

## SQUAMOUS CELL CARCINOMA ARISING IN PLANTAR ULCERS IN LEPROSY<sup>1</sup>

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Plantar ulcer is one of the common complications of leprosy. It is defined as "A chronic ulceration of the anaesthetic sole of the foot situated in well defined areas overlying a bony prominence, resistant to local or systemic therapy, and characterized by a marked tendency to recurrence" (?). Ulcers of this type are usually called "perforating ulcers" or "trophic ulcers." Carcinoma arising out of plantar ulcers seems to be extremely uncommon. It is not reported in literature known to the authors.

In this paper four cases of plantar ulcers that have undergone malignant changes are reported.

### CASE REPORTS

CASE No. 1 (C.L.H. 15).—A male aged 61 years who developed leprosy nearly 51 years ago, was first admitted as an inpatient in 1918. Since 1953 he has been persistently negative for acid-fast bacilli, and all his skin lesions have resolved. He has been classified as a case of resolved leprosy.

About 40 years ago he developed foot drop of the left leg. In the course of time the foot turned into an extreme varus position, so that he walked on his lateral malleolus. As a result he developed trophic ulceration distal to the lateral malleolus. The ulcer healed and broke down again from time to time. It became worse during the year and a half preceding this report and spread gradually over the entire lateral aspect of the foot.

On the right foot a drop developed about 20 years ago. Trophic ulceration of the metatarsal area and the lateral edge of the foot set in soon afterward. The ulcers healed and recurred several times, causing chronic osteomyelitis and gradual destruction of the metatarsal and distal tarsal bones. During the last six months preceding this report the ulcer began to get worse, gradually involving about two-thirds of the forefoot stump.

On physical examination in November 1960, there were no obvious skin lesions except for a little wrinkling of the ear lobes and face. There was complete anesthesia, including loss of deep sensation in the arms and legs, except for small areas on the extensor aspect of the

<sup>1</sup> Received for publication June 3, 1963.

arms. Both hands showed complete ulnar and median palsies, with the fingers clawed, contracted, and shortened to various degrees. There was bilateral foot drop. The forefeet were shortened from loss of the toes; only stumps were left on each foot.

The left foot was in an almost complete equino-varus position. Foot and ankle areas were warm, slightly swollen and red. The lateral aspect of the foot was the site of an ulcer of irregular outline, measuring  $4.5 \times 5.0$  cm. The ulcer was shallow, with overhanging edges, and its floor was covered with a small amount of slough and granulation tissue that bled easily. There was moderate seropurulent discharge from the ulcer, and some sinuses were found leading to the lateral malleolus and the lateral bones. No induration of the surrounding soft tissue was palpable. The inguinal lymph nodes were enlarged, soft, tender, and discrete.

The right foot showed a plantar ulcer involving the area of the second to the fourth metatarsal stump and adjoining tarsal area. It measured  $3.5 \times 5.0$  cm. The ulcer was nearly flat, and covered with granulation tissue similar to that of the other foot, except that the edges were not quite everted. The inguinal lymph nodes were a little enlarged, soft and discrete.

There was 0.5 per cent sugar in the urine and there were hookworm ova in the stools. The hemoglobin was 90 per cent and the bacterial index was negative.

The obstinate ulceration of the left foot, which did not yield to standard methods of treatment, aroused the suspicion of malignancy. In view of the hopeless deformity of the foot and the long standing sepsis, which had greatly weakened the patient, it was decided to amputate the leg. On December 8, 1960, the leg was amputated below the knee. A biopsy specimen taken from the edge of the ulcer revealed squamous cell carcinoma. A biopsy specimen of the inguinal lymph nodes, taken later, showed chronic lymphadenitis, but no evidence of tumor metastasis.

The ulcer on the right foot improved at first with renewed immobilization and vigorous antibiotic therapy, but then started to spread again. A biopsy specimen taken from its edge on January 21, 1961, showed marked hyperplasia of the epithelium, but no frank changes of malignancy. As the ulcer continued to enlarge and assumed the look of the malignant ulcer on the other foot, with overhanging edges, another biopsy specimen was taken in June 1961. This revealed a keratinizing epidermoid carcinoma. Consequently, this leg also was amputated, on June 22, 1961.

CASE No. 2 (C.L.H. 175).—A male patient, 33 years old, was first treated as an outpatient at an outstation clinic of this institution in 1952. He suffered from leprosy of tuberculoid type, which had started in 1949. He had a few hypopigmented, anesthetic, well-defined patches,

with slightly raised edges on his back, arms, and right leg. The lower third of the right leg and the foot were anesthetic to light touch and slightly thickened from filarial elephantiasis. There was a trophic ulcer on the right heel. Both lateral popliteal nerves were thickened, the right more so than the left. The bacterial index was negative.

