

# Wound Sleuth

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## Patient with a Painful Leg Ulcer

DR, a 74-year-old female, presented to Women's College Hospital Wound Care Clinic with a painful right lateral malleolar ulcer measuring 3 x 2.7 cm that had been present for nine months (see Figure 1). Other concurrent medical conditions included polycythemia rubra vera, glaucoma and hypothyroidism. Her medications were acetazolamide, levothyroxine, hydromorphone, nortriptyline, acetaminophen, acetylsalicylic acid, calcium, vitamin D, zinc, vitamin E and omega 3. She had been on hydroxyurea in the past for her polycythemia rubra vera, but that had been discontinued five months prior, as this was thought either to have caused the wound or to be contributing to its non-healing. The discontinuation of the hydroxyurea did not lead to any improvement in the status of the wound, however. Her main complaint was the pain she experienced from this wound and how it was affecting her functioning. She moved from her home to a retirement home because she required extra help with activities of daily living

and instrumental activities of daily living. Due to the pain, she suffered from reduced ability to ambulate, bathe, shop, house-keep, prepare meals and leave the home.

On examination, she had some mild varicosities and very mild edema in both legs. There was some dead tissue in the wound, which she refused to have debrided due to fear of worsening pain. We found strong pedal pulses bilaterally, and noted no physical findings of arterial disease in her feet.

### Question for the Reader

**Q** What would be the differential diagnosis of the underlying cause of this wound?

**A** Etiologies of the wound to be considered include:

- Venous stasis
- Hydroxyurea-induced ulcer<sup>1</sup>
- Arterial/angiosomal issue
- Infection
- Pyoderma gangrenosum

Prior to presenting at our clinic, the patient underwent the following investigations:

- Bone scan: suggestive of pos-



**Figure 1:** Lateral right leg wound that patient initially presented with

sible low-grade osteomyelitis and peroneal tenosynovitis

- Ankle-brachial indexes: found to be 1.0 in both legs
- Biopsy: showed increased neutrophils and bacteria, suggestive of infection

After the patient's presentation at the clinic, we conducted further investigations. A vascular surgeon saw her and determined that her clinical exam

and ultrasound findings indicated it was unlikely she had an angiosomal issue, so no computed tomography angiogram (CTA) was recommended.

Over time, she developed a new lesion on the medial aspect of the right leg and some superficial wounds on the left medial malleolus (see Figure 2).

Several times the wounds appeared to be infected, and she was treated with a variety of antibiotics. She grew methicillin-resistant *Staphylococcus aureus*, *Stenotrophomonas maltophilia* and *Serratia marcescens*. Eighteen months after presenting, the preliminary culture came back showing heavy growth of gram-positive bacilli. The final result would be low growth of other commensal bacteria that were not bacilli and therefore not being grown on the medium. After discussion with the microbiologist at the lab, we determined the best approach would be to biopsy the wound and have it tested for atypical bacteria (i.e., mycobacteria). A deep biopsy culture was sent for atypical bacteria and after several weeks returned showing *Mycobacterium chelonae*.

## The Infecting Bacteria

*Mycobacterium chelonae* is non-tuberculous, nonmotile, non-spore-forming, rapidly growing mycobacteria (RGM).<sup>2</sup> It was first described in 1903 by Freidmann, after he isolated the organism from a sea turtle.<sup>3</sup> *M. chelonae*, along with *M. fortuitum* and *M.*

*abscessus*, are the most common clinically significant RGMs. *M. chelonae* is characterized by its rapid growth in cultures, which usually take seven days to form mature colonies. The RGM group makes up approximately half of the validated mycobacterial species.<sup>4,5</sup>

These organisms are found in abundance in nature. More specifically, they have been isolated from tap, fresh and sea water sources, and also found in soil, dust and reptiles.<sup>5,6</sup> More concerning, they have been isolated from in-hospital environments, contaminated equipment and hospital tap water.<sup>7</sup> They are well known for their ability to withstand extreme environments and temperatures, and are resistant to chlorine water treatment and some industrial-grade detergents commonly used in hospitals and households.<sup>8,9</sup>

