Case Report

Verrucous carcinoma of the foot from chronic pressure ulcer

MY Lee¹, JC Shin*,², CI Park², DW Rha² and TK Sastry¹

¹Department of Physical Medicine and Rehabilitation, School of Medicine, University of North Carolina at Chapel Hill, NC, USA; ²Department of Rehabilitation Medicine, Yonsei University College of Medicine, Seoul, South Korea

Study design: This is a case report with literature review.

Objective: To describe a case of vertucous carcinoma, a rare histopathologic type, complicating a chronic pressure ulcer of duration less than 3 years.

Setting: The department of Physical Medicine and Rehabilitation, University of North Carolina at Chapel Hill, USA

Method: A 24-year-old African-American male with long-standing incomplete paraplegia visited the wound clinic due to a pressure ulcer that had lasted for more than 1 year on the medial side of the right foot. Despite conservative management for almost 2 years after the initial visit, the ulcer is suspected to have undergone malignant transformation. Histological study led to the diagnosis of verrucous carcinoma that necessitated transtibial amputation on the right foot.

Result: The carcinoma developed within 3 years, which was a relatively short time period for a pressure ulcer to have undergone malignant transformation. The diagnosis of verrucous carcinoma has never been reported as carcinoma complicating a pressure ulcer. No evidence of local recurrence or distant metastasis was seen in postoperative 10 months.

Conclusion: The possibility of malignant transformation should be kept in mind in cases of pressure ulcers that are unresponsive to treatment or that show morphological changes suspected to be cancerous. Furthermore, early detection and intervention increases the probability for successful outcome.

Spinal Cord (2004) 42, 431-434. doi:10.1038/sj.sc.3101606; Published online 23 March 2004

Keywords: Marjolin's ulcer; verrucous carcinoma; short duration of ulcer

Introduction

Malignant transformation of chronic wound, called 'Marjolin's ulcer' following the first description by Marjolin¹ in 1828 of carcinomatous degeneration in burn scars, is used to describe carcinoma developed in long-lasting pressure ulcers, stasis ulcers, burn scars, or osteomyelitis sinuses.

Malignant transformation of a pressure ulcer is very rare with a reported incidence of about 0.5%.² However, the mortality rate from pressure ulcers that turn malignant is very high compared with that for Marjolin's ulcers developed from other chronic wounds.^{2–4} The duration of the ulcer is very important, and the reported average period between ulcer development and malignant transformation ranges from 22 to 34 years.^{4–7} Carcinoma developed from these pressure ulcers is usually seen in the trunk area, that is, the sacral and ischial areas. $^{\rm 2-4}$

We encountered a case of pressure ulcer, that is, Marjolin's ulcer, which underwent malignant transformation within a short period of time (less than 3 years) into the very rare histopathologic type, verrucous carcinoma in the foot, which, is not a frequent site of malignant transformation. Thus, we report the case and present a literature review.

Case report

A 24-year-old African-American male visited the wound clinic on September 26th, 2000 due to a pressure ulcer that had developed about a year previously due to right, plastic ankle–foot orthosis (AFO). This patient was L3 incomplete paraplegia due to congenital spinal bifida. He wore a bilateral AFO and used bilateral forearm crutches for ambulation. He was independently np

^{*}Correspondence: JC Shin, CPO Box 8044, Department of Rehabilitation Medicine, Yonsei University College of Medicine, Seoul 120–752, South Korea

ambulatory and could carry out all daily living activities independently.

Physical examination revealed a pressure ulcer sized $3.5 \text{ cm} \times 2.0 \text{ cm} \times 0.5 \text{ cm}$ (length × width × depth), at stage 4 by National Pressure Ulcer Advisory Panel (NPUAP),⁸ in the first metatarsal area of the right foot on the medial side. Debridement of necrotic debris was performed, enzymatic ointment dressing was applied for softening and the lesion was debrided. A modified, new AFO was prepared for the purposes of relieving pressure at the pressure ulcer due to the right AFO.

Despite regular debridement of necrotic debris and change of dressing materials for 13 months after the initial visit until November 2001, the size of pressure ulcer did not change and wound bleeding was seen intermittently. No evidence of osteomyelitis was observed in the right foot according to laboratory and radiographic studies. The pressure ulcer became larger and histopathologic study in May 2002 of a debrided tissue sample showed evidence of atypical proliferative squamous lesion. However, physical examination in June 2002, 21 months after the initial visit, revealed evidence of hyperkeratosis surrounding the ulcer suspected of cancerous change (Figure 1).

