Necrotizing fasciitis in a dog

Necrotiserende fasciitis bij een hond

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ABSTRACT

A 7-year-old male intact Briard was presented with limping, fever and a painful swelling of the left hind leg. Physical examination revealed clinical findings consistent with a state of compensated shock, and demonstrated ecchymosis and an extremely painful edema of the left hind leg. Cytology of the extracellular subcutaneous fluid revealed large quantities of *cocci*. A bacteriological culture confirmed the presence of β-hemolytic *streptococci* of Lancefield group G. Necrotizing fasciitis was diagnosed based on the combination of the clinical findings, the culture results and the surgical findings. Two surgical interventions were performed and large amounts of necrotic and affected tissue were removed. After seven days of intensive treatment, the dog was discharged. Two weeks postoperatively, the dog had fully recovered, regained function of the limb, and the wound was completely healed.

SAMENVATTING

Een intacte, mannelijke briard van zeven jaar werd aangeboden met kreupelheid, koorts en een pijnlijke zwelling aan de linkerachterpoot. De hond was in compensatoire shock. Op het lichamelijk onderzoek vertoonde de patiënt een ecchymose en een zeer pijnlijk oedeem aan de linkerachterpoot. Op cytologie van de onderhuidse vochtopstapeling werd een groot aantal kokken aangetroffen. Een bacteriologische cultuur bevestigde de aanwezigheid van β-hemolytische streptokokken van de Lancefield groep G. Necrotiserende fasciitis werd gediagnosticeerd aan de hand van een combinatie van de klinische bevindingen, de bacteriologische cultuur en de bevindingen tijdens chirurgie. De patiënt onderging tweemaal chirurgie, waarbij grote hoeveelheden necrotisch en aangetast weefsel werden verwijderd. Na zeven dagen intensieve zorgen kon de hond de kliniek verlaten. Twee weken postoperatief verkeerde de hond in uitstekende conditie. Hij belastte zijn linkerachterpoot weer normaal en de wonde was volledig geheeld.

INTRODUCTION

Necrotizing fasciitis (NF) is a rare, rapidly progressive infection of the superficial fascia that has been described in humans, dogs and cats. In dogs, it is usually caused by *Streptococcus canis* (*S. canis*), a β-hemolytic bacterium of group G in the Lancefield grouping (Miller et al., 1996).

Streptococcus canis belongs to the normal flora of the skin and the mucosal surfaces of the respiratory, urogenital and gastrointestinal tract in dogs (Greene and Prescott, 1998). An infection with *S. canis* initiates as a local infection, when bacteria breach the skin or mucosal barrier. However, exotoxins (Streptolysin O and M protein) produced by *S. canis* can activate an inflammatory cascade that results in a systemic infection, and may lead to a systemic inflammatory response syndrome (SIRS) (DeWinter et al., 1999; Brady and Otto, 2001). The early phase of sepsis is associated with a hypercoagulable state that may progress to disseminated intravascular coagulation (DIC) (Ten Cate, 2000). In rare cases, the streptococcus toxic shock syndrome (STSS) can occur, presenting as shock and multiple organ failure (Miller et al., 1996).

It is difficult to distinguish NF from less severe soft tissue infections such as cellulitis. However,

Table 1. Criteria for systemic inflammatory response syndrome in dogs (Hauptman et al., 1997). Two or more criteria are needed for the diagnosis of SIRS.

Parameter	Feature
Heart rate	> 120 beats per minute
Respiratory rate	> 40 breaths per minute
Temperature	< 38.0 °C or > 40.0 °C
Leukogram	>18.000 white blood cells/µL

the early clinical suspicion of NF is essential, since delayed diagnosis results in a poorer prognosis, and might have fatal consequences for the patient (Jenkins et al., 2001). Delayed recognition of NF and the absence of radical surgery are the most important causes of the high mortality rates described in human patients (Childers et al., 2002). In NF cases, the infection spreads rapidly through the superficial fascia, resulting in swift necrosis of vast areas of fascia and tissue. Aggressive surgical debridement is mandatory to halt the spread of fascial necrosis (Edlich et al., 2010). In human NF, it has been reported that it is not possible to macroscopically detect the extent of tissue necrosis early in the course. Moreover, multiple surgeries are often necessary to adequately and completely remove all necrotic tissue (Edlich et al., 2010).

