

Squamous cell carcinoma of the foot arising in chronic ulcers in leprosy patients

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Summary Squamous cell carcinoma (SCC) of the foot is a rare sequelae of chronic ulceration secondary to leprosy neuropathy. Most of the tumours are relatively slow growing and tend to metastasize late. Survival after local excision is generally good. In this series of 17 patients so far there have been 3 deaths attributable to SCC, all of whom presented with locally advanced tumours and lymph node metastasis.

Introduction

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae* which predominantly affects skin and peripheral nerves. Damage to peripheral nerves occurs as a result of host immunity (reversal reaction, i.e. delayed-type hypersensitivity) to the presence of bacteria in nerves or as a result of fibrosis due to chronic inflammation in peripheral nerves.

This results in sensory, motor and autonomic loss in the affected limbs. As a result of paralysis of the dorsiflexors (damage to the common peroneal nerve) of the foot the forefoot is subjected to more pressure than usual with each step. Damage to the posterior tibial nerve results in anaesthesia of the plantar surface and some loss of cushioning in the foot due to wasting of the foot intrinsic muscles. Patients with insensitive feet are prone to recurrent wounds which often become secondarily infected. Secondary infection can lead to the absorption of digits. A proportion of patients with chronic ulcers (usually those present for more than 10 years^{3–5}) develop SCC¹ which is usually of low grade malignancy.

Materials

All patients with SCC who presented between January 1991 and June 1995 were included

in this series. There were 17 patients with SCC (15 male and 2 female). The normal male to female ratio for admitted patients is 4 : 1 at our hospital. The average age was 52 years (30–74 years). Some had clinically obvious SCC, while others had a chronic nonhealing ulcer with some suspicious features which led to a biopsy being done. Information on the duration of the ulcer was retrospectively extracted from case notes.

Results

There were 7 cancers on the left and 10 on the right foot. The average duration of an ulcer prior to clinically malignant transformation was 9.4 years (range 1–15 years). The earliest clinical sign of malignancy is a white pasty discharge from the central area of the ulcer when the edges are squeezed. It is believed that these are squamous cells produced by the cancer. Six patients had palpable inguinal lymph nodes on initial presentation. In 3 of these the nodes had settled within 6 weeks of surgery indicating infection as the most likely cause. In 3 patients the nodes persisted and were biopsied (all 3 were positive for cancer).

All patients underwent surgery. Nine patients had a Pirigoff amputation² (amputation of the foot with talocalcaneal arthrodesis) while 2 patients had a forefoot amputation. Four patients had a below knee amputation (BKA) and 2 underwent an above knee amputation (AKA).

There was one death within 4 weeks of surgery from widespread metastasis. One death occurred 14 months after a Pirigoff amputation (no local recurrence) presumably from metastatic disease. Another patient died of an intercurrent illness (undiagnosed hypothyroidism with severe depression). The other death was in the patient described in the following case study and illustrates the outcome if adequate primary treatment cannot be provided.

Case study

A female patient aged 74 initially presented with a hyperkeratotic lesion on the dorsum of her ankle. This was fully excised and skin grafted. Three months later she developed a recurrence of two nodules which when biopsied were positive for early SCC. She refused further surgery at that time. She returned 6 months later with a large fungating tumour on the anterior aspect of her ankle and again refused surgery. She was given oral Methotrexate, 20 mg weekly, and her tumour shrank over 3 months and finally completely disappeared. She was kept on oral Methotrexate, 20 mg every alternate week for a year, with no recurrence. As she seemed well her Methotrexate was stopped. Within 3 months her tumour recurred and this time did not respond to oral Methotrexate. She then developed a severe infection in the tumour and consented to BKA. However two days after BKA she developed gas gangrene which was treated by AKA with the skin flaps left open. She recovered from her surgery and returned home in the care of her son. Some 5 months after discharge she died at home of unknown cause—presumably metastatic carcinoma.

