Princess' Plight

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Introduction:

Cutaneous pythium and microbial infections significantly increases the potential for complications in wound healing. Oomycete sp. (*Pythium* and *Lagenidium* sp) are fungus-like organisms; however, they are not classified as a true fungi. Their cells walls lack chitin and consist of cellulose and β-glucans and the cytoplasmic membrane lacks ergosterol. An aquatic environment is necessary for the induction of biflagellate zoospores (Gaastra et al., 2010). *Pythium insidiosum* induces a granulomatous disease in various forms. Disease can be localized to the gastrointestinal tract, skin, blood vessels, eyes, or can become a systemic disease (Vanittanakom et al., 2004 and Gaastra et al., 2010).

Pythiosis is most commonly seen in immunocompetent horses and dogs. In horses the cutaneous form is more common, often found on the limbs and ventrum. However, in dogs, the gastrointestinal form is more common. Cutaneous pythium is characterized by non-healing, ulcerative wounds with chronic draining tracts located on the limbs, ventrum, perineum, tailhead, or abdomen in dogs (Thieman et al., 2011). At this time, zoonotic properties of *P. insidiosum* have not been reported (Gaastra et al., 2010). Until 2003, it was thought that *P. insidiosum* was the exclusive oomycete that caused clinical disease in mammals. However, there were six case reports published in 2003 which incriminated *Lagenidium* sp. as the infectious agent and caused a similar clinical presentation to *P. insidiosum* (Grooters et al., 2003).

The integument is the largest organ in the dog, consisting of 12% of the body weight in the adult canine (Pavletic, 2010). Its functions are numerous; however, serving as the first line of defense against microbial infection is vitally important. The introduction of microbial infections and mis-management of a wound lead to the delay in the healing process, as well as the potential for sepsis. Therefore, the proper management of wounds is critical to the life of the patient.

History and Presentation:

Princess was a 1-year old, intact female American Bulldog who was presented to her primary veterinarian on October 9th, 2018, for evaluation of a suspected skin infection. A large necrotic area caudal to her left shoulder was excised and a Penrose drain was placed on October 10th. Carprofen at 2.9 mg/kg orally every 24 hours and cephalexin at 29 mg/kg orally every 12 hours were prescribed for 7 days and 10 days respectively. It was noted on October 23rd, 2018, that a portion of the incision needed to be closely observed because it was not healing properly. On November 14th, 2018, a biopsy of the caudal left shoulder was taken for histopathology and culture and sensitivity. Cephalexin at 27 mg/kg orally every 12 hours was prescribed for another 10 days. Princess was referred to the MSU-CVM Small Animal Internal Medicine Service for further workup on December 17th, 2018. Her owner reported that she was painful and whined when she tried to lay down. Princess frequently visited a farm where she had access to stagnant water. Additionally, she was on a raw diet and was up to date on vaccines, flea, tick, and heartworm prevention.

Upon presentation, Princess was bright, alert and responsive. She weighed 37 kg (81.4 lb) with a body condition score of 7/9. She had a temperature of 103.8 °F, heart rate of 130 bpm, and her respiratory rate was obscured by panting. Her mucous membranes were pink and moist with a capillary refill time of less than two seconds. Caudal to the left shoulder, in the axillary region, there was a large ulcerative lesion that spanned from the left elbow halfway across the thorax, approximately 15 cm from the cervicothoracic spine and reaching midline ventrally, with evident muscle exposure of the triceps, latissimus dorsi, and the pectorals. The wound had a foul odor and produced serosanguinous discharge and appeared necrotic in the center. The remainder of Princess' initial physical examination was within normal limits.

Diagnostic Approach/Considerations:

On presentation, a complete blood count was performed which revealed an inflammatory leukogram characterized by mild neutrophilia with toxic changes and mild eosinophilia. The serum chemistry revealed a mild decrease in the ALT, moderate decrease in albumin, and a mild increase in globulins and CK. Thoracic radiographs were performed which revealed a large (approximately 16.4 X 7.8 cm), undulating in margin, convex, soft tissue opaque structure along the left thoracic body wall caudal to the left forelimb. Abdominal radiographs were performed and no irregularities aside from the soft tissue opaque structure caudal to the left forelimb were noted. An abdominal ultrasound revealed no ultrasonographic evidence of gastrointestinal pythiosis. Histopathology revealed severe cellulitis, myositis, eosinophilic and pyogranulomatous inflammation, with necrosis. Within some of the areas of pyogranulomatous inflammation there were small zones of clearing which suggested the presence of non-staining fungal hypha. Grocott methenamine silver stain (GMS) of the slide confirmed the presence of scattered, large, non-or sparsely branching, non-septate hyphae with "ragged," non-parallel cell walls. A pythium titer was sent to Auburn University and returned 95% positive at a 1:1000 dilution, 85% positive at a 1:2000 dilution, and 75% positive at a 1:4000 dilution. Based on Auburn's laboratory reference values, a positive test is consistent with being greater than 40% for all dilutions.

