Ultrasound-guided intracardiac xenotransfusion of canine packed red blood cells and epinephrine to the left ventricle of a severely anemic cat during cardiopulmonary resuscitation

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Abstract

Objective – To describe the use of an ultrasound-guided intracardiac xenotransfusion of canine packed red blood cells (pRBC) to the left ventricle of a severely anemic cat during cardiopulmonary resuscitation (CPR).

Case Summary – An 8-year-old previously healthy neutered female cat was presented with severe weakness after she had disappeared for 1 month. On presentation, the cat was in hypovolemic shock, laterally recumbent, and severely anemic with massive flea infestation. Within minutes of admission, the cat became agonal and suffered cardiopulmonary arrest. CPR was immediately initiated; however, attempts to gain IV access during CPR were unsuccessful. As the cat’s blood type was yet unknown, 10 mL of canine pRBC was transfused directly into the left ventricular chamber using ultrasound guidance, as well as 0.02 mg/kg of epinephrine using a similar technique. The cat regained cardiac activity and once the jugular vein was cannulated it received 20 additional mL of canine pRBC intravenously. The packed cell volume and total plasma protein following the intracardiac transfusion were 0.09 L/L [9%] and 30 g/L [3.0 g/dL], respectively. Subsequent blood typing revealed the cat had type B blood. The cat was discharged 3 days post-CPR and was alive and doing well 3 months following discharge.

New or Unique Information Provided – This is the first reported case of ultrasound-guided intracardiac canine-to-feline xenotransfusion during CPR.

Keywords: CPA, CPR, feline, transfusion

Case Description

A 2.3 kg, 8-year-old, previously healthy, indoor-outdoor, neutered female domestic short-hair cat was presented for severe weakness. A month prior to admission the cat disappeared and was found a day prior to presentation. The cat had lost a significant amount of body weight, was weak, but able to drink, eat, and walk around the house. The next day the cat became laterally recumbent, non-responsive, and was immediately presented for veterinary evaluation and promptly referred for further care.

On presentation, the cat was in severe hypovolemic shock. The cat was minimally responsive, tachypneic (respiratory rate 84/min), hypothermic (body...
temperature was below detection limit [32°C, 89.6°F]), and bradycardic (pulse rate 140/min) with weak peripheral pulses, pale mucous membranes, and severe dehydration (estimated 10–12%). The cat was extremely cachectic (body condition score 1/9) and was massively infested with fleas. Flow-by oxygen was supplemented and attempts to gain IV access were initiated.

Within minutes from admission, the cat deteriorated and became agonal. The cat became unconscious, was gasping for air and went into cardiopulmonary arrest (CPA). As the CPA was witnessed, cardiopulmonary resuscitation (CPR) was immediately initiated. The cat was intubated with a size 4 endotracheal tube, 100% oxygen was supplemented with manual positive ventilations using a bag valve mask (eg, Ambu) and chest compressions were initiated. Attempts to gain IV access via the cephalic, saphenous, femoral, and jugular veins failed. A 0.04 mg/kg epinephrine\textsuperscript{a} was administered directly into the endotracheal tube.

