

# Clinical characteristics of infectious ulceration over tophi in patients with gout

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## Abstract

**Objective:** The aim of this study was to investigate the clinical characteristics of infectious ulceration over tophi in patients with gout.

**Methods:** Participants were recruited from the First Affiliated Hospital of Wenzhou Medical University. The clinical characteristics of the patients and wound characteristics were recorded.

**Results:** Of the 38 enrolled patients, 18 were found to have infectious ulceration over tophi. *Staphylococcus aureus* was the most common pathogen and was identified in nine patients. Patients with infection were significantly older (69.6 vs. 60.1 years) and had a worse quality of life than those without infection. Patients with infection also had a significantly longer ulcer duration (125.6 vs. 54.2 days), larger ulcer size (2.47 vs. 1.99 cm<sup>2</sup>), a higher rate of tissue necrosis in the ulcer bed (55.6% vs. 20.0%), a lower rate of callus at the edge (27.8% vs. 70.0%), and a higher moisture level than did patients without infection. Additionally, patients with infection had significantly delayed wound healing (35.3 vs. 20.3 days) compared with patients without infection.

**Conclusions:** Older patients with a long ulcer duration and larger ulcer size are more susceptible to infection. Infection can lower patients' quality of life and delay wound healing.

## Keywords

Gout, tophi, infection, ulceration, *Staphylococcus aureus*, wound healing

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## Introduction

Gout is an inflammatory arthritis caused by deposition of monosodium urate monohydrate crystals within joints during chronic hyperuricemia.<sup>1</sup> Gouty tophi are a manifestation of prolonged, uncontrolled hyperuricemia and result from deposition of urate crystals in soft tissues, tendon sheaths, bony

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prominences, and joints.<sup>2</sup> The presence of tophi impacts many aspects of the patient's life, causing pain, restricted joint range of motion, joint deformity, and complications such as infection and ulceration.<sup>3</sup> These ulcerated tophaceous gouty lesions are susceptible to infection, and the main indication for surgery in patients with tophaceous gout is sepsis or infection of ulcerated tophi.<sup>4</sup> Even after adequate surgical debridement and infection control, balancing these potential advantages against the risks associated with surgery, especially poor wound healing and infection, remains challenging.<sup>5</sup> Therefore, we performed the present study because of the importance of analyzing the clinical characteristics of infectious ulceration over tophi in patients with gout to reduce and control infection and improve outcomes.

## Patients and methods

### Patients

Patients who underwent surgery for infectious or noninfectious ulceration over tophi at The First Affiliated Hospital of Wenzhou Medical University from July 2013 to July 2017 were prospectively recruited. Gout was diagnosed according to the American Rheumatism Association subcommittee on classification criteria.<sup>6</sup> A clinical diagnosis of infection was based on the presence of the following criteria: local redness, tenderness or pain, swelling or high temperature, local purulent discharge, and isolation of microorganisms from microbiological cultures of discharge.

The study protocol was approved by the Wenzhou Medical University ethics review committee. All patients provided verbal consent to participate.

### Clinical characteristics of patients

The following data were recorded: demographic characteristics (age and sex), fever,

body mass index, estimated glomerular filtration rate, serum urate, serum albumin, comorbidities (diabetes, hypertension, and heart disease), gout duration, tophi duration, and urate-lowering therapy.

### Assessment of pain and quality of life

Pain was assessed by patients' self-evaluation on a 100-mm visual analog scale (0 mm, no pain; 100 mm, maximum pain).<sup>7</sup> The patients were asked to complete the 100-point Cardiff Wound Impact Schedule to assess the effect of ulcers on quality of life (0, worst quality of life; 100, best quality of life).<sup>8</sup>

### Wound characteristics

The ulceration site, duration, and size were recorded. Ulcer size was determined by multiplying the longest and widest diameters in millimeters. According to previous studies, we adapted the Tissue, Inflammation/Infection, Moisture, Edge/Epithelialization (TIME) wound assessment tool to evaluate tissue necrosis in the bed, callus at the edge, and moisture level.<sup>9,10</sup> The skin grafting rate and wound healing time were also recorded.

### Statistical analysis

Statistical analysis was conducted using SPSS Statistics, Version 16 (SPSS Inc., Chicago, IL, USA). Data are expressed as percentage, mean  $\pm$  standard deviation, or median (interquartile range), where appropriate. The t test for two independent samples or  $\chi^2$  test was used to compare differences between the two groups. A *p* value of  $<0.05$  was regarded as statistically significant.