Pathophysiology:

Biflagellate zoospores, the infective component of *P. insidiosum,* have the ability through chemotaxis, to become encysted on decaying or injured plant tissue. Through this chemotaxis, injured mammalian tissue is also susceptible to *P. insidiosum*. After contact with injured plant or mammalian tissue, a sticky amorphous glycoprotein secreted from the surface of the biflagellate

zoospore permits adhesion to the tissue (Gaastra et al., 2010). Once activated by the host's body temperature, germ tube or hypha are produced and further infiltration into the tissue is achieved. Ravishankar et al. (2001) determined that *P. insidiosum* does not exert enough pressure to penetrate undamaged skin by mechanics alone. However, in vitro, *P. insidiosum* exhibits high levels of secreted proteinase activity. The correlation between these enzymes and their role in tissue destruction has not been established for *P. insidiosum* but have been implicated in other animal mycoses (Aspergillus) (Ravishankar et al., 2001 and Cole, 1996). The immune system responds to the *P. insidiosum* hyphae through a Th2 response characterized by the release of IL-4, IL-5, IgE and subsequent eosinophil and mast cell degranulation, causing extensive tissue damage (Mendoza, 2005).

Treatment and Management:

Historically, cutaneous pythium has a poor response rate with medical management, itraconazole and terbinafine. These antifungal therapies target ergosterol in the fungal cell membrane, however, *P. insidiosum* isolates lack these components. There are cases in the literature of cures after using various antifungal drugs (azoles, terbinafine, amphotericin B). The in vitro itraconazole and terbinafine treatment of *P. insidiosum* isolates, showed a synergistic effect in 40%. However, there was poor correlation to in vivo studies with rabbits (Argenta et al., 2011). Multimodal therapy should be pursued for the treatment of *P. insidiosum*. Dependent on the location, recommendations include amputation and wide excision. However, quantification of wide excision isn't explicitly stated in the literature. In 2011, a case report from the University of Florida detailed 5-cm skin margins and 2 fascial planes deep similar to an invasive neoplasm. Additionally, advanced imaging (computed tomography) and cytology should be used to determine adequate surgical margins and the spread of *P. insidiosum* to draining lymph nodes.

Based upon CT findings, the palpable lesion may expand several centimeters into normally appearing skin. While not neoplastic, cutaneous pythium is treated as an aggressive neoplasm (Theiman et al., 2011).

Mefenoxam 22% (Subdue MAXX Fungicide, Syngenta Crop Protection, Inc [Greensboro, NC]) is an agricultural fungicide for the treatment of plants infected with *Pythium* sp. In vitro, mefenoxam significantly inhibits the growth of *P. insidiosum.* It has recently been studied for efficacy in the treatment of gastrointestinal pythiosis due to historical poor response rates. In a case report by Hummel et al. (2011) a non-resectable case of gastrointestinal pythiosis was managed medically with itraconazole and terbinafine. Intraconazole was stopped due to itraconazole-induced cutaneous vasculitis. A 22% solution of mefenoxam was started at 4 mg/kg orally every 12 hours. After receiving mefenoxam and terbinafine for 18 months anti-P. *insidiosum* levels had decreased to 12%. Ultrasonographic findings resolved except a mild jejunal lymphadenopathy and mild segmental jejunal thickening (Hummel et al., 2011). Treatment of cutaneous pythium with mefenoxam has not been described in the literature.