There are only few reports of NF in the veterinary literature. The concepts of the diagnosis and treatment of canine NF are therefore greatly derived from human medicine. Currently, the treatment in dogs is initiated mainly on a diagnosis that is based on the combined presence of high fever, extreme and disproportional pain and swelling of the skin (Naidoo et al., 2005). The presence of these signs should give rise to a high level of suspicion of NF. Bacterial culture and histopathology results provide a definite diagnosis of NF (Naidoo et al., 2005; Wong and Wang, 2005).

In this case report, a dog with NF is described. Comparisons are made between the clinical findings in this canine case and the recognized parameters in human NF.

CASE REPORT

A 7-year-old male intact Briard was presented with persistent fever and a history of an acute onset of limping and edema of the left hind leg for five days. The referring veterinarian initially made a tentative diagnosis of a ruptured cranial cruciate ligament, and prescribed an NSAID. The dog was represented to the same veterinarian the following day because worsening was seen; the swelling of the left hind leg had worsened. A blood sample was taken, and a fine needle aspirate (FNA) of the swelling as well as a urine sample were submitted for bacteriological culture and sensitivity testing. Oral antibiotics (Marbocyl®, marbofloxacine, Vétoquinol, Magny Vernois, France) were added to the treatment. However, the general condition of the dog deteriorated within the next 24 hours. The laboratory results were not yet known when the dog was referred.

Upon presentation at the referral clinic, the general physical examination showed a nonambulatory, lethargic dog. The dog was febrile (40.3°C) and tachypneic (respiratory rate of 40 breaths per minute). A heart rate of 120 beats per minute and strong femoral pulses were found. Mucous membranes were hyperemic and capillary refill time (CRT) was shortened (< 1 second). These clinical findings were consistent with a state of compensated shock and SIRS (Table 1). Lymphadenopathy of the left popliteal lymph node was found, and an extremely painful swelling of the left hind limb, extending from the hip towards the tarsus, was present. Pitting edema was present as well as was a large ecchymosis (Figure 1). Neurological examination of the affected hind limb did not show any abnormalities.

A complete blood count (CBC) and serum biochemistry were performed. The results are summarized

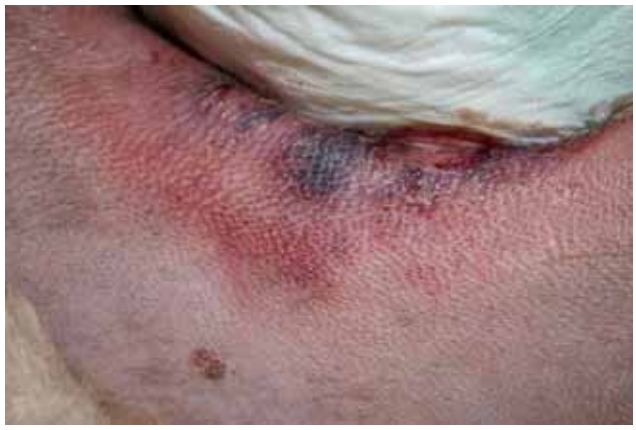

Figure 1. The left hind limb of the patient before surgery, demonstrating the macroscopic skin lesions. Note the ecchymosis and edema.

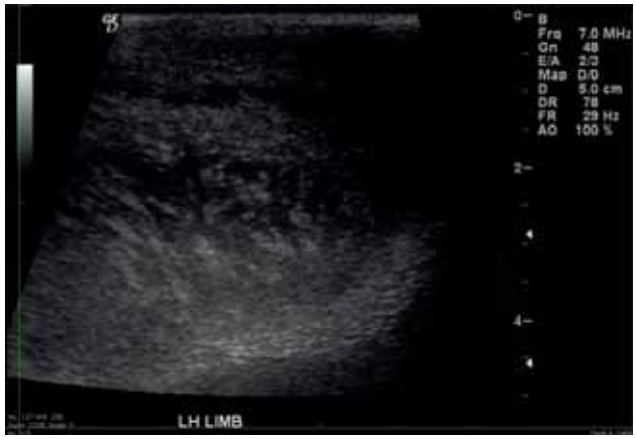

Figure 2. Ultrasound of the left hind leg, mediodistal of the stifle. It shows a subcutaneous swelling. Note a large heterogeneous area with multiple small hypoechoic areas interspersed with hyperechoic tissue ('cobblestone appearance').

Table 2. Comparison of the laboratory results of the patient. Values above the reference range in red, values below the range value in blue.

