# Squamous Cell Carcinoma Arising in Chronic Ulcers in Leprosy

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*Squamous cell carcinoma (SCC) arising in chronic ulcers of leprosy patients is uncommon. A retrospective analytical study of 416 biopsy specimens of chronic ulcers during 1976-2000 occuring on the extremity of leprosy patients was performed. Pathologic examination showed that 217 specimens (52.2%) were reported as pseudoepitheliomatous hyperplasia (PH). A total of 102 (24.5%) specimens reported as SCC, involving 100 individual patients (69 males, 31 females). SCC was localized on the lower extremity in 87 specimens (85.3%). No significant difference was observed between left and right foot using Chi-square test. The sole was the commonest site of involvement, and then the heel. SCC on the upper extremity which was much less common, presented in 15 specimens (14.7%). The tumor was localized on the palm in 10 specimens (right: 9, left: 1).*

*SCC in chronic ulcers of leprosy patients were much more common on the lower extremity than on the upper extremity. Most of the tumors on the upper extremity were localized on the right palm. This emphasizes the need for an active policy of prevention of disability in leprosy control programs.*

***Keywords:*** *Squamous cell carcinoma, Chronic ulcers, Leprosy*

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The etiology of cutaneous SCC (Squamous cell carcinoma) is multifactorial. Both environmental and host factors are important. Although SCC occurs in chronic ulcers, its occurrence is uncommon[1]. SCC developing in chronic ulcers of leprosy patients was first described in 1942[2]. Most articles appearing on this subject concerned only individual case reports [3-21]. Only 5 articles have dealt with a larger series of patients, 13, 16, 12, 38 and 11 cases respectively[22-26]. In this article the authors report a series of 100 leprosy patients with SCC developing in chronic ulcers.

## Material and Method

Raj-Pracha Samasai Institute (RPSI), in Samutprakarn, Thailand, has been established as the national leprosy research and training institute since 1960. The pathologic service of RPSI has served as a referral center for pathologic study of biopsy specimens from leprosy patients from most parts of Thailand. A retrospective analytical study of pathologic sections from a skin biopsy of chronic ulcers occuring on the limb of leprosy patients was performed. The paraffin embedded tissue specimens were processed and stained with hematoxylin-eosin. Histopathologic features of tissue specimens were blindly examined by two independent examiners. The available information from request forms of such cases, such as age, gender, type of leprosy, site of biopsy, were reviewed and analyzed. Categories data was expressed as percentage and Chi-square test or Fisher's exact test was used to analyze the different between right and left. A p-value $< 0.05$ was used to indicated significance different.

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## Results

From 1976 to 2000, 416 biopsy specimens from chronic ulcers on the extremities of leprosy patients were received. A total of 391 (94.0%) biopsy specimens were from the lower extremity (right: 197, left: 194), 25 (6.0%) biopsy specimens were from the upper extremity

(right; 16, left: 9). Most of the ulcers on the lower extremity were on the sole (150 specimens, 36.0%) and foot (101 specimens, 25.8%). Most of the ulcers on the upper extremity were on the palm (14 specimens, 56.0%). Details of the site and number of chronic ulcers are shown in Table 1 and 2.

Pathologic examination of the 416 biopsy specimens showed that 217 specimens (52.2%) were reported as pseudoepitheliomatous hyperplasia (PH), 102 SCC (24.5%), 22 benign ulcer, 21 atypical PH, 34 atypical PH vs SCC, 9 SCC in situ etc. Details of the pathologic reports of chronic ulcers are shown in Table 3.

A total of 102 biopsy specimens from chronic ulcers were reported as SCC, involving 100 individual patients. Of the 100 patients, 69 (69%) were males and 31 (31%) females. The average age (male and female) at the time of diagnosis of SCC was 55 years (ranging from 32 to 78 years); the average age of males was 54 years (ranging from 32 to 78 years), the average age of females was 57 years (ranging from 41 to 74 years). Two patients (2%) had a history of SCC in a chronic ulcer on different sites.

