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Authors: Casey, Kelsey, and Dickinson, Amy

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Suspected symmetrical peripheral gangrene in a cat

Kelsey Casey and Amy Dickinson

Abstract

Case summary An 8-year-old female spayed domestic shorthair cat was presented for evaluation of non-specific lethargy and pain. It was diagnosed with septic shock secondary to wounds on the dorsum and required treatment with multiple vasopressors for circulatory support. During the course of hospitalization, it was weaned from vasopressors but subsequently developed symmetric skin necrosis and sloughing of the paws on the right thoracic and right pelvic limbs leading to a presumptive diagnosis of suspected symmetrical peripheral gangrene (SPG).

Relevance and novel information This report documents the first case of suspected SPG in a cat that received multiple vasopressors for treatment of septic shock. Early recognition, cessation of vasopressor therapy and surgical management are necessary for treatment of this condition.

Keywords: Sepsis; septic shock; gangrene; vasopressin; hydrocortisone; norepinephrine

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Introduction

In people, symmetrical peripheral gangrene (SPG) is a rare clinical syndrome frequently defined by symmetrical acral ischemic damage involving two or more sites in the absence of large vessel obstruction or vasculitis.[1] SPG can lead to significant morbidity and mortality often requiring multiple limb amputations in survivors.[2] SPG was reported once in a foal;[3] however, this is the first documented case of suspected SPG secondary to septic shock in a cat. It demonstrates the importance of recognition of SPG as a possible complication of sepsis and vasopressor therapy. Treatment for SPG primarily includes identification and treatment of the underlying cause, discontinuation of vasopressors, wound care, surgical debridement, and/or amputation of digits or limbs.

Case summary

An 8-year-old female spayed domestic shorthair cat presented for acute onset of lethargy and pain. It was an indoor/outdoor cat and not up to date with vaccinations. There was no known history of trauma nor recent medication administration.

On presentation, the cat had an elevated body temperature of 39.9°C (103.9°F; measured rectally). It was hypotensive, with a blood pressure of 80 mmHg measured by an ultrasonic Doppler flow monitor, and tachypneic at 60 breaths per min. It was painful at the level of the thoracolumbar spine, and had three small puncture wounds on its back. Serum biochemistry showed mild hyperglycemia 9.82 mmol/l (177 mg/dl) (3.88–8.88 mmol/dl [70–160 mg/dl]). Complete blood count was normal, with a white blood cell count of 17.27 $\times 10^9$/l (5.50–19.50 $\times 10^9$/l). The packed cell volume (PCV) and total protein (TP) were 41% (25–45%) and 7.5 g/dl (65–84 g/l [6.5–8.4 g/dl]), respectively. The cat tested negative for retroviral disease (feline leukemia virus/feline immunodeficiency virus) via point-of-care ELISA. Radiographs of the thorax and abdomen, interpreted by a board-certified veterinary radiologist, showed a mild diffuse bronchointerstitial pulmonary

Department of Emergency and Critical Care, Pittsburgh Veterinary Specialty and Emergency Center, Pittsburgh, PA, USA

Corresponding author:
Kelsey Casey DVM, Department of Emergency and Critical Care, Pittsburgh Veterinary Specialty and Emergency Center, 807 Camp Horne Road, Pittsburgh, PA 15237, USA
Email: kelsey.casey@bluepearlvet.com

