Aspects of tropical ulcerating diseases

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Chapter 4

Etiology and incidence of chronic ulcers in Blantyre, Malawi


Abstract

**Background** Little information is available on the incidence and etiology of chronic ulcers in the tropics. Therefore, the incidence and etiology of chronic skin ulcers were assessed in out-patients at the Department of Dermatology and in in-patients at the Departments of Dermatology, Surgery, Medicine, and Pediatrics, Queen Elizabeth Central Hospital (QECH), Blantyre, Malawi.

**Method** In a 10-week study period, 44 patients (31 males, 70%) with chronic skin ulcers were diagnosed from 6292 patients seen by the departments involved.

**Results** The mean age of patients with ulcers was 38 years (range, 9 months to 82 years). The most frequent cause of ulcers was bacterial infection \( n = 22 \), followed by malignancy \( n = 11 \) and trauma \( n = 7 \).

**Conclusion** In contrast with developed countries, venous and diabetic ulcers were uncommon. In addition to bacterial infections, a surprisingly large number of malignancies were found in this study. We speculate that human immunodeficiency virus (HIV) infection, which is seen with a high prevalence at QECH, is a contributing factor. Because of the large number of malignancies, we recommend early histopathologic investigation of chronic ulcers in this part of Africa.
Introduction

Chronic ulcers are an important cause of morbidity in developing countries. This may be explained by the poor socioeconomic conditions and poor health services. In contrast with developed countries, little is known about the prevalence and etiology of skin ulcers in these areas. One study from Nigeria reported that the most common etiologic factors of leg ulcers were trauma, diabetes mellitus, and sickle cell disease. Depending on the region, infectious causes, such as cutaneous leishmaniasis or Buruli ulcer, may be encountered. In contrast, venous ulcers on the legs are the most common cause of ulcers in developed countries, and are reported to be uncommon in tropical countries.

Data from Malawi are scanty; one study showed trauma to be the most important cause of chronic wounds. We undertook this study to investigate the incidence and etiology of chronic skin ulcers presenting to the Queen Elizabeth Central Hospital (QECH) in Blantyre, Malawi.

Methods

The study was performed at QECH, Blantyre, Malawi, which is the teaching hospital of the College of Medicine and the largest referral hospital in Malawi, with over 1000 beds. Blantyre is the commercial capital and main industrial center of Malawi with a population of around 800,000 people. The study was performed during a 10-week period in the dry season (May to July) when daytime temperatures were around 25–30 °C.

All patients presenting with chronic ulcers at the outpatient clinic of the Department of Dermatology were included; in addition, the wards of the Departments of Dermatology, Surgery, Medicine, and Pediatrics were visited twice daily and any patient who had an ulcer was recruited into the study, irrespective of whether this was the main reason for admission or a comorbidity. All patients were informed about the purpose and methods of the study and were included after written consent had been obtained. The study was approved by the College of Medicine Research and Ethics Committee.

Chronic skin ulcers were defined as round or irregularly shaped excavations of the skin that had resulted from a loss of the epithelium and dermis, or even deeper, and had existed for more than 4 weeks.

Data were entered onto a case record form: age, gender, previous treatment, and underlying disease (e.g. diabetes mellitus, leprosy or sickle cell disease). A detailed description of the ulcer was made, including the number, duration, location, size,
aspect of the surrounding tissue, shape, edge, presence of exudate, and color. The presence or absence of varicose veins was noted. The arterial circulation was examined by palpating the dorsalis pedis artery and the posterior tibial artery. Clinical signs of inflammation (redness, pain, swelling, and increased temperature) were noted. Ulcerating pyoderma was defined as a purulent ulceration with signs of inflammation. Secondary ulcerating pyoderma was defined as a purulent ulceration of a pre-existing skin lesion, for example eczema or insect bites. A first clinical diagnosis was made by two investigators (ACS, WHS); a second opinion was obtained by examination of digital pictures in The Netherlands (JEZ, WRF). Swabs for Gram stain and bacterial culture were taken from the wound surface after thorough cleaning with water-soaked gauze. The swabs were inoculated onto appropriate agar media and a Gram stain was performed. If required for diagnosis, 4-mm punch biopsies were taken from the edge of the ulcer after local infiltration with 1% lidocaine. The specimens were fixed in formalin and embedded in paraffin. Slides were stained with hematoxylin and eosin; when indicated, additional slides were stained with Ziehl–Neelsen stain for the detection of acid-fast bacilli and with periodic acid–Schiff (PAS) and silver stains for the detection of fungi. After initial reading in Malawi, two unstained slides of each biopsy were shipped to The Netherlands for confirmation. A final diagnosis was made by taking into account the clinical presentation and the results of the microbiologic and histologic examinations. The study had a case series design. In addition, the incidence of skin ulcers in each department was estimated as the number of patients presenting with ulcers divided by the total number of patients seen at the out-patient department or as admissions during the study period.

