“No Time to ‘Kid’ Around”

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College of Veterinary Medicine Class of 2022

Clinicopathologic Conference

March 11, 2022

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Introduction

Clostridium tetani is a ubiquitous, anaerobic, Gram-positive bacterium found in soil and feces that can manifest as a clinical, and potentially fatal, disease in mammals known as Tetanus.[9] Infection by *C. tetani* causes a non-contagious, afebrile neuromuscular disease characterized by spasmodic contractions as a result of exotoxins tetanolysin and tetanospasmin (TeNT) produced by the bacterium when they invade and proliferate in anaerobic environments, most commonly trauma or open wounds.[5, 9] Despite the World Health Organization's intentions of eradicating the disease by 1995, Tetanus still remains an important cause of human death in the developing world and in livestock and companion animal husbandry.[4] In veterinary medicine, common large animal practices such as castration, dehorning, and tail docking are among the more traditional causes of infection by *C. tetani* with small animals more likely becoming infected during surgery or after trauma where the skin barrier is compromised. [3, 4] Humans and horses are the most susceptible to infection because TeNT penetrates neural tissue more effectively than in cattle, small ruminants, canines, and felines who are more resistant by the toxin. [3,8] Research also reports that poikilotherms and birds are resistant to *C. tetani* due to the protective effects of cooling on slowing down the TeNT-receptor binding rate.[8] Ultimately, the danger lies in the retrograde axonal transportation of TeNT and the clinical signs produced in mammals.[8]

This case report will follow the classic presentation and clinical signs of a neonatal goat with a *Clostridium tetani* infection. The disease pathophysiology will be outlined using information gathered from past literature reviews and research. Then considerations will be given in regard to diagnostics, treatment protocols and preventive measures if clinical signs are

recognized. Finally, the neonatal goat's case will be revisited in regard to the necropsy and histologic findings.

History & Presentation

Neshoba was an approximately 21 day old Nigerian Dwarf buck who presented to the Mississippi State University College of Veterinary Medicine Food Animal Department on 5/5/2021 at 3pm after his owners found him that morning displaying neurological signs and appearing to be painful. The owners reported that at home he could not nurse due to the inability to open his mouth so they had been bottle feeding him in addition to offering him a handful of grain. He had also been dribbling bright yellow urine and passing dark, dry feces. The owners had recently had him disbudded and when the neurological signs started a couple days afterwards, they gave him B-complex, Procaine Penicillin G, and dexamethasone for suspected Polioencephalomalacia although with no improvement noted the morning prior to presenting to MSU-CVM.

On initial physical exam, Neshoba was bright, alert, and responsive. His vital parameters were elevated, with a heart rate of 180 beats per minute, a respiratory rate of 84 breaths per minute, and a temperature of 103.3 degrees Fahrenheit. All four limbs were in rigid extension, with the hindlimbs being more severely affected, which made his gait short and stilted. His abdomen and bladder were tight and distended on palpation. He was 6% dehydrated and was frequently dribbling urine. On neurological examination, all cranial nerves were intact however he was deep pain positive and, due to the extensor rigidity, was unable to withdraw any of his limbs in response.

Pathophysiology

A Gram-positive bacterium, *Clostridium tetani* is ubiquitous in the environment where it is found to germinate and multiply in alkaline soil of warm, humid regions.[3,8] The bacteria resides in the intestine in insignificant numbers as part of the normal intestinal flora, however when an opportunistic anaerobic environment, such as a wound, becomes overburdened by the volume of the bacterium, the organisms secrete a neurotoxin called tetanospasmin (TeNT), and a hemolysin called tetanolysin, which are responsible for the clinical signs.[5, 8] Tetanolysin is a pore-forming toxin that facilitates colonization in tissue and resistance to macrophages.[8] TeNT proliferates in the anaerobic environments where it interacts with demyelinated nerve endings and ultimately binds to gangliosides where it is then transported via retrograde transportation in acidic endocytic vesicles to the central nervous system (CNS).[2, 8] In the CNS, TeNT targets inhibitory interneurons that are responsible for the management of motor neuron activity.[2, 8] Specifically, the release of glycine and gamma-aminobutyric acid (GABA) is inhibited causing an excessive activation of motor neurons which manifests as extreme muscle contractions.[8] Because of this characteristic spastic paralysis, Tetanus often results in death from asphyxiation as the muscles responsible for respiration and the diaphragm become paralyzed.[5, 6, 8]

The success of the toxin's ability to cause disease is ultimately dependent on two key features: the packaging and delivery of TeNT in acidified vesicles[2, 8] and the unique retrograde axonal transportation of that vesicle.[2,3,7,8] These characteristics set Tetanus apart from its sister disease Botulism and affords it its characteristic clinicals signs that subsequently relate to how it is diagnosed.