A wide excision biopsy was performed in June 2002. Gross anatomy showed the core of a hyperkeratotic lesion at the medial base of the first metatarsal area with a central tract, which tracked down to the periosteum. Histopathologic study revealed the typical blunt papillary projections of a well-differentiated epithelium with little atypia. These findings combined to support diagnosis of verrucous carcinoma (Figure 2). At the time of diagnosis, no evidence of distant



Figure 1 Photograph taken after wide excision biopsy. The ulcer measures $3.5 \text{ cm} \times 4.2 \text{ cm} \times 1.2 \text{ cm}$ (length \times width \times depth), with a dirty granulating base surrounded by a hyperkeratotic area and minimal serous drainage

1a



Figure 2 Histopathologic study shows typical blunt papillary projections (1a and b) of well-differentiated epithelium with little atypia (2)

metastasis or bony involvement was present according to staging workup including the magnetic resonance imaging study of the right leg. The patient was transferred to the department of orthopedic surgery and underwent right trans-tibial amputation on September 6th, 2002. At 10-month follow-up in July 2003, he showed no evidence of local recurrence of the pressure ulcer or distant metastasis.

Discussion

Pressure ulcers in patients with spinal cord injury (SCI) are a common complication, with Fuhrer *et al*⁹ reporting that 33% of patients had at least one pressure ulcer, of whom 13.6% had stage 3 or 4 pressure ulcer according to a community-based survey of SCI patients. The complications of pressure ulcers include soft-tissue

100

abscess, heterotopic ossification, pelvic abscess, osteomyelitis, sepsis, etc.¹⁰ Malignant transformation is one of the rare complications of pressure ulcers. Mustoe *et al*² reported two malignancies out of 356 pressure ulcers in a group of 992 SCI patients, and most reports in the literature have presented an incidence of around 0.5%.

The most frequent sites of pressure ulcer carcinoma development have been the sacrum and ischium.²⁻⁴ However, a carcinoma complicating a pressure ulcer developed in the distal extremity, as seen in the present case, is very rare.^{11,12} The four hallmark clinical signs of malignant transformation of chronic wound, as reported by Esther *et al*,¹³ are: (1) appearance of a mass; (2) new onset of pain; (3) a change in odor of the drainage; and (4) change in the character, volume, or appearance of the drainage. We observed bleeding from the wound and hyperkeratotic change in the present case.

The most frequent type of malignancy from pressure ulcers is squamous cell carcinoma, whereas basal cell carcinoma, adenocarcinoma, variety of sarcoma, and melanoma are rarely observed.¹⁴ To the best of our knowledge, the present case is the first report of verrucous carcinoma as a pressure ulcer carcinoma. Ackerman¹⁵ described verrucous carcinoma for the first time in the oral cavity and its characteristics are defined as a well-differentiated, slow-growing neoplasm with a tendency for local recurrence but not for metastasis. Since the epithelium shows little atypia, verrucous carcinoma is difficult to differentiate from benign lesions such as verruca vulgaris, reactive epidermal hyperplasia, keratoacanthoma, and hyperkeratotic basal cell epithelioma.¹⁶ Niebauer¹⁷ negated the effectiveness of biopsy using simple curettage in the diagnosis of pressure ulcer carcinoma and instead recommended deep tissue biopsy including subcutaneous tissue. We also observed an atypical proliferative squamous lesion according to the histopathologic study of debrided tissue in May 2002. It was difficult to confirm a diagnosis of malignancy from this observation alone, and the diagnosis was finally confirmed in July 2002 using wide excision biopsy. Therefore, deep tissue biopsy is needed to confirm diagnosis when a pressure ulcer is suspected to have undergone cancerous change.

Clinically, it was reported that metastasis of regional lymph nodes is rare and that a low mortality rate is seen with verrucous carcinoma.¹⁶ We also found no evidence of distant metastasis including regional lymph node metastasis in the present case. Furthermore, no evidence of new onset metastasis or local recurrence was observed during the 10-month follow up after transtibial amputation performed on September 6th, 2002. However, it is known that carcinoma developed from pressure ulcers shows highly aggressive behavior with a high mortality rate compared with secondary malignancy developed from chronic wound including burn scars, chronic venous ulcers, and sinuses due to osteomyelitis. Therefore, continual follow-up is necessary in the present case despite the absence of any evidence of local recurrence or metastasis of regional lymph nodes at 10 months.