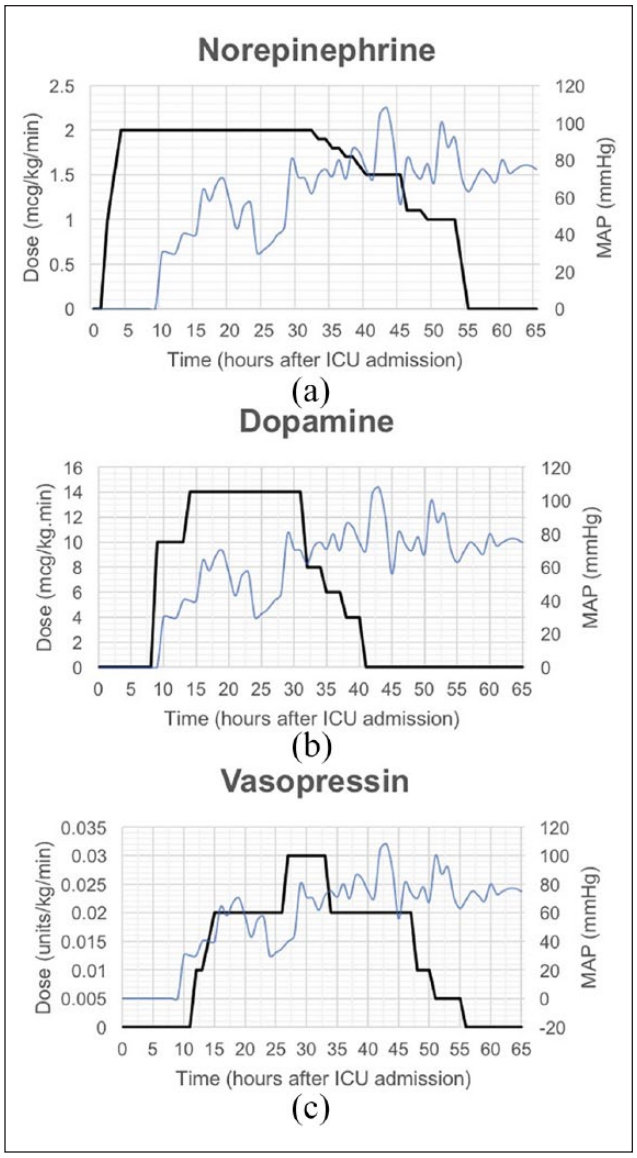

Figure 1 Doses of (a) norepinephrine, (b) dopamine and (c) vasopressin, as well as mean arterial blood pressure (MAP) from admission to the intensive care unit (ICU) to cessation of vasopressor support

pattern, a normal abdomen, normal skeletal structures, and soft tissue swelling and gas noted dorsal to the lumbar spine concerning for cellulitis.

Initial treatment included two intravenous (IV) crystalloid fluid boluses (9 ml/kg each, lactated Ringer's solution [LRS]), after which the Doppler blood pressure increased to 98 mmHg. The cat was then started on a rate (60 ml/kg/day) of IV LRS for approximately 3 h. It was also given an injection of IV buprenorphine (0.01 mg/kg). Hospitalization was declined by the owner, so the cat was discharged home with oral transmucosal (OTM) buprenorphine (0.01 mg/kg OTM q8h) and oral amoxicillin/clavulanic acid (11.16 mg/kg PO q12h). A culture of the wound was initially declined by the owner.

At home, the cat continued to be lethargic and became anorexic. It re-presented to the hospital approximately 23 h after its initial assessment. The cat was obtunded, had a body temperature of 37.7°C (99.9°F; measured rectally), a respiratory rate of 50 breaths per min and a heart rate of 180 beats per min. An IV catheter was placed in the right cephalic vein. The cat was severely hypotensive (Doppler blood pressure 30 mmHg) and hypoglycemic at 1.9 mmol/dl (35 mg/dl [75–125 mg/dl]). A focused assessment with ultra sonography for trauma examination was negative. The skin on the dorsum was warm to the touch, and a subcutaneous fluid pocket was suspected. A fine-needle aspirate of the area was obtained, and cytology was consistent with septic suppurative inflammation. A sample of the fluid was submitted to a reference laboratory for aerobic culture. An abdominal ultrasound, performed by a board-certified veterinary radiologist to rule out evidence of penetrating abdominal wounds, showed no significant findings. A PCV/TP (43% and 6.3 g/dl, respectively) and venous blood gas (normal) were performed.

