The “Kee” to my Heart

A case report of calf poly serositis and septicemia

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Introduction

Neonatal calves that did not receive adequate protective immunity are especially predisposed to rapidly developing bacteremia and a systemic inflammatory response. Septicemia, a common cause of fatality in the neonate, can be managed with supportive care and diagnostics when economically indicated.

Clinical signs of septicemia can begin as vague, and include dull to obtunded mentation, fever, respiratory distress, diarrhea, and petechiation of mucous membranes. Systemic effects include cavitary effusion, massive fibrin production, and polyarthritis. A history of complete or partial failure of passive transfer is frequently implicated[3]. The prognosis for long-term survival of a calf with this level of systemic sepsis is poor to grave due to the adhesions caused by the fibrin long after the systemic infection is cleared. Along with respiratory disease and diarrhea, calf septicemia can have a major economic impact[5].

Clearing the septic process relies heavily on supportive care and broad-spectrum antimicrobial administration. Evacuation of effusions can be both diagnostic and therapeutic, and may guide antimicrobial use[2,3]. This report will discuss a case of polyserositis stemming from failure of passive transfer of immunity and includes both diagnostic and treatment options.

History and presentation

An approximately 5-day old, 110 lb Charolais cross bull calf presented to MSU-CVM Food Animal Services on the morning of January 8th, 2019 for a non-specific history of unthriftiness and acute recumbency. His dam had been down for some time following his birth, but was standing and alert when she presented to MSU-CVM. He had not been observed to nurse

from his dam. A primary veterinarian passed a gastric tube and supplemented him with 2 liters of colostrum the day prior. He was referred to MSU-CVM after his continued decline in condition.

The calf was too weak to ambulate and was carried into the clinic. He was increasingly dull, though still aware of his surroundings. Vitals included a temperature of 101.8 F, pulse of 160 beats per minute, and a respiration rate of 64 breaths per minute. His gums were muddy to brick red, with a capillary refill time of 3 seconds. Moderate scleral injection was present bilaterally. He had no suckle reflex. Diffusely loud and harsh lung sounds were heard on thoracic auscultation. The heart was barely audible, and peripheral pulses were weak and thready. Extremities were cold to the touch, with no effusion or heat palpated in his appendicular joints. His umbilicus was swollen and warm. He was estimated to be 10% dehydrated. All peripheral lymph nodes palpated within normal size and shape.

Pathophysiology of disease

The septicemic process can begin through a number of ways, including abomasal perforation or hematogenous spread from local infection. Failure to attain adequate colostrum intake is a risk factor for infection through these routes [1]. Ruminants possess a cotyledonary placentation, where patches of endometrium, the cotyledons, engage with patches on the allantochorion to form placentomes, the sole form of communication of nutrients to the fetus from the dam. This type of placentation does not facilitate transport of maternal globulins *in utero.* If not infected with disease *in utero,* a normal calf is born without any circulating immunoglobulins[1,3].

The neonatal calf attains IgG through absorption by gastrointestinal pinocytosis through the ingestion of colostrum. The ability to absorb IgG begins to drop sharply within the first 4-6

hours of life, and ceases completely by 24 hours of life[1]. Nursing as early as possible after birth has been associated with peak IgG absorption. Quality, or high IgG concentration in the colostrum, is preferred over quantity, or liters of colostrum alone. Colostrum IgG concentrations decrease by 3.7% by the hour after calving, so milking and supervised feeding of calves is often utilized in the commercial setting. Refractometry is often used as a means of evaluating adequate colostral IgG concentrations[4].

Because of immature and naïve immune function *in utero,* during, and immediately post birthing, infection of the neonatal calf can occur easily at any of these times. Common routes include through the blood from the dam, infected placenta, umbilical stump, respiratory tract, gastrointestinal tract, and any external wounds. Of diseases affecting new born calves, septicemia can be especially devastating. Once bacterial pathogens enter the blood and circulate, they seed other sites such as joints, lungs, the gastrointestinal tract, the liver, and the heart. Often, Gram-negative pathogens, such as *Escherichia coli* and *Salmonella spp.* are implicated. These pathogens are well-known to produce endotoxins which can cause more systemic inflammation and shock, greatly reducing chances for survival[3].

