in 37 cases (60.7%) and total excision in 2 cases (3.2%). Lymph node dissection was performed in all patients, and the postoperative course was straightforward. Radiotherapy was used in 16 cases (8.5%). It was adjuvant in 12 cases (75%). Doses ranged from 8 to 120Gy. Chemotherapy was administered in 62 cases (32.8%). It was palliative in 20 cases, curative in 18 cases and adjuvant in 24 cases. Carboplatin + paclitaxel was used in 47 cases. Table 5 shows the different molecules used during chemotherapy. Favorable progression after treatment was in 39 cases (20.6%). Recurrence was noted in 2 cases, pulmonary and hepatic metastasis in 3 cases, and death in 5 cases.

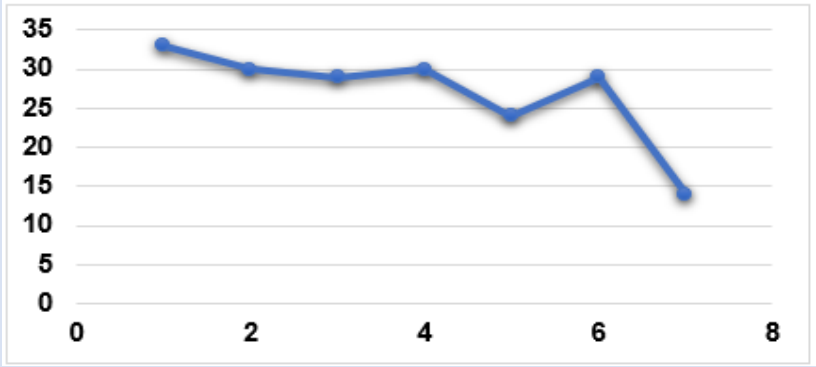

Figure 1: Epidemiological incidence of cutaneous squamous cell carcinoma over a period of 7 years.

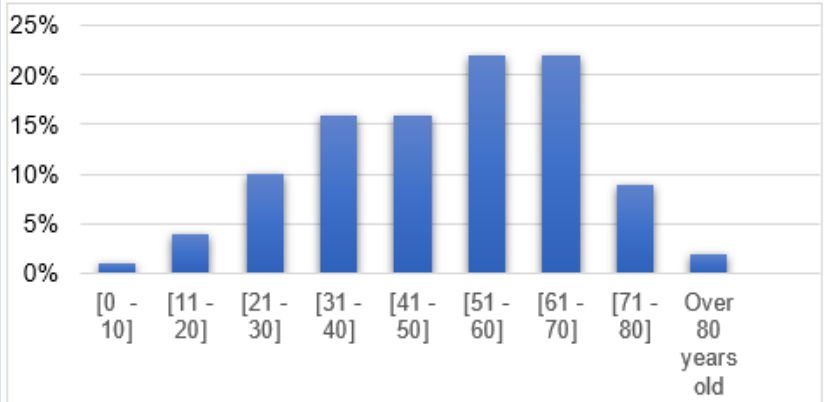

Figure 2: Distribution of patients according to age group.

Table 1: Distribution of patients by geographical origin in Senegal

Regions	Number	Percentage (%)
Dakar	94	49,7
Thies	29	15,4
Diourbel	15	8
Louga	10	5,3
Saint-Louis	7	3,7
Fatick	5	2,7
Kaolack	5	2,7
Kaffrine	4	2,1
Tambacounda	3	1,6
Kolda	3	1,6
Matam	2	1
Ziguinchor	1	0,5
Sedhiou	1	0,5
Kédougou	1	0,5

Figure 3: Ulcerative budding cutaneous squamous cell carcinoma developed in a chronic leg ulcer

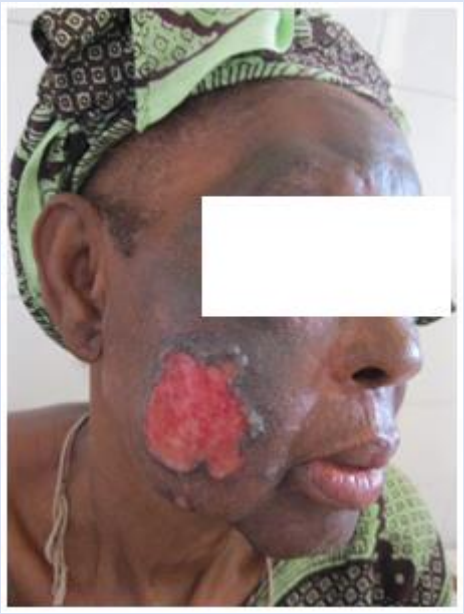

Figure 4: ulcerated squamous cell carcinoma associated with cosmetic skin whitening

