

**SIGNALMENT:**

Jazz, a 4-year-old castrated male Labrador retriever weighing 33.7 kg. Case log #63

**HISTORY:**

Jazz first presented to the Foster Hospital for Small Animals in July of 2010. At the time he was tetraparetic with evidence of progressive lower motor neuron signs. He was presumptively diagnosed with idiopathic polyradiculoneuritis, also known as coonhound paralysis. This is an inflammatory disease affecting primarily the ventral nerve roots and the peripheral nerves. It is generally characterized by pelvic limb weakness progressing to tetraplegia. Spinal cord reflexes are weak to absent though pain sensation remains intact. It is suspected to be caused by contact with raccoon saliva or feces. The owners live in a wooded area and Jazz was known to ingest raccoon feces. With supportive care he made a full but gradual recovery.

On September 7, 2012 Jazz presented to our hospital with neurologic signs consistent with lower motor neuron disease again, including marked muscle weakness and tetraparesis. These signs were similar to his previous episode in 2010, though less severe. It was presumed that this was a relapse of his previous idiopathic polyradiculoneuritis. His symptoms showed marked improvement after one night of hospitalization so he was discharged the next day.

Four days later I spoke with the owner when he called to report that Jazz's urine appeared to be bloody and he seemed less energetic. I instructed the owner that it would be best to bring Jazz in to have him rechecked. It was possible that Jazz had acquired a urinary tract infection secondary to the indwelling urinary catheter that was placed during his recent hospitalization.

Jazz's owner brought him in for recheck that morning. Urinalysis and urine cultures were performed and he was sent home with antibiotics for a presumptive urinary tract infection. Jazz re-presented to the emergency service that afternoon. The owners reported that he was breathing more heavily and seemed to be getting worse. Urinalysis results were not suggestive of urinary tract infection but revealed pigmenturia. No evidence of hemolysis was detected on examination of blood smear or saline agglutination. A complete blood count and serum chemistry were drawn and submitted. The doctor offered hospitalization, but the owners elected to take him home again.

Lab work revealed a leukocytosis of 17k (reference range: 2.8-11.5k), an increased alanine transaminase (ALT) 1261 IU/L (reference range: 14-86 IU/L), aspartate transaminase (AST) 9534 IU/L (reference range: 9-54 IU/L), and severely increased creatine kinase (CK) 298263 IU/L (reference range: 22-422 IU/L). CK is a leakage enzyme and increases with muscle activity. Elevation of CK, especially to this degree, is an indication of damage to the muscle. AST is commonly measured as a marker of liver health. However, it is also found in skeletal muscle. Given his markedly elevated AST and CK, and his progressive neuropathy there was concern that Jazz had developed a thromboembolism. The owner was contacted and asked to return to the hospital for admission and further assessment.

**INITIAL PHYSICAL EXAMINATION:**

Upon presentation to the hospital Jazz was bright, alert, and wagging his tail. He was tetraparetic and required a gurney to be transported into the hospital. At triage I obtained a set of vital parameters on Jazz, which revealed a normal heart rate, 110 beats/minute (bpm), and he was panting. Upon auscultation his heart and lung sounds were also normal and peripheral pulse quality was fair. However, he was pyrexia, with a rectal temperature of 103.9°F (39.9°C). Given the elevations in serum markers of muscle enzymes from earlier that day, concerns were raised about the potential of an ischemic myopathy. I obtained peripheral blood samples from both a hind and forelimb to run a glucose differential, which is commonly performed to support suspicion of aortic thrombus. The results were essentially the same, making the possibility of thrombosis seem less likely.

**INITIAL INTERVENTIONS:**

Once Jazz was admitted to the hospital, I placed an 18 gauge cephalic intravenous catheter. Blood was drawn from the IV catheter for submission of tick borne disease titers (Borrelia, Anaplasmosis, Ehrlichiosis, Rocky Mountain Spotted Fever), Leptospirosis IFA, and Neospora PCR, as well as a bedside PCV/TS, which was within normal limits. Along with the attending veterinarian, I took three view chest radiographs, which were clear of metastasis and showed a normal cardiac silhouette. I administered a 250 mL bolus of Lactated ringer's solution (LRS) to address the pyrexia and mild dehydration. Jazz was then started on maintenance LRS (50 mL/kg/day). A course of antibiotic therapy, doxycycline (5 mg/kg q 12 hr) and clindamycin (11 mg/kg IV q 12 hr), was initiated to treat for possible tick borne diseases or protozoal disease. I also administered a loading dose of N-acetylcysteine (70 mg/kg IV), a free radical scavenger. Despite therapy, over the course of the rest of my shift his temperature gradually increased to 104.9°F. Jazz remained bright, alert, and responsive and continued to move around the cage, though he remained non-ambulatory. Suspecting his elevated temperature was secondary to inflammation or an infectious process, no cooling measures were taken at this time. However, using sterile technique I drew blood cultures for submission to the lab.