As the cat’s blood type was yet unknown, and feline packed red blood cells (pRBC) were not readily available, approximately 3 minutes postinitiation of CPR, chest compressions were interrupted for approximately 30 seconds, to allow intracardiac transfusion of 10 mL of canine pRBC into the left ventricle using ultrasound guidance. The procedure was performed by 2 experienced board-certified emergency and critical care veterinarians. The cat was in right lateral recumbency, the left hemithorax was quickly clipped and sprayed with alcohol and the left ventricle was identified using a 6.5 megahertz ultrasound microconvex probe.\textsuperscript{b} The myocardium was penetrated using a 21 Ga catheter\textsuperscript{c} and 10 mL of canine pRBC were transfused as a bolus into the left ventricle, followed by 0.02 mg/kg epinephrine\textsuperscript{a} using a similar technique. Subsequently, return of spontaneous circulation (ROSC) was achieved and chest compressions were terminated. The cat regained slow cardiac activity, demonstrated with the ultrasound probe, and evidenced with an ECG monitor, and 0.04 mg/kg atropine\textsuperscript{d} was administered IV. Within a few minutes the jugular vein was cannulated using a 20 Ga catheter\textsuperscript{c} and secured. An additional 20 mL of canine pRBC were transfused IV over 20 minutes, followed by 20 mL of a balanced crystalloid solution,\textsuperscript{a} and 5 mL of 25% dextrose in water for injection. Sinus arrhythmia was achieved and the cat was placed on positive pressure ventilation\textsuperscript{e} (synchronized intermittent mandatory ventilation, pressure-cycled, 100% oxygen). After approximately 20 additional minutes the cat was breathing spontaneously and the ventilator settings were changed to continuous positive airway pressure with pressure support. Due to the prolonged time lag from initiation of CPR until spontaneous breathing resumed (approximately 35 min), mannitol\textsuperscript{f} (1 g/kg IV over 20 min) was administered to reduce potential cerebral edema. As the cat remained rigid and had a few episodes of myoclonal activity, diazepam\textsuperscript{g} 0.5 mg/kg, IV, was administered twice, 10 minutes apart. To reduce possible adverse reactions in response to the xenotransfusion, diphenhydramine\textsuperscript{h} 2 mg/kg, IM, once, and dexamethasone\textsuperscript{i} 0.3 mg/kg, IV, once, were administered as well.

Once the cat was stabilized on the ventilator, it was clipped, cleaned, and bathed in order to remove the copious amounts of fleas from its hair coat. Fipronil 0.29%,\textsuperscript{k} was gently sprayed and an ampule of Selamectin\textsuperscript{l} was applied. In addition, an orogastric tube was inserted and nitenpyram\textsuperscript{m} was administered enterally. The previously placed 20 Ga jugular catheter was replaced with a 5.5 Fr, 8 cm, double-port jugular catheter\textsuperscript{n} using a modified-Seldinger technique.

A CBC,\textsuperscript{o} sampled following the intracardiac transfusion, revealed severe anemia (PCV, 0.09 L/L [9%], reference interval [RI] 0.30–0.55 L/L [30–55%]) with low total plasma protein (TPP) (30.0 g/L [3.0 g/dL], RI: 55–75 g/L [5.5–7.5 g/dL]), a low WBC count (5.9×10\textsuperscript{9}/L [3.9×10\textsuperscript{9}/μL, RI: 6.3–19.66×10\textsuperscript{9}/L [6.3–19.66×10\textsuperscript{9}/μL]) and a moderate thrombocytopenia (platelets count 75×10\textsuperscript{9}/L [75×10\textsuperscript{9}/μL, RI: 156–626×10\textsuperscript{9}/L [156–626×10\textsuperscript{9}/μL]) (Table 1). Blood smear evaluation confirmed the thrombocytopenia and revealed mature neutrophils with no left shift or toxic changes. Anisocytosis, polychromasia, hypochromia, Howell-Jolly bodies, and abundant-nucleated red blood cells (47%) were also noted. The corrected WBC count was 3.1×10\textsuperscript{9}/L (3.1×10\textsuperscript{9}/μL) with type-B blood typing and a positive auto-agglutination test.

Repeat PCV/TPP after the full xenotransfusion administration was 0.15 L/L [15%] 32.0 g/L [3.2 g/dL]. Measurement of electrolytes\textsuperscript{p} revealed a significant hypocalcemia 0.67 mmol/L (2.7 mg/dL) (RI: 1.12–1.32 mmol/L [4.5–5.3 mg/dL]) and a mild hyperchloremia (111.5 mmol/L, RI: 98.0–107.0 mmol/L). The hypocalcemia was treated with 0.5 mL/kg IV over 20 minutes of 10% calcium gluconate.\textsuperscript{q}

The cat was administered IV crystalloids\textsuperscript{s} (3.4 mL/kg/h) supplemented with 2.5% dextrose\textsuperscript{r} and metoclopramide\textsuperscript{e} 1 mg/kg/day, IV CRI. Cefazolin\textsuperscript{t} 20 mg/kg, IV, every 8 hours, iron dextran\textsuperscript{u} 10 mg/kg, IM, once, and vitamin B\textsubscript{12}\textsuperscript{e} 250 μg, SQ, once, were also administered.