The cat was admitted to the intensive care unit and treated with ampicillin–sulbactam (30 mg/kg IV q8h), enrofloxacin (7 mg/kg IV q24h), metronidazole (9.8 mg/kg IV q12h), vitamin C (30 mg/kg IV q8h), maropitant citrate (1 mg/kg IV q24h), famotidine (1 mg/kg IV q24h) and a fentanyl constant rate infusion (CRI; 4 µg/kg/h). A single bolus of dextrose (1 ml/kg 25% IV) was given, and the cat was started on an infusion of LRS with 5% dextrose and 40 meq/l potassium chloride (85 ml/kg/day). The cat was sedated with fentanyl (4 µg/kg IV) and midazolam (0.18 mg/kg IV), and the wound was opened surgically, debrided and lavaged with sterile saline. A wet-to-dry tie over bandage was placed. A 5 Fr × 8 cm double-lumen catheter was placed in the left jugular vein. An indwelling urinary catheter attached to a closed collection system was also placed. An attempt to place an arterial catheter in the left dorsal pedal artery was unsuccessful.

The cat remained hypotensive (Doppler blood pressure 30–40 mmHg) despite IV fluids and resolution of hypoglycemia. A norepinephrine CRI was started, and the dose incrementally increased (Figure 1a) due to persistent hypotension. An arterial cut-down was performed, and an arterial catheter was placed in the right dorsal pedal artery for continuous invasive blood pressure monitoring. The cat continued to be hypotensive with a mean arterial blood pressure (MAP) of 30 mmHg. A dopamine CRI was started and the dose was incrementally increased (Figure 1b). The cat continued to have refractory hypotension (MAP 40 mmHg) and a low-dose vasopressin CRI was initiated (Figure 1c). The vasopressors were administered via the jugular catheter. Owing to concern for possible critical illness-related corticosteroid insufficiency, the cat was started on a hydrocortisone CRI (0.08 mg/kg/h).

The following day the cat was more responsive and able to lift its head. Dextrose supplementation was discontinued. The wet-to-dry bandage was replaced, and IV enrofloxacin, ampicillin–sulbactam, metronidazole, maropitant, hydrocortisone CRI and vitamin C were continued. The norepinephrine, dopamine and vasopressin CRIs were continued (Figure 1). The dopamine dose was decreased and eventually discontinued (Figure 1b). The norepinephrine dose was decreased (Figure 1a) and the vasopressin dose was unchanged (Figure 1c).

On the third day of hospitalization the cat was able to maintain sternal recumbency and ate a small amount of food. Motor function and pain sensation were present in all four of the limbs, but the cat was unable to stand or walk. The cat appeared less painful and the fentanyl CRI was decreased (2 µg/kg/h). The wet-to-dry bandage was changed with no additional sedation. The norepinephrine and vasopressin doses were decreased, and the CRIs were eventually discontinued (Figure 1a,c). The cat's MAP stayed between 70 and 80 mmHg overnight and through the next day (Figure 1a–c).

On day 5 of hospitalization the cat was anesthetized and a 7 mm Jackson-Pratt drain was placed under the wound, and the wound was closed by a board-certified veterinary surgeon. During surgery, the cat was briefly hypotensive (MAP 45 mmHg) and treated with dopamine (5 µg/kg/min). The hypotension resolved and the dopamine was discontinued on recovery from general anesthesia. A recheck PCV that day was 19%. The anemia was suspected to be secondary to dilution from IV fluids, blood sampling and surgical blood loss. At the discretion of the attending clinician, a blood type (Alvedia QuickTest) was performed (type A) and the cat was given one unit of compatible feline packed red blood cells. The cat started eating readily and was transitioned to oral amoxicillin/clavulanic acid, enrofloxacin and OTM buprenorphine.

The culture of the wound was reported as scant growth of a coagulase-negative *Staphylococcus* species sensitive to amoxicillin and amoxicillin/clavulanic acid, and resistant to enrofloxacin. The oral enrofloxacin was discontinued.

