

Tetanus in Sheep - Evaluation of New Successful Treatment Strategy

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ABSTRACT

Background: Tetanus, caused by the neurotoxin of *Clostridium tetani*, is a significant bacterial disease in sheep. Outbreaks are frequently observed following invasive procedures, such as shearing, ear tagging, and castration, which disrupt the skin's integrity and create entry points for the anaerobic bacteria. Tetanus toxin inhibits inhibitory neurotransmitters within the central nervous system at sensory receptors and neuromuscular junctions, leading to muscle rigidity, spasm, and eventual paralysis. While the standard treatment regimen encompasses the administration of antibiotics, antitoxins, and supportive therapy, the overall prognosis for tetanus remains guarded.

Cases: This report details 2 cases after an outbreak of tetanus within a flock of 7 female Suffolk sheep, each approximately 3 years old and weighing 45 kg, located on a farm ranch in the Rio Grande do Sul which is the southernmost state of Brazil. Tragically, the outbreak resulted in the deaths of 5 animals, underscoring the severity and rapid progression of the disease. The 3 remaining sheep were subsequently transported to the Large Animal Clinic of the Veterinary Medical Teaching Hospital (HCV) of the Universidade Federal do Rio Grande do Sul (CGA-UFRGS) in Porto Alegre city for urgent treatment. The 1st sheep arrived at the clinic, presenting with severe clinical signs indicative of advanced tetanus, including lateral recumbency, pronounced muscle rigidity affecting all limbs and the head, and sialorrhea. Due to the animal's poor prognosis and the severity of its condition, euthanasia was deemed the most humane course of action. The 2 remaining sheep exhibited varying neurological involvement, with clinical signs ranging from subtle head tilting and pelvic limb extension to more pronounced muscle stiffness and spasms. Both animals were immediately placed on a comprehensive treatment protocol that combined procaine and benzathine penicillin to combat the bacterial infection, anti-tetanus serum to neutralize circulating toxins, midazolam and acepromazine for sedation and muscle relaxation, methocarbamol for further muscle relaxation, and supportive care to address nutritional and hydration needs. Notably, in a novel therapeutic approach, 1 of the sheep received intrathecal administration of anti-tetanus serum to directly target toxins within the CNS, aiming to mitigate the pronounced neurological symptoms. Both animals responded favorably to the treatment strategy. They were subsequently discharged in good health, with no reported relapses or complications due to the procedure or treatment reported by the owner.

Discussion: Tetanus outbreaks in sheep can rapidly escalate, with the progression of clinical signs reflecting the advancing neurological damage caused by the tetanus toxin. The presence of tachycardia and tachypnea, coupled with progressive neurological symptoms such as head tilting, limb extension, and muscle spasms, indicates the necessity of prompt and aggressive intervention. In this case, the intrathecal administration of tetanus antitoxin proved to be a critical component of the successful treatment strategy. By directly targeting the toxins within the central nervous system, this approach supplemented the standard systemic treatment and effectively reversed the neurological symptoms observed in the most affected sheep. While tetanus is often associated with a high mortality rate in small ruminants, this case report demonstrates that combining standard therapy with intrathecal antitoxin administration can significantly enhance survival rates, as commonly observed in equine medicine. The positive outcome also underscores the importance of early diagnosis, aggressive treatment, and the potential for broader application of this technique in treating tetanus in sheep.

Keywords: *Clostridium*, tetanus, sheep, intrathecal, methocarbamol.

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INTRODUCTION

Tetanus is a disease caused by neurotoxins produced by the bacterium *Clostridium tetani*. Tetanus toxin induces paralysis, binding to sensory receptors and neuromuscular junctions and ascending to the central nervous system (CNS). There, it inhibits the release of inhibitory neurotransmitters, resulting in increased muscular rigidity and often leading to the death of infected animals [3,26].

In sheep, tetanus commonly occurs following procedures such as docking, shearing, castration, vaccination, or injectable pharmaceuticals, particularly anthelmintics [19,25]. The infection is typically associated with trauma from these procedures, which creates a hypoxic environment in the tissue, providing ideal conditions for the anaerobic growth of *C. tetani* [2].