The patient was placed on antileprosy treatment with diamino-diphenyl sulfone. The skin lesions responded well and resolved completely in the course of time. The ulcer on the right heel did not resolve, however. The patient was admitted to the hospital on March 2, 1955. After saucerization and several scrapings, the ulcer almost healed and the patient was discharged in July 1957. On October 17, 1959 he was readmitted with a large ulcer covering the lateral aspect of the right heel and ankle area up to the lower third of the leg (Fig. 1). Some sinuses inside and outside the ulcerated area led to covered and bare bone and were discharging foul smelling pus. The inguinal lymph nodes were enlarged, tender, soft, and discrete.



FIG. 1.—Specimen of the amputated foot showing a typical malignant ulcer involving the heel and spreading up the leg. (Case No. 2).

The ulcer did not respond to the usual treatment with immobilization and antibiotics. The granulation tissue kept growing profusely until the whole ulcerated area was slightly elevated and the edges were everted. The patient was weak and toxic. As there was a suspicion of malignancy, a biopsy specimen was taken from the edge of the ulcer on May 7, 1960. It revealed epidermoid carcinoma (Figs.

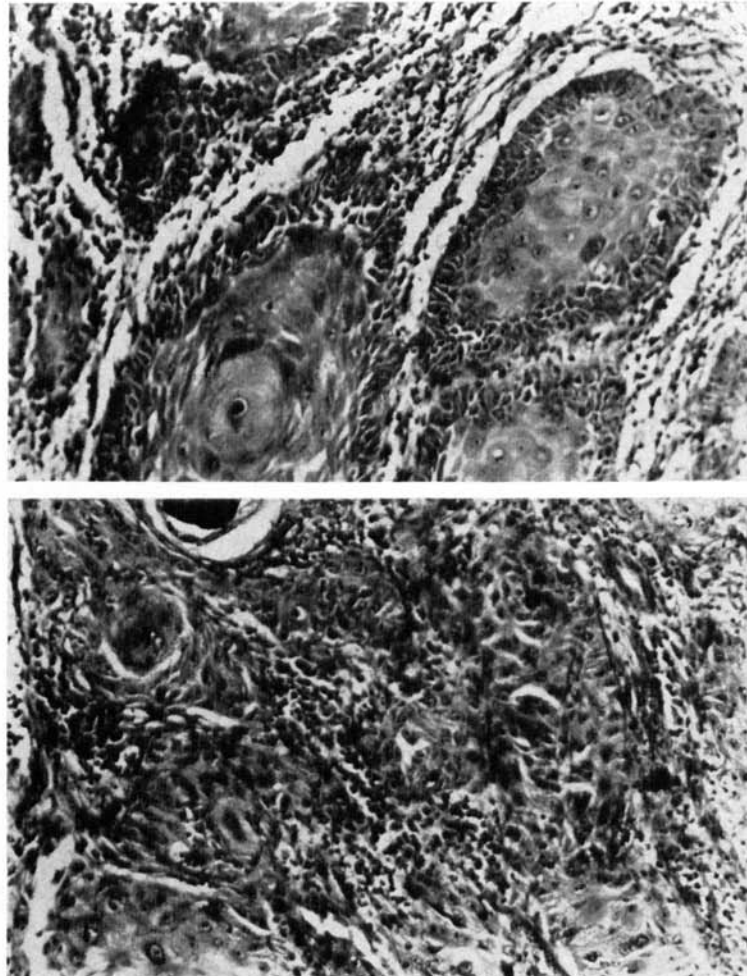


FIG. 2.—Photomicrograph showing a low grade squamous cell carcinoma. There are also collections of chronic inflammatory cells.

FIG. 3.—Another area in the tumor showing cellular pleomorphism and anaplasia. Note the cell nests.

2 and 3). The leg was amputated at the site of election below the knee on May 18, 1960. A biopsy of the inguinal lymph nodes, on June 18, 1960, showed involvement by both tuberculosis and secondary epidermoid carcinoma. Thereafter a block dissection of the right inguinal lymph nodes was carried out. A recurrence involving the inguinal skin, discovered on February 2, 1961, was excised as radically as possible on March 2, 1961. The resulting skin defect was covered by a plastic procedure. The wound healed soundly and, when the patient was last seen, on June 13, 1961, there was no evidence of fresh tumor growth. A specimen of tissue from the last operation was reported as a keratinizing epidermoid carcinoma.

CASE No. 3 (S.L.R.S. 4716).—A male aged 53 years was admitted as an inpatient on August 19, 1960. Thirty-five years previously he had noticed hypopigmented patches on his trunk and extremities. Five years after this he developed a claw-hand deformity of each hand. For the last ten years he had had repeated cracks and ulceration of the right heel. Two years previous to this report a blister appeared in the right heel, which broke down to form an ulcer. This did not heal, and gradually increased in size for several months in spite of treatment.

On physical examination the patient was found to have patches of atrophic skin on the upper and lower extremities, which were partly anesthetic to light touch. Both hands below the wrist and both legs below the knee were totally anesthetic to light touch. The right lateral popliteal nerve in the popliteal fossa and right posterior tibial nerve behind the medial malleolus, were markedly thickened and hard. On the right heel there was a fungating ulcer measuring 8 cm.  $\times$  6 cm. with an irregular margin (Fig. 4). The edges were raised and everted.