Results

Clinical findings
In the study period, 3320 patients (12 with chronic ulcers; 3.6/1000) were seen as out-patients in the Department of Dermatology, and 44 patients (one with a chronic ulcer; 23/1000) were admitted. In the other clinical departments these numbers were: Medicine, 1650 admissions (four chronic ulcers; 2.4/1000); Surgery, 688 admissions (23 chronic ulcers; 34/1000); Pediatrics, 590 admissions (four chronic ulcers; 6.8/1000). All 44 patients (0.7% of all patients screened) who were diagnosed as having a chronic skin ulcer consented to be enrolled into the study. The age range was 9 months to 82 years, with a mean age of 38 years. The mean age in children was 4.5 years and in adults was 43.5 years. The age distribution is shown in Fig 1.
The mean duration of the ulcers at the time at which the patients were enrolled in the study was 4.5 months (range, 1 month to 3 years; median, 19.1 months). In seven patients (16%), ulcers had been present for more than 6 months (in three for more than 1 year). Seven patients (16%) had a history of trauma; one ulcer was a result of a traffic accident; others were caused by decubitus (three; 7%) and snake bite or crocodile bite (three; 7%).

In the majority of patients (30; 68%), the ulcers were on the legs or feet. Of these, 16 patients had multiple ulcers, including eight who had bilateral ulcers. Two other patients had multiple ulcers spread over the body (Fig. 2). The total number of patients with multiple ulcers was therefore 18 (41%). The size of the ulcers ranged from 2 mm × 2 mm to 370 mm × 110 mm. Clinically, infection was suspected in 15 patients (13 of whom had ulcerating pyoderma); eight patients were thought to have a malignancy and seven had a traumatic ulcer. None of the patients showed clinical venous or arterial insufficiency. None of the patients was diabetic. In 14 patients, a clinical diagnosis could not be made.

Histopathologic findings

Histologic examination was performed in 34 (77%) of the 44 patients; four patients refused to have a biopsy taken and, in six patients, a biopsy was not indicated on the basis of the clinical picture. Eleven patients had malignancies, six (55%) of which were squamous cell carcinoma, four (36%) were Kaposi’s sarcoma, and one was dermatofibrosarcoma protuberans. An inflammatory reaction suggestive of infection was noted in 20 biopsies (59%).

Figure 1. Age and sex distribution of study population.
Microbiology

Cultures were performed in 41 patients (93%); *Staphylococcus* spp. grew in 12 (29%) of the cultures. Other isolates included *Proteus* spp. (10, 24%), *Escherichia coli* (six, 15%), β-hemolytic streptococci group A (one, 2%), non-group A streptococci (three, 7%), *Klebsiella* spp. (one, 2%), *Pseudomonas* spp. (three, 7%), *Salmonella* spp. (two, 5%), and *Cryptococcus neoformans* (one, 2%); three (7%) cultures yielded no growth (Fig. 3).

Cultures from six (46%) of the 13 patients with a clinical diagnosis of (secondary) ulcerating pyoderma yielded growth of streptococci and/or *Staphylococcus*. 

**Figure 2.** Location of ulcers.

**Figure 3.** Results of wound cultures.
Bacterial cultures revealed pathogens in 12 of the 20 patients in whom biopsy showed an inflammatory reaction; nine of these were *Staphylococcus aureus*, two were non-hemolytic streptococci, and one was SY-hemolytic streptococci.