In 87 specimens (85.3%) the SCC was localized on the lower extremity (right: 47, left: 40). The tumor was described as being on the sole in 34 specimens (right: 21 (44.7%), left: 13 (32.5%)), 11 specimens on the heel, 4 on the toe, 11 on the ankle, leg and knee, 2 on the buttock, and 3 on the amputation stump (Table 1). In the remaining 22 specimens, the tumor was either localized elsewhere on the foot (forefoot or dorsum) or it was not possible to determine the origin of the tumor exactly due to its extent and severe deformity of the foot.

In 15 specimens (14.7%) the SCC was localized on the upper extremity (right: 11, left: 4). The tumor was localized on the palm in 10 specimens (66.7%), (right: 9, left: 1).

**Table 1.** The site and number of chronic ulcers and SCC on chronic ulcers on the lower extremity

| Site | Right | | Left | |
|---|---|---|---|---|
| | Ulcer (%) | SCC (%) | Ulcer (%) | SCC (%) |
| Toe | 16 (8.12) | 3 (6.39) | 14 (7.22) | 1 (2.5) |
| Sole | 77 (39.09) | 21 (44.68) | 73 (37.63) | 13 (32.50) |
| Heel | 19 (9.64) | 6 (12.77) | 14 (7.22) | 5 (12.50) |
| Foot | 50 (25.38) | 9 (19.15) | 51 (26.29) | 13 (32.50) |
| Ankle | 14 (7.11) | 2 (4.25) | 22 (11.34) | 2 (5.00) |
| Leg | 10 (5.08) | 3 (6.38) | 7 (3.61) | 2 (5.00) |
| Knee | 1 (0.50) | 0 - | 3 (1.55) | 2 (5.00) |
| Thigh | 0 - | 0 - | 3 (1.55) | 0 - |
| Buttock | 2 (1.02) | 1 (2.13) | 1 (0.51) | 1 (2.50) |
| Amputation stump | 8 (4.06) | 2 (4.25) | 6 (3.08) | 1 (2.50) |
| Total | 197 (100.00) | 47 (100.00) | 194 (100.00) | 40 (100.00) |

**Table 2.** The site and number of chronic ulcers and SCC on chronic ulcers on the upper extremity

| Site | Right | | Left | |
|---|---|---|---|---|
| | Ulcer | SCC | Ulcer | SCC |
| Finger | 1 | 0 | 1 | 0 |
| Palm | 13 | 9 | 1 | 1 |
| Hand | 0 | 0 | 2 | 1 |
| Wrist | 1 | 1 | 1 | 1 |
| Arm | 1 | 1 | 2 | 1 |
| Elbow | 0 | 0 | 2 | 0 |
| Total | 16 | 11 | 9 | 4 |

**Table 3.** Pathologic reports of chronic ulcers

| Pathologic reports | Number of specimens (%) |
|---|---|
| Pseudoepitheliomatous hyperplasia (PH) | 217 (52.16) |
| Ulcer | 22 (5.29) |
| Atypical PH | 21 (5.05) |
| Atypical PH vs Squamous cell carcinoma (SCC) | 34 (8.17) |
| Carcinoma in situ (CIS) | 9 (2.16) |
| SCC, well differentiated | 64 (15.39) |
| SCC, moderately differentiated | 13 (3.13) |
| SCC, poorly differentiated | 25 (6.01) |
| Basal cell epithelioma | 5 (1.20) |
| Malignant melanoma | 2 (0.48) |
| Sarcoma | 2 (0.48) |
| Others | 2 (0.48) |
| Total | 416 (100.00) |

## Discussion

The chronic ulcers and tumors were usually localized on the foot, the most common site of neuropathic ulcers in leprosy patients[25]. No significant difference was observed between left and right foot, in contrast to the report of Richardus and Smith in that the left foot was involved nearly twice as often as the right foot[25]. The sole was the commonest site of involvement in the present series; the heel was identified as the origin of the tumor in only 11 cases, while the sole was affected in 34 cases. However, 3 patients in the present series developed SCC on the amputation stump, which has rarely been reported before[27]. Another noteworthy finding was that 2 patients had SCC on the buttocks. These patients had severe deformities of hands and feet, this is an obstacle for

mobilization. Bed- or chair- ridden patients would eventually succumb to chronic ulceration and SCC on the buttocks.