Immunotherapy with *P. insidiosum* derived antigens has been described as a potential modality of treatment. In the late 20th century, a cell mediated hypersensitivity reaction and production of antibodies through the humoral immune system were found after horses became infected with *P. insidiosum* (Mendoza, 2005). Immunotherapy with *P. insidiosum* immunogens was 100% successful in the treatment of equine pythiosis with lesions less than 20 days old, the cure rate for lesions greater than two months old was 20-40%. Multi-modal therapy (surgery and immunotherapy) increased the cure rate to 90%. Immunotherapy treatment in cats and dogs has been significantly less rewarding, with a 33% success rate. A proposed explanation for the decreased response rate is the time to definitive diagnosis; dogs often present very late in clinical

disease. The immunogens shift the body's response from a Th2 to a Th1 response. The Th1 response triggers production of interleukins (IL-2), IFN-γ inducing cytotoxic T-lymphocyte production and the activation of macrophages and increases in IgG (Mendoza, 2005).

The basic phases of wound healing are essential to know in the treatment of any wound, but specifically a wound complicated by many factors. The inflammatory phase (early vascular and late cellular) is directly proportional to the severity of the inciting trauma (Hararl, 1993). Initially, to control hemorrhage the vessels are vasoconstricted, quickly followed by vasodilation (Pavletic, 2010). The late cellular phase is characterized by the arrival of neutrophils, macrophages, and lymphocytes at the wound. Fibroplastic (proliferative) phase is considered to occur 5-20 days after injury. Neovascularization, migration of fibroblasts and reestablishment of the epidermis occur in this phase (Pavletic, 2010). Angiogenesis is essential for the continued success of a healing wound. In its absence, fibroblasts can't be recruited to produce collagen. The final step in the proliferative phase is epithelialization, where epithelial cells lose their binding properties and migrate until other epithelial cells are reached. The final phase of wound healing is the maturation and remodeling phase where Type III Collagen decreases and Type 1 Collagen increases taking up to a year. Scars only reach 70-80% of the original tensile strength (Pavletic, 2010).

When wounds diverge from the normal physiological course of healing and become fixed in one phase, likely the inflammatory stage, wounds can become chronic. Various reasons lead to the persistence of one phase, but bacterial infections and increased motion of the wound are expected inciting causes. Overcoming the fixed inflammatory phase is crucial to the successful management of these wounds (Gist, 2009).

Delivering antibiotics at concentrations high enough to provide clinical treatment of microbial infections can be a challenge. The controlled release of vancomycin from Poloxamer 407 gels was described in a study by Veyries et al. (1999). The Poloxamer 407 gel allowed the vancomycin to be in intimate contact with infected tissues. Rats tolerated a single dose very well and the local vancomycin concentration remained high for greater than 24 hours. Overtime, the gel matrix dissolves, not requiring removal. Additionally, there were no changes in the effectiveness of the vancomycin (Veyries, 1999).

There are six principles in wound management. Prevention of further wound contamination can be reduced by the application of topical antimicrobial ointment and a protective bandage until further steps can be taken to treat the wound. Sterile lube should be placed onto the wound bed, to prevent contamination from fur, which may serve as a continued source of infection (Pavletic, 2010).

The debridement of dead and dying tissue can become the most involved step in wound management. Nonselective debridement such as wet to dry bandages, are aggressive and a faster method, though not specific to necrotic tissue, viable tissue may also become traumatized. Selective debridement is less aggressive and a slower method. Autolytic methods include hydrogels utilize the body's own enzymes to rehydrate and liquefy eschar and promote sloughing (Dabiri et al., 2016). Alginate dressings (alginic acid), and zinc, sodium, or calcium salts are added to the acid. A local hemostatic effect is promoted by the activation of prothrombin locally. Hygroscopic agents (honey and sugar-applied at least 1 cm thick), draw fluid from the wound, often requiring frequent bandage changes. Honey (Manuka) also has antimicrobial properties due to its high osmolarity and acidity. Enzymatic methods use proteolytic enzyme preparations such

as, collagenase to digest tissue (Dabiri et al., 2016). Biotherapeutic debridement consists of the use of medical grade maggots (Pavletic, 2010).

Foreign debris and gross contaminants such as soil, organic debris should be removed from the wound bed. Pressure lavage, using an 18-gauge needle with a 35mL syringe, perpendicular to the tissue, pushed at full force, delivers 8 pounds per square inch (psi) to the wound bed. Isotonic solutions (normal saline or lactated Ringer's solution) will aid in the removal of microscopic contaminates. Depending on the size and contamination of the wound the volume of fluid used varies (Pavletic, 2010).