Table 1. Detailed profile of patients

| Pt | Year | Sex Age | Side/Site | Duration of ulcer (years) | Lymph nodes | Pathology | Surgery | Outcome |
|-----|------|---------|-------------|---------------------------|-------------|----------------------------|------------------------|---------------------------------------|
| BBT | 9/91 | M/40 | R forefoot | 4 | Yes | Poorly diff. | AKA | Died 4/52 |
| SMT | 1/94 | M/45 | R forefoot | 10 | Yes | Benign epith. SSC in LN | Pirigoff | No local recurrence. Died at 14/12 |
| BK | 1/92 | F/74 | R ank dor. | 13 | No | SCC | AKA | Died 1994 |
| HB | 9/93 | M/64 | R forefoot | 1 | No | Cornu cutaneum | Forefoot Amput. | Died Hypothyroid |
| SD | 9/93 | M/30 | R heel | 4 | No | SSC | BKA | Not seen since |
| SR | 9/93 | M/50 | L forefoot | 14 | Yes | | Pirigoff | Well since 1993 |
| GP | 4/93 | M/58 | L short ft | 35 | No | | Pirigoff | Well since 1993 |
| TK | 3/93 | F/54 | L midfoot | 5 | No | Well diff SCC | Pirigoff | Well since 1993 |
| EKN | 4/94 | M/63 | L forefoot | 8 | No | SCC—early invasiveness | Forefoot Amputation | Well |
| KB | 3/94 | M/43 | L lat bord. | 7 | Yes | Cornu cutaneum | Pirigoff | Well since 1994 |
| GR | 4/94 | M/60 | R heel | 5 | Yes | SCC well diff | BKA | Well since |
| SMG | 6/94 | M/65 | L heel | 3 | No | SCC well diff | BKA | Well since |
| DBT | 7/94 | M/55 | L forefoot | 9 | Yes | SCC well diff | Pirigoff | Well since |
| KBM | 3/93 | M/40 | R forefoot | 15 | No | SCC early invasiveness | BKA | No recurrence But BK stump wounds |
| KBB | 3/95 | M/35 | R lat bord. | 15 | Yes | SCC well diff | Pirigoff | Well since |
| BRS | 3/95 | M/45 | R instep | 8 | No | SCC well diff | Pirigoff | Well since |
| DL* | 9/94 | M/62 | R lat bord | 3 | No | SCC | Pirigoff | Well since |

Discussion

These patients were all treated at Anandaban Leprosy Hospital which is the referral hospital for reconstructive surgery for leprosy patients from the Central and Eastern regions in Nepal. Nepal is a developing country with very basic health services and has a largely rural population of 20 million living in villages among the foothills of the Himalayas. Patients with malignancy often present late with fungating tumours, as health is a lower priority than ensuring a food supply for the following year and other obligations to family.

Most day-to-day transport is on foot and patients often have to walk for days to the nearest basic health facility. Most of these patients had a local amputation, usually a Pirigoff amputation (as compared with a BKA). In Nepal, where the terrain is hilly, this amputation is far superior to a below knee amputation, after which the patient is constantly dependent on scarce prosthetic services. The patient is also able to walk within their home without any form of footwear and to squat when going to the toilet (a cultural prerequisite). Thus preservation of leg length and the use of simple footwear rather than complicated prosthetic devices are vital components in the rehabilitation of patients requiring amputation.

The duration of ulcers prior to malignant change was 9.4 years (range 1–15 years). It is likely that this duration is inaccurate for some of these patients. In general, rural villagers in Nepal have very loose concepts of time and this information was extracted retrospectively from case notes.

The high male to female ratio (7 : 1) may reflect a true greater risk as men in Nepal

walk much greater distances, and carry heavier loads than women. This would predispose those with insensitive feet to a much greater risk of chronic wounds and hence SCC. However women in Nepal are much less likely to present for hospital care (the ratio of men to women affected by leprosy is 2:1 but the ratio of admitted patients 4:1). One risk is the small margin of clearance available (often 1–2 cm of macroscopically normal tissue) but SCC in leprosy is usually a low grade malignancy^{4,5} with moderately well-differentiated tissue. None of the patients who had a Pirigoff amputation have had any local recurrence.

Often the pathologist finds it difficult to differentiate the lesion from a benign basal cell epithelioma. In one patient (SMT) initially reported as a benign basal cell epithelioma, keratotic type, persistent inguinal lymph nodes were biopsied 6 weeks after the initial amputation, because they had not reduced in size despite an absence of infection. These lymph nodes showed well-differentiated SCC. On review of the initial specimen a small focus of invasive SCC was found. The difficulty in diagnosing these lesions has been documented, with some patients requiring up to 6 pre-operative biopsies for a definitive diagnosis in one series.⁵

The histological features include hyperplasia of epidermis showing hyperkeratosis, parakeratosis, and papillomatosis associated with lymphocytes and plasma cell infiltration in upper dermis and some cells with a large nucleus and disappearance of basement membrane suggesting well-differentiated squamous cell carcinoma.

It is essential that patients are taught self-care routines⁶ in order to prevent chronic wounds and thus the development of SCC. Patients need to be instructed in a daily routine of skin care (inspection, soaking, scraping, oiling and exercise) as well as methods of wound avoidance to prevent wounds and wound care to help heal the wounds quickly. In addition to teaching patients these principles we provide them with leaflets in Nepali to help them remember what they have been taught.

Conclusion

SCC in chronic plantar ulcers in leprosy are usually well differentiated and only metastasize late. There can often be difficulty in making a firm diagnosis from the histology. Pirigoff's amputation is a valuable procedure in the preservation of leg length in patients requiring amputation for SCC in leprosy.

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