

Post-burn squamous cell cancers in Nigerians

L. M. IREGBULEM

Department of Plastic Surgery, The National Hospital for Orthopaedic and Plastic Surgery, Enugu, Nigeria

Summary—Eighteen patients with post-burn skin cancers seen at Enugu over an 8-year period have been reviewed. All the tumours were well differentiated squamous cell carcinomas. The mean age of the patients was 36 years and the incubation period of 17.5 years was shorter than in previously reported studies. An aggressive policy in the treatment of these tumours by surgery alone has resulted in an 87% 5-year survival rate for lower limb tumours. When secondary tumours due to pre-existing dermatological diseases are excluded, post-burn skin epitheliomas constituted the largest group of squamous cell skin cancers seen in Enugu, Nigeria.

The association between unstable scars and skin cancers is well documented in the surgical literature (Marjolin, 1828; Treves and Pack, 1930; Arons *et al.*, 1965; Swanbeck and Hillstrom, 1969). Cruickshank *et al.* (1963) pointed out that Marjolin did not recognise that the warty ulcers he described in 1828 in long-standing burn scars were malignant. This was recognised by Smith (1850) and Marjolin's name given to them by da Costa in 1903. Such secondary tumours have been seen with disturbing frequency in post-burn scars in Nigerians in whom they constitute a large proportion of all the cutaneous cancers encountered in the author's unit. A review of 18 such cancers and the protocol for their management is presented in this paper.

Materials and methods

In the 8 years between January 1975 and January 1983, 30 patients with cutaneous squamous epitheliomas involving various parts of the body were seen. In every instance, a preliminary diagnosis was made on the basis of the history and clinical findings which took adequate cognisance of Ewing and Warren's postulates summarised below, *viz*:

- (i) The tumour site was previously intact.
- (ii) The initiating trauma was authentic and severe.
- (iii) The tumour originated within the boundaries of the injury.
- (iv) There was an adequate latent period.
- (v) The tumour was compatible histologically with the anatomic location (Ewing, 1935; Warren, 1943).

In all the burn scar carcinomas, tell-tale signs of

previous burn injury (residual peripheral scarring and pigmentary changes) were invariably present. A histological confirmation of the tumour by biopsy was made. On the basis of these findings, 18 tumours were labelled "post-burn squamous cell carcinomas" and analysed for anatomical distribution, age, sex, histological type, incubation or latent period, *etc.*

Results

The aetiology of the 30 squamous cell cancers is shown in Table 1 on the basis of previous thermal injury, mostly flame burns.

Table 1 Aetiology of 30 squamous cell carcinomas of the skin seen in Enugu (1975-1983)

Post-burn	Osteomyelitis/chronic discharging sinus	Chronic ulceration	arising spontaneously
18	4	5	3
60%	13.3%	16.7%	10.0%

Age and sex distribution are given in Table 2. The ages ranged from 14 to 58, the mean being 36 years. The sex ratio was approximately three males to one female.

Two clinical types of post-burn squamous skin cancers were encountered:

- (i) The nodular, fungating ulcers which were characteristically malodorous. This variety was often deeply infiltrating at presentation (Fig. 1).
- (ii) The dry, flat variety. These were normally mobile and non-infiltrating (Fig. 2).

Table 2 Sex, age and latent period (18 post-burn cancers)

Sex	M	M	F	M	M	F	F	M	M	F	M	M	M	M	M	M	F	
Age at presentation	58	57	50	46	44	41	38	37	36	36	35	30	29	27	22	21	20	15
L.P.	13	20	20	17	30	25	15	15	11	22	21	15	25	21	16	10	15	11

There were 14 tumours of the nodular, fungating variety and four flat lesions confined mostly to the upper limbs and back.

Histopathology of the tumours

Microscopically, all 18 lesions were well differentiated squamous cell cancers showing marked keratinisation and abundant mitotic figures. Infiltration with large lymphocytes and plasma cells was associated with the degree of tumour ulceration. No basal cell carcinomas, sarcomas or melanomas were seen in this series. The important differential diagnosis was pseudoepitheliomatous hyperplasia.



Fig. 1

Figure 1—Nodular fungating post-burn carcinoma of the knee. Note dense scarring and pigmentary changes.



Fig. 2

Figure 2—Albino male with dry malignant ulcer of the right forearm and extensive post-burn hypertrophic scarring and contractures of the elbow, wrist and digits.

Metastasis

Regional lymph glands were palpable in one case at presentation and proved to be positive at biopsy. There were no metastases to distant sites.