Passive drains, active drains, and vacuum-assisted closure (VAC) Systems can be used to help established adequate wound drainage. The Penrose drain utilizes capillary action for the movement of fluid along the drain and out a gravity-dependent incision. Active drains, such as Jackson-Pratt drains, used in deep wounds, drawing fluid out. Utilize a closed suction system. VAC systems create a uniform vacuum across the wound surface, which draws fluid out. The system may be kept on continuously or intermittently (3 minutes on, 5 minutes off) and may also help with bacterial clearance. The VAC may be needed for several days before the wound is ready for surgical closure (Pavletic, 2010).

Promotion of a viable vascular bed supports the development of granulation tissue. Finally, selection of an appropriate method of closure must be achieved. Depending on the extend of the wound, it may take several days to answer this question. Contraction and epithelization without surgical intervention may be achieved. Surgical closure using direct apposition of adjacent tissues, skin flaps or free grafts may be considered (Pavletic, 2010).

Free grafts are harvested from one area of the body and moved to a distant location, without a direct blood supply. Harvested grafts have a pale or white appearance due to the vasospasm of the vessels. Shortly after graft placement, networks of fibrin strands contract, resulting in closer apposition of the graft and the wound bed. These networks act as scaffolding for the movement of fibroblasts, leukocytes, and phagocytes and begin the transition into fibrous tissue. Vessels within the graft dilate and through capillary action from the recipient bed nutrients are transferred, known as plasmatic imbibition. This mechanism leads to increased concentrations of hemoglobin and its breakdown products giving the graft a purplish to cyanotic appearance which peaks at 48-72 hours post grafting. A lack of venous drainage additionally causes edema of the graft. Vessels of similar sizes from the graft and recipient bed begin to anastomosis together. Inosculation allows normal perfusion to return to the graft 5-6 days after placement. Revascularization occurs at a rate of 0.5 mm/day. The tissue returns to a normal pale pink color, 14 days after placement. Avascular necrosis is characterized by persistently pale coloration of the graft, leading to eventual necrosis (Tobias, 2012). Material (purulent exudate, serum, or blood) between the graft and recipient bed, increased motion, or fibrinolysis secondary to bacterial infection (*Klebsiella* and *Pseudomonas* sp.) delay or prevent the graft from completing the revascularization process, leading to graft necrosis. (Pavletic, 2010).

On December 19th, 2018 Princess was placed under general anesthesia for a left forelimb amputation and closure of the extensive wound caudal to her shoulder. The thoracic wound was covered with an Ioban and a #10 scalpel blade was used to make an encircling skin incision around the left forelimb and the thoracic wound 5 cm from diseased tissue. The remainder of the forelimb amputation was performed following the procedure outline by Tobias (2012). A full thickness skin graft measuring, 20 X 8 cm with tapered ends was harvested from the dorsal

thorax and subsequently prepared for placement. The graft was secured to the ventral abdomen and the remainder of the incision was apposed with 3-0 Nylon in a simple interrupted pattern. Four, 6 cm, pieces of sterilized Velcro were sutured to the skin using simple interrupted sutures from mid thorax to cranial abdomen to relieve tension and stretch the skin. Lap sponges and an Ioban were placed on the incision. The left forelimb and associated pre-scapular and axillary lymph nodes were submitted for histopathology. Princess recovered well in the intensive care unit post-operatively. She received lactated ringer's solution intravenously at maintenance, a fentanyl CRI at 3 mcg/kg/hr, lidocaine CRI at 30 mcg/kg/hr, and a ketamine CRI at 5 mg/kg/min. Her bandage was evaluated every hour for strike through. Princess was on cefpodoxime at 10 mg/kg orally every 24 hours, previously prescribed by the primary veterinarian.

On December 21st, 2018 Princess was sedated with dexmedetomidine (2.5 mcg/kg) and hydromorphone (0.1 mg/kg) intravenously. The thoracic bandage was changed due to excessive strike through, it was noted that the serosanguinous exudate was coming from the caudal aspect of the skin graft. Additionally, there were 2-6 mm zones of blanched, pale tissue, where the graft was meshed diffusely. The fentanyl, ketamine, and lidocaine CRIs were discontinued and she was started on Tylenol #4 at 2 mg/kg orally every 8 hours, gabapentin at 6 mg/kg orally every 8 hours, Cerenia at 1 mg/kg intravenously every 24 hours. Hydromorphone at 0.05 mg/kg intravenously was available as needed for rescue. The biopsy results were consistent with an oomycete infection (*Pythium insidiosum* or *Lagenidium* sp.). GMS staining confirmed the diagnosis of *Pythium insidiosum.*

