Ulcerated tophaceous gout

Girish K Patel, Wendy L Davies, Patricia P Price, Keith G Harding

ABSTRACT

Gout is often considered a disease of an excessive lifestyle, a ‘malady of kings’. Today, more than 1% of the European and US populations are afflicted with gout, although ulceration over gout tophi remains uncommon. We describe four cases of ulceration associated with gout tophi to highlight the clinical presentation, complications and a management strategy.

Key words: Ulcer • Gout

Gout is a common inflammatory arthropathy that is estimated to affect 1.4% of the UK adult population, similar to the incidence observed in many other countries (1–3). Overall, the incidence of gout has steadily risen between the 1970s and 1990s, but now appears to have plateaued (3,4). The prevalence of gout is greater in the elderly, such that 4% of individuals over 65 years of age are affected (1–3). Chronic gout results from persistent hyperuricaemia typically over a period of greater than 5 years, due either to delayed or ineffective treatment, which can predispose to the formation of tophi that are characterised histologically by a subcutaneous accumulation of monosodium urate crystals surrounded by chronic mononuclear and giant cell inflammation (5). Typically such tophi develop on the ear helix, over the olecranon processes, achilles tendons, around the knee, as well as within and around the toe and finger joints (6). In general, gout tophi are painless and rarely become infected, although their presence can dramatically impair quality of life (7). Yet despite the propensity for sites of potential trauma, surprisingly ulceration over gout tophi remains uncommon, even in the presence of quite large nodules. In this report we describe four patients with ulcerated tophaceous gout to highlight this complication and the complex issues related to wound management.

The four cases with idiopathic gout are described, two females and two males, mean age 78 years (range 74–84 years). One male was diagnosed with myelodysplasia and initiated on hydroxycarbamide 1 year prior to presentation, when his blood count showed haemoglobin 9.3 g/dl, white blood count 12.4 × 10⁹/l and platelet count 571 × 10⁹/l.

Tophaceous gout had been diagnosed prior to the development of ulceration in three patients, 30, 20 and 2 years earlier; two of whom had received treatment with allopurinol 18 and 12 years prior to the ulceration. The two female patients were both started on allopurinol after ulceration had occurred.

Two patients at the time of presentation, prior to initiation of therapy, had elevated serum uric acid levels: 0.38 and 0.39 mmol/l (normal range 0.1–0.36 mmol/l). Also two patients had multiple comorbidities (Table 1), one of whom had a history of peripheral vascular disease of the affected limb.

All patients have evidence of tophaceous gout at multiple sites (Figure 1). Three patients had an ulcer that developed over a gout tophus on a toe, while a male patient had ulceration overlying the heel. In all cases the skin surrounding the wound was thinned and appeared ‘stretched’. Two wounds developed over the great toe and the other on the small toe, all involving the distal metatarsophalangeal joint. Within the small ‘punched out’ ulceration, a hard gout tophus

Key Points

- ulceration over gout tophi is both extremely painful and debilitating
- all patients with gout are at risk of multiple comorbidities that can adversely impact wound healing
- topical hydrogels can be used to facilitate debridement of the tophus
Table 1 Clinical details of the three patients with ulceration over a gout tophus

