“This Little Piggy” had to Go

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Introduction

The management on chronic, non-healing wounds can often be a frustrating and time-consuming process. Although there is no breed predilection for this condition, there are predisposing factors, such as infection, age, endocrine disorder, and many more, that can contribute to a wound not healing appropriately.[1,4] A number of conditions that can cause a delay in wound healing can cause any wound to become a chronic, non-healing wound.[1]

History and Presentation

Rhett is a 3-year-old, male intact, Labrador Retriever that presented to Mississippi State University College of Veterinary Medicine (MSU-CVM) Small Animal Surgery Department on January 8, 2020, for a chronic, non-healing wound. He also presented with a history of possible food and/or environmental allergies and was being fed a Purina ProPlan Veterinary Diet HA dry canine kibble. He was treated by his referring veterinarian (RDVM) for recurrent infections of his left forepaw at the level of the 4th digit starting in February of 2019. On December 6, 2019, his RDVM amputated his 4th digit. The left forepaw was healing well after surgery, but approximately one week post-operatively, the surgical site dehisced and started producing purulent material. Rhett's culture and sensitivity on December 19, 2019, grew *Pseudomonas aeruginosa, Escherichia coli,* Methicillin-resistant *Staphylococcus pseudointermedius* (MRSP)*,* and *Enterococcus faecalis.* He was receiving amikacin injections, marbofloxacin orally, trazodone orally, and gabapentin orally when he presented to MSU-CVM.

On physical exam, Rhett was bright, alert, responsive, and anxious. He weighed 33 kg with a body condition score (BCS) of 5/9. Vital parameters included a temperature of 103.8°F, a heart rate of 96 beats per minute, and he was panting. His mucus membranes were pink and moist with a capillary refill time (CRT) of less than 2 seconds. Thoracic auscultation revealed no crackles, wheezes, murmurs, or arrhythmia. A cough could not be elicited. Eyes, ears, and nose were clean and clear with no signs of discharge. Abdominal palpation was unremarkable. Peripheral lymph nodes palpated smooth and symmetrical with no evidence of lymphadenopathy. There was a wound between digits 3 and 5 on the left forelimb where the 4th digit was amputated. The wound was hyperemic with multiple, small openings that were effusing a small amount of serosanguinous fluid from them. The remainder of the physical exam was within normal parameters.

Diagnostic Approach and Considerations

Based on Rhett's history and physical examination findings, we were able to diagnose him with a chronic, non-healing wound. However, we still needed to investigate what the underlying cause of his wound was in order to initiate the appropriate therapy. Differentials for the cause of chronic wounds include the following: infectious (bacterial or fungal), foreign body, and neoplasia (least likely).[12] A typical diagnostic work-up for a chronic limb wound can include a combination of the following dependent on history and physical examination findings: bacterial and fungal culture and sensitivity, direct smear of the wound, skin scraping, histopathology, and diagnostic imaging.[10,12]

At the time of presentation, a minimum database was collected that consisted of a complete blood count (CBC), serum biochemistry, and urinalysis. These tests were performed to make sure he was not showing signs of systemic infection, to check his liver and kidney values prior to anesthesia, and to check his urinalysis for any signs of kidney damage caused by amikacin administration. The minimum database did not reveal any significant abnormalities. Rhett was also scheduled for computed tomography (CT) of both forelimbs in order to rule out a foreign body that could be acting as a nidus for infection and the perpetuation of his chronic wound. CT revealed an enhancing, fluid attenuated pocket at the level of the 4th metacarpal bone that was most consistent with an abscess, but other differentials included granuloma, neoplasia, or a foreign body.