Virulence factors from the bacteria often implicated play a large role in causing septicemia and eventual inflammation of serous membranes. Well known virulence factors include lipopolysaccharide (LPS) and capsular antigens, such as K1. LPS contains a side chain of oligosaccharides, a polysaccharide, and a lipid. LPS is well-known to stimulate innate immune responses through activation of toll-like receptor (TLR-4). Activation of TLR-4 stimulates inflammatory cytokines to recruit inflammatory cells to the site of infection, which is disseminated in cases of bacteremia[7]. Collateral damage is a common occurrence of this specific immune response. Damage to vascular endothelium can result in leakage, edema, and exudative

effusion[5]. Cattle readily produce fibrin in the face of bacterial infection as they have few neutrophils in storage. The fibrin is utilized to trap the bacteria where it is present in body cavities. Fibrinopurulent cavitary effusions are a common sequela of endotoxemia[1,7].

Presenting clinical signs for calf septicemia include lethargy, recumbency, scleral injection, brick red mucus membranes, fever, prolonged capillary refill time, diarrhea, omphalitis, and polyrthritis. Bacterial seeding to the lungs can result in pulmonary abscessation and pneumonia, with concurrent respiratory abnormalities and hypoxemia clinically.

Diagnostic approach

In any severely diseased calf less than 5 days of age, failure of passive transfer should be considered highest on the differential list as an inciting cause[4]. The gold standard diagnostic test for FPT is radial immunodiffusion for serum IgG levels. This test can be cost-prohibitive and has a slow turnaround time. ELISA Snap tests for IgG levels exist as well. They are fast and simple to use but are not as sensitive to decreased IgG. A common method of evaluating quantity of circulating IgG is refractometry to measure total proteins in serum. At a cutoff of 5.0 being indicative of FPT, this method was found to have a sensitivity of 83%. This method tends to be the most economic, yet still accurate, method of evaluation for FPT calves. Refractometry is also often used as a screening method in production circles to determine adequate colostral intake in calves and which ones may be at risk for illness[4].

Presumptive diagnosis of neonatal septicemia is reliant on non-specific clinical signs and the patient history[3]. A more definitive diagnosis can be obtained via blood culture. For this, the skin surrounding the patient's jugular vein is clipped as aseptically scrubbed. In a sterile fashion, 10 mL of whole blood are drawn. The needle is changed and the blood is transferred to a culture

bottle. A negative culture does not necessarily mean that septicemia is not present. Varying factors, such as antibiotic use, can interfere with growth. Additionally, cultures of pleural, peritoneal, and joint effusions, as well as cerebrospinal fluid can be utilized if blood culture is unrewarding[2,3].

Landmarks for thoracocentesis in cattle should be chosen via ultrasound. If ultrasound is unavailable, the ventral sixth and seventh intercostal space should be chosen. The area should be shaved, sterily prepped, and 2% lidocaine should be given subcutaneously where the procedure will occur. A stab incision should be made on the cranial aspect of the sixth or seventh rib to avoid intercostal vessels and nerves. A 3-inch teat cannula may be inserted through this incision, with the expectation of a pain response on stabbing through the pleura. An extension set with a 3-way stopcock may be attached, and fluid can be drained with a 60 mL slip tip syringe[2].

The same materials and methods may be used for abdominocentesis, with the preferred areas being either the cranial abdomen or the caudal flank. The stab incision must be made through several layers of muscle for each site. Pericardiocentesis should be performed at the cranioventral third of the left fifth intercostal space. A 16-18 gauge, 3-3.5 inch spinal needle may be used instead of the teat cannula for this procedure if the teat cannula is unable to pierce the pericardium. Known risks of this procedure are the initiation of arrhythmias and hemopericardium[2].

Cytologically, large numbers of neutrophils which may be degenerate, intracellular bacteria, and extracellular bacteria should be seen[2].