Chronic ulcers and SCC on the upper extremity were much less common. Interestingly, the tumor was on the palm in 10 cases, with 9 cases on the right palm, a feature rarely reported before[10,25]. This is because the right hand is the dominant hand, so it is predisposed to repeated injury and chronic ulcers.

Pathologic examination of 102 SCC specimens were usually reported as SCC, well differentiated (62.7%). In the remaining 24.5% were SCC, poorly differentiated and 12.7% SCC, moderately differentiated. In 1932, Broders introduced a histologic classification system for SCC based on keratinocyte differentiation that is still used today[28]. Broders found, in cutaneous SCC, that the more differentiated the tumor, the less aggressive it is. Since then, the claim that more differentiated SCC is less prone to metastasis and recurrence and is associated with a higher survival rate has been substantiated in cutaneous SCC[29,30].

It has been a question that SCC arising in chronic ulcers in some cases are really instances of pseudoepitheliomatous hyperplasia (PH)[18,22]. This is considered benign and therefore would justify more conservative therapeutic modalities. Fleury and Opromolla[23] remarked that the distinction between a hyperplastic pseudoepitheliomatous reactivity and a well differentiated SCC is very difficult. The authors encountered this problem of distinction in at least 21 specimens reported as atypical PH and 34 specimens reported as atypical PH vs SCC. It is clear that pathologic reports cannot be conclusive in deciding on therapeutic measures. Biopsies are not always from the right place or not taken deep enough into the tumor mass, and pathologic features can be difficult to interpret. Clinical features such as the extent of the ulcerous fungating process, regional lymph node enlargement and radiological evidence of bone involvement must be taken into consideration. The surgeons in Thailand are in favor of below-knee amputation as the treament of choice for SCC on the foot, because a suitable prosthesis can be provided to keep disability and possible subsequent recurrent ulceration of the stump to a minimum.

Carcinomas arising from chronic lesions, including burn and x-ray scars, ulcers, osteomyelitic sinuses, traumatic wounds, and fistulas have relatively high metastatic rates, generally more than 20%, and are associated with a poor prognosis[31,32]. However, in patients with SCC on the extremity, regional lymph nodes are often enlarged due to the infected tumor on the extremity. Only when regional lymph nodes fail to resolve after amputation or clinically suspect enlarged lymph nodes, is further histologic investigation indicated[33]. In the present series, node dissection was done in 73 inguinal (right: 28, left: 45) and 2 axillary (right: 1, left: 1) lymph nodes. The pathologic results showed that metastatic SCC presented in 21 (28.8%) inguinal (right: 9, left: 12) and 2 axillary lymph nodes.

SCC arising in chronic ulcers of leprosy patients cannot be considered rare and should be recognized in time. They lead to considerable disability (amputation, often below the knee) and even to death due to metastatic spread. The occurrence of SCC in chronic ulcers emphasizes once again the need for an active policy of prevention of disability in leprosy control program.