The cat’s massive flea infestation was suspected to be the main cause of its anemia; however, the positive auto-agglutination test indicated a process of hemolysis, possibly secondary to Mycoplasma hemofelis infection, which is transmitted via flea bites. Due to financial restraints, PCR for M. hemofelis was not performed and oxytetracycline\textsuperscript{w} 10 mg/kg, SQ, every 24 hours, was empirically administered. Due to the low TPP
concentration, 1 unit of matched type B feline fresh frozen plasma was administered.

Approximately 2 hours after presentation, the cat was extubated and oxygen was supplemented via a face mask. Monitoring included continuous ECG and blood pressure measurements. Vital signs were recorded every 2 hours. Six hours after presentation the cat regained mentation, ate a small amount of food and remained stable overnight.

Repeat CBC performed on day 2 revealed a stable PCV and improvement in the TPP (0.15 L/L [15%] and 82.0 g/L [8.2 g/dL]), with a wide red blood cells distribution width (RDW) (20.5%) and a high mean corpuscular volume (MCV) (58.6 μm³) indicating regeneration (Table 1). Direct blood smear confirmed the presence of a regenerative anemia and mild neutrophil toxicity. No significant abnormalities were noted in the serum biochemical panel except for a mild hypoaalbuminemia, and mild increases in urea and creatine kinase activity (Table 2). As the cat was still anemic, an additional iron dextran injection and a multivitamin injection were administered. During a second follow-up examination 1 month after discharge, the cat was deemed normal. No abnormalities were noted on physical examination, serum biochemical analytes or PCV/TPP.

Discussion

To the authors’ knowledge, this is the first reported case of successful intracardiac xenotransfusion of canine pRBC into the left ventricle of a cat during CPR. Canine-to-feline xenotransfusion was first described in 1962. Recently, Bovens et al reviewed 62 reported cases in the literature describing xenotransfusion ranging from 5–130 mL of canine whole blood administered to cats, and concluded that anemic cats receiving canine blood improve clinically within hours. Weingram reported...
Table 2: Serum electrolytes and biochemistry results* of an 8-year-old neutered female cat with severe anemia due to massive flea infestation

