Failure of Passive Transfer and Its Sequelae in Calves

Laken S. Russell

Mississippi State University

College of Veterinary Medicine

Class of 2019

Clinicopathologic Conference

Advisor: Amelia R. Woolums, DVM, MVSc, PhD, DACVIM, DACVM

December 14, 2018

Introduction

The terminology "passive transfer" refers to the movement of maternal immunoglobulin, or antibody, from dam to offspring. In all neonatal ruminants, passive immunity is strictly conferred post-calving through consumption of colostrum, a cow's first mammary secretions. This provides protection against infections until endogenous antibody concentrations are adequate to protect the calf. Adequate and timely consumption is vital because the ability to absorb colostrum wanes a short period of time after birth, and the calves that do not receive adequate colostrum suffer failure of passive transfer (FPT). FPT itself is not a disease, but it can make calves more susceptible to infection, leading to increased neonatal and pre-weaning morbidity and mortality and decreased average daily gain. Although FPT calves can survive with improved environmental husbandry and hygiene, they are still at greater disadvantage than their counterparts, imposing added expense to the operation overtime. Furthermore, despite occurring most frequently in dairy calves, it is also seen in beef calves, neonatal swine, and lambs. For this reason, FPT is of economic concern to many livestock producers, making prevention through strict herd management highly recommended.[1, 8, 10] Presented in this paper is the pathophysiology of FPT, its diagnosis, treatment options, and prevention with reference to a case seen at Mississippi State University College of Veterinary Medicine Animal Health Center.

History and Presentation

A five week old Charolais-Angus cross bull calf, known as "Elmo," presented to the MSU-CVM Food Animal Service on October 6, 2017. The owner, Mr. John Hardy, had not witnessed Elmo's calving, and found him abandoned in his pasture on October 4, 2017. Elmo's dam was not only reluctant to let him nurse, but she also had "balloon teats," so it was suspected that the calf had received minimal to no colostrum, leading to concerns that he had FPT. Elmo willingly nursed once via bottle for Mr. Hardy but became increasingly lethargic and inappetent within a short time.

On presentation, Elmo was dull but alert and responsive. His body condition was normal for a neonatal calf, and he received a body condition score of 5/9. It was noted that his head appeared misshapen, and although his left eye (OS) was normal, the right eye (OD) was buphthalmic with profuse periorbital swelling, epiphora, and corneal opacity. He was estimated to be 10% dehydrated based on skin tent and oral mucous membrane parameters. Elmo's temperature was on the low end of normal at 100.9 F (101-103 F), he had a low normal heart rate at 80 beats per minute compared to the normal range for most calves (80-100 bpm), and his respiratory rate was elevated at 36 breaths per minute with louder than normal lung sounds bilaterally evident on thoracic auscultation. Urination was observed to be normal, and his umbilicus was dry and soft on palpation without evidence of heat, swelling, or discharge. His carpi and tarsi palpated within normal limits without heat, swelling, or apparent discomfort; however, he was observed knuckling over on his left rear fetlock when walking. The remainder of his physical exam was normal.

Diagnostic Approach/Considerations

FPT, now more accurately deemed failure of transfer of passive immunity, refers to a calf's serum maternal antibody concentration that is normally gained post-partum via suckling.[1, 8, 10] The immunoglobulin (IgG) concentration in a calf's blood can be measured by many methods that differ in accessibility, speed, and accuracy. Comparison of the results to established guidelines aids the diagnosis of adequate passive transfer versus partial (pFPT) or complete failure (FPT). The only diagnostic methods that directly measure the serum concentration of IgG are the enzyme linked immunosorbent assay (ELISA) and the gold standard for measurement of serum IgG concentration, radial immunodiffusion (RID). Other methods, including sodium sulfite precipitation, zinc sulfate turbidity, refractometry, and whole blood glutaraldehyde coagulation, estimate concentration based on serum total proteins and may be more affordable and practical in field work.[1, 4, 10] Measurement of serum gamma-glutamyl transferase (GGT) activity can also be used to estimate the adequacy of passive transfer.[4] Refractometry is often employed by practitioners and producers due to its ease of use, reasonable accuracy, affordability, and application as a herd monitoring tool.[9, 10] This method was employed by the Food Animal Service when evaluating Elmo Hardy.