The standard treatment involves intravenous administration of anti-tetanus serum, intramuscular benzathine penicillin, and supportive therapy [2]. This report aims to present a situation involving 2 sheep diagnosed with tetanus, describing the clinical signs observed, the therapeutic interventions implemented, and the clinical progression of the animals, and evaluating new techniques for treating tetanus in sheep.

CASES

A 2-year-old Suffolk sheep weighing approximately 50 kg was brought to the Large Animal Clinic (CGA) at the Veterinary Medical Teaching Hospital (HCV) of the Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, Rio Grande do Sul, Brazil. The sheep was from a flock of 7 animals on a farm ranch, where 4 had recently died. When the animals were purchased, the farmer was unaware that they had not been vaccinated against tetanus. Upon arrival at the farm, the sheep underwent routine ear tagging and shearing on November 24 and 28, respectively. Shortly after these procedures, the sheep exhibited clinical signs, including muscle rigidity, lateral recumbency, anorexia, sialorrhea, and extension of the head and limbs.

These symptoms are almost always associated with *Clostridium tetani* infection, which produces a disease called tetanus, which is frequently seen in this region of Rio Grande do Sul. Once there are no necropsy findings, the disease is normally diagnosed by its symptomology, and the toxins produced by the microorganism are the main cause of the disease.

The sheep presented to the hospital showed clinical signs similar to those of the other affected animals in the flock. During the consultation, the owner mentioned a prior veterinary practitioner visit during which penicillin¹ [Penfort® - 40,000 IU, IM] was administered to each survivor. While this treatment temporarily slowed disease progression, it did not prevent the other animals from succumbing to the infection. This sheep presented tachycardia (116 bpm), tachypnea (160 rpm), fever (40.5°C), ruminal atony (0:2'), hyperemic ocular mucous membranes, sialorrhea, severe muscular rigidity, and lateral recumbency with the extension of the head and limbs.

Given the animal's poor prognosis, euthanasia was deemed necessary. The procedure was initiated with pre-anesthetic administration of xylazine² 10% [Xilazin® - 0.01 mg/kg, IV], and once sedation was achieved, euthanasia was carried out using a combination of ketamine 10%² [Cetamin® - 3 mg/kg, IV] and midazolam³ [DORMire® - 0.06 mg/kg, IV], followed by intrathecal administration of lidocaine 2%⁶ [60 mL].

The last 2 sheep in the flock, both approximately 3 years old and 45 kg, were transported directly to the hospital after the death of the 1st sheep. Sheep 1: displayed tachycardia (96 bpm), tachypnea (104 rpm), ruminal atony (0:2'), and early neurological symptoms, such as subtle head tilting and extended pelvic limbs. Sheep 2: was in worse condition, presenting tachycardia (128 bpm), tachypnea (92 rpm), ruminal atony (0:3'), and more pronounced neurological signs, including head tilting, neck stiffness, and extended pelvic limbs.

On the 1st day of hospitalization, both sheep received the following treatment: procaine and benzathine penicillin¹ [Penfort® - 40,000 IU/kg, IM], anti-tetanus serum⁴ [Vencosat® - 50,000 IU diluted in 1,000 mL of Lactated Ringer's Solution, IV], midazolam hydrochloride³ [DORMire® - 0.25 mg/kg, IM], vitamin supplement⁵ [Bionew® - 1 mL/kg, IM], and food supplement⁵ [Glicopan® - 5 mg/kg, orally].

The following morning, the treatment was adjusted to include acepromazine⁵ [Acepran® - 0.03 mg/kg, IM] and methocarbamol⁵ [Descontrax® - 10 mg/kg diluted, IV], along with food supplement⁵ [Glicopan® - 5 mg/kg, orally] and 1 more dose of anti-tetanus serum⁴ [Vencosat® - 50,000 IU diluted in 1,000 mL of Lactated Ringer's Solution, IV]. During the week, the treatment with procaine and benzathine penicillin¹ [Penfort® - 40,000 IU/kg, IM] and acepromazine⁵ continued [Acepran® - 0.03 mg/kg, IM] following the

leaflet, including food supplement⁵ [Glicopan® - 5 mg/kg, orally] as supportive therapy.

