

Successful xenotransfusion from a domestic dog (*Canis familiaris*) to an Andean fox (*Lycalopex culpaeus*)

Sucesso da xenotransfusão de um cão doméstico (Canis familiaris) para uma raposa andina (Lycalopex culpaeus)

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ABSTRACT

An Andean fox was transferred to the Wildlife Hospital of the Universidad San Francisco de Quito for evaluation of injuries caused by a run over. Clinical signs of hypovolemic shock were detected. Radiographies showed multiple pelvic fractures and free fluid in retroperitoneal cavity. The presumptive diagnosis was hemorrhagic shock caused by blood loss secondary to a pelvis fracture. An emergency xenotransfusion using blood from a domestic dog was performed without acute transfusion reactions observed. This is the first report of successful xenotransfusion between a domestic dog and an Andean fox presenting a procedure that could be applied in emergency situations.

Keywords: Blood transfusion. Hemorrhage. Hypovolemic shock. Run over.

RESUMO

Uma raposa andina foi levada ao Hospital da Vida Selvagem da Universidad San Francisco de Quito para avaliar os ferimentos causados por um atropelamento. Sinais clínicos de choque hipovolêmico foram detectados. Radiografias mostraram múltiplas fraturas pélvicas e fluido livre na cavidade retroperitoneal. O diagnóstico presuntivo foi um choque hemorrágico causado por perda sanguínea secundária a uma fratura pélvica. Uma xenotransfusão de emergência foi realizada com o sangue de um cão doméstico sem reações agudas transfusionais. Este é o primeiro relato bem sucedido de xenotransfusão entre um cão doméstico e uma raposa andina, demonstrando que é um procedimento que poderá ser considerado em situações de emergência.

Palavras-chave: Transfusão. Hemorragia. Choque hipovolêmico. Atropelamento.

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The Andean fox (*Lycalopex culpaeus*) is distributed along the Andes from southern Colombia to southern Chile and Argentina (Martínez et al., 2018). The species is globally classified as Least Concern by the IUN Red List of Threatened Species (Lucherini, 2016), but as Vulnerable in Ecuador, where the main threats are anthropogenic factors (Zapata-Ríos et al., 2011). In this sense, with the rapid expansion of the road network, collisions with wildlife have become one of the main causes of mortality for many species; only on Brazilian roads it is estimated that more than two million mammals could die per year (González-Suárez et al., 2018).

A juvenile free-ranging male Andean fox was transferred to the Wildlife Hospital of Universidad San Francisco

de Quito (USFQ) after being found immobile on a road shoulder in the province of Pichincha, Ecuador. At the clinical evaluation, extreme depression was observed and chemical restraint was not needed for physical examination and sample collection. The animal weighed 4.4 kg and physical exam revealed altered mental status (stupor), pale mucous membranes, prolonged capillary refill time (5 s), tachypnea (48 breaths/min), tachycardia (190 beats/min), hypotension (80 mmHg), hypothermia (36.4 °C) and severe dehydration (10%). Laboratory tests revealed normochromic normocytic anemia (hematocrit 22%, hemoglobin 73 g/L, erythrocytes $3.2 \times 10^{12}/L$, MVC 68.7 fL and MCHC 331 g/L), hypoproteinemia (38 g/L), hypoalbuminemia (17.6 g/L), high lactate levels (4 mmol/L), prolonged partial thromboplastin time (33 s), prothrombin time (10 s) and hematuria (250 RBC/ μ L) (Table 1).

Radiography series (Sharp Ray LWX-20P) demonstrated multiple pelvic fractures and free fluid in retroperitoneal cavity. Pelvic fractures are regularly associated with high-impact soft tissue injuries and vascular lesions that can produce significant retroperitoneal hemorrhages in dogs (Cabassu, 2005). Besides that, states of mental depression, pale mucous, poor peripheral perfusion, increased heart rates, low blood pressure and hypothermia are commonly associated with hypovolemic shock in small animals (De Laforcade & Silverstein, 2009). In addition, the anaerobic metabolism produced by poor tissue perfusion increases the lactate concentration, being widely accepted as an indicator of shock in animals (Pang & Boysen, 2007). The presumptive diagnosis for the Andean fox was a hypovolemic shock secondary to the retroperitoneal hemorrhage caused by the multiple pelvic fractures.