**Table 1.** Final diagnoses.

<table>
<thead>
<tr>
<th></th>
<th>number</th>
<th>Mean duration in weeks</th>
<th>Mean ages in years</th>
</tr>
</thead>
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<tr>
<td><strong>Trauma N= 7</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Snake/crocodile bite</td>
<td>3</td>
<td>15</td>
<td>39</td>
</tr>
<tr>
<td>Trauma after traffic accident</td>
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<td>4</td>
<td>45</td>
</tr>
<tr>
<td>Pressure sore</td>
<td>3</td>
<td>8</td>
<td>42</td>
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<td><strong>Infection N=22</strong></td>
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<tr>
<td>Ulcerating pyoderma</td>
<td>13</td>
<td>7</td>
<td>34</td>
</tr>
<tr>
<td>Sec. Ulcerating pyoderma</td>
<td>7</td>
<td>21</td>
<td>22</td>
</tr>
<tr>
<td>Cryptococcoma</td>
<td>1</td>
<td>4</td>
<td>50</td>
</tr>
<tr>
<td>Cancrum oris</td>
<td>1</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td><strong>Malignancy N=11</strong></td>
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<td></td>
<td></td>
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<tr>
<td>Squamous cell carc.</td>
<td>6</td>
<td>53</td>
<td>48</td>
</tr>
<tr>
<td>Kaposi sarcoma</td>
<td>4</td>
<td>38</td>
<td>52</td>
</tr>
<tr>
<td>Dermatofibrosarcoma protuberans</td>
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<td>44</td>
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<tr>
<td><strong>Miscellaneous N=4</strong></td>
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</tr>
<tr>
<td>Chronic aspecific ulcer</td>
<td>4</td>
<td>49</td>
<td>65</td>
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</table>

The final diagnoses are shown in Table 1. Infection was found in 22 patients (50%), mainly ulcerating pyoderma; 11 patients (25%) had a malignancy, seven had traumatic wounds, and four had miscellaneous causes.

**Discussion**

This study shows an incidence of chronic ulcers that was lower than expected. Bacterial ulcers are the main cause of chronic ulcers in our setting. Of these infectious causes, ordinary ulcerating pyoderma is most common. It is not known why pyoderma is common in many tropical countries. Environmental factors, such as small trauma to the skin, may contribute; streptococci or staphylococci may be more virulent, although this has never been investigated. Intrinsic factors, including general condition, human immunodeficiency virus (HIV) infection, age, and nutritional status, may also play a role.
A surprisingly large number of malignancies were found. The occurrence of squamous cell carcinoma in long-standing chronic ulcers in Africans is well recognized. Delayed wound healing results in chronic inflammation, which can give rise to the phenomenon of “scar cancers.” Most patients did not report a long duration of their ulcers. One may speculate that these malignant ulcers existed for a much longer period than reported by the patients. A recent study at QECH showed an HIV prevalence of 70% and 36% amongst medical and surgical admissions, respectively. In our study group, HIV prevalence may therefore be suspected to be high; five patients had acquired immunodeficiency syndrome (AIDS)-defining illnesses (four Kaposi’s sarcoma and one cryptococcoma). HIV infection might contribute to impaired wound healing. There is also evidence that suppressed cell-mediated immune responses and angiogenesis, and reduced apoptosis, as seen in HIV infection, may favor the development of malignancies. We speculate that this might explain the large number of malignancies seen in this study.

No diabetic, venous, or arterial ulcers were found. This is in contrast with the results observed in developed countries, and also in studies performed in other African countries, in which diabetes, in particular, seems to be an important cause of chronic ulcers.

Mycobacterial ulcers, which have been reported to occur in Malawi, were not detected in this study.

In conclusion, bacterial infections are the most common cause of chronic skin ulcers in Malawi. A surprisingly large number of malignancies were found in this study. One may speculate that HIV infection is a contributing factor. Because of the large number of malignancies, we recommend early histopathologic investigation of chronic ulcers in this part of Africa.

Acknowledgements

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References
