MALIGNANT TRANSFORMATION OF PLANTAR ULCERS IN LEPROSY

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SYNOPSIS

Malignant change in neuropathic ulcers in leprosy patients is not as rare as previously believed since reports from few countries have highlighted this phenomenon. This paper describes 4 patients at the Tampoi Leprosarium, 8 km north of Johor Bahru who had non-healing plantar ulcers for several years and presented with cauliflower-like growths. Three of them had below knee (BK) amputation while the other had excision of the neoplasm. All of them showed changes in the underlying bones. The need for early detection of malignancy by performing multiple biopsies when clinical impression overides histological interpretation and avoidance of traumatic surgery in leprosy patients who had already been handicapped by the stigma and deformity of the disease are emphasized.

INTRODUCTION

Development of ulcers over the plantar aspects of the feet is an important but preventable complication in leprosy. The loss of sensation as a consequence of neural involvement of the disease and the subsequent exposure to trauma are predisposing factors. Proper medical advice on the care of the anaesthetic hands and feet and good patient-compliance could avert such an undesirable event. Although it is accepted that chronic ulcers such as gastric ulcer can turn malignant the exact aetiopathogeneis is not known. In leprosy, the causes incriminated for cancer development from trophic ulcers are chronic osteomyelitis, calcaneal spur (1) and administration of dapsone which is a proven carcinogen in animals (2). Chronicity of the plantar ulcers due to trauma causes prolonged destruction of tissues, demanding constant replacement of parts with disturbance of normal growth mechanism. Therefore, 'chronic irritation', once a scapegoat of carcinogenesis may be incorporated into the multistep concept of cancer development as a promoting factor (3).

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The first report of malignancy arising from trophic ulcers came from South India in 1964 by Job and Riedel (4) who documented 4 leprosy patients and noted that carcinoma arising from plantar trophic ulcers was rare. Two years later Riedel presented another 4 cases (5). Henceforth, reports have appeared from other parts of India (1,6,7), Brazil (8), Nigeria (9), Ethiopia (10) and Egypt (11). This is the first report from Malaysia of 4 patients, 3 of them with squamous cell carcinoma grade 1 and 1 with verrucous carcinoma.

CASE REPORTS

CASE 1

A 72-year old Chinese male was seen at the skin clinic in January 1985 with a proliferative growth over the left forefoot. He was a case borderline leprosy on treatment with Inj. hydnocarpus oil weekly from 1937 – 1951 and Inj. sulphone 1 cc biweekly from 1951 – 1968. Later he was given oral dapsone and currently he is on multiple drug therapy (MDT) for multibacillary leprosy. He developed an ulcer for 20 years at the site of the growth which was managed with oral antibiotic and local antiseptic. He noticed the ulcer growing fast recently, the border becoming wider and everted reaching a size of 9 × 10 × 2 cm extending to the instep of the foot. It wa a cauliflower-like growth, fungating and foul-swelling with purulent discharge oozing out from the numerous sinuses. The ipsilateral inguinal lymph nodes were tender and enlarged. He also presented with saddle nose, bilateral hand deformities and pain at the site of the lesion. Biopsy from the edge of the ulcer showed pseudo-epitheliomatous hyperplasia. X-ray of left foot showed complete distortion of the normal anatomy of the bones with regards to the bone density, configuration, articular margins and articulation. Almost all the metatarso-phalangeal joint articulations had been disrupted. Since there was a strong and valid suspicion of malignancy, biopsy was repeated at the centre which showed hyperplasia of squamous epithelium with foci where demarcation of basal cell layer became blurred. Third biopsy with deeper tissue was compatible with squamous cell carcinoma. The lymph nodes resolved after pseudomonas infection responded to gentamycin. Left BK amputation was done on 20.5.85 and he had an uneventful post-operative recovery. Subsequently, he was fitted with the prosthesis and currently he is doing well without any manifestation of distant secondaries in the lymph nodes, liver or the lung.