	Reference values	Patient
Hematology and serum biochemistry		
Leukocytes	7,5-9 10^9/l	15,4 10^9/l
Band neutrophils	0-0,1 10^6/l	6 10^6/l
RBC	5,5-8,5 10^{12}/l	5,97 10^{12}/l
Hct	44-57%	47,50%
RDW	14-17%	14,3%
MCV	60-77 fl	60,6 fl
Hgb	9,3-12,4 mmol/l	7,8 mmol/l
MCH	1,05-1,43 fmol/l	1,31 fmol/l
PLT	200-460 10^9/l	269 10^9/l
PT	7,2-9,9 sec	67,7 sec
aPTT	13,2-18,2 sec	36,5 sec
Fibrinogen	100-460 mg/dl	430 mg/dl
D-dimers	<0,5 mg/dl	4,79 mg/dl
Na	136-154 mmol/l	132 mmol/l
K	2,7-5,0 mmol/l	3,5 mmol/l
Cl	97-115 mmol/l	110 mmol/l
Albumine	20-30 g/l	14 g/l
Total protein	60-80 g/l	57 g/l
Globulin	25-45g/l	45 g/l
Glucose	2,2-8,2 mmol/l	4,5 mmol/l
BUN	<12 mmol/l	7,9 mmol/l
Creatinine	44-159 µmol/l	96 µmol/l
Total bilirubin	0-15 µmol/l	17 µmol/l
AST	<44 units/l	78 units/l
ALP	<123 units/l	189 units/l
Urinalysis		
Protein/Creatinine ratio (UPC)	<0,5	4,94
Urine specific gravity	1.015-1.035	1.049
Glucose	Neg.	Neg.
Urine sediment		
RBC	<25/µl	223/µl
WBC	<25/µl	54/µl
Urine culture	Neg.	β-hemolytic *Streptococcus* Group G

in Table 2. A mild neutrophilic leukocytosis, prolonged prothrombine time (PT) and an activated partial thromboplastine time (aPTT), increased D-dimers, hypoalbuminemia, hypoproteinemia and hyponatremia were present. Urinalysis showed an active sediment, increased urinary protein/creatinine ratio (UPC) and hypersthenuria. An ultrasound of the left hind limb was performed, and demonstrated a severe heterogeneous swelling of the subcutaneous tissue from the hip towards the tarsus. The subcutaneous fat showed an increased echogenicity with multiple small hypoechoic areas interspersed. Scattered small pockets with cellular fluid were present proximal to the stifle joint (Figure 2). Some fluid was aspirated under ultrasonographic guidance. The left popliteal and left medial iliac lymph nodes were enlarged, but showed a normal aspect. Cytology of the aspirated fluid revealed suppurative inflammation with a large amount of intra- and extracellular *cocci* and degenerative neutrophils. A presumptive diagnosis of phleg-

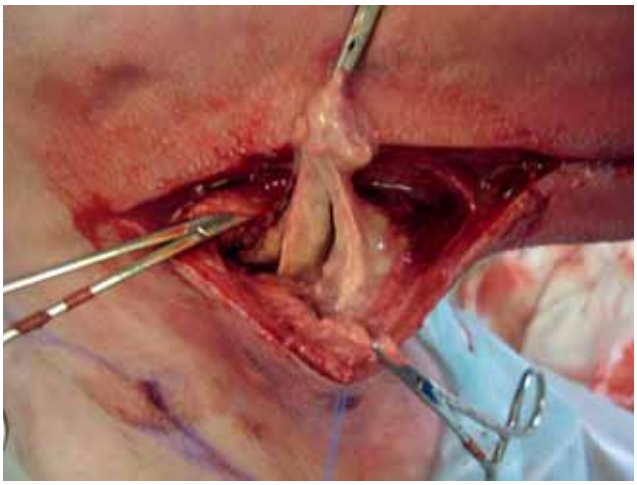

Figure 3. During surgical debridement at the level of the medial tibia, caudomedial to the stifle joint and distal to the darkened skin, extensive necrosis of the fascia can be observed.

mon was made, pending the results of culture and sensitivity tests performed by the referring veterinarian.