**FURTHER INTERVENTIONS:**

Over the course of the day Jazz's condition continued to deteriorate. He became dull and stuporous. His temperature continued to increase, 105.2°F at the start of my next shift. Over the course of the day attempts were made to actively cool Jazz as a temperature greater than 105.9°F can cause multi-organ dysfunction syndrome (MODS). In case this was an immune-mediated disease process, a treatment course of intravenous immunoglobulin (IVIG) was begun that evening. IVIG modulates the expression and function of the Fc receptors of antibodies, which bind to antigens that are attached to infected cells or pathogens. It also interferes with the activation of the complement system and production of cytokines, and affects the activation and effector functions of T and B cells, thus attenuating the autoimmune response.

At approximately 11 pm the second shift technician reported that Jazz's temperature was too high to read (>108°F). I noticed that he had generalized muscle tremors. He was found to have no gag reflex and his respirations were extremely labored. The IVIG

transfusion was discontinued and he was given a dose of diphenhydramine (2 mg/kg) intramuscularly. We quickly moved Jazz to a treatment table. He rapidly decompensated and exhibited an agonal breathing pattern and was bradycardic with barely palpable pulses. As the doctor intubated him, another technician began cardiac compressions at approximately 100-120 compressions per minute while I administered a dose of intravenous atropine (0.4 mg/kg). While providing cardiopulmonary resuscitation (CPR) the thorax was compressed by one third of its circumference, and then allowed to fully expand between compressions, to provide the greatest effect on intrathoracic pressure.

There are currently two methods utilized to generate forward blood flow during CPR. The first is the cardiac pump method, which suggests that forward blood flow is directly due to compression of the heart through thoracic wall compressions. The thoracic pump method postulates that blood flows from the thorax because intrathoracic pressure exceeds extrathoracic vascular pressure causing blood to fill the heart chambers. In both methodologies, blood flow is restricted to the venous-to-arterial direction due to venous valves that prevent retrograde flow. In smaller patients, weighing less than 7 kg, the cardiac pump method is believed to provide primary blood flow. In larger dogs, like Jazz, where it is more difficult to directly compress the heart, the thoracic pump method is believed to provide forward blood flow.

Jazz was hooked up to 100% oxygen and manual ventilation was initiated at approximately 20 breaths per minute. When ventilating him pressure was not maintaining within the circuit. I suggested rechecking endotracheal tube placement. Upon examination it was found that the endotracheal tube was too short so it was removed. I re-intubated him with a 10 mm endotracheal tube. Within two minutes Jazz had return of spontaneous circulation and respirations. ECG showed sinus tachycardia. When breathing on his own, Jazz remained hypercapnic with an end tidal CO<sub>2</sub> (ETCO<sub>2</sub>) of 70-80 mmHg as measured via capnography. His ETCO<sub>2</sub> improved to less than 50 mmHg only with manual ventilation. Persistent hypercapnia is an indicator of hypoventilation and so mechanical ventilation was indicated. The attending clinician contacted the owners and permission was granted to begin mechanical ventilation. I assisted another technician in setting up the mechanical ventilator. At the same time, I instructed/assisted another technician in placing an arterial catheter. I then set up and began direct blood pressure monitoring. I also placed a 10 fr foley urinary catheter and hooked Jazz up to a closed collection set, to monitor urinary output. Lastly, I inserted a rectal temperature probe. He was given a 500 mL bolus of LRS and then LRS was restarted at a rate of 50 mL/kg/day.

Jazz was positioned in sternal recumbency to facilitate maximum bilateral lung expansion. Because he continued to initiate his own breaths, the ventilator was set to spontaneous mode with pressure support added. Fraction of inspired oxygen (FIO<sub>2</sub>) was set at 80%, and positive-end expiratory pressure (PEEP) was set at 5 cmH<sub>2</sub>O. His blood pressure was stable at 125/65 mmHg. He continued to have sinus tachycardia, 180-210 bpm. His SpO<sub>2</sub> was 97-99%, as measured via pulse oximetry. His ETCO<sub>2</sub> improved on the ventilator, dropping to 35-45 mmHg. Jazz was persistently hyperthermic at 106.2°F (41.2°C). To address the hyperthermia, I wet Jazz down with cool water, I positioned large flat ice packs directly under his abdomen, his fluid line was run through an ice bath, and a cooling fan was positioned near him. A bolus of solu-medrol was administered (30 mg/kg) and then a constant rate infusion (CRI)

was started at 1.5 mg/kg/hr due to suspicion of a fulminating auto-immune process. He was also given a 3 mcg/kg bolus of fentanyl and started on a CRI at 3 mcg/kg/hr for pain management and sedation while being ventilated.