Induction time of the tumour

This was calculated as the latent period from the burn injury to the time when the tumour was diagnosed. It ranged from 10 to 25 years with a mean of 17.5 years (Table 2). However, since many patients in this part of the world consult the specialist only as a last resort, considerable disparity exists between the time of cancer diagnosis in hospital and the time when the malignant change occurred in the ulcer. The actual latent period is therefore somewhat less than that calculated above.

Distribution of lesions

The lower leg was the most commonly affected part, accounting for over two-thirds of all lesions.

There was distinct predilection for the pretibial area (Tables 3 and 4).

Tumour size

The tumour size ranged from 1 × 7 cm to 10 × 10 cm but most lesions averaged 7 × 8 cm.

Treatment

The mainstay of treatment was surgery. Chemotherapy and radiotherapy were not regularly available and consequently neither was employed in the management of these patients.

In lesions of the lower limb where regional lymph glands were not palpable, surgery consisted of amputation of the limb at an appropriate level. Previous experience had shown that in nodular, fungating lesions of the lower limbs, local surgery, no matter how proficient, was followed invariably by local recurrence within weeks.

Eight patients were treated in this way; all are alive and well during a follow-up period ranging from 4 to 8 years and are free from regional node involvement. Seven of these patients have survived

for more than 5 years, giving a 5-year survival rate of 87%.

One patient who presented with a lesion of the lower limb and inguinal gland involvement was treated initially with wide local excision and inguinal clearance. Amputation was performed subsequently when the tumour recurred locally. However, the patient developed extensive groin metastases (Fig. 3) and died 15 months from the date of his first operation. Five patients with tumours at sites other than the lower limbs were treated by adequate local excision and skin coverage. All five are alive and well at follow-up periods ranging from 2 to 7 years.

Three patients in this series with lower limb cancers were lost to follow-up, having refused the recommended treatment. One patient with extensive post-burn cancer of the left groin area died before any form of treatment could be initiated. When these four untreated cases were excluded, 14 patients were available for study. Thirteen of these are still alive, 10 at 5 years and over, giving a 5-year survival rate of 71% for all post-burn skin cancers.

Table 3 Distribution of post-burn epidermoid carcinoma of the skin in Nigerians (N = 18)

Scalp		1
Face preauricular		1
Chest		0
Upper limb	upper arm	1
	forearm	1
	hand	0
Abdomen		0
Back		1
Groins		1
Thighs		1
Knees	front	2
	popliteal	1
Lower leg	upper 1/3	1
	middle 1/3	5
	lower 1/3	2

Discussion

It is widely believed that skin cancers are rare in blacks. For instance, they constituted only 1.5% of all malignant tumours seen in blacks at the West Tennessee Cancer Clinic (Fleming *et al.*, 1975). In Nigeria, however, pre-existing dermatological disease, *i.e.* albinism, is often associated with multiple basal or squamous cell skin cancers. When this group of cancers is excluded, burn scar cancers constituted the commonest squamous skin malignancy encountered in Nigeria. Of 30 squamous skin cancers seen over an 8-year period, 18 (60%) arose in association with a previous thermal injury, which contrasts with the 1.7 to 6.8% of all epidermoid carcinomas in other reports (Treves and Pack, 1930; Sirsat and Shrikhande, 1967;

Table 4 Sites of incidence of post-burn skin cancers

Site	Arons <i>et al.</i> (1965)		Sirsat & Shrikhande (1967)		Mouly (1960)		Iregbulem (1986)	
Lower limb	9	41%	23	52%	9	56%	13	72%
Upper limb	4	18.2%	11	26%	3	19%	2	11%
Trunk	2	9%	10	22%	1	6%	1	6%
Head and neck	7	31.8%	0	—	3	19%	2	11%
Total	22	100%	44	100%	16	100%	18	100%



Fig. 3

Figure 3—A 20-year-old Nigerian amputee with extensive inguinal gland metastases from post-burn epithelioma of the right knee.

Nancarrow, 1983). This difference supports the suspicion that once the protective pigment in blacks is damaged there is an increased tendency to neoplastic change. In Nigeria most burn wounds unfortunately are treated by dressings alone and the resulting scars are often depigmented. They are also often unstable. Treves and Pack (1930) believe that repair and regeneration in marginal epithelium which result from recurring ulceration in poorly vascularised scar tissue lead to neoplastic change. Other workers (Gilman *et al.*, 1955; Sirsat *et al.*, 1963) have emphasised the importance of the alteration in connective tissue, probably hyalinisation, and the presence of exogenous collagen with fibrinoid change, in burn scars. These changes are said to precede post-burn malignancy which they

induce by initiating abnormal metabolic activity. Castillo and Goldsmith (1968) have postulated that the presence of a depressed immunological state surrounding a burn may lead to the development of burn carcinoma.