Initial treatment included oxygen therapy (100%) in an oxygen cage, fluids (lactated Ringer's, Viaflex Baxter, S.A, Valle del Cauca, Cali 760002, Colombia; 13 mL/kg/hr iv.), antibiotherapy (ceftriaxone, Vitrofarma S.A, Cundinamarca, Bogotá 11001, Colombia; 22 mg/kg iv q 12 hr and

metronidazole, Procaps S.A, Atlántico, Barranquilla 080002, Colombia; 10 mg/kg iv q 12 hr), analgesia (fentanyl, Viteco S.A, Bogota 111411, Colombia; 3 μ g/kg, bolus iv once), antioxidant (acetyl cysteine, Zambon Group S.p.A, V. della Chimica, 936100 Vicenza, Italia; 30 mg/kg iv once) through a 22-gauge catheter placed in the cephalic vein and bleeding prophylaxis (vitamin K, Invet S.A, Cundimarca, Medellín 110221, Colombia; 5 mg/kg sq sid).

Usually, emergency indications for transfusions commonly includes anemia and coagulopathy (Rozanski & De Laforcade, 2004). Specifically, if anemia is associated with hypovolemia and the patient show signs of tissue hypoxia (tachycardia, tachypnea, mental depression and significant increase in blood lactate levels), the hematocrit (HTC) should not be allowed to decrease below 25-30% (Lichtenberger, 2004). In addition, dehydration status reduces blood volume, which cause a relative increase in HCT by hemoconcentration (Willard & Tvedten, 2011). Therefore, it was determined that an emergency blood transfusion was necessary according to the HTC (22%; Micro Hematocrit Centrifuge DSC-030 MH, Miami Florida 33166) and severe dehydration presented by the Andean fox.

Blood transfusions between specimens of the same species is always the best option, however xenotransfusion may be an option for some wild species when a homologous donor is not available (Martony et al., 2016). In the present case, access to a homologous donor was unattainable; therefore, an emergency xenotransfusion was performed with whole fresh blood from a domestic dog (*Canis familiaris*). A healthy 4-year old male neutered Labrador Retriever weighing 35 kg, with normal reference ranges for hematological parameters (hematocrit 54%, hemoglobin 180 g/L and erythrocytes $8 \times 10^{12}/L$), was selected as the potential blood donor. Blood smear and Anigen Rapid CaniV-4 Kit® (Idexx Laboratories, Inc, Westbrook, Maine 04092 USA) tests were negative. Forty-five milliliters of whole blood were collected from the cephalic vein into a sterile

Table 1 – Vital signs and blood values of Andean fox (*Lycalopex culpaeus*) before and after blood xenotransfusion from a domestic dog (*Canis familiaris*)

PARAMETER (units)	D1 BT	D1 AT	D2 AT	D3 AT	D4 AT	D5 AT	D13 AT	D53 AT	REF. RANGE ^a
RR (breaths/min)	48	24	30	26	25	30	28	20	(20-40)
HR (beats/min)	190	168	120	117	121	116	120	132	(70-180)
SP (mm Hg)	80	90	98	98	104	111	115	118	(90-160)
T (°C)	36.4	37.9	38.2	38	38.5	38.4	38.6	39	(37.5-39)
HTC (%)	22	33	32	32	29	30	39	45	(35-54)
TPP (g/100 mL)	3.8	6.0	6.8	7.2	7.2	6.8	7.6	6.3	(5.7-7.3)
PT (seconds)	10	7	7	ND	ND	ND	7	7	(5-9)
PTT (seconds)	33	21	21	ND	ND	ND	18	17	(4-18)
CRT (seconds)	5	5	3	2	2	2	2	2	(<2)

D = day; BT = before transfusion; AT = after transfusion; REF. RANGE = reference range; RR = respiration rate; HR = heart rate; SP = systolic pressure; T = temperature; HTC = hematocrit; TPP = total plasma protein; PT = prothrombin time; PTT = partial thromboplastin time; CRT = capillary refill time; ND = not determined.^aTo our knowledge, there are no published reference values for Andean fox, so reference values for domestic dog were used (Birchard, 2006).

transfusion bag (Industrias Plásticas Médicas S.A, Mexico, Distrito Federal 06760, México) with acid-citrate-dextrose (7 mL blood/1 mL ACD) (Lichtenberger, 2004).