Hematological values can also be indicative of ongoing septicemia. In a complete blood count, expected changes include extreme fluctuations in neutrophil count, which include either a

profound immature neutrophilia and a severe neutropenia, neutropenia with no left shift if early in the course of disease, or neutrophilia with or without a left shift if infection has been present for several days. In calves, it is also expected to see elevated fibrinogen. In end-stage disease, thrombocytopenia and prolonged clotting times may be expected, due to disseminated intravascular coagulation. As with neonatal diarrhea, metabolic acidosis is a common finding in the septic calf, and may progress to lactic acidosis. Hypoglycemia is common in septic patients. Elevations in acute phase proteins, such as haptoglobin are also to be expected[3,5].

Case progression

The calf was admitted for hospitalization. Blood was drawn for a PCV and total protein, which returned as 50% and 4.2 g/dL, indicating dehydration and complete failure of passive transfer. Due to financial limitations, a complete blood count and serum chemistry was not pursued. Initial blood glucose level read as 66 mmol/L.

Around 4 pm on January 9th, due to severe respiratory compromise, the decision was made to ultrasound his lung fields. Ultrasonographic examinations revealed diffuse comet tails bilaterally. On the ventral aspect of the lungs bilaterally, moderately-sized pockets of effusion with floating fibrinous tags along the pleural surface were seen. Radiography revealed a severe alveolar pattern in the gravity dependent lung fields, made evident by air bronchograms and lobar signs. An unstructured interstitial pulmonary pattern was also visible in the craniodorsal lung fields. Decreased serosal detail was present in the visible abdomen. A thoracocentesis was elected for therapeutic and diagnostic value.

The lungs were ultrasonographically evaluated once more with the calf standing. The left side of the thorax was chosen for the procedure as the volume of fluid present was greatest. A

sterile clip and prep were performed, followed by an incisional block with 2% lidocaine. A stab incision was made in the skin overlying the cranial 7th intercostal space. A 3-inch teat cannula was carefully advanced into the plural cavity. Using 60 cc slip tip syringes, approximately 0.6 L of fluid was evacuated from the chest. The fluid was frothy, clear yellow, slightly malodorous, and had visible fibrin clots. A total protein of this fluid was 2.3 g/dL. The fluid was submitted for analysis, which returned as an exudate with intracellular bacteria seen. Aerobic culture of the fluid yielded a *Pasturella* sp; antimicrobial susceptibility testing was not performed due to financial constraints. Continued ultrasonographic evaluation also revealed pericardial and peritoneal effusion with fibrin seen throughout.

Treatment and management

Neonatal septicemia carries a high mortality rate. There are 3 goals to managing the septic calf: the first is to control bacterial load, the second is to regulate the inflammatory response, and the third is to provide supportive care[3]. Venous access via a jugular catheter should be established. Of these, parental antibiotic therapy should be the most urgent step, as controlling the bacteremia will lessen the severity of the inflammation and ease some clinical signs[3,6]. In hypovolemic calves, placing the head below the heart may help visualize the filling of the jugular vein when occuled[7]. The most reliable first selection is a third or fourth generation cephalosporin, such as ceftiofur (10 mg/kg every 24 to every 8 hours, IM or IV), sodium ampicillin (10-20 mg/kg every 8 hours IV), or florfenicol (20 mg/kg every 12 hours, IV, extralabel use). Florfenicol should not be used in calves that will be processed for veal. To cover a broader spectrum of bacteria, adjunct antibiotics may include procaine penicillin G (0.15-0.22 mL/kg, intramuscularly or subcutaneously every 24 hours) or ampicillins. Antibiotics can be changed dependent on bacterial identification[3].

Non-steroidal anti-inflammatory drugs, such as flunixin meglumine (1.1-2.2 mg/kg intravenously every 24 hours for up to 5 days) can also be administered to limit the cardiovascular effects of endotoxic shock, and to mitigate pain and fever. Flunixin is preferable over other NSAIDs, such as meloxicam, for its known endotoxin-modulating effects. NSAID use should be executed with caution in the severely dehydrated patient, due to the risk for abomasal ulceration and kidney damage.