A fusion podoplasty procedure was performed on January 9, 2020, in order to remove all of the necrotic tissue between digits 3 and 5 and to explore the pocket seen on CT at the level of the distal 4th metacarpal bone. At the time of surgery, the diseased tissue was collected and submitted for histopathology and a bacterial culture and sensitivity. No foreign body was found at the time of surgery and the articular surface and small amount of unhealthy bone of the 4th metacarpal bone were removed in order to reduce inflammation around it. Following the surgical procedure, a Modified Robert Jones bandage with a spoon splint was placed to the level of the proximal antebrachium in order to provide weight bearing support to the surgical site as it heals. Based on his history at presentation, we were concerned that Rhett still harbored a MRSP infection. One study out of Sweden found that patients that underwent surgery and were hospitalized in a veterinary clinic were exposed to MRSP from both human and animal contact points[2]; this was a concern based on Rhett's history of digit amputation, multiple visits and rounds of antibiotics for recurrent infection of the left forepaw, and his latest bacterial culture and sensitivity. Rhett's tissue biopsy was diagnosed as fibrotic and granulomatous lesions with draining tracts and bacteria present. His culture and sensitivity revealed methicillin-resistant *Staphylococcus intermedius* and *Enterococcus faecalis*.

Rhett was hospitalized overnight for post-operative pain management and monitoring. Based on the latest culture and sensitivity report from his RDVM, he was placed on meropenem 10 mg/kg intravenously every 8 hours and chloramphenicol 60 mg/kg orally every 8 hours. He was also prescribed hydromorphone 0.2 mg/kg intravenously every 4 hours for pain and carprofen 2.2 mg/kg orally every 12 hours for inflammation. His bandage was changed the morning of January 10, 2020. His incision was intact, and it was not swollen, red, or warm to the touch. The bandage was replaced, and Rhett was discharged with instructions for bandage changes with his RDVM, continued monitoring of his kidneys due to amikacin administration, activity restriction, bandage monitoring, and prescriptions of acetaminophen with codeine 1.8 mg/kg orally every 8 hours for 10 days, carprofen for 3 days at the same dosage as above, metronidazole 7.5 mg/kg orally every 12 hours for 3 days for the diarrhea he developed in hospital, marbofloxacin 6 mg/kg orally every 24 hours for 14 days, and amikacin 15 mg/kg subcutaneously every 24 hours for 14 days.

Unfortunately, Rhett presented to MSU-CVM Small Animal Surgery Department on January 15, 2020, for dehiscence of the fusion podoplasty site. Open wound management was performed in order to manage the multi-drug resistant infection and to allow the wound to heal by second intention.

Pathophysiology

Wound healing can be broken down into three major stages, which are inflammation and debridement, proliferation, and maturation; it is a dynamic process in which all stages overlap one another.[1,4,5,7,8] Immediately after injury, the inflammatory and debridement step begins and the area undergoes vasoconstriction. This vasoconstriction lasts for approximately five to ten minutes and allows for the control of hemorrhage and the formation of a fibrin-platelet clot that fills the defect.[4,5,7,8] After the clot is formed, vasodilation of the vessels around the wound occurs. This allows a transudate containing complement, antibodies, plasma proteins, and immune cells to enter the wound space.[4,5] Neutrophils and macrophages are the key immune cells that respond to injury during the inflammatory and debridement stage. Neutrophils appear within six hours of injury and continue to increase for two to three days post-injury, whereas macrophages appear within twelve hours of injury.[4,7,8] The goal of the inflammatory and debridement step is to allow for the formation of a healthy granulation tissue bed, which provides a contact surface for epithelialization in later stages of wound healing.[5,7]

Approximately three to five days post-injury, the proliferative phase of wound healing begins, which will last for approximately eight days.[4,7] The proliferative phase is predominated by endothelial cells, epithelial cells, and fibroblasts, who's proliferation is stimulated by macrophages in the inflammatory stage, and includes processes such as angiogenesis, epithelialization, and collagen production.[4,5,7] Fibroblasts arise from undifferentiated mesenchymal cells that migrate along the fibrin strands of the fibrin clot into the wound matrix.[7] They are responsive for forming type III collagen that is folded in a triple helical structure in order to form fibrous tissue and the strength needed for wound healing.[4,7] This combination forms granulation tissue over the wound. Granulation tissue forms at a rate of 0.4 to 1 millimeter per day and is relatively resistant to infection.[7] The goal of the proliferative stage is to achieve wound closure by replacing the tissue lost at the time of injury.[4]