Various studies have reported latency periods between ulcer development and malignant transformation ranging from 22 to 34 years,^{4–7} suggesting a minimum of 20 years. However, the pressure ulcer of our case turned malignant within a short period of less than 3 years, indicating a latency period much shorter than that of other cases previously reported. Thus, although longstanding ulceration is an important factor affecting the process of malignant transformation of pressure ulcer, the possibility of malignant transformation of pressure ulcer having a significantly shorter period of duration should also be kept in mind.

In conclusion, clinicians need to consider the possibility of malignant transformation from the beginning, regardless of the duration, when a pressure ulcer wound does not respond to conservative treatment, bleeds frequently, or shows morphologic changes suspected of cancerous change in the wound bed or its margin. Furthermore, biopsy performed with a sufficient amount of tissue obtained from the wound, including tissue from the wound bed and a deep portion, will aid in obtaining a good prognosis through early diagnosis and effective treatment.

References

- 1 Marjolin J-N, Ulcère. *Dictionnaire de Medecine*, Vol 21, Pratique 1828.
- 2 Mustoe T, Upton J, Marcellino V, Tun CJ, Rossier AB, Hachend HJ. Carcinoma in chronic pressure sores: fulminant disease process. *Plast Reconst Surg* 1986; 77: 116–121.
- 3 Ceuppens A, Wylock P, de Raeve H. Carcinoma in a pressure sore. *Br J Plast Surg* 1997; **50:** 382–383.
- 4 Grotting JC, Bunkis J, Vasconez LO. Pressure sore carcinoma. *Ann Plast Surg* 1987; **18**: 527–532.
- 5 Giblin T, Pickrell K, Pitts W, Armstrong D. Malignant degeneration in burn scars: Marjolin's ulcer. *Ann Surg* 1965; **162**: 291–297.
- 6 Schlosser RJ, Kanar EA, Harkins HN. Surgical significance of Marjolin's ulcer: with report of three cases. *Surgery* 1956; **39:** 645–653.
- 7 Treves N, Pack GT. Development of cancer in burn scars: analysis and report of thirty-four cases. *Surg Gynecol Obstet* 1930; **51**: 749–782.
- 8 Salcido R, Goldman R. Prevention and management of pressure ulcers and other chronic wounds. In: Braddom RL (ed) Physical Medicine & Rehabilitation, 2nd ed., W.B. Saunders Company: Philadelphia, 2000, pp 645–664.
- 9 Fuhrer MF *et al.* Pressure ulcers in community resident persons with spinal cord injury: prevalence and risk factors. *Arch Phys Med Rehabil* 1993; **74:** 1172–1177.
- 10 Yarkony GM. Pressure ulcers: a review. Arch Phys Med Rehabil 1994; 75: 908–917.
- 11 Stankard CE, Cruse CW, Wells KE, Karl R. Chronic pressure ulcer carcinomas. *Ann Plast Surg* 1993; **3**: 274–277.
- 12 Dumurgier C, Pujol G, Chevalley J, Bassoulet H, Ucla E, Stchepinsky P. Pressure sore carcinoma: a late but

fulminant complication of pressure sores in spinal cord injury patients: case reports. *Paraplegia* 1991; **29**: 390–395.

- 13 Esther RJ, Lamps L, Schwartz HS. Marjolin ulcers: secondary carcinomas in chronic wounds. *J South Orthop Asso* 1999; **8**: 181–187.
- 14 Gan BS, Colcleugh RG, Scilley CG, Craig ID. Melanoma arising in a chronic ulcer. J Am Acad Dermatol 1995; 32: 1058–1059.
- 15 Ackerman LV. Verrucous carcinoma of the oral cavity. *Surgery* 1948; **23:** 670–678.
- 16 Ho J, Diven DG, Butler PJ, Tyring SK. An ulcerating verrucous plaque on the foot Verrucous carcinoma (epithelioma cuniculatum). Arch Dermatol 2000; 136: 547–551.
- 17 Niebauer JJ. Development of squamous-cell carcinomata in sinus tracts of chronic osteomyelitis. *J Bone Joint Surg Am* 1946; **28:** 280–285.