Journal of Plastic, Reconstructive & Aesthetic Surgery (2010) 63, 1705–1711

JPRAS
An International Journal of Surgical Reconstruction
www.JPRASurg.com

Long-term outcome of squamous cell carcinoma of the upper and lower limbs☆

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Received 8 April 2009; accepted 1 October 2009

KEYWORDS
Skin cancer;
Squamous cell carcinoma (SCC);
Limb

Summary Cutaneous squamous cell carcinoma (SCC) is the second most common malignant skin tumour in the European population, with an annual estimated age-standardised incidence of 1–6 per 1000. After the head and neck, the upper and lower limbs are the most common sites affected with 14% of SCCs occurring in these areas. SCC has the potential to be a highly aggressive tumour but there are no recent studies looking at the long-term outcome of patients with extremity SCC. A retrospective study was performed of 243 patients with a total of 517 upper and lower extremity SCCs who had been followed up for at least 4 yrs. All patients' lesions were studied at one institution and data was collected from the Medical and Histopathology records. We found that there is only a low rate of recurrence or metastasis for extremity SCCs and that patients had a good prognosis overall.

Cutaneous squamous cell carcinoma (SCC) is a significant and increasing public health problem.[1–3] Its incidence in the Caucasian population is reported to be 1–6 per 1000 and this is rising.[4] It is more common in men than women, in geographic areas with greater sun exposure and at increasing number of years of sun exposure/age.[5] It occurs most frequently on the head and neck (84%), with the upper and lower limbs being the second (13%) and third (1%) most common sites affected, respectively.[6,7] In one study of Australian women, the arm was found to be more commonly affected than the head and neck.[8]

SCC appears to arise in genetically susceptible people who are exposed to various risk factors, the commonest being Ultraviolet (UV) radiation (UV-B > UV-A).[2] Other recognised risk factors include fair skin (including albinism), exposure to ionising radiation and arsenic, defective DNA-repair (xeroderma pigmentosa), immunosuppression (transplant patients, long-term steroid use, Human immunodeficiency virus (HIV), lymphoma or leukaemia), infection (human papilloma virus, leprosy) and chronic skin disorders such as ulcers.[2]

A number of factors have been identified to increase the risk of metastasis of extremity SCCs, including site (sole of the foot), those arising in a chronic (Marjolin's) ulcer or

☆ This work has not been presented at any meeting.

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doi:10.1016/j.bjps.2009.10.003

Bowen's disease, tumour diameter >2 cm or depth >4 mm, poor differentiation, perineural invasion and host immunosuppression. Many of the risk factors for high-risk SCC were originally determined in patients with head and neck SCC.[9]

The British Association of Dermatologists and the British Association of Plastic Surgeons have published guidelines for the management of cutaneous SCC.[10] These guidelines recommend that histological diagnosis should be based on a minimum dataset consisting of: pathological pattern, cell morphology, degree of differentiation, Broder's grade, level of dermal invasion, presence of perineural or lymphovascular invasion and margin of excision.[10]

Most studies of cutaneous SCC do not differentiate between the prognosis of lesions at different anatomical sites.[11] The majority of cutaneous SCCs arise in the head and neck and so there is little recent data on the prognosis of extremity SCCs. Our retrospective study aimed to address the management of extremity SCCs in our hospital, with particular focus on diagnosis, risk factors (UV exposure, albinism, ionising radiation, arsenic, defective DNA-repair, immunosuppression, infection, chronic skin disorders) and prognosis. Since the majority of recurrent and metastatic disease is detected within two years of the primary tumour and 100% of second primary SCCs are detected by four years,[5,12,13] our study followed up patients for a minimum of four years.

Methods

A list of patients with extremity SCCs was formed by searching the Histopathology database at our hospital for cutaneous SCC reports over an eight year period (1997–2004 inclusive). All reports of upper and lower limb SCCs were selected. Lesions placed proximal to the buttock and groin crease or the acromion and axillary apex were excluded. Second opinion reports of lesions treated at other hospitals were also excluded. The pathological information was extracted according to the minimum dataset[10] and any relevant clinical information was recorded. The patients' medical records were then examined for a full history including comorbidities, risk factors, and the complete details of all their SCCs. If patients were deceased and no cause of death was noted in their medical records, the General Practitioner was contacted for further information.

Results

From the Histopathology database at our hospital, 243 patients were identified with upper and/or lower limb SCCs between the years 1997–2004. 120 patients had upper limb lesions, 96 had lower limb lesions and 27 patients had lesions on both the upper and lower limbs. These patients had 569 associated histology reports relating to their SCCs from presentation up to October 2008. Of these reports, seven were for lymph node biopsies or lymphadenectomy (four patients) and four were for biopsies of dermal deposits (one patient). Of the 558 histology reports of skin lesion biopsies or excisions, a total of 516 separate SCC lesions were identified. Including the patient with dermal deposits at presentation, but no primary lesion histology report, we had reports relating to a total of 517 separate SCC cases. 42 histology reports related to lesions that were excised or biopsied more than once due to incomplete excision.

Within this patient group of 243 people, there was a preponderance of females (59%) over males (41%). At their first presentation, the patients' age ranged from 39 to 99 yrs, with a median of 77 yrs. The mean follow-up from initial presentation of the first SCC (in cases of multiple SCC) was 6.2 yrs, with a maximum of 22 yrs. All patients had a minimum of 4-years' follow-up except for 56 of the 89 patients who died during the study. More SCCs were found on the upper limb (62%) than the lower limb (38%) (Table 1). The most common site in the upper limb was the hand and in the lower limb was the lower leg. A total of 65 (27%) patients had multiple SCCs on the limbs and 50 (21%) had SCCs elsewhere on the body (e.g., head and neck, back, chest, abdomen and perineum). Of those patients with multiple limb lesions, there was an average of 5.2 lesions per patient. The greatest number of limb lesions in one patient was 39.

The majority of the surgical procedures (skin biopsies, excisions and lymph node dissections) were performed by Plastic Surgeons (65%); a large number of the procedures were performed by Dermatologists (33%) and the remainder (2%) was done by General Surgeons, Orthopaedic Surgeons, Renal Doctors, Vascular Surgeons, General Practitioners and an A&E Doctor.

Histology reports

A total of 558 cutaneous lesion reports and four dermal deposit reports were examined from 243 patients. These covered 517 separate lesions, with some lesions having multiple reports due to repeated sampling.

The lesion diameter was reported in 23% (126) cases and depth was reported in 35% (194) cases (Table 2). Differentiation was reported in 86% (477) cases. Invasion was specified in 83% (463) of the reports, with the structural level of invasion specified for 18% (100) of cases and perineural or lymphovascular invasion for 33% (184) cases. The pathological pattern was included in 8% (42) of reports, 0.4% (2) stated cell morphology and none stated Broder's grade.

Completeness of excision was specified in 77% (428) of reports. Measurement of the deep margin was made in 33% (186) of samples and the peripheral margin in 33% (186). Both measurements were recorded in 31% (170) of samples.

Size

Of the 126 lesions with diameter reported, 13% (16) were >2 cm diameter and two of these patients had local recurrence. None of these patients had metastatic disease.

Of the 194 lesions for which depth was reported, 33% (64) were >4 mm. Three of these patients had local recurrence and one had metastatic disease.

Differentiation

449 reports noted the differentiation of the SSC. The majority of SCCs were well (40%) or moderately (30%) differentiated, with only 8% being poorly differentiated. The remaining 22% were reported as SCC in situ.