The mean age of the patients in this series was 36 years, which contrasts sharply with an average of 58 years quoted by other workers (Arons *et al.*, 1965; Stromberg *et al.*, 1977). However, the M:F ratio of about 3:1 agrees with the figures from other series. The present study also shows a mean latent period of 17.5 years (range 10 to 25 years) compared to periods of 28.5, 32.0, 36.3 and 38.0 years quoted by other workers (Lawrence, 1952; Mouly, 1960; Arons *et al.*, 1965; Sirsat and Shrikhande, 1967).

It would appear from the foregoing that post-burn scar carcinomas in Nigerians have a distinct predilection for the younger age group and have the shortest mean incubation period of any published series. The earlier development of such cancers in Nigerians and their frequent occurrence in the lower limbs may not be unconnected with prevailing socio-economic factors. Such ulcers in this environment are frequently exposed to sustained empirical treatment by all and sundry, repeated trauma and infection.

Post-burn squamous skin cancer in Nigerians does not appear to be an aggressive disease. Most patients in this series presented with long-standing large fungating lesions (average size 7×8 cm). In spite of this, only one instance of metastasis to the regional lymph nodes was noted and none occurred at distant sites. This would conform with the views of Sevitt (1957), Bowers and Young (1960) and Mouly (1960) that burn scar carcinomas were unlikely to metastasise. In the series by Glass *et al.* (1964) carcinomas of the lower extremities with antecedent lesions, *e.g.* burns, osteomyelitis, stasis, ulcers, *etc.* metastasised in 2 out of 13 cases, while similar carcinomas which appeared in apparently normal skin metastasised in 8 out of 13 cases. Our findings seem to substantiate this view. However, higher estimates of 30% or more have been reported by other workers for whom post-burn cancers must represent a more aggressive disease (Taylor *et al.*, 1941; Arons *et al.*, 1965; Sirsat and Shrikhande, 1967).

Our 5-year survival rate of 71% may, in part, be due to the aggressive policy in the Unit whereby lower limb tumours without regional node involvement were treated by amputation of the limb at the appropriate level. This procedure was invariably followed by an improvement in the appetite, a rise

in the haemoglobin level, appreciable gain in weight and a feeling of well-being in the affected patients.

Lesions in other parts of the body were usually amenable to adequate surgery which involved wide local excision of the tumour including the scar field.

Since all the tumours in this series were well differentiated, it could be argued that their less aggressive characteristic favourably influenced the prognosis. Recent evidence, however, suggests that the degree of squamous differentiation of a tumour does not necessarily determine its invasive ability. Dellon *et al.* (1975) have shown that the tendency of a tumour to recur depends instead on a balance between its invasive capability and the host's immunocompetence.

The presence of clinically involved regional lymph nodes at the time of presentation or during the course of the disease is considered of serious prognostic import. The one patient in this series who presented with involvement of the groin lymph glands died within 15 months of the diagnosis in spite of what was considered adequate surgery.

Bostwick *et al.* (1976) reported the early post-operative development of metastases in six patients with scar carcinomas. They attribute the behavioural pattern of such tumours to their origins in an "immunologically privileged site devoid of the normal immunosurveillance mechanisms". It is presumed that breaching of such scar barriers by local surgery accelerates the process of tumour dissemination. In our previous experience, regional node metastasis after excisional surgery was more likely to occur in the lower limbs. This is probably because of its rich lympho-venous supply.

The management of those patients with lower limb tumours in which the regional lymph nodes are already involved with tumour is more problematical. From what has been said, ablation of the limb and simultaneous removal of the regional lymph nodes would seem to be the treatment of choice. Such a line of treatment is now being evaluated in this Unit but the great reluctance of many Nigerians to accept amputation as a form of therapy is recognised.

The occurrence of carcinoma in previously grafted skin or at sites where previous skin grafts have failed has been reported by several workers (Treves and Pack, 1930; Mouly, 1960). However, this is generally regarded as an uncommon finding and no instances of such cancers have been encountered in this Unit.

Post-burn carcinoma in Nigerians is undoubtedly

an avoidable disease which prophylactic measures can help to eradicate. Public education in the prevention of burn injuries is of paramount importance and is being relentlessly pursued. Additionally, appropriate surgical measures, *viz.* the timely application of skin cover for full thickness burns and the excision and subsequent tissue replacement or realignment of tight and ulcerating burn scars, must be rigidly applied. Prompt referral to a specialised Unit is advocated in extensive partial thickness burns and all cases of full thickness burns.

Acknowledgements

I would like to thank Professor Arnold Levene, Department of Histopathology, Royal Marsden Hospital, London, and Professor W. Onuigbo, Department of Morbid Anatomy, College of Medicine, University of Nigeria, Enugu, for their help with the histology of these tumours.