CASE 2

A 60-year old Chinese female with borderline leprosy since 1949 presented with a large growth over the right foot of 3 months duration. She had an ulcer over the forepart for about 18 years without good response to treatment. Biopsy of the lesion was in favour of squamous cell carcinoma. X-ray showed erosions and destruction of the bones of the forefoot. Inguinal lymph nodes were not enlarged. BK amputation was performed on 14.9.85. In May 1986 she developed an abscess of the right popliteal fossa with discharging sinuses. She had enlarged inguinal lymph nodes. Patient was suspected to have metastasis to the knee and groin. Wedge biopsy was taken from the edge of the sinus in popliteal fossa which showed epithelial hyperplasis. Since there was no improvement of her condition, biopsy was repeated and computed tomograph (CT) scan of the abdomen was done to rule out secondaries. Second biopsy showed features of squamous cell carcinoma and CT scan did not show abdominal secondaries. Metastasis to the knee being confirmed, she was thought to have further spread since her condition deteriorated. Radical surgery in the form of hind-quarter amputation was not contemplated. While she was awaiting radiotherapy, she died.

CASE 3

A 72-year old male with borderline leprosy was seen with fungating growth at the sole of left foot (Figure 1). He had an ulcer over the heel of 3 years duration. There were few non-tender inguinal lymph nodes. X-ray of the foot showed destruction and absorption of several phalanges. The calcaneum was sclerosed with irregular margins compatible with chronic destructive osteomyelitis. Biopsy of lesion showed squamous cell carcinoma. BK amputation was done on 28.12.85. Three months later the inguinal lymph nodes became larger. A wide clearance of the lymph nodes was done and biopsy showed total replacement of a node by metastatic deposits of well-differentiated squamous cell carcinoma. The incision at the inguinal region healed well. He is fitted with the prosthesis and no other distant secondaries have been discovered so far.

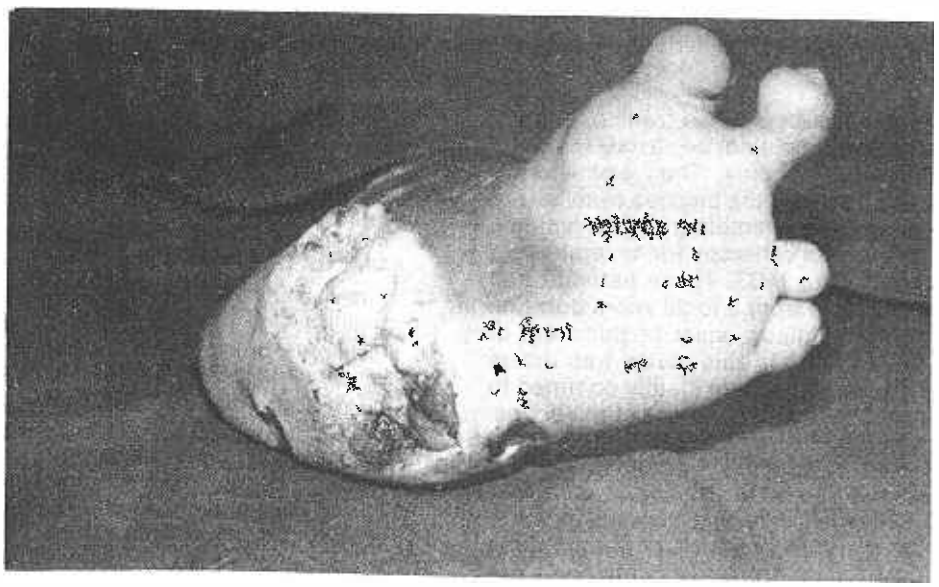

Figure 1 Squamous cell carcinoma involving the left heel of case 3.