Clinically, *M. chelonae* is known to infect immunocompromised patients in which the infection is reported to have a wide range of manifestations, including skin and soft tissue infection, lymphadenitis, osteomyelitis, prosthetic valve endocarditis, keratitis, line infection, pulmonary disease or disseminated infection.<sup>10-12</sup>

Immunocompetent patients are also susceptible to infection by these organisms; however, the infection tends to be limited to skin and soft tissue.<sup>13</sup>

Skin and soft tissue infection by *M. chelonae* has been reported to be associated with tattooing using contaminat-



**Figure 2:** Medial right leg wound that developed in time

ed ink, or after surgeries in which non-sterile techniques or contaminated materials were used.<sup>13-15</sup> There are a wide variety of cutaneous manifestations of *M. chelonae* infection depending on the patient's immune status. Many descriptions of this infection have been reported in the literature, including single or multiple subcutaneous erythematous violaceous papules and nodules, pustular lesions, hemorrhagic crusts, cellulitis, ulcers, draining sinuses with discharge, and abscesses.<sup>10,13,14,16</sup> All of these lesions can be either painless or painful; however, larger lesions tend to be associated with pain.<sup>10</sup> Lower and upper extremities are the most common site of manifestation, although face and scalp lesions have been reported.<sup>10</sup> A history of trauma is not specific to *M. chelonae* cutaneous



**Figure 3:** Right lateral leg wound after deep debridement



**Figure 4:** Wound with allograft applied



**Figure 5:** Wound on lateral right leg showing signs of healing

infection, as many reported cases have denied a history of trauma.<sup>10</sup> Most reported cases share the fact that these lesions are chronic in nature and tend to be mistaken for other more common causes of skin lesions, like common bacterial infections and vasculitis that fail to improve with their respective treatments.<sup>10,13,14,16</sup> In immunocompromised patients, the infection tends to have a more disseminated picture, presenting with five or more lesions.<sup>10</sup> Clinicians can establish a diagnosis after isolating the organisms either from cultured discharge or skin biopsy.<sup>10,16</sup>

RGMs, including *M. chelonae*, are well known to be strongly resistant to standard antimycobacterial therapy.<sup>17</sup> The suggested initial therapy for *M. chelonae* cutaneous infections includes a combination of

clarithromycin with either tobramycin, imipenem or amikacin, along with wound care.<sup>16,17</sup> *M. chelonae* has been shown to have an excellent susceptibility to single antimicrobial agents like clarithromycin,<sup>18</sup> but due to emerging resistance to single agents, the use of a minimum of two agents is recommended.<sup>19,20</sup> Therapy should be guided using *in vitro* susceptibility patterns for the isolated organism.<sup>16</sup> The duration of antimicrobial therapy hasn't been established yet. The literature suggests treatment for a minimum of one to four months and continued until all lesions are healed with no recurrence.<sup>10,13,14,16,20</sup> Surgical excision and cryotherapy should be considered for resistant lesions if amenable.<sup>16,20</sup>

## Treatment

Following the diagnosis of *M. chelonae* infection, we performed a surgical debridement of the infected area (see Figure 3). A specialist in infectious disease at the Toronto General Hospital elected to treat the patient with six months of combination antibiotic treatment of clarithromycin and ciprofloxacin. The wound on the lateral malleolus was now 3 x 3 cm, and the wound on the medial aspect of the leg was 1 x 1 cm. Because the lateral malleolus wound was so deep with all layers of the dermis removed, a dehydrated human amnion/chorion membrane allograft was applied weekly (see Figure 4). The wounds began healing well (see Figure 5). Shortly after the six months of antibiotics were completed, the wounds healed over and were in the final stage





**Figures 6a and 6b:** Lateral and medial wounds in the remodeling stage of healing

of healing: the remodelling stage (see Figures 6a and 6b). Pain decreased to a more tolerable level though the patient felt more comfortable continuing with a bandage.