References

- Arons, M. S., Lynch, J. B., Lewis, S. R. and Blocker, T. G. (1965). Scar tissue carcinoma. Part 1: A clinical study with special reference to burn scar carcinomas. *Annals of Surgery*, **161**, 170.
- Bostwick, J., Pendergrast, W. J. and Vasconez, L. D. (1976). Marjolin's ulcer: an immunologically privileged tumour? *Plastic and Reconstructive Surgery*, **75**, 66.
- Bowers, R. F. and Young, J. M. (1960). Carcinoma arising in scars, osteomyelitis and fistulae. *Archives of Surgery*, **80**, 564.
- Castillo, J. L. and Goldsmith, H. S. (1968). Burn scar malignancy in a possible depressed immunologic setting. *Surgical Forum*, **19**, 511.
- Cruickshank, A. H., McConnell, E. M. and Miller, D. G. (1963). Malignancy in scars, chronic ulcers and sinuses. *Journal of Clinical Pathology*, **16**, 573.
- Da Costa, J. C. (1903). Carcinomatous changes in an area of chronic ulceration, or Marjolin's ulcer. *Annals of Surgery*, **37**, 496.
- Dellon, A. Lee, Potwin, C., Chretien, P. B. and Rogentine, C. N. (1975). The immunobiology of skin cancer. *Plastic and Reconstructive Surgery*, **55**, 341.
- Ewing, J. (1935). Bulkley lecture: modern attitude toward traumatic cancer. *Archives of Pathology*, **19**, 690.
- Fleming, I. D., Barnawell, J. R., Burlison, P. E. and Scott Rankin, J. (1975). Skin cancer in black patients. *Cancer*, **35**, 600.
- Gilman, T., Bronks, D., Penn, J. and Roux, M. (1955). Abnormal elastic fibres. *Archives of Pathology*, **59**, 733.
- Glass, R. L., Spratt, J. S. Jr and Perez-Mesa, A. (1964). Epidermoid carcinomas of lower extremities. *Archives of Surgery*, **89**, 955.
- Lawrence, E. A. (1952). Carcinoma arising in the scars of thermal burns with special reference to the influence of the age at burn on the length of the induction period. *Surgery, Gynecology and Obstetrics*, **95**, 579.
- Marjolin, J. N. (1828). Ulcère verruqueux. *Dictionnaire de Médecine*, **21**, 46.
- Mouly, R. (1960). Cancer in burn scars ("Marjolin's ulcers"). Transactions of the International Society of Plastic Surgeons, 2nd Congress 1959. Edinburgh: E. & S. Livingstone.

- Nancarrow, J. D.** (1983). Cicatricial cancer in the South-West of England: a regional plastic unit's experience over a 20-year period. *British Journal of Surgery*, **70**, 205.
- Sevitt, S.** (1957). *Burns, Pathology and Therapeutic Applications*. London: Butterworths.
- Sirsat, M. V. and Shrikhande, S. S.** (1967). Histochemical studies on squamous cell carcinoma of the skin arising in burn scars with special reference to histogenesis. *Indian Journal of Cancer*, **3**, 157.
- Sirsat, S. M., Vandrewalla, A. H. and Khanolkar, V. R.** (1963). Histochemical and electron microscopic study of epidermal neoplasms. *Indian Journal of Dermatology and Venereology*, **29**, 43.
- Smith, R. W.** (1850). Observations upon the warty ulcer of Marjolin. *Dublin Quarterly Journal of Medical Science*, **9**, 257.
- Stromberg, B. V., Keiter, J. E., Wray, R. C. and Weeks, P. M.** (1977). Scar carcinomas; prognosis and treatment. *Southern Medical Journal*, **70**, 821.
- Swanbeck, G. and Hillstrom, L.** (1969). Analysis of etiological factors of squamous cell skin cancer of different locations. *Acta Dermato-Venereologica*, **49**, 427.
- Taylor, G. W., Nathanson, I. T. and Shaw, D. T.** (1941). Epidermoid carcinoma of the extremities with reference to lymph node involvement. *Annals of Surgery*, **113**, 268.
- Treves, N. and Pack, G. T.** (1930). The development of cancer in burn scars. An analysis and report of 34 cases. *Surgery, Gynecology and Obstetrics*, **51**, 749.
- Warren, S.** (1943). Minimal criteria to prove causation of traumatic or occupational neoplasms. *Annals of Surgery*, **117**, 585.

The Author

Lawrence M. Iregbulem, FRCS(Ed), FRCS, Consultant Plastic and Reconstructive Surgeon, The National Hospital for Orthopaedic and Plastic Surgery, P.M.B. 01294, Enugu, Nigeria.

Requests for reprints to the author.

Received 24 October 1986.

Accepted 6 April 1987 after revision.