On presentation, a blood sample was taken from Elmo to measure his packed cell volume (PCV) and total protein (TP). He had a PCV of 36%, which is normal, and his TP was 4.4 g/dL. When using refractometry, a resulting TP < 5.2 g/dL equates to complete FPT, a TP between 5.2-5.5 g/dL is partial FPT, and a TP > 5.5 g/dL signifies adequate passive transfer. Based on these guidelines and his TP, Elmo was diagnosed with complete FPT. Due to financial concerns associated with Elmo's treatment, poor prognosis, and long term management, Mr. Hardy donated him to the Food Animal Service for educational use.

Pathophysiology

Calves are born agammaglobulinemic due to the bovine epitheliochorial placentation. With this type of placenta, all of the maternal tissue layers are retained, creating a separation of the fetal and maternal circulation and preventing transfer of antibodies across the placenta to the fetus in utero.[2, 10] A calf's passive immunity can only be obtained after parturition when it consumes colostrum. Colostrogenesis is the transport of antibodies from maternal circulation to the mammary gland mediated by lactation hormones. It is initiated weeks before parturition and stops abruptly a few days before calving. The largest component of colostrum is immunoglobulin, and in cattle, IgG1 is the predominant type. The concentration of IgG in colostrum varies; higher concentrations are found in multiparous cows, beef cows, and Jerseys while it is generally decreased in first lactation cows, cows with periparturient mastitis, and most dairy breeds due to high volume dilution.[1, 8, 10]

Following consumption of colostrum, a neonatal calf's small intestinal enterocytes absorb antibody by non-selective transcytosis that diminishes in effectiveness over the first 24-36 hours of life. This waning is referred to as "closure" of the intestine. It is initiated by intake of a calf's first meal, no matter the content, and it is what makes timing of ingestion so vital.[1] Regardless of the range of time to closure, optimal absorption takes place in the first 4 hours after parturition and decreases quickly by the 12 hour mark. Even when fed similar volumes and concentrations of colostrum, calves that receive it as soon as possible post-partum have been shown to have significantly higher serum IgG concentrations compared to those fed later on. Calves with serum IgG concentrations of <1000 mg/dL 48 hours after birth are considered to have FPT. To achieve adequate transfer, a calf must be able to stand and walk to his dam, locate the teats, and suckle appropriately for a long enough duration to intake at least 7.5-10% of its body weight within the first 4 hours of its life. The most common and likely cause of FPT in beef calves is delayed suckling; however, the dam also plays a role in that she must stand for her calf, form a bond with it, produce IgG concentrated colostrum, and be free of teat abnormalities that would prevent appropriate suckle by the calf.[8, 9, 10]

Treatment and Management

Slow intravenous (IV) administration of plasma at 20 ml/kg is the cornerstone of treatment for FPT. Use of whole blood is acceptable, but the dosage must be increased. To cut costs, plasma or whole blood can be given intraperitoneally. Transfusion reactions are not a common occurrence in calves, but they should still be monitored closely during the transfusion for dyspnea, gastrointestinal signs, lethargy, and abrupt changes in temperature and pulse. Comorbidities should also be addressed in the treatment plan with appropriate diagnostics and therapy. Evaluation of husbandry practices to reduce the calf's exposure to pathogens and administration of injectable, broad spectrum antimicrobials are recommended. Close monitoring for sequelae of FPT, such as respiratory disease, neonatal diarrhea, sepsis, septic arthritis, and omphalitis, should also be performed.[8, 9, 10] In neonatal calves, FPT is actually the most common cause of sepsis, a systemic inflammatory response to infection. The most frequently implicated organism is *E. coli*, emphasizing the importance of environmental cleanliness in herd management. The clinical signs of sepsis are many and can include: omphalitis, edematous extremities, meningitis, hypopyon, pneumonia, pyrexia, and joint swelling. Treatment is directed toward control of the infection, amelioration of clinical signs, and supportive care as needed.[6]