## References


1. Grossman D, Leffel DJ. Squamous cell carcinoma. In: Freedberg IM, Eisen AZ, Wolff K, et al, eds. Fitzpatrick's dermatology in general medicine. New York: McGraw- Hill, 2003: 737-47.
2. Hayashi Y, Fukuda S. Cancroid from leprotic mal perforans du pied. La Lepro 1942; 13: 9.
3. Riedel RG. An additional note on malignancy in plantar ulcers in leprosy. Int J Lepr 1966; 34: 287-8.
4. Michalany J. Malignant tumours of the skin among leprosy patients. Int J Lepr 1966; 34: 274-86.
5. Boopalray JM, Muthusami TC. Squamous cell carcinoma arising from trophic ulcers. Lepr India 1979; 51: 74-7.
6. Troy JL, Grossman ME, Walter RR. Squamous-cell carcinoma arising in a leprous neurotrophic ulcer: report of a case. J Dermatol Surg Oncol 1980; 6: 659-61.
7. Andersen JG. Malignant degeneration in chronic ulceration of the leg and foot in leprosy patients; two case reports. Lepr Rev 1982; 53: 265-9.
8. Kumar K, Kant M. Squamous cell carcinoma developing in trophic ulcers in leprosy: a case report. Ind J Lepr 1984; 56: 656-7.
9. Bobhate SK, Sisodia SM, Kherdekar M. A case of squamous cell carcinoma in plantar ulcer in leprosy. Ind J Lepr 1984; 56: 653-5.
10. Reddy NBB, Srinivasan T, Krishnan SAR, Bhusnurmath SR. Malignancy in chronic ulcers in leprosy: a report of 5 cases from Northern Nigeria. Lepr Rev 1985; 56: 249-53.
11. Anilkumar G, Patil SD. Squamous cell carcinoma developing in trophic ulcer in leprosy: a case report. Ind J Lepr 1985; 57: 879-82.
12. Mohamed KN. Malignant transformation of plantar ulcers in leprosy. Singapore Med J 1987; 28: 432-5.
13. Arora SK, Mukhija RD. Squamous cell carcinoma in trophic ulcer cases. Ind J Lepr 1987; 59: 100-2.

14. Ozkan T, Yuksel A, Saylan T, Erding N, Sutlas M, Mat C. Carcinoma in plantar ulcers of leprosy patients: a report of 4 cases from Turkey. Lepr Rev 1988; 59: 356-7.
15. Majoroh TO, Imongan WI. Carcinoma in plantar ulcers of leprosy patients. Trop Geogr Med 1988; 40: 365-8.
16. Anilkumar G, Khedker MY, Bhume JI, Jawade GK. Malignant transformation of trophic ulcer in leprosy. Ind J Lepr 1988; 60: 385-8.
17. Naik R, Bharathi S, Bai BM. Squamous cell carcinoma developing in trophic ulcer in leprosy. Ind J Lepr 1988; 60: 380-4.
18. Duvauchelle D, Goldstein N. Cauliflower growths in ulcers of leprosy: a question of malignancy. Hawaii Med J 1989; 48: 129-31.
19. Riedel RG, Adhikari S. Malignancy in plantar ulcers in leprosy. Lepr Rev 1990; 61: 400-1.
20. Girdhar M, Mohan L, Arora SK, Gupta M, Basu PK, Mishra SD, Mukhija RD. Squamous cell carcinoma developing in trophic ulcers of leprosy: report of 2 cases. Ind J Lepr 1990; 62: 126-8.
21. Furuta M, Obara A, Ishida Y, Harada N, Ozaki M. Leprosy and malignancy: Autopsy findings of 252 leprosy patients. Int J Lepr 1990; 58: 697-703.
22. Srinivasan H, Desikan KV. Cauliflower growths in neuropathic plantar ulcers in leprosy. J Bone Joint Surg 1971; 53: 123-32.
23. Fleury RN, Opromolla DVA. Carcinoma in plantar ulcers in leprosy. Lepr Rev 1984; 55: 369-78.
24. Sane SB, Mehta JM. Malignant transformation in trophic ulcers in leprosy: a study of 12 cases. Ind J Lepr 1988; 60: 93-9.
25. Richardus JH, Smith TC. Squamous cell carcinoma in chronic ulcers in leprosy: a review of 38 consecutive cases. Lep Rev 1991; 62: 381-8.
26. Karthikeyan K. Squamous cell carcinoma in plantar ulcers in leprosy: a study of 11 cases. Ind J Lepr 2003; 75: 219-24.
27. Mahaisavariya B, Mahaisavariya P. Marjolin's ulcer complicating a poorly fabricated prosthesis. Injury 1991; 22: 423-4.
28. Broders AC. Practical points on the microscopic grading of carcinoma. N Y State J Med 1932; 32: 667.
29. Lund H. How often does squamous cell carcinoma of the skin metastasize? Arch Dermatol 1965; 92: 635-7.
30. Shiu MH, Chu F, Fortner JG. Treatment of regionally advanced epidermoid carcinoma of the extremity and trunk. Surg Gynecol Obstet 1980; 150: 558-62.
31. Mouly R. Cancer in burn scars ("Marjolin's Ulcers"). Trans Int Soc Plast Surg 2nd Congress, 1959. Edinburgh: E & S Livingstone, 1960: 130-42.
32. Hejna WF. Squamous cell carcinoma developing in the chronic draining sinuses of osteomyelitis. Cancer 1965; 18: 128-32.
33. Dinehart SM, Pollack SV. Metastases from squamous cell carcinoma of the skin and lip. J Am Acad Dermatol 1989; 21: 241-8.