The patient was stabilized with isotonic crystalloid fluid therapy (NaCl 0.9%®, B-Braun, Melsungen, Germany) administered initially as a bolus at 45 ml/kg over 10 minutes. After normalization of the mucous membrane color and capillary refill time, crystalloid fluid therapy was continued as a continuous rate infusion to cover maintenance requirements and ongoing losses. A fresh frozen plasma transfusion and unfractioned heparine (Heparine Leo®, Leo Pharma, Ballerup, Denmark, at an initial dose of 200 units/kg IV, and continued SC q6h) were administered to treat an arising DIC, suggested by the prolonged PT and aPTT. Amoxycilline-clavulanic acid (Augmentin®, GSK, London, United Kingdom) was administered at 20 mg/kg IV q8h, as well as clindamycine (Antirobe®, Pfizer, Zaventem, Belgium) at 13 mg/kg PO q12h. A mucopolysaccharide polysulphate cream (Hirudoid®, Sankyo, Tokyo, Japan) was applied to the skin q8h. The following morning, the general status of the dog had improved, but the limb had developed a purple discoloration that was progressing proximally and distally. Additionally, there was an area of black, necrotic skin measuring 2 cm in diameter on the caudomedial aspect of the stifle. The bacteriological cultures of the FNA and urine sample taken by the referring veterinarian both revealed multiple colonies of β-hemolytic *streptococci* of Lancefield group G, indicating NF. Immediate surgical intervention was performed. The patient was premedicated with morphine HCL (Morphine HCL®, Sterop, Brussels, Belgium, 0.1 mg/kg IV). Anesthesia was subsequently induced with midazolam (Dormicum®, Roche, Brussels, Belgium, 0.5 mg/kg IV) and fentanyl (Fentanyl®, Janssen, Beerse, Belgium, 5 µg/kg IV). A small additional dose of propofol (Propovet®, Abbot, Berkshire, United Kingdom, 1 mg/kg IV) was required to facilitate endotracheal intubation. After the endotracheal intubation, anesthesia was maintained with isoflurane (Isoflo®, Abbott, Berkshire, United Kingdom) vaporized in 100% of oxygen using an anesthetic rebreathing system. In the operating theatre, the patient was positioned in dorsal recumbency with the left hind leg fixed to a standard, allowing full access to the leg. An incision was made at the level of the medial tibia, three centimeters distal to the darkened skin. A large amount of exudate (800 ml) was encountered subcutaneously, and the fascial layer was affected extensively (Figure 3). The muscles underneath the fascia were not macroscopically affected, but the overlying epidermis and dermis were severely traumatized. There was a large pus-filled pocket stretching from the middle of the tibia to the sciatic bone, where an additional small incision was made. All of the macroscopically affected tissue was debrided. Two Penrose drains were placed in the pocket; their ends were fixed through the intact skin with a single interrupted suture in nylon (3/0 Ethilon®, Johnson&Johnson/Ethicon, Diegem, Belgium). A stab incision was made through intact skin at the medial aspect of the stifle and at the medial aspect of the tarsus, a few centimeters cranial to the tibial incision line, to allow exit of the distal ends of the drains (Figure 4). The skin edges were loosely appositioned with a cruciate suture pattern in 3/0 nylon. The incision line was covered with an absorbent compress, and a padded bandage was applied to the whole limb.

The following day, extra skin necrosis became apparent on the caudomedial side of the hind limb. The affected skin was clearly delineated on day four. The suture line was partially reopened, and the necrotic skin was removed. The underlying subcutaneous tissues looked healthy, and a fair amount of granulation tissue was present. Several blood clots were removed, and the subcutaneous tissues were flushed with saline

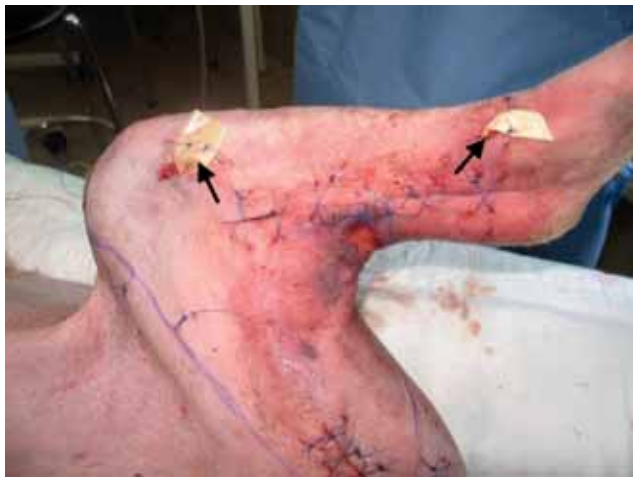

Figure 4. After extensive surgical debridement, two Penrose drains were placed in the pocket and tunneled subcutaneously to exit proximally and distally to the tibial incision line. The ends of both drains were fixed by a transfixing suture (small arrows). The skin edges were loosely appositioned with non-resorbable suture materials in a cruciate suture pattern.