After Elmo's diagnosis on October 6, 2017, a 16 gauge IV catheter was placed for administration of 900 ml of plasma. Following the transfusion, he received a balanced electrolyte solution, Normosol-R, to address his estimated 10% dehydration. Due to his respiratory signs, he was started on Nuflor (florfenicol), initially at a single dose of 20 mg/kg intramuscularly (IM) but from October 8-20, 2017, he received 40 mg/kg subcutaneously (SQ) every 4 days. Atropine ophthalmic drops were applied every 12 hours in his right eye (OD), and triple antibiotic ophthalmic ointment was applied every 8 hours OD. Full physical exams were performed every 12 hours with emphasis on temperature, pulse, and respiration (TPR) as well as palpation of his joints and umbilicus. He was weighed daily; received small, frequent feedings with calf milk replacer; was given free access to calf starter; and his stall was kept clean and dry.

However, between October 8 through 14, Elmo developed a waxing and waning fever of 103.3-104.8 F. Banamine (flunixin meglumine) was given IV at 1.1 mg/kg for its anti-inflammatory benefits, and the fever subsided until October 8. Increased lung sounds and wheezes were heard on auscultation by October 15; due to his new respiratory signs and persistent fever, he received a single dose of Draxxin (tulathromycin) at 2.5 mg/kg SQ and Clostridium type C & D antitoxin. An ultrasound evaluation was performed to assess his lungs and umbilical structures on October 16. Mild comet tails were noted bilaterally in his lungs, and there were no remarkable findings at his umbilical structures. Despite improvement in his ocular signs OD and subsequent discontinuation of his ophthalmic medications, he developed mild ventral hypopyon and blepharospasm OD, so atropine was resumed and his ophthalmic ointment was changed to a triple antibiotic with hydrocortisone. An ophthalmology consult on October 17 revealed synechiae and a cataract OD as well, which were both attributed to ongoing inflammation of anterior uveitis caused by bacteremia, presumably resulting from his FPT. His ophthalmic ointment was discontinued and switched to one containing dexamethasone for better anti-inflammatory effect. Elmo intermittently produced flecks of frank blood in his feces, so ranitidine treatment was initiated at 50 mg/kg orally (PO) every 8 hours in case of abomasal ulceration.

A persistent fever of unknown origin surfaced on October 21. From then through October 29, persistent effusion, warmth, stiffness, and discomfort at the walk progressed until it encompassed his carpi and right tarsus. Suspicion of septic polyarthritis was high, though confirmatory culture of fluid collected by arthrocentesis or blood cultures were not performed due to financial constraints. Septic arthritis is an important cause of calf lameness, leading to serious damage and permanent effects if not treated promptly and adequately. The ideal diagnostic strategy combines arthrocentesis with repetitive joint lavage to allow cytologic analysis of the collected fluid and to reduce infectious organisms and inflammatory products within the joint space. Recommendations say that joint lavage should be repeated every 24 to 48 hours, or until cytologic abnormalities of synovial fluid samples have improved. While not a definitive method of diagnosis, gross observation of synovial fluid is useful in differentiating between septic and non-infectious causes of "joint ill" or lameness. For instance, synovial fluid sampled from an infected joint space can have decreased viscosity, cloudiness, presence of fibrin, and yellow discoloration, depending on severity and duration of the infectious process. Prognosis is influenced by several factors, including the time of presentation, age and value of the animal, which joints are affected and how many are involved, type of microorganism isolated, and concurrent disease. Prognosis for recovery from septic arthritis is always guarded, but in cases of septic polyarthritis, with infection of more than 2 joints, prognosis is poor.[3, 5, 7]

Elmo was sedated with xylazine at 0.04 mg/kg and ketamine at 0.08 mg/kg and arthrocenteses and copious lavage of his affected joints were performed on October 21, 23, 26, and 29. Common infectious organisms in septic arthritis include staphylococci, streptococci, and coliforms that reach the location through trauma or hematogenous spread.[3, 5, 7] Gram stain performed on Elmo's synovial fluid samples by students revealed a predominately gram negative cocci population. However, this result did not correlate with the most likely pathogens of concern and is subjective to user error. It is possible the crystal violet or de-colorizer steps of gram staining were incorrectly performed, and the actual population was gram positive cocci. Yet, this was never confirmed and empirical treatment commenced.