Two hours after the initiation of mechanical ventilation Jazz's  $\text{ETCO}_2$  and blood pressure remained stable and his  $\text{FIO}_2$  was weaned down to 40%. However, his temperature had only dropped by 1°F (0.5°C) and his heart rate remained above 180 bpm. I also observed that his urine production appeared low (not measured at this time). I discussed this with the clinician, as I felt Jazz was behind on fluids. I administered another 500 mL bolus of LRS and increased his fluid rate to just over 1.5 times maintenance at 100 mL/kg/day.

Over the course of the next two hours Jazz's temperature began to come down. When his temperature reached 103.6°F (39.8°C), I removed his fluid line from the ice bath. By the time his temperature reached 103.2°F (39.5°C), I had removed all cooling elements, except the fan. This was to ensure that he did not become hypothermic cooling progressed. When his temperature dropped below 103°F (39.4°C), Jazz was dried and was placed on padded bedding to prevent decubitus ulcers. His heart rate had improved, though it remained elevated at 140-150 bpm, with a normal sinus rhythm. His urinary output was improving, measured at 1.5 mL/kg/hr. His urine color was very dark which could be consistent with myoglobinuria due to muscle damage. I also drew an arterial blood gas, from the arterial catheter, which showed Jazz had a compensating metabolic acidosis: pH=7.34, partial pressure  $\text{O}_2$  ( $\text{pO}_2$ )=215.8 mmHg on  $\text{FIO}_2$ =40%, partial pressure  $\text{CO}_2$  ( $\text{pCO}_2$ )=31.7 mmHg, bicarbonate ( $\text{HCO}_3^-$ )=17.2 mmol/L. The ratio of arterial oxygen concentration to the fraction of inspired oxygen (P:F ratio) was calculated=537 showing that Jazz had a normal gas exchange and was not suffering from acute lung injury or acute respiratory distress syndrome (ARDS). ARDS is the impairment of gas exchange caused by inflammation of the lung parenchyma and is typically associated with a P:F ratio less than 200. There is also an associated systemic release of inflammatory mediators causing inflammation and hypoxemia, and can contribute to multi-organ failure.

The point of care analysis also revealed a BUN=51 mg/dL (18.2 mmol/L) (reference range: 7-28 mg/dL/2.5-10 mmol/L), creatinine=1.2 mg/dL (106.1  $\mu\text{mol/L}$ ) (reference range: 0.2-2.1 mg/dL/17.7-185.6  $\mu\text{mol/L}$ ), PCV=43%, TS=6.6 g/dL. All other values were within normal limits. The elevated BUN with normal creatinine could signify ongoing dehydration but could also be suggestive of early acute kidney injury. I notified the overnight doctor of the results of the arterial point of care analysis, and she chose to continue fluid therapy with no changes.

Jazz's temperature dropped as low as 102.4°F (39.1°C). However, towards the end of the night his temperature began to climb again. When his temperature reached 103.2°F (39.6°C) I placed ice packs in his groin region, and his temperature stabilized at 102.9°F (39.3°C). Also, towards the end of the night Jazz began to exhibit purposeful movement, moving his head and forelimbs. I administered a 0.2 mg/kg dose of diazepam to keep him relaxed so he could remain on the ventilator.

**OUTCOME:**

During the course of the following morning Jazz's temperature began to climb again, reaching a temperature of 106.3°F (41.2°C). Additionally, lab work revealed worsening azotemia with decreasing urinary output. The attending veterinarians discussed continuous renal replacement therapy with the owners. However, the owners were concerned that without a definitive diagnosis this would only be prolonging Jazz's suffering so they elected to humanely euthanize him. A necropsy was performed revealing lesions in the skeletal muscles consistent with muscular necrosis and degeneration. Damage to the respiratory muscles was the likely cause of Jazz's respiratory deficiencies, which ultimately lead to hypoxia and a centrilobular hepatopathy. A likely diagnosis of muscular dystrophy or hereditary myopathy was made based on post-mortem examination.