On day 6 the paws on the right thoracic and right pelvic limbs became swollen, edematous and cold to the touch. The right cephalic IV catheter and right dorsal pedal arterial catheters were removed. Vascular access via the central venous catheter was maintained. On day 7 the paws on the right thoracic and right pelvic limbs continued to be cold to the touch, painful and became discolored. The skin on the paw pads of the right thoracic and right pelvic limbs started to slough in a symmetrical fashion (Figure 2). A line of demarcation dividing affected tissue and normal healthy skin was noted on the limbs (Figure 3). Strong pedal pulses could be detected via ultrasonic Doppler flow monitor in all four limbs, despite continued skin sloughing. Clopidogrel (3.35 mg/kg PO q24h) was started on day 7 and continued until the paws fully healed.

The cat remained normotensive (MAP >70 mmHg) throughout the rest of the hospital stay. Continued wound care in the hospital included daily wet-to-dry bandage changes and hydrotherapy at the discretion of the attending clinician. The cat was discharged after 11 days with soft padded bandages in place on the right thoracic and right pelvic limbs. The paws fully healed with continued outpatient treatment by a board-certified veterinary surgeon (necrotic skin debrided and bandage changes over the following 2 weeks). The cat became ambulatory with mild residual pelvic limb weakness.

Figure 2 Sloughing of the skin on the right forelimb

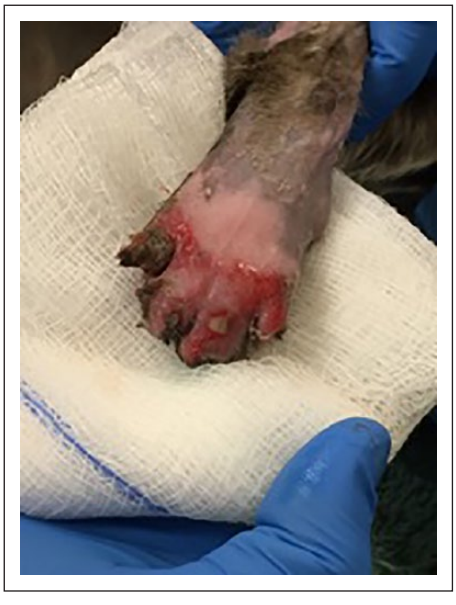

Figure 3 A line of demarcation on the right forelimb

Discussion

SPG is defined by symmetrical distal ischemic necrosis involving two or more sites in the absence of large vessel obstruction or vasculitis.[1] In people it is a well-documented clinical syndrome. SPG has been previously reported in a foal that developed ischemic necrosis of the distal limbs, and ultimately died of sepsis secondary to enteric salmonellosis.[3] This is the first documented case of suspected SPG in a small animal patient.

The clinical syndrome of SPG was first described in 1891.[4] The pathophysiology of SPG is incompletely understood, but is thought to be a result of impaired peripheral perfusion secondary to reduced cardiac output, and is exacerbated by peripheral microcirculatory vasoconstriction.[5] A low-flow state in the microvasculature, as well as disseminated intravascular coagulation (DIC), are commonly present in patients that develop SPG. Activation of neutrophils and release of vasoactive substances are thought to contribute, especially in patients with sepsis.[1] Many causes of infectious (bacterial, protozoal, viral) and non-infectious SPG have been described in the human literature.[6] Causes of non-infectious SPG are numerous and include neoplasia, pulmonary embolism, pancreatitis, frostbite and trauma.[2,6,7] The use of vasopressors for the treatment of septic shock has also been reported as a cause of SPG.[2,5,8,9,10] The cat described in this report had several predisposing factors, including infection, decreased peripheral circulation secondary to persistent and prolonged hypotension, sepsis and vasopressor use.