Supportive care should include correction of dehydration and metabolic derangements, oxygen supplementation, and nutrition supplementation[3,6]. Plasma transfusions are necessary in a patient with a history of failed passive transfer. Bovine frozen plasma is given at dose of 20-30 mL/kg. The transfusion is started slowly, gradually increasing in speed until the dose is given. Vital parameters should be monitored every 5 minutes to ensure that an anaphylactic event is not occurring. In severe cases, the patient may use up the immunoglobulins given and require multiple transfusions.

The intravenous fluid therapy plan should include consideration of the patient's maintenance requirement, the existing deficit, and losses due to diarrhea or effusions. Hypoglycemia is common in the septic patient, and in these cases, glucose should be supplemented. Normal saline or Plasmalyte with 5% dextrose added is an accepted choice. The maintenance rate is 50 mL/kg over 24 hours; higher rates may be used judiciously in patients with dehydration and/or shock. Lactated Ringer's Solution should be avoided in the acidic patient due to lactate in the solution. Higher amounts of dextrose in the fluids, though acceptable, have been known to cause phlebitis over extended periods of time[3].

Septic calves often cannot nurse, so nutritional supplementation is paramount. The calf should ingest 10-15% of its body weight in milk every 24 hours. If stimulation to nurse in not

fruitful, then esophageal tube feeding should be considered. Tube feeding can provide the calf with nutrition in the short term, but should not be considered a long-term method of nutritional supplementation due to the possibility of the calf failing to close its esophageal groove and becoming a ruminal drinker. In calves with a high economic value where tube feeding is not well tolerated by the GI tract, total parenteral nutrition should be considered[3].

At presentation, a guidewire central catheter was placed in the calf's right jugular vein. He was bolused 1 L of 5% dextrose, followed by 1.5 L of 2.5% dextrose, after which his blood glucose improved to 189 mmol/L. His umbilicus was dipped in 7% iodine. He was transfused 917 grams (917 mL) of bovine plasma. He was placed on Plasmalyte A at a maintenance rate of 375 mL/hr.

Throughout the rest of the day, the calf's respiratory effort started to increase. On auscultation, no crackles could be heard, but rather, excess grunting. Abdominal fluid could be heard sloshing around on ballottement. The calf began to open-mouth breathe, vocalize intermittently, and his tongue became progressively cyanotic. Nasal flow by oxygen was commenced at 4L/min. Flunixin meglumine at 1.1 mg/kg was given IV, and 6.6 mL of procaine penicillin was given SQ. 2 mL Naxcel was given IV. A blood glucose taken at 4 pm read 26 mmol/L. The calf was then bolused with 100 mL of 2.5% dextrose. He was changed to this as a maintenance at 260 mL/hr.

The calf was supervised around the clock. Overnight, he was examined every 4 hours. He remained normothermic, but respiration and heart rates remained increased. A bottle was offered to him every 2 hours, and he was assisted to stand every 6 hours, with recumbency switched every 2 hours. Three times overnight, he defecated solid feces with specks of frank blood. His suckle began to strengthen took in ½ of a pint of milk independently. While short of his needed

requirements, he was not tube fed at any time overnight. Blood glucose stayed in the range of 40 mmol/L.

At 6 am the morning of January 9th, his blood glucose was 124 mmol/L, and he was able to stand independently. Two hours later, at his 8 am physical exam, his temperature was 101.2 F, his pulse was 172 bpm, and his respiration was 132 breaths per minute. His mucous membranes improved to pink in colors, and capillary refill time was about 2 seconds. His extremities were warm to the touch. Contrary to just 2 hours earlier, the calf was too weak to stand. His blood glucose was found to be 24 mmol/L. A 100 mL bolus of 3.5% dextrose was given.

Throughout the day, therapy was continued for the calf as previously described, with the fluid rate being decreased to 110 mL/hr. A 10 AM PCV/TP was improved at 30% and 4.6 g/dL. Around 1 PM, the calf's glucose was 30 mmol/L. Shortly before that he stood with assistance and suckled 1 pint of milk. Throughout the afternoon, he made several unsuccessful attempts to stand on his own.