## *โรคมะเร็งชนิด squamous cell carcinoma ที่เกิดขึ้นในแผลเรื้อรังในผู้ป่วยโรคเรื้อน*

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*โรคมะเร็งชนิด squamous cell carcinoma (SCC) ที่เกิดขึ้นในแผลเรื้อรังในผู้ป่วยโรคเรื้อนพบไม่บ่อยนัก รายงานนี้ได้ศึกษาแบบย้อนหลังระหว่าง พ.ศ. 2519 ถึง พ.ศ. 2543 ในชิ้นเนื้อจำนวน 416 ชิ้น ที่ตัดจากแผลเรื้อรังตามมือเท้าของผู้ป่วยโรคเรื้อน โดยศึกษาลักษณะการเปลี่ยนแปลงทางจุลพยาธิวิทยา และวิเคราะห์ข้อมูลทั่วไปของผู้ป่วยและตำแหน่งของแผล ผลจุลพยาธิวิทยาส่วนใหญ่พบว่าชิ้นเนื้อ 217 ชิ้น (52.2%) เป็น pseudoepitheliomatous hyperplasia 102 ชิ้น (24.5%) เป็น SCC จากผู้ป่วย 100 ราย (ชาย 69 ราย, หญิง 31 ราย) SCC เกิดขึ้นบนแผลที่เท้า 87 ราย (85.3%) มีความแตกต่างอย่างไม่มีนัยสำคัญของจำนวน SCC บนเท้าซ้ายกับเท้าขวา โดยใช้ Chi-square test sole และ heel เป็นตำแหน่งบนเท้าที่พบ SCC มากที่สุด SCC บนแผลที่มือพบน้อยกว่าที่เท้ามาก คือพบเพียง 15 ชิ้น (14.7%) ในจำนวนนี้ 9 ชิ้นพบจากฝ่ามือข้างขวา 1 ชิ้นพบจากฝ่ามือข้างซ้าย*

*SCC ที่เกิดขึ้นในแผลเรื้อรังในผู้ป่วยโรคเรื้อน พบที่เท้าบ่อยกว่าที่มือมาก SCC ที่มือมักพบอยู่ที่ฝ่ามือข้างขวา SCC มีผลทำให้ผู้ป่วยพิการจากการผ่าตัดตัดแขนขารักษามะเร็ง และอาจทำให้ผู้ป่วยเสียชีวิตจากมะเร็งแพร่กระจาย จึงจำเป็นต้องมีการเน้นย้ำถึงกิจกรรมการป้องกันความพิการในผู้ป่วยโรคเรื้อนเพื่อป้องกันการเกิดแผลมะเร็งต่อไป*