In people, up to 85% of patients with SPG are also diagnosed with DIC.[7] The cat's coagulation profile (prothrombin time/partial thromboplastin time, D-dimer, fibrinogen, anti-thrombin activity) was not evaluated during the course of hospitalization, so it is not possible to determine if the cat suffered from DIC. However, DIC is a known complication of sepsis,[11,12] so it is possible that undiagnosed DIC contributed to the development of SPG. The cat had no known pre-existing risk factors for peripheral thromboembolic disease.

SPG is suspected at the first sign of coldness, pallor, cyanosis or pain in the extremity.[1] Pulses are often palpable in the initial stages of the disease as microthombi concentrate in the small vessels rather than large vessels.[1,2] Fur on veterinary patients inhibits early recognition of pallor and cyanosis of the skin. Critically ill cats are often hypothermic, which may inhibit early recognition of coldness in the extremity.

Doppler ultrasound examination can be used to support the diagnosis of SPG and can show normal blood flow in large peripheral arteries.[1] Histopathology is required to make a definitive diagnosis. Histopathologic changes may be non-specific but can include microthrombi in the lumen of the capillaries, intraluminal deposition of fibrin and subtle extravasation of red blood cells in the absence of inflammatory infiltrates.[1] Large vessels lack evidence of thrombi.[2] Sparing of major arteries and absence of histopathologic evidence of inflammatory cells differentiates SPG from other conditions that cause a similar clinical appearance such as cutaneous vasculitis, Raynaud's gangrene or chemical injury.[1] Given the lack of histopathology in this case virulent systemic calicivirus can be considered as a possible cause[13], though this is considered unlikely given the lack of prodromal upper respiratory signs. Cutaneous vasculitis is also considered, but is thought to be less likely owing to lack of pinnal lesions, as well as lack of lesion recurrence.[14]

Treatment for SPG is largely anecdotal and ineffective at reversing gangrene. Most importantly, the inciting cause of SPG should be identified and treated. Previously described therapy includes treatment with anticoagulants (heparin, clopidogrel), recombinant tissue plasminogen activator, IV nitroprusside, topical nitroglycerine ointment, local or IV infusion of an alpha-blocker (phentolamine, chlorpromazine), phosphodiesterase inhibitors (sildenafil), IV infusion of a prostaglandin (iloprost) and hyperbaric oxygen therapy.[6,8,15,16,17] Immediate reduction or discontinuation of vasopressor therapy should be pursued to reduce peripheral vasoconstriction. Ultimately, most patients suffering from SPG require digit or limb amputation.[1] Amputation should only be considered after a line of demarcation is noted, in order to spare any viable tissue.[6,17,18,19]

There are case reports of skin necrosis in people receiving peripheral IV low-dose vasopressin therapy. Those patients were thought to have skin necrosis secondary to extravasation of vasopressin into the soft tissues.[20] However, there is also a case report of skin necrosis in a human patient receiving low-dose vasopressin therapy in a central venous catheter.[21] This suggests that SPG can occur in patients receiving low-dose vasopressin, regardless of the site of infusion. Veterinary patients receiving vasopressin for treatment of septic shock should be closely monitored for this complication.

Conclusions

This the first documented case of suspected SPG secondary to sepsis and vasopressor therapy in a small animal patient. While there is a strong clinical suspicion for SPG in this case, it was not definitively diagnosed with histopathology. SPG has mortality rates as high as 40%, making early recognition of this clinical syndrome important.[2] Frequent assessment of perfusion of the limbs and early cessation of vasopressor therapy in veterinary patients suffering from septic shock are indicated to avoid this potentially life-threatening complication.

Conflict of interest The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical approval This work involved the use of client-owned animal(s) only, and followed internationally recognised high standards ('best practice') of individual veterinary clinical patient care. Ethical Approval from a committee was not therefore needed.

Informed consent Informed consent (either verbal or written) was obtained from the owner or legal guardian of all animal(s) described in this work for the procedure(s) undertaken.

ORCID iD Kelsey Casey https://orcid.org/0000-0003-0615-7650

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