On December 23rd, 2018, the mesh skin graft was diffusely white with serosanguinous exudate from the cranial and caudal aspects. On the craniodorsal aspect of the mesh skin graft

the apposed tissue to the graft was dark green to black in appearance. Terbinafine at 10 mg/kg orally every 24 hours and omeprazole at 1 mg/kg orally every 12 hours were started. On December 25th, 2018, the left craniodorsal aspect of the mesh skin graft was dehisced and retracted from the apposing skin. The meshing of the graft has widened and on the caudoventral aspect of the graft there was dehiscence from the apposing skin. Additionally, the cotton bandage was saturated with a green serosanguinous discharge, which had a putrid odor. A bacterial culture and sensitivity were taken at this time, Princess was started empirically on chloramphenicol at 30 mg/kg orally every 8 hours.

On December 26th, 2018, Princess was sedated, there was increased dehiscence, with only slight apposition in two regions of the graft. The meshing on the graft coalesced into several large sections, which revealed the underlying wound bed to be absent of granulation tissue. The necrotic graft was removed, edges of the remaining wound were sharply debrided, and it was flushed with 3L of sterile saline. A large amount of sugar was placed into the wound bed and packed with lap sponges to fill the dead space. The previously described Velcro was removed, and six new pieces were sutured onto the left lateral thorax (two cranial, caudal, and ventral to the wound). An Ioban was placed over the thoracic wound and four more pieces of Velcro were placed craniodorsal to caudoventral and caudodorsal to cranioventrally.

On December 27th, 2018, Princess was sedated, and the wound bed was flushed with 3L of sterile saline. A VAC System was placed in the wound bed and secured with an Ioban to obtain negative pressure. The Velcro straps were tightened by 0.5-1.0 cm every 12 hours to expediate skin stretching. Two days later, the VAC System was discontinued due to the inability to obtain continuous negative pressure.

On December 30th, 2018, Princess was sedated, and granulation tissue was still not seen at this time, a calcium alginate dressing was placed into the wound bed (16 X 14 cm) and a soft padded bandage was placed. The bacterial culture and sensitivity revealed growth of *Pseudomonas aeruginosa, Proteus mirabilis,* and *Staphylococcus intermedius* all susceptible to amikacin and gentamicin. Princess was started on amikacin at 16 mg/kg subcutaneously every 24 hours and itraconazole at 5 mg/kg orally every 24 hours. Chloramphenicol and cefpodoxime were discontinued at this time. Amikacin, an aminoglycoside with efficacy against gram-negative organisms with limited gram-positive activity (*Staph* and *Strep* species) (VIN Veterinary Drug Handbook, 2017). A three-fold increase in the urine GGT:Creatinine ratio is indicative of early nephrotoxicity from aminoglycoside use (Rivers *et al.,* 1996). Serial urinalysis were also performed to monitor for the production of casts. A urinalysis was performed and there were no clinically significant abnormalities as well as a urine GGT:Creatinine ratio was obtained and was 0.2 U/g. Princess's ratios did not exceed a three-fold increase. The calcium alginate was removed, flushed and replaced every 48 hours for six days. During this time a healthy bed of granulation tissue was achieved and became exuberant prior to surgical closure.

On January 10th, 2019 Princess was placed under general anesthesia for closure of the wound dehiscence from the failed mesh skin graft. The wound bed (16 X 14 cm) was flushed with 2L of sterile saline. Skin edges of the wound were sharply debrided to reveal healthy; bleeding tissues and the edges of the wound were undermined. The edges of the wound were then advanced in order to re-appose them in a "Y" shape. A 10 mm Jackson Pratt drain was placed in the subcutaneous space and secured with a purse string and a Chinese finger trap of 2-0 Nylon. Subcuticular cruciate, simple interrupted, and near-far-far-near sutures were placed to appose subcuticular tissue with 2-0 PDS. The skin was apposed with 3-0 Nylon in a cruciate

pattern. Princess recovered from anesthesia with no complications and received hydromorphone at 0.1 mg/kg intravenously. The remainder of the night she received hydromorphone every 4 hours subcutaneously at 0.05 mg/kg. Additionally, she was started on Benadryl at 2.5 mg/kg orally every 8 hours due to severe razor burn.