## Results

In total, 38 consecutive patients with ulceration over tophi were enrolled in this study, and infections were identified in 18 patients. As shown in Table 1, *Staphylococcus aureus* was the most common microorganism

identified (9 of 18 patients with ulcer infection over tophi). Other pathogens identified were *Pseudomonas aeruginosa* in six patients, *Acinetobacter baumannii* in two patients, and *Shewanella algae* in one patient. The clinical characteristics of those with and without infection are shown in Table 2. Those with infection were older than those without infection ( $69.6 \pm 10.3$  vs.  $60.1 \pm 13.8$  years,  $p < 0.01$ ). Patients with infection also had higher rates of fever, obesity, and comorbidities such as diabetes, hypertension, and cardiovascular disease than patients without infection, but the differences were not significant. There were also no significant differences in the

gout duration, tophi duration, albumin level, urate level, estimated glomerular filtration rate, or urate-lowering therapy between the two groups. Both groups had high visual analog and Cardiff quality of life scores, and there were significant differences between the two groups in well-being scores and physical symptoms and daily living scores ( $p = 0.02$  for both) as shown in Table 3.

The wound characteristics are shown in Table 4. Ulcers were mostly located in the foot in both groups. Patients with infection had a longer ulcer duration and larger ulcer size than those without infection ( $p < 0.01$  and  $p = 0.04$ , respectively). The rate of tissue necrosis in the ulcer bed was 55.6% in patients with infection and 20.0% in those without infection ( $p = 0.01$ ). The rate of callus at the edge was 27.8% in patients with infection and 70.0% in those without ( $p < 0.01$ ). Most patients with infection had moderate to large levels of exudates, and the moisture level was significantly different between the two groups ( $p < 0.01$ ). There was no difference in the rate of skin grafting. Patients with infection had delayed

**Table 1.** Etiology of infectious ulceration over tophi in patients with gout.

Organism	Number	Percentage (%)
<i>Staphylococcus aureus</i>	9	50.0
<i>Pseudomonas aeruginosa</i>	6	33.3
<i>Acinetobacter baumannii</i>	2	11.1
<i>Shewanella algae</i>	1	5.6
Total	18	100

**Table 2.** Clinical characteristics of patients with gout with or without infectious ulceration over tophi.

Variable	Infection (n = 18)	No infection (n = 20)	p-value
Male	18 (100.0)	19 (98.7)	1
Age, years	$69.6 \pm 10.3$	$60.1 \pm 13.8$	$< 0.01$
Fever	3 (16.7)	0 (0.0)	0.10
Diabetes	10 (55.6)	5 (25.0)	0.09
Hypertension	9 (50.0)	7 (35.0)	0.51
Heart disease	8 (44.4)	7 (35.0)	0.74
Gout duration, years	$14.4 \pm 7.6$	$13.3 \pm 7.9$	0.47
Tophi duration, years	$5.6 \pm 3.6$	$5.9 \pm 2.9$	0.25
BMI, kg/m <sup>2</sup>	$28.6 \pm 5.7$	$27.3 \pm 7.1$	0.63
Albumin, g/L	$32.3 \pm 8.7$	$34.4 \pm 8.3$	0.20
Serum urate, $\mu\text{mol/L}$	$486.5 \pm 161.6$	$487.7 \pm 130.4$	0.96
eGFR, mL/min/1.73 m <sup>2</sup>	$50.5 \pm 24.8$	$48.3 \pm 24.5$	0.64
Urate-lowering therapy	10 (55.6)	10 (50.5)	0.78

Data are presented as n (%) or mean  $\pm$  standard deviation.

BMI, body mass index; eGFR, estimated glomerular filtration rate.

**Table 3.** VAS scores and Cardiff quality of life scores of patients with gout with or without infectious ulceration over tophi.

Items	Infection (n = 18)	No infection (n = 20)	p-value
VAS score	44.6 ± 12.3	42.3 ± 14.8	0.43
Social life	64.29 ± 19.8	62.54 ± 24.7	0.51
Well-being	68.5 ± 14.6	54.4 ± 21.2	0.02
Physical symptoms and daily living	67.1 ± 15.2	53.1 ± 18.5	0.02

Data are presented as mean ± standard deviation. VAS: visual analog scale.

**Table 4.** Wound characteristics and outcomes of patients with gout with or without infectious ulceration over tophi.

Variable	Infection (n = 18)	No infection (n = 20)	p-value
Location			0.88
Foot	13 (72.2)	14 (70.0)	
Hand	4 (22.2)	4 (20.0)	
Other	1 (5.6)	2 (10.0)	
Ulcer duration, days	125.6 ± 72.3	45.2 ± 24.1	<0.01
Ulcer size, cm <sup>2</sup>	2.47 ± 0.78	1.99 ± 0.75	0.04
Tissue necrosis in bed	10 (55.6)	3 (20.0)	0.01
Callus at edge	5 (27.8)	14 (70.0)	0.02
Moisture level			<0.01
Dry	0 (0.0)	6 (30.0)	
Exudates +	2 (11.1)	10 (50.0)	
Exudates ++	5 (27.8)	3 (15.0)	
Exudates +++	11 (61.1)	1 (5.0)	
Skin grafting	4 (22.2)	1 (5.0)	0.17
Wound healing time, days	35.3 ± 22.4	20.3 ± 13.8	0.02

Data are presented as n (%) or mean ± standard deviation.

wound healing compared with those without infection ( $p = 0.02$ ).