FIG. 4.—Photograph of the specimen showing a fungating malignant ulcer in the heel (Case No. 3).



FIG. 5.—Specimen of the amputated foot with the large plantar ulcer in the metatarsal region, showing grossly all the characteristics of a malignant ulcer (Case No. 4).

There was no induration of the surrounding tissue. On the lateral side of the heel there was a sinus discharging pus. The right inguinal lymph nodes were enlarged and matted together. They were firm, but not fixed to the surrounding tissue.

Urine examination showed no significant abnormality. There were hookworm ova in the stools. The hemoglobin was 9.75 gm. per cent. Skin smears were negative for acid-fast bacilli.

This was a case of resolved leprosy with bilateral ulnar-median nerve palsies. It was felt that the plantar ulcer had undergone malignant change. A biopsy of the heel ulcer, made on August 22, 1960, proved that the lesion was a squamous cell carcinoma. Amputation below the knee, at the site of the election, and block dissection of the right inguinal lymph nodes, were carried out. The lymph nodes did not show any evidence of tumor.

CASE No. 4 (C.M.C.H. 46115).—A male aged 46 years was admitted as an inpatient on August 30, 1960, with a history of leprosy for 30 years. Five years previously a small ulcer had developed at the plan-

tar aspect of the left foot. In spite of all available treatment it did not heal. During the last four months the ulcer began to increase in size, spread to the surrounding tissue, and became painful.

This was a case of resolved leprosy with a plantar ulcer of the left foot. The ulcer was extensive, involving the plantar surfaces of the heads of all the metatarsals and spreading to the dorsum of the left foot. It measured  $10 \times 12$  cm. The edges were irregular, raised and everted (Fig. 5). The base of the ulcer was necrotic and friable. The ulcer bled easily on touch. The left inguinal glands were enlarged. Urine examination revealed no abnormality. The hemoglobin was 12 gm. per cent. Clinically the ulcer appeared malignant, and a biopsy was made on September 9, 1960. Histopathologic examination revealed a squamous cell carcinoma. Amputation below the knee at the site of election, and block dissection of the left inguinal glands, were carried out. The lymph nodes showed metastatic tumor deposits.

#### DISCUSSION

In a study of 2,479 patients at Polambakkam in Chingleput District, South India, it was found that 9.3 per cent had plantar ulcers on one or both feet. In Nigeria 11 out of every 100 feet of leprosy patients undergoing treatment showed ulcers. Malignant transformation was not reported in any of them.

At the Schieffelin Leprosy Research Sanatorium at Karigiri between 25 and 30 per cent of nearly 2,000 patients attending the outpatient department regularly have or have had plantar ulcers. Only one case showed carcinomatous change. It seems to us that the development of a carcinoma in a plantar ulcer is extremely rare.

There are many known factors causing squamous cell carcinoma in skin. Arsenical cancers, actinic cancers, X-ray and radium cancers, are well known. Carcinomatous changes have been reported in association with lupus vulgaris, syphilis, varicose ulcers, osteomyelitis, and chronic sinuses associated with other lesions.

In all of the four cases described in this report there was a history of chronic ulcer for a period of more than five years. In one case the ulcer was present for nearly 20 years. In three cases there was definite evidence of chronic osteomyelitis. Therefore, chronic ulceration and chronic osteomyelitis seem to be the main causative factors in these malignant plantar ulcers. In all four cases the skin was totally anesthetic to touch and pain. Only deep sensation was present. Superficial sensory loss had not prevented the ulcers from turning malignant.

The diagnosis of malignant degeneration does not seem to be too difficult. One is not likely to think of this possibility, however, because of the rarity of the condition. The chronicity of these plantar ulcers is notorious. It may be that more cases with this complication will be detected if careful examination is made and if the fact is borne in

mind that malignant change may be encountered in such ulcers in anesthetic feet. The following points may be helpful diagnostically: history of long-standing ulceration; poor response to adequate treatment (immobilization, control of sepsis, and removal of dead bone); and appearance of the ulcer, with everted edges and size out of proportion to the mechanism causing it. The diagnosis should be confirmed by an adequate biopsy of the lesion.

#### SUMMARY

Four cases of squamous cell carcinoma arising in plantar ulcers in leprosy patients are described. It is pointed out that malignant changes can occur in denervated tissue and that chronic ulceration and chronic osteomyelitis with sinus formation may be the main etiologic factors.

#### RESUMEN

Son descriptos cuatro casos de carcinoma de células escamosas originados en úlceras plantares en pacientes leprosos. Se pone de manifiesto que los cambios malignos pueden ocurrir en tejido denervado y que la ulceración crónica y la osteomielitis crónica con formación de trayectos sinuosos puede ser el factor etiológico principal.

#### RESUMÉ

Quatre cas de cancer à cellules squameuses développés sur des ulcères plantaires de malades de la lèpre sont décrits. Les auteurs soulignent que des transformations malignes peuvent survenir dans des tissus dénervés et que l'ulcération chronique de même que l'ostéomyélite chronique avec formation de sinus peuvent être les facteurs étiologiques principaux.

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