Diagnostics

As a result of *C. tetani's* unique pathophysiology and affinity for the central nervous system (CNS), diagnosis of Tetanus is primarily made on clinical signs alone, particularly the spastic paralysis and failure to respond to therapy.[6, 8] Less commonly, *C. tetani* can be identified via Gram stain of a contaminated wound revealing a Gram-positive drumstick-like spore. [8] Isolation via this method however, is difficult given that only a small amount of TeNT is required to develop signs and levels of bacteria is typically low in a contaminated wound.[8] Other, less common diagnostic methods include wound culture, polymerase chain reaction (PCR), and serology.[8] The latter two are not often performed given the limitations in PCR detection and the need for high antibody concentrations of TeNT in order to produce adequate diagnostic results.[8] Thus, diagnosis is made by clinicals signs, ruling out other disease processes and response to treatment.

Treatment & Prevention

Research in human medicine categorizes Tetanus based on inciting cause and signs: neonatal, cephalic, generalized, and local.[6] While veterinary medicine does not commonly employ these categories as it does not affect the method of treatment as readily as in human medicine, the distinctions are beneficial for identifying clinical signs and possible origin of infection.[6] Neonatal Tetanus typically presents with opisthotonos and seizures caused by poor umbilical hygiene and can be managed via maternal immunity during pregnancy though vaccination.[4] Cephalic Tetanus manifests as spasms localized to the head following head trauma, eye injury, or procedures such as tonsillectomies.[7] Generalized and local Tetanus commonly present with muscle spasms and/or rigidity in all musculature or to specific body parts

respectfully.[7, 8] Treatment and management for the disease however remains the same across all categories. In acute cases, wound cleaning is the most important factor followed by Tetanus antitoxin and a seven day course of antibiotic therapy, most commonly metronidazole or penicillin.[6] Tetanus antitoxin can be given once intramuscularly, however, because the antitoxin only inactivates free TeNT it is less effective in chronic cases where the toxin has already had time to bind to receptors in the CNS.[6] In all cases, vaccination is a mainstay of therapy since an individual's immunity may not necessarily develop upon recovery from the disease.[6]

Other therapies to consider include muscle relaxants and hospitalization in a quiet, stress-free environment. Benzodiazepines are the muscle relaxant of choice as this class of drug augments gamma-aminobutyric acid's (GABA) effects on the lower motor neuron GABAA receptor.[6] In more seriously diseased human patients, the use of Propofol, a GABAA receptor modulator, has also been reported.[6] Additionally, a calm resting environment is important for the prevention of triggering excess spasms via sensory stimuli. A 2019 case study in a fifteen day old goat with Tetanus reports that a treatment protocol aimed at eliminating the bacteria, controlling muscle spasms, and supportive care, should see improvement of clinical signs by the second day of treatment – their protocol consisted of Procaine penicillin, Tetanus antitoxin, Deriphylline, Meloxicam, Diazepam, and intravenous dextrose.[9]

Control of muscle spasms induced by *C. tetani* with the use of Botulinum toxin has also been recently proposed although there is limited clinical experience with its use in resolving Tetanic muscle ridigity.[6] Botulism, an infection caused by *Clostridium botulinum,* causes a neuromuscular disease characterized by flaccid paralysis, and undergoes the same initial pathway as Tetanus toxin in that both bacteria's exotoxins undergo axonal and trans-synaptic

transportation to the CNS, although the *C. botulinum* toxin has less transport affinity than *C. tetani* and thus remains in the lower motor neurons where it inhibits the release of acetylcholine and finally the activation of voluntary muscle activity.[6] An article in the 2013 Journal *Toxins* reports that in six cases studies the Botulinum toxin was successful in controlling muscle rigidity and spasms with improvement seen within four days after starting treatment, and in patients who were resistant to muscle relaxants, the toxin was used for the treatment of residual muscle rigidity.[6] The drawback of this research however, centers on the lack of data on the use of Botulinum toxin on large truncal musculature that are commonly affected with Tetanus, the slow onset of action, and the risk of overdosing which could lead to accidental, and prolonged, manifestation of a true Botulism infection.[6]

Management of Tetanus focuses on prophylactic immunization through vaccination protocols starting at a young age with routine boosters as needed or following injury.[1] As is the case in livestock animals, the most important time to vaccinate against tetanus is at the time of castration and dehorning. One survey from 2010 looked at common husbandry practices by 189 bovine practitioners in the Unites States and found that 52% of veterinarians will administer prophylactic Tetanus toxoid injections prior to castration and 90% will concurrently vaccinate and dehorn at the time of castration.[4] Of the 98 respondents who use Tetanus vaccines, 26 gave the vaccine prior to any method of castration while only 7 gave it if the castration was performed surgically and 65 gave the vaccine if the castration was performed non-surgically.[4] The most common adverse effect was stiffness/ altered gait and recumbency, which was reported in more than half of the surgical castrations, and swelling, which was more commonly noted in the non-surgical castrations.[4] “Rarely” and “Never” were the most common responses for Tetanus being

an adverse effect in cattle who had received either method of castration however this survey did not contain any information on post-castration diagnostics used and the author indicated the need for more research in this area in regard to effective management practices.[4]