CASE 4

A 60-year old Chinese male with borderline leprosy was seen with a verrucous, fungating growth extending from the lateral margin to the instep of the right foot. He had a non-healing, slightly, painful ulcer for about 4 years. Inguinal lymph nodes were not enlarged and were non-tender. A deep biopsy of the growth was consistent with verrucous carcinoma. X-ray of the right foot and ankle showed periosteal reaction at the lower end of the tibia and fibula which resembled fusion of these bones. Except for the talus and calcaneum, the rest of the tarsal and metatarsal bones along with the phalanges did not show normal congigurasion, articular margins and density. The tarso-metatarsal and metatarso-phalangeal joints had been disrupted. Pockets of luscencies within the bone was indicative of chronic infection. Excision of the growth was done, thus preserving the foot. Full-thickness skin grafting was done successfully. He is doing well with no distant metastasis.

DISCUSSION

The incidence of cancer in leprosy patients may be increasing but their vulnerability to malignancy is almost similar to that of the general population. In a large survey of 60,000 histopathological slides of leprosy patients, 539 showed features of carcinoma of the skin (12). In another study 33 of the 195 (16.9%) deaths in leprosy were due to cancer (13). Within a period of 2 years the author has encounted 4 cases of malignant changes from trophic ulcers amont 567 leprosy patients. Squamous cell carcinoma is a malignant tumour arising from the epidermal cells. Verrucous carcinoma is a variant of squamous cell carcinoma which is slow-growing, warty and locally invasive with absent or very rare metastasis. It occurs in three areas such as the mouth, genitalia and feet. It was first recognized as a distinct entity by Ackerman (14) who originated the term and described 31 patients with verrucous growths in the buccal mucosa and lower gingiva and attributed to tobacco-chewing as the main cause. These tumours, also called as oral florid papillomatosis had a male predominance of 5:1. Secondly, it presents at the perianal, perineal regions and genitalia as Bushke-Lowenstein tumour (giant condylomala accuminata) (15,16) Aird (17) et al described the third variety as a 'peculiar-tumour' of the foot, epithelioma cuniculatum in 3 patients who had fungating warty growths at the fore part of the feet with clefts and tunnels intercommunicating the sinuses which appeared like burrows of the rabbit warren.

Of the 4 patients described, 3 had frank malignancy and their affected feet could not be saved, 1 had the features of verrucous carcinoma. Their age was 60 years and above and acquired the disease even before the introduction of specific chemotherapy for leprosy. They were on dapsone monotherapy for several years and currently converted to MDT. These patients had non-healing plantar ulcers from 3 to 20 years duration which represents the insidious onset of this form of cancer. One of the patients in this series had ulcers over the heel and the growths were mainly confined to the forepart of sole with the involvement of the bones. All of them had deformities attributable to the diseases process in many parts of their body.

The author wishes to stress the importance of a large, deep and if necessary repeat biopsy since the site of taking the material helps in confirming the diagnosis, and that tissue from the centre and not from the edge of the lesion as in case 1 may show characteristic features (6). Early diagnosis will initiate a speedy and prompt intervention and thereby prevent or reduce matastasis. Enlargement of inguinal lymph nodes should not pose much concern for they may resolve after control of infection or after amputation (6). The striking similarity in their presentation point out to a vital fact that if the disease is arrested and deformity prevented we may not encounter such incidence any longer! These patients with borderline leprosy are in good health at the time of writing except case 2, who died of terminal cancer.

Verrucous carcinoma resembles viral wart and it is of utmost importance to differentiate the latter with which it was assumed to be similar. Histology will help us in this regard (17,18). Verrucous carcinoma shows features of marked hyperkeratosis, parakeratosis and acanthosis, with the absence of vacuolated cells in the epidermis which is a characteristic feature of wart. The broad strands of tumour invading the dermis often contain keratin-filled cysts. Nuclear atypism and horn pearls may be absent. The early detection of verrucous carcinoma which poorly responds to radiotherapy cannot be over-emphasized because owing to the slow-growth, excision carries a good prognosis, and therefore the affected anatomical structure can be preserved. This is of great importance to leprosy patients because many of them who live in leprosarium with deformities had already lost the quality of life; what have they got to lose further?

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