(NaCl 0.9%®, B-Braun, Melsungen, Germany). The Penrose drains were removed as they were only mildly productive; the exit sites were closed with a simple interrupted suture in 3/0 nylon. Two vacuum drains were placed proximal and distal to the incision. The subcutaneous layer and the incision were closed with a continuous suture and a continuous intradermal suture with poliglecaprone 25 (3/0 Monocryl®, Johnson&Johnson/Ethicon, Diegem, Belgium). Skin staples (Leukoclip SD® 6.9mm x 3.9mm, Smith&Nephew, Zaventem, Belgium) were added for extra stability. A padded bandage protected the limb.

Pain management during the first 24 hours following surgery was achieved with morphine (0.1 mg/kg IV q4h). A transdermal fentanyl patch (Duragesic® 100 µg/h, Janssen, Beerse, Belgium) was placed on the clipped thorax at the end of surgery, and covered the pain management for three consecutive days starting from the day after surgery. Fluid therapy consisted of a crystalloid solution (Hartmann®, B-Braun, Melsungen, Germany) at maintenance rate and an isotonic solution (Sterofundin-B®, B-Braun, Melsungen, Germany) at maintenance rate.

The wound healed well, and the patient regained weight bearing on the affected left hind leg. The day following the second surgery (day five), the padded bandage was replaced by a tie-over dressing (changed q12h) with a honey-based ointment (Dermazyme®, Melivet, Ecuphar, Oostkamp, Belgium) to achieve a local bactericidal effect and to further promote the recovery of the damaged skin by decreasing inflammatory edema. The vacuum drains produced about 1 ml q8h. Three days after the second surgery (day seven), the vacuum drains were no longer productive, and were disconnected. The suture line looked healthy, and had nearly completely healed. Pain medication had been gradually reduced, and stopped completely on day seven. On day eight, the patient was discharged. Antibiotic treatment was continued for eight more days after discharge, and the owner was advised to change the dressings daily. Fifteen days after the second surgery (day nineteen), the wound was completely healed, and the staples were removed (Figure 5). The patient regained full function of the limb; only a slight limp was detectable.

Contact with the owners two years after surgery learns that the patient has been doing well ever since. Only after intense exercise, a very slight limp can be observed in the left hind limb, which quickly resolves after rest.

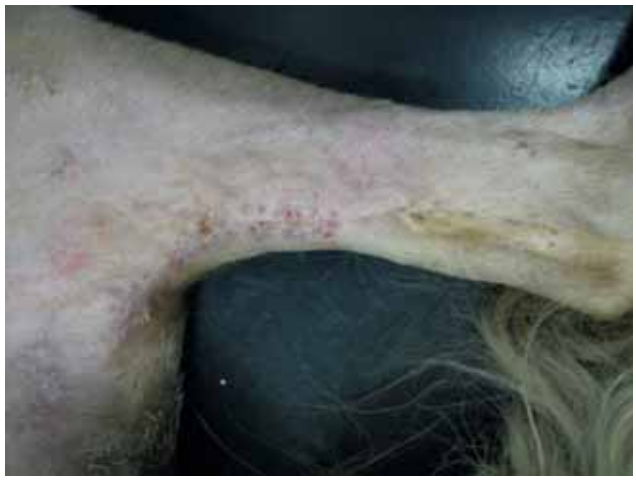

Figure 5. Fifteen days after the second surgery, nineteen days after admission, the wound was completely healed and the staples were removed.

DISCUSSION

Necrotizing fasciitis (NF) in dogs is an uncommon but potentially fatal condition (Kulendra and Corr, 2008). Inadequate awareness of this condition and the lack of pathognomonic physical examination findings impair recognition by veterinarians. In both human and canine patients, immediate surgical therapy is paramount in the successful treatment of NF, and any substantial delay in the surgical intervention considerably increases both the morbidity and mortality rates (Naidoo et al., 2005; May et al., 2009).