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Day 0</th>
<th>Day 1</th>
<th>Day 10 (1 week post discharge)</th>
<th>Day 30 (3.5 weeks post discharge)</th>
<th>RI† (SI units)</th>
<th>RI† (US units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin (g/L) [g/dL]</td>
<td>28 [2.8]</td>
<td>24 [2.4]</td>
<td>37 [3.7]</td>
<td>22–46</td>
<td>2.0–4.6</td>
<td></td>
</tr>
<tr>
<td>Alkaline phosphatase (U/L)</td>
<td>23</td>
<td>28</td>
<td>114</td>
<td>27–101</td>
<td>14–71</td>
<td>14–71</td>
</tr>
<tr>
<td>Alanine transaminase (U/L)</td>
<td>155</td>
<td>26</td>
<td>1.0 [0.08]</td>
<td>0.0–3.4</td>
<td>0.0–0.2</td>
<td></td>
</tr>
<tr>
<td>Amylase (U/L)</td>
<td>809</td>
<td>1213</td>
<td>2.2–2.7</td>
<td>9.0–10.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspartate transaminase (U/L)</td>
<td>821</td>
<td>49</td>
<td>17–58</td>
<td>15.0–21.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total bilirubin (μmol/L) [mg/dL]</td>
<td>11.4 [0.7]</td>
<td>0.85 [0.05]</td>
<td>79 [0.9]</td>
<td>97.2–194.4</td>
<td>1.1–2.2</td>
<td></td>
</tr>
<tr>
<td>Calcium (mmol/L) [mg/dL]</td>
<td>2.1 [8.4]</td>
<td>2.4 [9.9]</td>
<td>2.2–2.7</td>
<td>9.0–10.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ionized calcium (mmol/L) [mg/dL]</td>
<td>0.6 [2.7]</td>
<td></td>
<td></td>
<td>1.1–1.3</td>
<td>4.5–5.3</td>
<td></td>
</tr>
<tr>
<td>Cholesterol (μmol/L) [mg/dL]</td>
<td>4.0 [155]</td>
<td>6.5 [247]</td>
<td>3.3–6.6</td>
<td>89–258</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatine kinase (U/L)</td>
<td>&gt;40,000</td>
<td>623</td>
<td>73–280</td>
<td>73–280</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chloride (mmol/L) [mEq/L]</td>
<td>111</td>
<td>120</td>
<td>17–126</td>
<td>117–126</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total CO₂ (mEq/L) [mmol/L]</td>
<td>18.8</td>
<td>11.6</td>
<td>15.0–21.0</td>
<td>15.0–21.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine (μmol/L) [mg/dL]</td>
<td>7.0 [0.8]</td>
<td>65 [0.7]</td>
<td>79 [0.9]</td>
<td>97.2–194.4</td>
<td>1.1–2.2</td>
<td></td>
</tr>
<tr>
<td>γ-glutamyl transpeptidase (U/L)</td>
<td>2.3</td>
<td>0</td>
<td>0.0–6.0</td>
<td>0.0–6.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose (mmol/L) [mg/dL]</td>
<td>4.7 [85.6]</td>
<td>4.4 [80.7]</td>
<td>3.5–6.5</td>
<td>63.0–118.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potassium (mEq/L) [mmol/L]</td>
<td>4.1</td>
<td>4.4</td>
<td>3.5–4.5</td>
<td>3.5–4.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium (mEq/L) [mmol/L]</td>
<td>143</td>
<td>151</td>
<td>135–148</td>
<td>135–148</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phosphorus (mmol/L) [mg/dL]</td>
<td>1.2 [3.8]</td>
<td>1.4 [4.6]</td>
<td>1.0–2.0</td>
<td>3.2–6.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total protein (g/L) [g/dL]</td>
<td>26.7 [75.3]</td>
<td>28.4 [79.7]</td>
<td>21.38</td>
<td>13.7–25.2</td>
<td>38.5–70.6</td>
<td></td>
</tr>
</tbody>
</table>

*SI units are depicted in parentheses, while US units (when different from the SI ones) depicted in brackets.
†Reference interval.

Ultrasound-guided intracardiac xenotransfusion

xenotransfusing 5 mL of canine pRBC that also resulted in rapid improvement of the recipient cat with no complications noted.3

As opposed to dogs, cats exhibit naturally occurring autoantibodies against feline red blood cell antigens of other types, potentially inducing severe adverse reactions, including shock, anaphylactic and anaphylactoid reactions, and even death, if unmatched blood is transfused.4 In addition, availability of feline blood is often limited and it is technically more challenging to collect it due to patient size and behavior. In light of this, xenotransfusions may be of significant importance, especially in geographical areas with higher incidence of type B and AB blood groups, such as Australia and Israel.5 In addition, feline transfusions are cost-prohibitive for some owners and in critical need of blood, such as in the present case, the time spent to perform blood typing may be crucial.