**Discussion**

Tophi are present in approximately 12% to 35% of patients with gout.<sup>1,11</sup> The presence of tophi has been associated with significant morbidity, including poor quality of life and increased use of healthcare resources.<sup>3</sup> Superficial tophi are especially vulnerable to local trauma with ulceration

and subsequent susceptibility to infection.<sup>4,5</sup> These ulcerated and infectious tophaceous gouty lesions increase the risk of further tissue breakdown and delay healing.<sup>12</sup> Previous studies have focused mainly on surgical treatment of ulcerations over tophi and subsequent wound healing.<sup>13-15</sup> To the authors' knowledge, the present study is potentially the first prospective study of such ulcerations and also potentially the first to examine the involved pathogens.

In the present study, the main microorganisms involved were *S. aureus* (50.0%) and *P. aeruginosa* (33.3%). Yu et al.<sup>16</sup> analyzed the clinical features of 30 patients with gout and concomitant septic arthritis and found that *S. aureus* was the most common microorganism (53.3%). Weng et al.<sup>17</sup> also analyzed the characteristic features of 14 patients with coexisting gouty arthritis and septic arthritis and found that 10 infections were due to *S. aureus* (71.4%). However, we used the superficial discharge as the sample for microbiological culture, whereas the above studies used the joint effusion for culture.

Patients with infection were significantly older than those without infection in this study. Compared with younger patients, older patients often have poor nutrition, poor self-management ability, and more comorbidities. Although there were no significant differences, we found higher rates of obesity and comorbidities such as diabetes, hypertension, and heart disease in the infection group, and these underlying comorbidities may have increased the risk of infection and impeded wound healing, which is consistent with previous studies.<sup>10,15</sup>

In this study, only three patients, including one with septic shock, had signs of systemic infection such as fever. These findings indicate that the infectious ulceration over the tophi was mainly localized infection. Almost all previous studies of patients with gout and infection have described septic arthritis. However, septic arthritis could be considered an infectious diffusion. In the studies by Yu et al.<sup>16</sup> and Weng et al.,<sup>17</sup> most patients with septic arthritis had tophi (83.3%–92.5%), and whenever ulceration was present over the tophi it most often involved the knee joint. These findings indicate that the tophus itself may be a risk factor for infection. However, when ulceration was present, infection was more likely to occur. Alappatt et al.<sup>18</sup>

described patient with gout with an ulcerative area over a large tophus in the right olecranon bursa who developed *S. aureus* polyarticular septic arthritis and sepsis syndrome.

Ulceration over tophi in patients with gout can lead to pain and affect patients' quality of life. In our study, infection worsened the pain and patients' quality of life. The effects of living with chronic malodorous wounds has been infrequently investigated, but such studies have highlighted the impact on health-related quality-of-life outcomes, altered body image, and withdrawal from social activities together with a detrimental effect on sexual expression and depression.<sup>19,20</sup>

In the present study, the infectious ulcerations occurred mainly in the foot (72.7% patients); none were present in the knee, which was the joint area most commonly involved by bacteria in other studies.<sup>16,17</sup> In our recent study of risk factors for ulceration over tophi in patients with gout, 77.8% of 113 patients had ulceration on the foot, and friction was the major cause of tophi ulceration.<sup>21</sup> In the present study, patients with infection had a significantly longer ulcer duration and larger ulcer size than those without infection, indicating that both a longer ulcer duration and larger ulcer size may be risk factors for infectious ulceration over tophi in patients with gout.

The TIME wound assessment tool was developed based on the concept of wound bed preparation to promote acceleration of the wound healing process.<sup>9,10</sup> In this study, we found that the infected wounds had significantly more tissue necrosis in the bed, less callus at the edge, and a higher moisture level than the uninfected wounds. These factors predicted poor wound healing, and patients with infection had definitely delayed wound healing than those without, which is consistent with previous studies.<sup>22–24</sup>

In summary, this study has revealed the clinical characteristics of infectious ulceration over tophi in patients with gout. The key finding is that infectious ulceration over tophi is mainly localized, and most infections are caused by *S. aureus* or *P. aeruginosa*. Older patients with a long ulcer duration and large ulcer size are more susceptible to infection. Infection can lower patients' quality of life and delay the wound healing time. However, a limitation of this study is the small number of patients, which affected the statistical analyses; further studies should include more patients.

### Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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