The bacterium *Streptococcus canis* was described by Devriese et al. (1986). Its pathogenic role in dogs was described in 1996 by Miller et al. in a series of seven dogs that had severe systemic disease and shock, associated with a β-hemolytic *S. canis* (Lancefield Group G) infection. Out of these seven systemically ill dogs, four had associated NF. Since then, NF in dogs has been reported by others (Prescott et al., 1997; Jenkins et al., 2001; Gerdin and Pintar, 2003; Naidoo et al., 2005; Kulendra and Corr, 2008; Csiszer et al., 2010). A detailed description of the stepwise treatment of NF in a dog was first reported by Jenkins et al. (2001). The dog in the current report was the first recognized NF case treated at the veterinary clinic of the Faculty of Veterinary Medicine, Merelbeke (UGhent, Belgium). During the following three years, another six dogs were diagnosed with NF at the Faculty of Veterinary Medicine in Merelbeke. All NF patients underwent drastic surgical debridement, and they were all treated with a successful outcome.

The initial physical examination of the reported dog revealed increased body temperature, hyperemic mucous membranes, shortened CRT and tachypnea. These abnormalities are compatible with septic SIRS and compensated distributive shock (Brady and Otto, 2001). In human and canine patients, typical clinical signs of NF include fever, edema and necrosis of the affected area (Wong and Wang, 2005; Naidoo et al., 2005). The localization in the limb and the swelling and intense pain that is disproportionate to the findings on physical examination are consistent with the other reported veterinary cases of NF (Jenkins et al., 2001; Gerdin and Pintar, 2003; Naidoo et al., 2005; Csiszer et al., 2010). Necrotizing fasciitis may occur in any region of the body. However, the extremities are the most common reported site in canine patients (Jenkins et al., 2001; Naidoo et al., 2005). Cutaneous signs begin with a diffuse swelling with spreading erythema.

As the lesion progresses, the skin develops ecchymosis (Jenkins et al., 2001). Discoloration of the skin can be difficult to appreciate in intensely pigmented dogs (Jenkins et al., 2001) but was easily noticeable in the case described.

Documented findings on cytology in human patients include degenerative neutrophils and a large amount of intra- and extracellular gram-positive *cocci* (Wong and Wang, 2005). This corresponds to the cytologic findings in this canine patient as well as in four other reported cases of canine NF (Jenkins et al., 2001; Gerdin and Pintar, 2003; Naidoo et al., 2005; Csiszer et al., 2010). In some cases, *streptococcus* species may be recognized by their typical chainlike formation. However, microscopic examination of the *cocci* in the present case did not reveal a chainlike formation. Therefore, an initial diagnosis of a phlegmon with *cocci* was made. The diagnosis was amended immediately after the culture results were available. The identification of chains of *cocci* under the microscope should alert the clinician to suspect NF, but may never rule out NF if absent. Histopathology may serve as a confirmation of the diagnosis of NF, but was not performed in the current case. In human patients suspected of NF, it is good practice to obtain tissue specimens for bacterial culture and for histopathology in all patients without exception because the results determine the need for repeated debridement and thorough follow-up (Wong and Wang, 2005).

Radiographs of the affected limb were not taken. In some cases, subcutaneous air may be present and visible on the radiograph, supporting the suspicion of NF. However, this finding is inconsistently reported in the veterinary literature, and its absence does not exclude it (Jenkins et al., 2001). A more versatile imaging tool capable of assisting in the early diagnosis of NF, is ultrasonography. In human patients, ultrasonography may reveal fascial thickening, swelling of subcutaneous tissue, perifascial fluid collections, gas within the soft tissue and increased echogenicity of the subcutaneous tissue with interconnected thin anechoic spaces ('cobblestone appearance') (Tsai et al. 1996; Chau et al., 2005; Edlich et al., 2010; Wronski et al., 2011). In the veterinary literature, ultrasonographic findings have been described in three cases of canine NF so far (Gerdin and Pintar, 2003; Kulendra and Corr, 2008; Csiszer et al., 2010). In these cases, ultrasonography identified significant fluid accumulation between the fascial planes of the affected limb. Indicative findings in the present case were the 'cobblestone appearance' of the subcutaneous tissue and the fluid filled pockets. Although ultrasonography can mostly not differentiate between infected and non-infected fluid (Edlich et al., 2010), it allows for guided aspiration of this abnormal fluid, even in the early course of the disease. Additional advantages of ultrasonography are that it is a low-cost and readily available technique, sedation or anesthesia is not required, and that it may be performed on the intensive care unit (Yen et al., 2002). More advanced medical imaging techniques, such as computed tomography (CT) or magnetic resonance imaging (MRI), might further assist in the early diagnosis of NF. However, in the human literature, there is controversy about their benefit in the diagnosis of NF (Beltran et al., 1988; Rahmouni et al., 1994; Arslan et al., 2000; Edlich et al., 2010). Some authors claim that CT and MRI are superior diagnostic tools for the early detection of NF because of an unparalleled resolution and contrast at the level of the soft tissues and a high sensitivity for detecting exudate (Beltran et al., 1988; Rahmouni et al., 1994). According to others, their high sensitivity may overestimate the extent of deep fascial involvement, making the differentiation between NF and cellulitis not reliable (Arslan et al., 2000). To the authors' knowledge, CT and MRI have not yet been used as diagnostic tools in canine cases of NF.