## Discussion

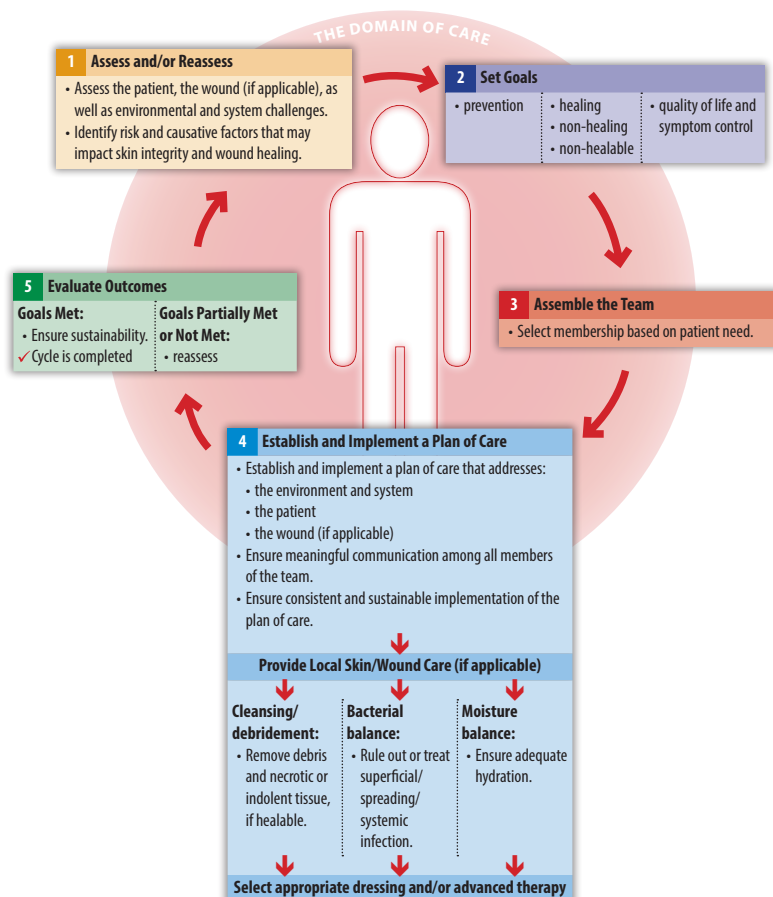
In this particular case, it was confusing as to why the wounds kept increasing in size and number despite good wound care, adequate circulation and reasonable nutrition. We believed this wound should be a healable wound. We had no reason to believe it should be a non-healable wound.

Treating infections and targeting the easily grown bacteria did not help, and the wounds continued to worsen. This patient suffered from polycythemia rubra vera, which is a myeloproliferative neoplasm causing the bone marrow to produce too many red blood cells and sometimes too many white blood cells and platelets. The medication she was on prior to presentation, hydroxyurea, could have led to the initiation or non-healing of the wounds; however, the wounds were progressing even after this treatment was stopped.

The patient continued to have issues with pain control and decreasing function despite attempts to correct these. She was afraid of any debridement in case it might add to the pain, but finally agreed once *M. chelonae* was suspected.

This case shows that we should consider using aids

### Assess/Reassess ▶ Set Goals ▶ Assemble Team ▶ Establish and Implement ▶ Evaluate



**Figure 7:** The Wound Prevention and Management Cycle

## Key Points

- ✓ We did not know the etiology of the wound but were able to find the cause for its not healing (infection).
- ✓ It is important not to label a wound as “non-healable” just because it is not healing as expected. Further investigation may be needed.
- ✓ When treating an older adult, consider how the wound may be affecting their daily functioning.

such as The Wound Prevention and Management Cycle (see Figure 7). When a wound is not healing as expected, we need to reassess what we are doing and readdress our goals. For DR, we still believed healing was possible. Our main clue was the preliminary swab culture result that showed we had gram positive bacilli that we could not grow within the ordinary culture growth times. We needed to add more members of our team—including the lab microbiologist and infectious disease specialist. We had to open our minds to what other etiologies might exist. In particular, the case of DR demonstrates the need to look at deep cultures for slower growing organisms such as mycobacteria and fungi. 📌

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