Cats do not exhibit naturally occurring antibodies against canine erythrocytes.2 In all cases of xenotransfusions documented, cross match performed prior to the transfusion revealed no major incompatibilities and only 2 cases of minor incompatibilities were reported.2 Agglutination between canine red blood cells and the feline recipient’s plasma developed 4–7 days posttransfusion, and hemolysis was evident 7–21 days post transfusion.1 Severe acute adverse reactions have not been reported in cats receiving xenotransfusions.5 Minor clinical signs such as tachypnea, mild pyrexia, and icterus, are also common following interspecies transfusions.2,4

Immediate fatalities have not been reported following the first canine-to-feline xenotransfusion, nor as a result of a second xenotransfusion administered within 6 days after the first one.1,6 In contrast, 93.7% of cats receiving a second xenotransfusion 7 days or more after the first transfusion exhibited signs of anaphylaxis (eg, dyspnea, cyanosis, salivation, depression, coma) and 66% of the reported cases died.1,6 Therefore, as much as it is unlikely, it is important to make sure previous xenotransfusions had not been performed and xenotransfusions should not repeated after 6 days from the first administration.

Although first-time xenotransfusion of canine blood appears to be safe in cats, it is important to note that the lifespan of canine whole blood in the cat is significantly shorter than that of feline blood (4 versus 30 days).7,8 Therefore, in cases of chronic anemia or an anemia that is likely to continue despite blood transfusions (eg, anemia secondary to chronic kidney disease, neoplasia, or bone marrow suppression), canine blood transfusions are not likely to last long in the recipient and feline blood

is optimal. In acute cases of regenerative anemia, as reported herein, bone marrow regeneration is expected to occur rather quickly and canine blood transfusion can be lifesaving if no matched feline blood is available, and provided that the cat did not previously receive a canine blood transfusion.

In addition to blood products, hemoglobin-based oxygen carriers (HBOC), such as Oxyglobin, can be used when blood type is unknown or when matched blood components are unavailable. Oxyglobin has oxygen carrying capacities and colloid properties that allow expansion of circulatory volume that could be beneficial in cases of severe hypovolemia and anemia\(^9\) such as in the cat reported herein. Although Oxyglobin is labeled only for dogs, it has been used in other species, including cats\(^9,10\). In cats, rapid administration of HBOCs or presence of heart disease can lead to pulmonary edema and pleural effusion due to volume expansion.\(^9\) Unfortunately, Oxyglobin has not been available in many countries for a number of years and to our knowledge is currently not being produced.

As no intravenous route was available during CPR, the reported cat received epinephrine as well as 10 mL of canine pRBC directly into the left ventricle. Intraosseous access was not attempted, despite being the preferred route of drug administration during CPR when IV access is unsuccessful.\(^11\) Although intraosseous access may have been faster to achieve, it may take twice as long to administer the same volume of blood intraosseously compared to intravenously.\(^12\)

Intraventricular administration of drugs during CPR has been described in the human literature since the early 1900s.\(^13,14\) Reported complications after intraventricular drug administration include coronary artery laceration, pericardial effusion, and pneumothorax.\(^15–17\) In an article published in 1990, cardiac action was restored in half of the patients that were administered intraventricular injections of epinephrine and isoproterenol during CPR.\(^17\) Nonsurviving patients were autopsied and it was concluded that the consequences of the intraventricular injections were not serious.\(^17\) However, unless injected during open chest thoracotomy, injection into the left ventricle was not easily achieved.\(^16\) In 1983, Sabin et al\(^16\) postmortally evaluated 18 patients who died after unsuccessful CPR that included multiple intraventricular drug administration attempts, and in only 72% of the patients was the heart punctured at all during CPR. In 28% of the patients, injections were into the right ventricle and in 11% into the left. This report lacks consistency in the injection site used and the authors did not specify what was the desired injection location.\(^16\)

Ultrasound-guided techniques have been routinely incorporated into veterinary emergency and critical care,\(^18\) including focused assessment with sonography for trauma for early detection of abdominal fluids, thoracic-focused assessment with sonography for trauma for detection of pleural effusion, pneumothorax and pericardial effusion\(^19\) and ultrasound-guided jugular vein catheterization to gain rapid vascular access.\(^20\) Based on the difficulty of injecting the left ventricle, and due to reported complications, Plunkett and McMichael recommended to avoid intraventricular injections during CPR in veterinary patients, unless during an open chest CPR.\(^11\) However, with the increased availability of bedside ultrasound and proficiency of emergency clinicians in certain ultrasonographic techniques, this recommendation may need to be revisited as its use during CPR could improve accuracy of intraventricular site injection when appropriate.