In humans, the 'finger test' is a bedside procedure that may raise the index of suspicion of NF (Andreasen et al., 2001). During this procedure, a two-centimeter stab incision is made in the affected area under local anesthesia, and a gentle probing with the index finger is performed at the level of the deep fascia. The lack of bleeding, the presence of foul smelling pus and the lack of tissue resistance to blunt finger dissection are features of a positive 'finger test' (Andreasen et al., 2001). A 'finger test' was not performed in the patient of the present case, because the test was unknown to the authors at that time, nor has it been described in any of the reported canine cases. However, it is an easy and low-cost test that could potentially be a useful diagnostic tool in veterinary medicine as well.

In human medicine, there is a consensus that early, radical and complete surgical debridement is the primary, life-saving treatment for NF in human patients (May et al., 2009; Edlich et al., 2010). The importance of early diagnosis is underscored by studies that report the significant benefit to the outcome and prognosis associated with early and aggressive debridement (May et al., 2009; Edlich et al., 2010). Reassessment and re-exploration of the affected area within 48 hours are warranted, and debridement should be continued until the infection is completely halted (Wong and Wang, 2005; Edlich et al., 2010). Tissues that appear viable during the first surgical exploration may develop into necrotic tissue (Andreasen et al., 2001). Toxin-induced vasoconstriction leads to secondary thrombosis of the supplying vessel, resulting in progressive necrosis of skin and subcutaneous tissue (Childers et al., 2002). Such inadequately perfused tissue promotes progressive bacterial growth, and the infectious process continues to spread if not halted by surgical means (Childers et al., 2002). Aggressive debridement removes the source of infection and toxins. By removing the infarcted tissue, the penetration of antibiotics is improved (Mulla, 2003). Medical therapy in the absence of surgical debridement is futile because of its poor antibiotic penetrance (Wong and Wang, 2005). Naidoo et al. (2005) reported on a canine case of NF in which

the owners declined aggressive surgical debridement. Despite supportive care, broad-spectrum antibiotic therapy and open wound drainage, the fasciitis rapidly progressed, and the dog needed to be euthanized within 46 hours of admission. The dog described in the current case report underwent aggressive surgical debridement as soon as the presumptive diagnosis of a phlegmon with *cocci* changed into a tentative diagnosis of NF. At the initial surgery, all macroscopically affected tissue was removed. However, in accordance to the human literature (Childers et al., 2002), more necrotic tissue developed, and a second surgical debridement was necessary within 48 hours.

While awaiting culture results, initial antibiotic treatment should be broad based (Edlich et al., 2010). Recommendations for human NF patients include a combination of penicillin or cephalosporins for gram-positive and gram-negative coverage, along with clindamycine or metronidazole for anaerobic coverage (Bisno and Stevens, 1996; Childers et al., 2002). Due to thrombosis of the blood vessels that supply the affected area, there is very little effect on the primary infection site (Wong et al., 2003), but the early use of broad-spectrum antibiotics is essential for lowering the systemic bacterial load (Brady and Otto, 2001). The antibiotic treatment helps to arrest the progression of early sepsis into severe sepsis or septic shock and multiple organ failure (Brady and Otto, 2001; Wong et al., 2003). Generally, β-hemolytic *streptococci* are sensitive to penicillins. Therefore, these antibiotics should always be included in the initial therapy (Morgan, 2010). Clindamycine, however, does not only inhibit the bacterial protein synthesis, hereby suppressing the synthesis of tumor necrosis factor-α and decreasing the progression of STSS, it also suppresses the synthesis of bacterial toxins by *S. canis*, thus slowing the toxin-mediated tissue destruction (Edlich et al., 2010). Neither the amount of bacteria nor the bacterial growth stage at the time of initiating the therapy affect the efficacy of clindamycine, which is nowadays considered the drug of choice in human NF patients (Edlich et al., 2010). In accordance to the human literature, initial broad-spectrum antibiotic therapy is also recommended for canine patients (Naidoo et al., 2005). Monotherapy with fluoroquinolones is not recommended in dogs. The veterinary literature documents a limited clinical activity against streptococcal species, despite the in vitro bacterial sensitivity (Miller et al., 1996). Furthermore, fluoroquinolones may aid the initiation of STSS by causing a bacteriophage induced lysis of *S. canis* and superantigen expression. These superantigens induce T-cell proliferation and the excessive release of host cytokines, which may lead to a toxic shock syndrome (Ingrey et al., 2003).