Maturation is the final, and arguably the most important, stage of wound healing in which collagen is remodeled to form a strong scar.[4,5] Approximately 30% of the collagen in granulation tissue is type III collagen. Type III collagen is thin and glycosylated, making the parallel matrix it forms weak.[7] Through the process of maturation and remodeling, type III collagen is replaced by type I collagen to add stiffness and rigidity to the tissue. At the conclusion of maturation, only about 10% of the final scar contains type III collagen.[7] At an ideal healing rate, the collagen matrix is completed at four to five weeks, but maturation of the collagen matrix continues for twelve to eighteen months after the initial injury.[4,7] In wounds healing by second intention, reorganization and maturation of collagen offers wound contraction at a rate of 0.6 to 0.8 millimeters per day.[7]

The above pathophysiology is how an acute wound would heal without becoming a chronic wound. Any incident that causes disruption as it heals can transform an acute wound into a chronic wound; some examples of these inciting events include: infection, tension on the wound, pressure on the wound created by a hematoma or fluid accumulation in the dead space under the wound, the animal licking or biting the wound, poor perfusion, etc.[1,4] More specific to the limb of a dog, non-healing wounds are often due to infection, either bacterial or fungal, foreign body, osteomyelitis or orthopedic implant infection, neoplasia, or perivascular injections.[1,4,12,13]

Often times, chronic wounds manifest as sinus tracts, ulcerative lesions, or a combination of the two.[12] Ulcerative lesions are observed as "a bed of chronic, unhealthy granulation tissue which is thick and fibrotic[12]," whereas sinus tracts are cylindrical ulcers that do not heal due to the persistence of poor granulation tissue caused necrotic tissue, foreign body, or some other cause of irritation.[1,12,13] In Rhett's case, our top two differentials for the cause of his chronic wound were bacterial infection and/or the presence of a foreign body because we could see an ulcerative lesion with poor granulation tissue externally and we suspected a sinus tract due to the enhancing pocket near the 4th metacarpal on CT.

Acute wounds transform into chronic wounds when continued infection, trauma, or irritation from a foreign body causes a sustained inflammatory response, which can result in continued trauma of the wound bed.[1] Infection can cause delayed wound healing by weakening the collagen matrix and thus the wound as a whole.[1] This is one explanation of how wound dehiscence can occur in surgically corrected wounds, such as with Rhett's fusion podoplasty site.

Common bacterial etiologies in chronic wounds include the following: *Staphylococcus aureus, Staphylococcus epidermidis, Pseudomonas sp., Streptococcus sp., E. coli,* and *Proteus sp.*[1,5,12]

Treatment and Management Options

The management strategies for chronic wounds are based on culture and sensitivity in order to select appropriate antibiotics, lavage the wound in order to remove contaminants, debridement of devitalized tissue, allowing for drainage of the wound, bandaging the wound to protect it from contamination, and wound closure when appropriate.[7] The first step in deciding how to manage a chronic wound is to classify the wound in order to decide if surgical intervention is warranted or if medical treatment is indicated.[6,12] Some of the factors to consider when you classify the wound include the following: time since initial insult, how contaminated the wound is, tissue damage sustained, location of the wound, overall health of the patient, etc.[7] Rhett's wound was classified as "dirty" because the wound contained devitalized tissue with purulent discharge at the time of presentation.[3] The initial decision was to perform surgical management with the fusion podoplasty and then medical management with long term systemic antibiotics based on his history, the CT findings, and his bacterial culture and sensitivity.