Barsan et al\(^21\) evaluated the differences between peripheral, venous, central venous, and intraventricular (left ventricle, via thoracostomy) injections of lidocaine to dogs. No significant difference was found in effective serum concentrations or in time to peak serum levels between the different routes of administration; however, duration of effective concentrations was the longest in the intraventricular group.\(^21\) Intraventricular administration of drugs or blood products has not been evaluated in the recent reassessment campaign on Veterinary Resuscitation (RECOVER) guidelines for veterinary CPR.\(^22\) Intraventricular administration of blood has been reported only once in the human literature, in 1945, by a Soviet doctor that administered sodium chloride, glucose, and citrated blood, intraventricularly to 2 soldiers that were wounded during combat; both eventually survived.\(^23\)

A recent prospective study evaluating 121 dogs and 30 cats undergoing in-hospital CPR reported improvement in the rate of ROSC in cats compared to previous veterinary studies, increasing from 42–57%.\(^24–27\) Despite this, survival to discharge rates remained unchanged, and are reportedly 3–9.6%.\(^24–27\) In one study, cats with severe anemia and shock were less likely to survive CPR.\(^28\)

The major limitation of the present report is the inability to prove beyond doubt that ROSC was a direct result of the intracardiac injection of pRBC. Whether intravenous or intracardiac use of canine-to-feline xenotransfusions can improve survival rates in anemic cats undergoing CPR remains to be elucidated.

We conclude that intraventricular canine-to-feline xenotransfusion is feasible, and injection of canine pRBC and epinephrine into the left ventricle of the heart could be considered during CPR in cases of severe anemia when no intravenous access, a matched feline pRBC unit or HBOC are available. In addition, this case highlights the important contribution of ultrasound use in the emergency setting.
Footnotes

a Adrenaline, Teva Pharmaceuticals, Petach Tikva, Israel.
b Edan Instruments Inc. 6.5 MHz microconvex probe - dups 60, Nanshan Shenzhen, China.
c Delta Med, Viadana, Italy.
d Atropine, Teva Pharmaceuticals.
e Lactated Ringer’s solution, Teva Pharmaceuticals.
f T bird ventilator, AVS 3, San Diego, CA.
g Osmotrol 20%, Baxter International Inc., Deerfield, IL.
h Assival, Teva Pharmaceuticals.
i Diphenhydramine, Tamar Inc., Rishon Lezion, Israel.
j Dexacort forte, Teva Pharmaceuticals.
k Fipronil 0.29%, Frontline solution, Merial Limited, Duluth, GA.
l Selamectin, Revolution, Pfizer, New York City, NY.
m Capstar, Nitenpyram, Basel, Switzerland.
Contra-line 6.5 inch, BioMetrix, GD Breda, the Netherlands.
Advia 120, Siemens Medical Solutions Diagnostics GmbH, Erfurt, Germany.
Coabs integra 400 plus, Hoffmann-La Roche, Basel, Switzerland.
B Braun, Melsungen, Germany.
Teva Pharmaceuticals.
Pramin, Rafa Laboratories, Jerusalem, Israel.
PanCefazolin, PanPharma, Luirité, France.
Endofer, Farto, Ozanno Emilia, Italy.
Bodeka, Teva Pharmaceuticals.
Engamycin, Dexel Pharma Ltd, Or Akiva, Israel.
Cardell veterinary monitor 9401 BP, Midmark, Versailles, OH.
Doxylamine, Dexel Pharma Ltd.
Prednisolone, Rekah, Holon, Israel.
Multivitamin, V.M.D n.v.s.a, Arendonk, Belgium.

References