<table>
<thead>
<tr>
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<th>VW</th>
<th>CW</th>
<th>VM</th>
<th>TW</th>
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<tbody>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Female</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Preceding history of gout (years)</td>
<td>30</td>
<td>0</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>Serum urate level at presentation (normal range 0·1–0·36 mmol/l)</td>
<td>0·31</td>
<td>0·38</td>
<td>0·33</td>
<td>0·32</td>
</tr>
<tr>
<td>Gout treatment</td>
<td>Allopurinol</td>
<td>Allopurinol</td>
<td>Allopurinol</td>
<td>Allopurinol</td>
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<tr>
<td>Coexisting morbidities</td>
<td>Maturity onset diabetes, diabetic retinopathy, diabetic neuropathy, chronic venous insufficiency, asthma</td>
<td>Peripheral vascular disease, ischaemic heart disease, hypertension, cerebrovascular disease</td>
<td>Hypertension, ischaemic heart disease, chronic venous insufficiency</td>
<td>Hypertension, maturity onset diabetes, hypercholestaemia</td>
</tr>
<tr>
<td>Concomitant medication</td>
<td>Metformin, gliclazide, indomethacin</td>
<td>Dipyridamole, atenolol, isosorbide mononitrate, furosemide, diltiazem, calcium carbonate</td>
<td>Amiloride hydrochloride</td>
<td>Simvastatin, atenolol, metformin, gliclazide</td>
</tr>
<tr>
<td>Wound site</td>
<td>First distal MTP joint</td>
<td>First distal MTP joint</td>
<td>Fifth toe distal MTP joint</td>
<td>Heel</td>
</tr>
<tr>
<td>Wound size (diameter, cm)</td>
<td>1·5</td>
<td>0·98</td>
<td>0·2</td>
<td>2 × 1</td>
</tr>
<tr>
<td>Ankle brachial pressure index</td>
<td>Frequent</td>
<td>Frequent</td>
<td>0·6</td>
<td>0·98</td>
</tr>
<tr>
<td>Frequency of wound pain</td>
<td>Frequent</td>
<td>Frequent</td>
<td>1·12</td>
<td>Frequent</td>
</tr>
<tr>
<td>Total duration of the wound (months)</td>
<td>23</td>
<td>32</td>
<td>36*</td>
<td>16</td>
</tr>
</tbody>
</table>

*Patient died from an unrelated cause before the wound had healed.
was palpable in the base of all, with no evidence of overlying granulation tissue formation (Figure 2). The ankle brachial pressure and arterial duplex were normal in three patients. Repeated X-ray of the affected digit and heel, as well as blood tests did not support the presence of underlying osteomyelitis. Yet despite the relative small size of these wounds, chronic pain that was worsened by weight bearing and walking necessitated the regular use of analgesics in all four patients. Added to this the wounds were resistant to conventional wound care, three wounds had been present for over 3 years and the heel wound for 6 months.

The patients were all evaluated to exclude coexistent osteomyelitis and peripheral vascular disease, which have the potential to further complicate the wound and influence treatment decisions. In all four cases, the gout tophus at the base of the wound at presentation was hard and associated with tenderness on palpation. To soften the tophus, a hydrogel was applied on the wound, which was comforting and also sufficient for it to dissociate and be removed gradually at monthly clinic visits. Yet the prolonged nature of these wounds led to a dramatic adverse effect on the otherwise good quality of life of these patients (Table 2). The Cardiff Wound Impact Schedule\textsuperscript{©} (8) was used to determine the detrimental effect of these wounds on three patients and compared with the mean scores recorded for patients with chronic venous leg ulcers, healed and unhealed. For each category in the Cardiff Wound Impact Schedule\textsuperscript{©}, each patient with ulceration over the gout tophus showed lower scores and therefore greater health-related quality of life disability.

Gout is a disorder of purine metabolism, caused by long-standing hyperuricaemia, which results in monosodium urate crystal deposition in and around joints (9,10). Uric acid is the final metabolite of human purine metabolism and exists as intravascular urate because of physiological pH. The normal serum levels of urate are close to the solubility limit, and at concentrations above 0.38 mmol/l (hyperuricaemia) it can form monosodium urate crystal (11,12). In 90% of patients, hyperuricaemia is because of impaired renal excretion, which maybe triggered by genetic polymorphisms in genes that encode renal urate transport proteins: SLC22A12 (URAT), SLC2A9 (GLUT9), ABCG2

Table 2 Comparison of mean scores Health Quality of Life for each domain assessed by Cardiff Wound Impact Schedule\textsuperscript{©}