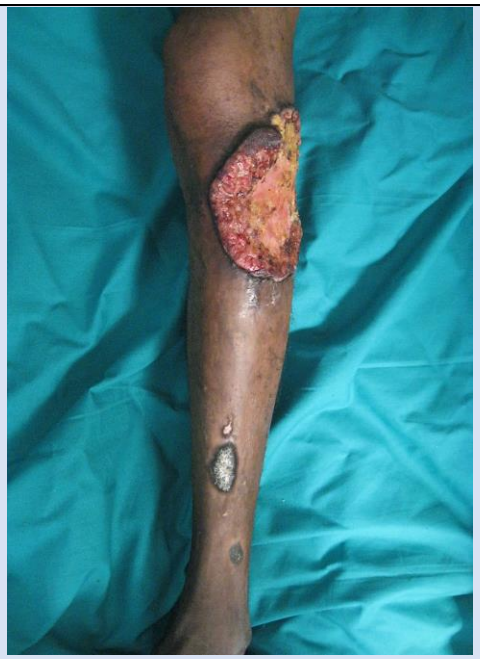

Figure 5: Budding ulcerative cutaneous squamous cell carcinoma developed on a verrucous lichen of the leg

Table 2: Topography of cutaneous squamous cell carcinoma lesions

Topography	Number	Percentage (%)
Legs	58	30,6
Trunc	36	19,1
Lip mucous membranes	31	16,4
Genital mucous membranes	21	11
Upper limb	18	9,6
Scalp	14	7,4
Face	9	4,6

Table 3: Histopathological features of squamous cell carcinoma

Histopathological features of squamous cell carcinoma	Number	Percentage (%)
According to the degree of differentiation		
well-differentiated squamous cell carcinoma	137	72,4
moderately differentiated squamous cell carcinoma	43	22,7
Anaplastic squamous cell carcinoma	9	4,7
According to the degree of infiltration		
Squamous cell carcinoma in situ	8	42,1
Microinvasive squamous cell carcinoma	2	1,05
Invasive squamous cell carcinoma	179	94,7

Table 4: Distribution of patients according to pre-neoplastic dermatoses.

Preneoplastic dermatoses	Types	Number	Percentage (%)
acquired	Burn scars	23	43
	Chronic ulcer	21	39
	Buschke Lowenstein tumor	2	4
	Lupus discoid	1	2
Congenital	Albinism	6	11
	Xeroderma pigmentosum	1	2

Table 5: Distribution of patients according to chemotherapy protocols

Protocols	Number	Percentage (%)
Carboplatin-paclitaxel	47	77
Carboplatin- paclitaxel Capecitabine- gemcitabin	3	5
Cisplatin- 5 fluorouracil	3	2
Capecitabin	3	5
Carboplatin-paclitaxel -Capecitabin	2	3
Carboplatine- paclitaxel-gemcitabin	1	2
Methotrexate – 5fluororacil	1	2
Paclitaxel	1	2
Carboplatin - adriamycin	1	2

Table 6: Epidemiological characteristics of cutaneous squamous cell carcinomas according to country

	Our Study	Ivory Coast [12]	Guadeloupe [13]	Madagascar [14]	United States [15]
Number of cases	189	10	551	18	90
Middle age	51ans	34ans	65ans	47ans	65ans
Sex ratio	1,28	2,33	1,1	1,13	1,3
Predominant clinical forms	Ulcero-budding carcinoma	Ulcero-budding carcinoma	Ulcero-budding carcinoma	Budding carcinoma	Ulcerated carcinoma
Topography					
	Limbs (40,2%)	Limbs (100%)	Cephalic extremity (38,3%)	Cephalic extremity (44%)	Limbs (100%)
	Céphalique (39,4%)	-	Limbs (20,1%)	Limbs (42%)	-
	Trunk (36%)	-	Trunk (15,1%)	Trunk (8,5%)	-
	Genital (11%)	-	Genital (12,2%)	-	-