Because the sheep were used to grazing, their diet during hospitalization consisted of fresh leaves collected daily, without alfalfa or concentrated feed. They were housed in a stall with low light and minimal noise to reduce stress and kept together to provide mutual comfort. Clinical examinations were conducted twice daily to monitor their progress, but by the afternoon of the 2nd day of hospitalization, Sheep 2 showed no signs of recovery. With the owner's consent, it was decided to administer anti-tetanus serum intrathecally to alleviate the neurological symptoms. Before the procedure, the sheep fasted for 7 h, and its vital signs were assessed to confirm it was stable enough for the intervention.

The procedure began with administering xylazine 2% as a pre-anesthetic [Xilazin® - 0.1 mg/kg, IM]. After approximately 10 min, the sheep were positioned in the right lateral recumbency to avoid rumen compression. The cervical region, in an area of 10 cm x 10cm, underwent trichotomy, followed by antisepsis with chlorhexidine (2% detergent) applied in circular motions and removed with alcohol 70%, repeated 3 times. Additionally, a subcutaneous block with lidocaine⁶ was done at 2% (2 mL) to reduce discomfort during the procedure.

An ultrasound was used to locate the atlanto-axial space (between C1 and C2) with the sheep's neck semi-flexed, ensuring precise needle placement. An epidural needle (20G) was carefully guided into this space, taking care to avoid spinal cord injury. No cerebrospinal fluid was aspirated, and 10 mL of anti-tetanus serum⁴ [Vencosat® - 10,000 IU] was administered. The sheep remained conscious throughout the procedure and had its vital signs monitored continuously.

The sheep did not show adverse neurological or locomotor effects immediately after the procedure, nor in the following days. With the successful administration of the serum, both sheep remained hospitalized for 3 more days. They continued receiving treatment with acepromazine⁵ [Acepran® - 0.03 mg/kg, IM], methocarbamol⁵ [Descontrax® - 10 mg/kg diluted, IV], procaine and benzathine penicillin¹ [Penfort® - 40,000 IU/kg, IM], and food supplement⁵ [Glicopan® - 5 mg/kg, orally]. They were discharged 5 days after admission to the hospital, considering the remission of clinical symptoms, and according to the owner's report, both animals remained alive and healthy until the submission of this manuscript.



Figure 1. Sheep 1 hospitalized with suspected tetanus, presenting severe muscle rigidity with extension of head and limbs.



Figure 2. Sheep 2 hospitalized stayed together in a stall with low luminosity and silence to reduce stress. The animal is in a "saw-horse" position and has acute tachypnea.



Figure 3. The administration of the antitoxin intrathecally was done in a controlled environment with the guidance of an ultrasound. A- The sheep underwent trichotomy and antiseptic followed by a subcutaneous block with lidocaine 2%. B- An ultrasound was used to ensure the correct placement of the needle (20G) into the atlantoaxial space, and 10,000 UI of anti-tetanus serum was introduced into the subarachnoid space without aspirating cerebrospinal fluid. C- After 24 h of the procedure, the sheep did not show any signs of sequelae related to the procedure and had already shown improvement in clinical signs.



Figure 4. A- The day of the discharge, when both sheep were in almost complete remission of the disease. B- The remaining sheep from the flock 10 days after the discharge from the hospital.

DISCUSSION

Clostridial diseases, particularly tetanus, enterotoxemia, and botulism, were the most prevalent in the region where this outbreak occurred, accounting for approximately 90% of cases diagnosed at the Veterinary Pathology Sector (SPV) - UFRGS between 1996 and 2011 [20]. Therefore, it's not unusual to observe this disease in the region. It was proven that the absence of vaccination protocols was a critical factor in this outbreak, resulting in the death of 5 animals from the flock, and it's further emphasized in a 1994 report of a tetanus outbreak in horses, where unvaccinated individuals showed no survival [10]. This underscores

the necessity of preventive measures in managing clostridial diseases, considering the high cost of the treatment and its high mortality, therefore expensive and rarely achieving success [1], which may deter livestock owners from pursuing similar therapies, given the economic implications in production animals. Also, the lack of vaccination against tetanus can increase the prevalence of the disease on farms and worsen the prognosis of the sheep that contract the disease [17].