A fusion podoplasty is a salvage procedure that is used in cases with severe tendinopathies or in an attempt to control a chronic process, such as a wound or interdigital pyoderma.[7,10] A fusion podoplasty study found that wound dehiscence was a common complication of this procedure seen in five out of eight of the participants.[10] That same study also found that this procedure has favorable long-term outcomes with six of eight participants having complete resolution of their clinical signs, and the other two participates having mild weight-bearing lameness that was improved as compared to their pre-surgical lameness.[10] A long-term bandage with a spoon splint or some other supporting structure is indicated post-operatively in order to reduce the weight bearing forces on the incision site and to reduce the chances of surgical site dehiscence.[7,10,13]

After Rhett represented for the fusion podoplasty dehiscence, the decision making process lead to open wound management with healing by second intention, which relies on wound contracture and epithelialization.[5,12] Open wound management is indicated for wounds classified as “dirty” because this allows the veterinarian to assist in cleaning and debriding devitalized tissue.[5,8] Although there are many avenues and products that can be used to manage an open wound, this paper will focus on the treatment avenues utilized in this case.

A moist wound environment offers the ideal conditions for debridement, granulation tissue formation, and epithelialization. However, it also carries the risk of providing a favorable environment for bacterial colonization.[7] Alginate is one product that can be utilized to provide a moist wound environment. It is a polysaccharide derived from seaweed that absorbs exudates from the wound and creates a gel matrix that keeps the wound moist, fills the dead space, promotes autolytic debridement in the wound, and promotes granulation tissue development.[5,7,8,9,11] Medical-grade honey can also be used in addition to alginate in order to add moisture to a wound and provide a gel matrix infused with honey and its antimicrobial properties.[7,9]

The utilization of honey in wound management dates back centuries.[9] It possesses antibacterial properties, such as a low pH, approximately 3.6, to create an acidic environment, produces hydrogen peroxide, and contains inhibin.[8,9] Due to its hyperosmotic effect, it also helps inhibit microbial growth and reduces edema.[8,9] Honey also enhances autolytic debridement, granulation, and epithelialization by increasing the production of immune cells and by causing lymph transudates to entire the tissues at the borders of the wound.[8,9]

Throughout the management of Rhett's wound, a Modified Robert-Jones bandage with a spoon splint was maintained at all times. This bandage provided support and prevented contamination from hospital surfaces. The use of systemic antibiotics was guided by three separate bacterial culture and sensitivity results at different intervals in his management process. Once a healthy granulation tissue bed was achieved using Medi-Honey and Alginate, the decision to use compounded amikacin gel on the wound was based on culture and sensitivity results. This gel allowed systemic amikacin to be discontinued but still provided antibiotic support to the body in order to combat the multi-drug resistant infection while the wound continued to heal.

Prognosis

Rhett's prognosis was fair to good. Although it took many weeks of systemic antibiotics and open wound management with bandage changes and topical antimicrobials, we were confident that Rhett would regain full function of his left forelimb.

Case Outcome

As a part of open wound management, Rhett was hospitalized on January 15, 2020, and the bandage on his left forelimb was changed every day for approximately one week using Medi-Honey and silver alginate to debride the wound. Two cultures were taken in the first week to guide appropriate antibiotic choices. Once there was a healthy bed of granulation tissue, Rhett was switched to every-other-day bandage changes using Amikacin gel at 50 mg/ml for about 10 days (4 total bandage changes). His bandage change on 1/31/2020 discontinued the use of the Amikacin gel and a petroleum gauze was placed to keep the 3rd and 5th digits separated as they continued to heal. On February 3, 2020, his last bandage change was performed at MSU-CVM, and he was discharged on February 4, 2020. He continued to have his bandages changed two to three times a week with his RDVM. Communication with the client revealed that as of April 29, 2020, Rhett's left forelimb was no longer being bandaged and his wound had completely healed.

Conclusion

Chronic wound management is often a long process that requires constant evaluation of the wound, the course of treatment, and decisions to change the course of treatment when the circumstances call for it. Rhett's case is an excellent example of how decisions must be made to alter management strategies as each new problem arises. Chronic wound management can include a combination of surgical reconstruction, maintaining a moist wound environment when open wound management is elected, antiseptic lavage, and antimicrobial therapy guided by culture and sensitivity results.

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