Thirty-minutes before beginning the transfusion, the Andean fox was premedicated with antihistamine (diphenhydramine, Laboratorios Maymo S.A. Vía Augusta 302, Barcelona 08017, España; 0.2 mg/kg iv once) and corticosteroid (dexamethasone, Laboratorio Biosano S.A, Cerrillos, Santiago 9200000, Chile; 1 mg/kg iv once). Whole blood was transfused commencing at 3 mL/kg/h for the first 30-min and gradually increasing to a maximum of 10 ml/kg/h. The whole blood was administered through a 22-gauge catheter placed in the cephalic vein by using a blood transfusion (Jiangxi Hongda Medical Equipment Group Ltd, Minhe, Jiangxi 810800, China). No evidence of acute transfusion reaction was observed during or following the transfusion. Five hours after transfusion the patient began to show signs of stabilization (Table 1).

Patient's hydration state must be normal before the HTC properly reflects the degree of anemia, so after a hemorrhage it must be rehydrated to refill the blood volume before assessing the evolution of the anemia (Willard & Tvedten, 2011). Maintenance treatment included fluids (lactated Ringer's; 5 mL/kg/hr iv for 5 days), antibiotherapy (ceftriaxone; 22 mg/kg iv q 12hr for days and metronidazole; 10 mg/kg iv q 12hr for five days) and analgesia (fentanyl; continuous infusion rate of 3 µg/kg/h iv for 2 days, reducing the dose to 1 µg/day for three consecutive additional days). Oral analgesic (ketamine, Ketamina 50, Holliday Scott S.A, Beccar, Buenos Aires 1643, Argentina; 0.25 mg/kg po tid for seven days) and antibiotic (cefalexine, Afford S.A, Lomas de Zamora, Buenos Aires 1832, Argentina; 30 mg/kg po bid for seven days) mixed with food were started instead of the intravenous formulation after five days. Over the next few days the Andean fox improved clinically and blood parameters were found to fully normalize 12 days after transfusion (Table 1).

The domestic dog and the Andean fox are part of the same taxonomic family, Canidae, but they differ in gender and species. As far as the authors know, the typing of blood in the Andean fox has not been established, and the presence of natural antibodies against domestic canine blood remains unknown. Therefore, whole xenotransfusions of the domestic dog to the Andean fox entail potential adverse transfusion reactions. However, in a previous documented xenotransfusion with domestic dog blood to an island fox (*Urocyon littoralis clementae*) it was indicated that the success could be due to the absence of natural antibodies against the canine erythrocyte antigens in the fox (Martony et al., 2016). In this sense, cats also do not seem to have primary antibodies against canine antigens, which allows transfusions with blood from dogs to cats (Bovens & Gruffydd-Jones, 2013). So, the lack of natural

antibodies could also explain the favorable development of the case described in this document.

There was no acute transfusion reaction nevertheless four days later the fox's HTC dropped to minimum post-transfusion values (29%); at this point, the animal showed a correct hydration state, so the HTC value was considered real. This drop is consistent with the production of antibodies against canine erythrocytes detected in cats that received dog blood four to five days after transfusion as a consequence of destruction of the transfused erythrocytes in a delayed hemolytic reaction (Bovens & Gruffydd-Jones, 2013; Euler et al., 2016; Weingram et al., 2014). However, no adverse clinical signs were detected in the patient and the hematocrit began to increase after the fifth post-transfusion day, without the need of any additional treatment.

Finally, a second xenotransfusion could entail a higher risk of delayed reactions four to six days after the first transfusion (Bovens & Gruffydd-Jones, 2013; Martony et al., 2016). In the present study, this fact could be verified by performing compatibility tests with the blood of both individuals 53 days after the first transfusion; major and minor cross-matching test detected agglutination confirming that a second transfusion could prove fatal for the Andean fox.

In conclusion, the present study describes the first case of successful blood transfusion from a domestic dog to an Andean fox. This result is important for wild canids because donors or blood from homologous species are not normally available. Therefore, although future investigations are necessary, a single transfusion between dogs and foxes could be considered as an emergency procedure to save-life of critical specimens.

Conflict of Interest

The authors state that they have no conflicts of interest to declare.

Ethics Statement

This study was authorized by the Animal Ethics Committee of Universidad San Francisco de Quito USFQ, with approval protocol number 2018-011.

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