Discussion

We report 189 cases of SCC over a 7-year period in the oncology department of Aristide Le Dantec hospital. This department is the reference center for cancer management in Senegal and sub-Saharan Africa. In our study, we noted an incidence of 27 cases per year and a hospital frequency of 0.77% of SCC. This frequency is low compared with the general population, but higher than the last study by Dieng in 2004, who reported 80 cases in dermatology departments [2]. This seems to be linked to the increase in the number of dermatology departments in Senegal, which nevertheless refer confirmed SCC to the oncology department for therapeutic management. Epidemiology varies worldwide, depending on phenotype, environment and genetic predisposition [11]. Table 6 illustrates some of the particularities of SCC worldwide. In Africa, squamous cell carcinoma accounts for 56% of skin cancers in Senegal [16] and 37% in Madagascar [14]. The mean age of our patients was 51 years, in line with work reported in the literature [14,16,17,18]. The age of onset is higher in the phototype I and II population. In our series, we noted a predominance of females, in opposite to studies carried out in Madagascar and Ivory Coast [12,14], and a predominance of males in France [11]. In our study, we noted an average delay in diagnosis of 20 months; this delay in specialist consultation is also observed in Burkina Faso, with an average delay of 13.4 months [19]. The reason seems to be the patient's therapeutic itinerary, self-medication and difficulties in accessing specialized care. SCC was preferentially located in the lower limbs (30.6%) and the cephalic extremity (28.4%). This was linked to the presence of pre-neoplastic dermatoses [10]. We noted a genital location in 11%. The prevalence seems to be related to genital papillomavirus infections [20]. Patients with Geno dermatoses such as albinism and xeroderma pigmentosum had a predominantly cephalic localization of SCC. This strongly suggests the role of sun exposure in the occurrence of SCC in these patients. Other authors confirm the high prevalence of SCC in these patients [21, 22]. Cutaneous squamous cell carcinoma was predominantly verrucous on the lower lip. Hertog reports a significant role for smoking in SCC of the oral lip, in addition to other risk factors such as sun exposure, age, pre-neoplastic lesions and immunosuppression [23]. The ulcero-budding form of SCC was noted in 67.2% of our study. It occurred on pre-cancerous lesions such as chronic leg ulcers and burn scars. The tumors were in advanced stages at the time of diagnosis with a degree of deep invasion on histopathology. Metastases were frequent in 40.2% of cases. According to some authors, the risk of SCC metastasis is 20 to 40% higher in pigmented skinned individuals, compared with 1 to 5% in light-skinned populations [10]. The presence of a risk factor was noted in 121 cases (64%). With regard to Geno dermatoses, albinism is a major risk factor in tropical Africa, with several series reporting the precocity of SCC in this area [23]. In children with xeroderma pigmentosum, SCC are frequent, early and predominantly in photo-exposed areas. They pose therapeutic problems in the case of advanced stages tumors located at the cephalic extremity [24]. Several factors have been incriminated in the occurrence of SCC during voluntary cosmetic depigmentation of the skin. These included cumulative exposure to ultraviolet radiation, the use of hydroquinone, papilloma virus infections and immunosuppression [8]. Smoking, noted in 26.5 % of our study, is incriminated by some authors as a risk factor for lower lip SCC [25]. Surgical treatment was performed in 32.3% of cases. Surgery is the standard treatment for operable SCC, with cure rates varying according to the severity of the histological type [26]. Chemotherapy was palliative in 32.6% (n=20), curative in 29% (n=18) and adjuvant in 38.4% (n=24). The most commonly used protocol was the carboplatin-paclitaxel combination. Molecules considered active were cisplatin, bleomycin, 5-fluorouracil, methotrexate and Adriamycin [27]. Combination treatments such as cisplatin (D1, 100 mg/m2), 5-fluorouracil (D1 to D5, 650 mg/m2 /d), bleomycin (D1 to D5, 16 mg/m2 /d) achieve the highest response rates (80%). Complete remission is rare and often transient. EGFR (epidermal growth factor receptor) is expressed in SCC of the face and trunk, but also in SCC lymph node metastases, and its overexpression appears to worsen prognosis. It represents a new therapeutic target in SCC. Cetuximab is a chimeric human and murine monoclonal antibody. It has a high affinity for EGFR and inhibits cell maturation. A randomized phase III study [28] of 117 patients with metastases of SCC on the lip or face showed a better efficacy of the cetuximab/cisplatin combination compared with cisplatin alone, but with no significant increase in survival time. Radiotherapy was used in 8.5% of cases, it is useful in inoperable tumors, as well as in

neoadjuvant treatment. It is limited by the high cost, accessibility and availability in certain African countries [12,14]. Favorable progression was in 20.6% of our patients, with control of the SCC. This control rate is 95% in France after curative surgery, sometimes combined with the radiotherapy [29]. According to Alam, ten-year survival rates are less than 20% for patients with regional lymph node involvement and less than 10% for patients with distant metastases [30].

Conclusion

Cutaneous squamous cell carcinoma remains a rare and serious cancer in sub-Saharan Africa. There is a delay in diagnosis, with tumors that are clinically and histo-pathologically very advanced. Early surgical management is the main factor in curing the cancer. Prevention relies on early management of precancerous lesions, especially in people with acquired or genetic risk factors.

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