Additional control of Tetanus, more commonly seen in small animal medicine, involves the use of sterile surgical instruments and prevention of penetrating or debridement wounds. A retrospective study from *The Journal of the American Veterinary Medical Association* that collected data from cases of canine Tetanus found that dogs infected with *C. tetani* from surgical introduction were more likely to show more severe signs of disease than dogs who experienced external inoculation.[3] Furthermore, no association was noted in dogs who received early administration of antitoxin, antimicrobial therapy, or wound management and the progression of clinical signs or 28-day mortality, which strengthens the author's claim that the prognosis for canine tetanus is good and supports the fact that canines are more resilient to infection by *C. tetani.*[3]

Case Outcome

Neshoba did not undergo diagnostics during his stay in hospital, however, based on his history and clinical signs Tetanus was highly suspected. Neshoba's treatment consisted of Procaine Penicillin G, Tetanus antitoxin, and Acepromazine in addition to frequent monitoring of vitals and glucose. Because he had shown no signs of neurologic improvement the morning following the start of his hospitalization, the owners elected humane euthanasia due to poor quality of life and a necropsy in search of a definitive answer.

Necropsy & Histopathologic Findings

Neshoba presented to necropsy in an ideal body condition and minimal autolysis. The umbilicus and horn buds were dried and scabbed over with no evidence of previous inflammation. When the thoracic cavity was opened, there was appropriate negative pressure however the lungs were mottled dark red to pink. All sections of lung were soft and slightly wet and when placed in formalin floated. Roughly half of the trachea contained a small amount of pale pink to white stable foam. The gastrointestinal tract was grossly normal and contained a normal amount of ingesta and digesta throughout. The remainder of the abdominal cavity also did not have any evident gross pathology. No lesions were seen grossly on external examination nor on examination of the cut surface of the brain and spinal cord. Samples taken during necropsy included swabs of the umbilicus and horn buds for anaerobic culture.

Of the thirty organs sampled for histopathology only five samples – lung, trachea, horn bud, cerebrum, and cerebellum – contained abnormal findings and all other tissues were interpreted to be within normal limits for a young caprine. The trachea contained small, multifocal regions of disrupted epithelium and small mucosal hemorrhages; some areas of epithelium were flattened and covered the areas of disruption. Both tissues of brain showed small, eosinophilic, laminated structures most consistent with venous thrombi.

The most important histologic findings were in the horn bud sections which contained a significant amount of pathology consistent with the history of recent disbudding. The haired skin was covered by a thick fibrin mat composed of inflammatory cells, mainly neutrophils and degenerate neutrophils, and necrotic cellular debris was present in addition to multifocal coccid and rod-shaped bacterial colonies. The underlying epidermis and dermis were hypereosinophilic

with indistinct cellular architecture and streaming chromatin with necrosis characterized by both the epidermic and dermis showing regions of sloughing. The underlying tissue was thickened by proliferative fibrous connective tissue. Occasionally, the neighboring musculature contained small clusters of infiltrating neutrophils. The woven bone of the horn bud was also necrotic and the marrow of the deeper bone was made up of neutrophils and fibrin; fibroblasts were present indicating remodeling.

Incidentally, the lungs contained pathology suggestive of aspiration pneumonia from being bottle fed and/or nursing while laterally recumbent. The lungs contained a small amount of fibrin and large, round, homogenous, eosinophilic structures consistent with proteinaceous material, most likely milk. Additionally, the normal alveolar architecture contained multifocal areas of dilated capillaries and occasionally small portions of single ciliated columnar epithelial cells were present within the alveolar sacs. These affected alveoli frequently housed type 1 pneumocytes that sloughed into the alveolar space although there was no evidence of inflammation.

From these findings it is surmised that Neshoba aspirated milk while being laterally recumbent following nursing or hand feeding which caused an acute bronchopneumonia. A definitive cause for the source of infection could not be made from either the gross or the histologic findings, however the bacterial colonies present within the horn bud tissue is strongly speculated to have been the primary source of infection.

Conclusion

Neshoba's history of recent disbudding and the lack of improvement from at-home treatment for suspected Polioencephalomalacia placed Tetanus at the top of the differential list. It

can be surmised that the trauma from his recent disbudding was the anerobic environment where the bacteria entered, proliferated, and began releasing exotoxin, most significantly TeNT. This presumptive diagnosis was further confirmed by the lack of progression of his neurological signs while in hospital and the lack of gross findings on necropsy. The histopathology findings were also relatively unrewarding except for evidence of a mild aspiration pneumonia.

Overall, this case is an important reminder that veterinary medicine is not always about a lifesaving surgery or medication for the treatment of disease; vaccination protocols, hygiene, and environmental management are equally important. So don't wait until things get "baaad," go see your local veterinarian early and often.

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