Following each arthrocentesis, he received intra-articular infusions of Naxcel (ceftiofur sodium) at 1.1 mg/kg, +/- Banamine (flunixin meglumine) IV at 1.1 mg/kg. For increased antimicrobial coverage and effectiveness, 6.6 mg/kg of Excede (ceftiofur crystalline free acid) was administered at the base of his ear on October 21 and 24; in addition, Procaine Penicillin G (PPG) was initiated at 44,000 IU/kg SQ every 24 hours. Injectable oxytetracycline administration was started on October 29, and meloxicam tablets were given at 0.5-1 mg/kg PO every 24 hours for pain. Profuse, watery diarrhea developed on October 30, prompting the addition of a probiotic supplement to his regimen and submission of a fecal sample for *Salmonella* screening, which returned with negative results. An ophthalmology recheck of Elmo's right eye on November 1 deemed his hypopyon OD resolved and all ophthalmic medications were discontinued. At that exam, he was found to have reduced menace OD, suggesting permanently decreased vision.

Tennis ball to softball sized swellings progressively developed at sites of PPG injection, so warm packing was performed and PPG was discontinued on November 9. By November 11, 2017, 35 days after his initial presentation, Elmo's septic polyarthritis had shown continued improvement. He was almost fully transitioned off milk replacer to calf starter and Bermuda hay, and his vital parameters were consistently within the normal range. Therefore, he was transferred to a calf hutch outside of the Animal Health Center. He received injectable oxytetracycline through November 21, but at the end of his prescription, his fever of unknown origin returned and his right carpus became effusive and palpably warm. Having exhausted treatment options, a final attempt was made by administering oxytetracycline powder orally (PO) in increasing increments until a final dose of 22 mg/kg every 24 hours was achieved. With this Hail Mary attempt, Elmo's polyarthritis signs, fever, and cellulitis significantly improved and on December 19, 2018, the oxytetracycline powder was discontinued.

Prevention

Adequate immunoglobulin transfer is only one factor among several contributors to a calf's ability to thrive, albeit a very large one. The best approach to herd management is a multi-modal one. Aside from FPT, other factors that should be considered when attempting to reduce disease risk within a herd include: immunization programs; environmental factors, such as wind chill, temperature, and humidity; general hygiene/cleanliness; pathogen concentration and virulence; exposure to stresses, such as handling, transport, and medical procedures; and nutritional status.[1, 9] In Elmo's case, more frequent checks of the cows near the time of calving could help catch those that are unable to nurse immediately; however, this is a somewhat impractical task in small beef herds of the southeast where the calving season occurs year round.

Case Outcome

Electronic records place Elmo's finalized inpatient bill at $1,311.51; however, this does not include the cost of ongoing treatments performed after his transfer. Even though he made a miraculous recovery, Elmo still experiences occasional bouts of illness. Most recently, from July to August 2018, he had two febrile episodes and developed symptoms of respiratory disease suspected to be of viral origin. Elmo currently resides in a tiny herd with Abe, Dianna, and Swiss in one of the pastures at the College of Veterinary Medicine. He is still halter trained and is often used for teaching opportunities within the Food Animal Rotation and for the sampling needs of Dr. Amelia Woolums's research lab. The length of his therapy and the cost involved is often an infeasible consideration for many livestock producers, but Elmo is a unique case and excellent learning model that exemplifies the ability of a calf to live despite FPT and illustrates the long term consequences of such a fate.

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