In our described cases, it's believed that ear tagging and shearing was the entry to *C. tetani*, a pattern [2] that emphasizes factors or procedures deemed predisposing to the establishment of tetanus in domes-

tic ruminants, such as umbilical contamination, genital and placental contamination during the postpartum period, surgeries, vaccinations, and shearing [14]. Although tetanus is usually a sporadic disease, outbreaks have been associated with contaminated vaccines and injectable dewormers or following ear-tagging of unvaccinated sheep [17,22]. Diagnosing tetanus is typically based on clinical signs, case history, the presence of a wound, and disease progression [12].

From the report of the owner, previous animals in the flock had presented the disease in a fatal course, where the sheep, as until then had been standing, fell to the ground and usually died soon, with a general increase in muscle contractions [13]. In that regard, the clinical case is characterized by muscle rigidity, beginning in the head muscles and propagating to other groups in the body [13]. The 1st sheep to arrive in the clinic had the similar clinical signs described in the existing literature [14,22], with tetanus of the masseter muscles causing drooling of saliva and inability to eat or drink, which would lead to death from asphyxiation secondary to respiratory paralysis if euthanasia was not performed. Spasm causes retention of urine, opisthotonos, the curvature of the spine, and tail bending, when, ultimately, they cannot walk and lie in lateral recumbency with legs out stiffly, and head extended back [1].

The last 2 sheep arrived at the clinic in better conditions but still showed muscular stiffness and spasms [14]. Among these symptoms, the affected animals were hyperaesthetic, and while still able to walk, they appeared stiff-legged and turned without flexing their spines. Also, the literature [17,22] describes that the animal may be in a “saw-horse” stance or recumbent, as shown in Figure 2 of the sheep hospitalized.

The treatment aims to eliminate the infection, neutralize unbound toxins, relieve muscle spasms, and provide nursing care, and a protocol described in the literature [22] was utilized in this report. Initial penicillin administration by the 1st veterinarian may have extended the course of the disease, slowing bacterial growth without addressing circulating toxins, contrasting with other research [2] about the incubation period of *Clostridium tetani*, which can vary between 3 days and 4 weeks. Also, the age of the animals and the distance between the entry of the infection and the CNS are conditions that can favor its multiplication [13]. After the animal's admission to the clinic, penicillin

was chosen to continue the treatment given to the animals at high doses and frequency (22,000 - 44,000 IU/kg, IM) [9], where it had its crucial point of treatment in the use of high doses of penicillin in the 1st 2 days with 6 x 10⁶ IU of penicillin every 8 h, totalizing 5 applications and guaranteeing the survival of the animal.

The prognosis of tetanus is highly dependent on the stage of disease progression at the time of diagnosis, directly influencing the treatment outcome. Early detection significantly improves the chances of recovery and the disease offers much better prospects when it develops slowly after a prolonged incubation [13]. If the animal survives the second week, it must be considered, with significant probability, saved.

Neutralizing tetanus toxins requires antitoxin administration, which binds circulating toxins but cannot reverse the effects of internalized tetanospasmin [12]. In the standard treatment for tetanus in small ruminants [2,21] it is recommended the treatment utilized in this case [100,000 IU], where was used [50,000 IU diluted in 1,000 mL of Lactated Ringer's Solution, IV], for each sheep for 2 days straight, but not repeating doses of antitoxin for longer because of the risk of anaphylactic and anaphylactoid-type reactions [12]. Small ruminants treated with standard protocols have been described as having poor outcomes [2], contrasting with the outcome of sheep 1, which showed a great response, even after the long incubation time of *C. tetani*.

Supportive therapy is essential for managing tetanus and ensuring animal well-being during treatment. Electrolyte and energy balance correction using lactated Ringer's solution, bicarbonate, glucose, and muscle relaxants such as diazepam is recommended [2]. In this case, alternative relaxants, including midazolam, acepromazine, and methocarbamol, yielded satisfactory results. The last medication [22] indicates the use of methocarbamol to treat tetanus because of its indication as a muscle relaxant, at a dosage of 22 mg/kg, but because it's not well known the effects of this medication in sheep, using half of the predicted dosage was safer yet efficient to treat the disease without causing side effects. A combination of acepromazine, widely used in treating tetanus in horses [7], with buprenorphine and midazolam or diazepam is used to control painful convulsions and muscle spasms [12]. So, acepromazine was administered intravenously at a dose of 1 mg/kg at 6-h intervals to promote muscle

relaxation. This medication has a potent muscle relaxant effect and is commonly used in equine clinical practice [4].