<table>
<thead>
<tr>
<th>Domain</th>
<th>Healed leg ulcer</th>
<th>Non healed leg ulcer</th>
<th>Ulcerated gout</th>
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<tbody>
<tr>
<td>Physical</td>
<td>87.6</td>
<td>71.7</td>
<td>55.2</td>
</tr>
<tr>
<td>Social</td>
<td>84.7</td>
<td>76.1</td>
<td>57.7</td>
</tr>
<tr>
<td>Well-being</td>
<td>50.8</td>
<td>38.7</td>
<td>28.6</td>
</tr>
</tbody>
</table>

0 = worst and 100 = best, health-related quality of life.
and SLC17A3 (3,13–15). In addition, local tissue factors, particularly in joints, further reduce solubility and facilitate monosodium urate crystal deposition; these include temperature, pH, concentration of cations, hydration state and presence of extracellular matrix proteins (12). Thus, although hyperuricaemia is necessary to cause gout, but alone it is not sufficient; it is local tissue factors that determine the distribution of joints affected and gout tophus formation. The lower temperatures and propensity for osteoarthritis therefore result in the frequent involvement of the first metatarsophalangeal joint.

Deposition of monosodium urate crystals in the intrarticular joint space is associated with acute painful episodes on monoarthritis, the most common manifestation of gout. In this setting, intrarticular monosodium urate crystals activate the immune system via antigen-presenting cells (16,17). The development of tophi in patients with gout is related to the duration of the disease and typically is associated with untreated hyperuricaemia, and manifest in only 3–21% of patients with gout (18,19). Although gout has an overall male predominance, late-onset gout and the development of tophaceous gout are more frequent in females, which maybe related to the loss of the protective effects of oestrogen after menopause (20,21). Although uncommon, tophaceous gout may present without a preceding history of painful arthritis (20). The formation of tophi is associated with a chronic inflammatory cell infiltrate, consisting of macrophages that surround the often necrotic monosodium crystal-laden core (22). The difference in inflammatory response seen in chronic tophaceous gout, as compared with acute episodic intrarticular gout, may account for the lack of pain associated with gout tophi.

The skin overlying gout tophi often appears stretched and therefore it is surprising that ulceration remains uncommon. However, epidermal extrusion of monosodium urate crystals has been reported, by a mechanism reminiscent of other perforating dermatoses (23). The development of ulceration overlying a gout tophus presents a number of challenges to wound care professionals. First and foremost almost half the patients with gout have comorbidities, which can adversely impact on wound healing. As part of the metabolic syndrome, patients with gout are at greater risk of obesity, diabetes, hyperlipidaemia, hypertension, atherosclerosis and ischaemic heart disease (24–27). Of direct concern, as for one of our patients, is the risk of associated peripheral vascular disease that may further compound healing. Therefore, all patients with ulcerations overlying a gout tophus require careful evaluation of the peripheral circulation, as a minimum assessment an ankle brachial pressure index. In addition, gout tophi may present a conduit for microbial infection of the underlying and involved joint space, with a risk of osteomyelitis. While all our patients were investigated for the possibility of osteomyelitis, surprisingly osteomyelitis was not observed given the likely direct communication of the wound to the underlying joint, suggesting that monosodium urate or the surrounding chronic inflammation prevents bacterial colonisation. As it is also clear from our observations, the gout tophus also hinders the formation of granulation. To facilitate the formation of granulation tissue and thus facilitate wound healing, we have sought to hydrate and fragment the tophus using hydrogels together with gentle debridement. This patient approach achieved healing in three patients, one patient unfortunately died from an unrelated cause before healing was observed.

In summary, this report outlines the wound care issues surrounding the management of ulceration over a gout tophus. We also highlight the distress associated with these otherwise small wounds, the importance of comprehensive assessment of comorbidities, as well as a strategy to promote healing.

REFERENCES

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