The calf remained in intensive care overnight, with no changes in therapy. He only took ½ of a pint of milk at his 8 PM feeding time. On the morning of January 10th, his temperature had elevated to 104.8 F. He began to get restless and would have intermittent episodes of open-mouth breathing. A half dose of flunixin was given IV as a rescue. Blood glucose was 42 mmol/L. A fan was placed in front of the calf's cage.

Re-evaluation with ultrasound revealed that the effusion that had been removed the previous day had returned. The owner visited the calf. At this visit, the calf stood and nursed. The owner authorized one more day of treatment. A 4 PM PCV/TP read 36% and 5.0 g/dL. Due to the limited duration of therapy legally allowed he was switched off of Naxcel and onto

florfenicol as a first-line antibiotic. A blood glucose at 4 PM was 68 mmol/L. His clinical picture improved in the overnight hours, and he suckled 4 pints of milk independently in this time period, to include 2.5 during his 8 am physical exam on January 11th. He was standing with assistance well. An 8 AM glucose was 43 mmol/L.

On the afternoon of January 11th, the calf began to stand and ambulate on his own. Dextrose constant rate infusion was discontinued, and the calf was moved out of a dog kennel and into a stall. The owner showed up to visit that afternoon. Upon observing the calf's greatly improved clinical picture, and given financial constraints, he elected to take the calf home.

Case outcome

The calf was discharged on the evening of January 11th with florfenicol to be given subcutaneously every 4 days until January 30th, along with daily subcutaneous penicillin until January 30th, oral meloxicam to start daily and be tapered down to every other day until January 20th. The owner was instructed that the calf was in no way fully recovered, and that the calf needed to be fed a specific amount of milk daily for maintenance and growth. The owner was warned that if signs of lameness, lethargy, or distress should appear, he was to seek medical attention for the calf as this was a sign of sequelae from his severe septic event.

In pictures and videos sent to the student up to Jaunary 20th, 2019, the calf was doing well. He was ambulating with no signs of lameness, and nursing strongly. However, the calf presented to MSU-CVM on the afternoon of Jaunary 28th for bilateral swollen carpi. He presented non ambulatory and weak. He had a temperature of 101.5 F, pulse of 128 beats per minute, and respiration of 32 breaths per minute. He was estimated to be 8-10% dehydrated. Swelling and effusion were present in both carpi. On flexion and extension of his tarsi, his joints

were stiff, with an audible creaking noise heard. An abdominal fluid wave was present. Thoracic ultrasound revealed some residual fibrin in the pleural space. Visualization of abdominal viscera was not possible due to severe effusion and fibrinous adhesions. Ultrasound of the carpus revealed fibrin in the joint spaces.

Due to poor prognosis and extreme costs needed to save the animal, the owner elected to donate the calf to MSU-CVM. Abdominocentesis yielded 4 L of clear yellow, frothy, fibrinous fluid. Following this procedure, the calf was revealed to be in extremely poor body condition. Arthocentesis revealed fibrin in both carpi, both stifles, and the right tarsal joint. To prevent further suffering, the calf was humanely euthanized and sent to necropsy.

Necropsy findings included diffuse, severe fibrinosupprative peritonitis, pleuritis, and pericarditis, along with severe fibrinosupprative polyarthritis. There was 1 L of abdominal effusion and 200-300 mL of thoracic effusion. Fibrin mats were present throughout the viscera, with the abdominal viscera being adhered to one another. A sample of joint effusion had a TP of 5.4 g/dL, and cultured *Mycoplasma spp.*

The ultimate contributor to this calf's demise was disseminated polyserositis that was likely secondary to failure of passive transfer of immunity. The FPT in of itself was likely secondary to an unattended dystocia, which is suspected due to the size of the calf and the dam going down following his birth. A relapse in his clinical signs, along with the appearance of infection in the joints, can likely be attributed to continued infection with bacteria that were resistant to our antibiotic choices, as evidenced by our joint culture yielding *Mycoplasma spp*.

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