On January 12th, 2019, there was a 1 X 1 cm area of dehiscence at the center of the "Y" shaped incision. A sample for bacterial culture and sensitivity was taken at this time. Princess was pyrexic (103.5 °F) and was started on carprofen at 2.2 mg/kg orally every 12 hours. Culture revealed the growth of *Streptococcus canis, Proteus mirabilis,* and *Klebsiella pneumoniae ssp. pneumoniae.* Based on final sensitivity results she was started on cefoxitin at 30 mg/kg subcutaneously every 8 hours and the amikacin was discontinued. Cefoxitin, a second-generation cephalosporin (cephamycin) antibiotic highly active against gram-negative microorganisms. *Pseudomonas* strains are resistant to cefoxitin (Wallick and Hendlin, 1974). From January 12th to January 15th the area of dehiscence increased in size to 4 X 8 cm, and there were additional areas of dehiscence cranially and caudally, measuring 2 X 1 cm and 1 X 1 cm respectively. On January 16th, 2019, Princess was sedated, and the areas of dehiscence were lavaged with 2L of sterile saline and 25 mL of vancomycin Poloxamer Gel was placed on sterile gauze and into the wound bed. Every 48 hours for the next 6 days the vancomycin Poloxamer Gel was replaced in the wound bed. The dead space surrounding the wound remained static measuring 10 cm cranially and 3 cm ventrally. The Jackson Pratt drain was removed due to its low production.

On January 25th, 2019, Princess was placed under general anesthesia for the third time. The wound bed (4 X 8 cm) was flushed with 2L of sterile saline. A sample of the wound bed was taken at this time for bacterial culture and sensitivity. Skin edges were sharply debrided and undermined to reveal healthy, bleeding tissue. Edges of the wound were advanced in order to

reappose them in an “S” shape. A 10 mm Jackson Pratt drain was placed in the subcutaneous ventral space and secured with a purse string and Chinese finger trap of 2-0 Nylon. 25 mLs of vancomycin Poloxamer Gel was infused into the dorsal pocket above the wound. Subcuticular cruciate and near-far-far-near sutures were placed to appose subcuticular tissues with 2-0 PDS. The skin was closed with 2-0 Polypropylene suture in a cruciate pattern. Princess recovered from anesthesia and surgery with no complications. She received hydromorphone at 0.05 mg/kg subcutaneously every 6 hours post-operatively and Benadryl at 2.5 mg/kg orally every 8 hours.

On January 28th, 2019, the bacterial culture and sensitivity returned with growth of *Pseudomonas aeruginosa* with limited susceptibility. Based on these results the vancomycin Poloxamer Gel was discontinued and 25 mLs of amikacin Poloxamer Gel was placed into the wound bed though a releasing incision. There were no areas of wound dehiscence. On January 30th, 2019, the Equine Antibiotic Susceptibility Panel returned for the resistant *Pseudomonas aeruginosa* with susceptibility to ceftazidime, a third-generation cephalosporin with broad spectrum activity and the most active against *Pseudomonas aeruginosa.* Additionally, in patients with nephrotoxicity secondary to aminoglycoside administration, ceftazidime is an alternative (Richards and Brogden, 2012). She was started on ceftazidime at 30 mg/kg subcutaneously every 8 hours and the cefoxitin was discontinued. The Jackson Pratt drain was removed, and 25 mL of amikacin Poloxamer Gel was placed into the drain opening.

Case Outcome:

Pythiosis is treated in a multi-modal attack including radical surgery, antifungal drugs, immunotherapy, and more recently agricultural fungicide. After three surgical interventions, skin graft, wound VAC, two Jackson-Pratt drains, resistant bacterial infections, and treatment with intrawound Poloxamer Gel-antibiotic compound administration Princess was discharged on

February 1st, 2019 from the MSU-CVM Small Animal Surgery Service. She was sent home with acetaminophen with codeine (Tylenol #4), and gabapentin for three days, ceftazidime for 21 days, itraconazole and terbinafine until otherwise directed by a veterinarian, and trazodone as needed. Her owners were given instructions to begin mefenoxam 22% (Subdue MAXX Fungicide, Syngenta) once she returned home. Additionally, Princess was to have her incision checked and sutures removed on February 4th, 2019 by her primary veterinarian. An appointment was scheduled on March 1st, 2019 with the MSU-CVM Small Animal Internal Medicine Service to recheck her weight, CBC, serum chemistry, and a pythium titer. At this time, initiating immunotherapy was to be discussed. Unfortunately, Princess was lost to follow up prior to her recheck visit.

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