In the current case, the referring veterinarian administered marbofloxacine the day before referral. However, this isolated dose did not induce STSS. The subsequent antibiotic treatment consisted of amoxicillin-clavulanic acid, covering for most gram-positive *cocci*, and for some gram-negative rods and anaerobes. Clindamycine was added for an enhanced anaerobic coverage. The administration of both antibiotics was continued when culture and sensitivity results demonstrated the growth of *S. canis*, sensitive to both antibiotics.

In human medicine, tables and diagrams are available predicting the probability of NF based on several parameters (Childers et al., 2002; Wong et al., 2003; Wong et al., 2004; Wong and Wang, 2005; Edlich et al., 2010). These parameters include clinical signs, findings on cytology, medical imaging results, observations during surgery and results of the histopathology. An area of recent development is the analysis of changes in the hematologic and biochemical profile assisting the early recognition of NF (Wong et al., 2004). Sepsis and the associated SIRS cause changes in the hematologic and biochemical parameters. Less severe soft tissue infections, such as phlegmones and abscesses, rarely cause an inflammatory state severe enough to cause disturbances in these variables (Wong et al., 2004). Therefore, aberrations in these parameters aid the early recognition of NF, even before the culture results are available.

In the dog described in the current case report, a mild neutrophilic leukocytosis with a left shift indicated a possible infection. The presence of hypoalbuminemia in this patient could have been due to the compensation to hyperglobulinemia, a decreased synthesis due to negative acute-phase or impaired liver function, an increased loss at the infection site, or due to intravascular dilution (Mazzaferro et al., 2002). Both the PT and the aPTT were prolonged in this dog, and D-dimers were elevated, indicating DIC (Nelson and Couto, 1992). The SIRS induces an increased production of tissue factor and a decreased production of antithrombine, leading to hypercoagulability and possibly DIC (Brady and Otto, 2001).

In this patient, the calculated plasma osmolarity was slightly decreased (287 mOsm/L) due to hyponatremia. The presence of a distributive shock most likely stimulated anti-diuretic hormone (ADH) secretion and free water retention, hence causing hyponatremia (Heinrich et al., 2012). Hyperbilirubinemia and mild elevations in liver enzymes are common with sepsis, caused by the bacterial toxin- and TNF-mediated inhibition of the hepatocyte membrane pumps (Brady and Otto, 2001).

Urine culture revealed a bacterial urinary tract infection caused by the same *streptococcus* present in the wound. This confirms the hematological spread of the infection. The active sediment and increased UPC were secondary to the infection. To the authors' knowledge, aberrations in urinalysis have never been reported in association with canine NF.

Despite therapeutic advances in the treatment of NF in humans, the mortality rates for necrotizing soft tissue infections still remain high, and range from 6% to 76%, with a mean mortality rate of 34% (McHenry et al., 1995). In contrast, the prognosis in dogs with NF appears to be better. All of the eighteen described dogs

as well as all seven patients treated by the authors did survive to discharge, with the exception of two dogs, suggesting a mortality rate under 8%. One of these two dogs was the only one that had not been receiving surgical debridement as part of its treatment, suggesting that the mortality rate is even lower for patients receiving optimal care treatment, including aggressive surgical debridement.

CONCLUSION

Dogs may be affected by NF. Similar to the situation in humans, timely and aggressive surgical intervention in combination with antibiotic therapy is imperative to avoid fatalities. In the early phase of the disease, however, it might be difficult to differentiate between NF and other less severe soft tissue infections. Therefore, clinico-pathological findings compatible with NF should prompt early surgical exploration even before the results of bacterial culture are available. Because of the limited number of affected dogs reported so far, it has not yet been possible to acknowledge diagnostic value to specific clinical and laboratory parameters.

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