Additionally, advises isolating animals in dark, quiet stalls, the last 2 sheep were kept together due to stress when separated, but in a similar environment to the literature [2]. Also, it's preferable to keep the animal in the station instead of in suspension machines [24].

The treatment for tetanus in horses is no different [24], where the specific treatment made with the antitoxin or anti-tetanus serum is used in the dose of 300,000 IU or 200,000 IU intravenously and 100,000 IU intrathecal, the last one, after tranquilizing the animal. Intrathecal antitoxin administration is an adjunct to routine treatment in horses [6,15], so it was decided to experiment with it in treating sheep 2. Its efficacy lies in neutralizing unbound toxins in the CNS, unlike systemic antitoxin administration, which cannot reach it [6,15]. Some authors dispose the animal in dorsal recumbency, trichotomy, and skin antisepsis were performed in the atlantoaxial joint region, followed by the administration of 50,000 IU of tetanus antitoxin intrathecal, like this case, adapting to 10,000 IU (administered according to the different weight and species) [21].

An ultrasound-guided needle was inserted into the subarachnoid space, a technique similar described in horses [11]. With sedation with detomidine hydrochloride followed by morphine, providing superior central nervous system analgesia. Still, it has been shown that it is possible to have successful outcomes only with xylazine 2%, local skin blockage with lidocaine 2%, and restraint paramount [7]. Subsequently, continues obtaining a transverse image until the spinal cord and subarachnoid space are visible, just like we did in this case on the sheep [11]. To ensure the needle placement is correct, a distinct 'pop' or sudden loss of resistance is felt on the penetration of the dura mater. The same author also highlights that one disadvantage of this technique is the width of the subarachnoid space at this location, which is smaller than that at the atlanto-occipital site.

This report also aligns with other study [23], where intrathecal administration effectively managed tetanus, and the sheep demonstrated significant improvement after the administration. Tetanus antitoxin given intrathecally may even neutralize toxins already attached to the grey matter of the spinal cord, thereby preventing further disease progression and improving the survival rate [16,23]. There are reports where mepivacaine

hydrochloride had to be administered subcutaneously in 1 horse that reacted when the needle was introduced into the skin [18], a situation that did not occur in this report, despite the fear that this would happen.

In another reported case [4], treatment success was obtained by accessing the intrathecal route, using dissociative general anesthesia, and accessing the atlanto-occipital space, where 50 mL of cerebrospinal fluid was withdrawn, and 50 mL of tetanus antiserum was injected, differing from this report, where it was not possible to withdraw any fluid from the subarachnoid space. [8] describes another procedure in horses, where an application of 5.000 IU was realized, intrathecally with the animal subjected to dissociative anesthesia and local anesthesia with a good outcome.

This case shows similarities with the use of lidocaine 2% as subcutaneous blockage and the sedation with xylazine 2%, and with the outcome obtained by the technique. Even though these procedures were successful, this case could not strictly follow them due to the different species, the progress of the disease, and the absence of complete anesthesia. Also, although this technique has shown promise here, some studies report no improvement in some instances, highlighting variability in outcomes [10].

This case report examines 3 sheep affected by tetanus, each with varying treatments and outcomes. The successful treatment of Sheep 2 was notably attributed to the intrathecal administration of anti-tetanus serum, which proved crucial for neutralizing the toxin and facilitating recovery. This method represents not an innovative approach but a different and effective one in treating tetanus in sheep. Two days after the beginning of the treatment and the procedure, the animals showed improvement with remission of clinical signs, and 3 days later, they were discharged after 7 days of hospitalization.

Despite the successful outcome, this report has limitations, including the financial considerations associated with intensive treatment. Besides, previous reports demonstrate a higher prevalence of death outcomes rather than cure [2]. Nevertheless, this case illustrates the potential for intrathecal antitoxin administration to improve survival in medium to late-stage tetanus, where standard treatments alone may not suffice. The findings contribute valuable insights for future clinical practices and encourage further research into effective treatment strategies for clostridial diseases in sheep.

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