Article

Respiratory complications in dogs with tetanus: A retrospective study of 53 cases

Miriam Guedra, Stefano Cortellini, Karen Humm

Abstract — Tetanus can lead to respiratory complications, and the outcome of dogs affected by this disease is still largely unknown. This retrospective study aimed to evaluate the frequency and outcome of 53 dogs with tetanus and respiratory complications between February 2006 and January 2019.

Medical records from dogs diagnosed with tetanus admitted to a referral teaching hospital were reviewed. Fifty-three dogs were diagnosed with tetanus and respiratory complications were observed in 26.4% (14/53) of dogs; 8 developed aspiration pneumonia (AP), 5 developed upper airway obstruction (UAO) and 1 dog developed both. A total of 5 AP dogs were mechanically ventilated. Three dogs with UAO had tracheostomy tubes placed. Dogs with respiratory complications had a poorer outcome, with only 14.3% (2/14) surviving to discharge, compared to 94.8% (37/39) for dogs with no respiratory complications. Respiratory complications such as AP and UAO were common in dogs with tetanus, and this was associated with a poorer outcome.

Résumé — Complications respiratoires chez des chiens affectés par le tétanos : une étude rétrospective de 53 cas. Le tétanos peut entrainer des complications respiratoires et les conséquences de celles-ci sur le pronostic vital du patient sont souvent inconnues. Cette étude rétrospective d'observation a pour but d'évaluer l'incidence et les conséquences de complications respiratoires chez 53 chiens affectés par le tétanos entre février 2006 et janvier 2019.

Les dossiers médicaux de chiens ayant le tétanos et admis dans un hôpital de référence furent analysés. Cinquante-trois chiens furent diagnostiqués du tétanos et des complications respiratoires ont été observé dans 26,4 % (14/53) des cas; huit développèrent une pneumonie par aspiration (AP), 5 développèrent une obstruction des voies aériennes supérieures (UAO), un patient eut les deux. Trois patients avec une UAO reçurent une trachéostomie. Les patients avec des complications respiratoires avaient une évolution plus néfaste, avec seulement 14,3 % (2/14) qui survécurent jusqu'à la sortie de l'hôpital, comparativement à 94,8 % (37/39) pour les patients sans complications respiratoires. Les complications respiratoires chez les chiens souffrant du tétanos sont courantes et ces patients ont un pronostic vital plus mitigé.

(Traduit par les auteurs)

Can Vet J 2021;62:1202–1206

Introduction

Tetanus is a relatively uncommon canine neurological disease caused by *Clostridium tetani* (1). This disease is clinically diagnosed by recognition of the classical clinical signs of a stiff gait, protrusion of the third eyelids, enophthalmos, *risus sardonicus,* and trismus (1,2). Respiratory complications can develop as part of the disease progression in both humans and dogs (3–5). A canine tetanus severity scale ranging from Classes I to IV, based on a human classification system, has been described, with Class IV patients (the most severely affected) potentially experiencing periods of apnea or respiratory arrest (4). In the corresponding human classification system, some patients with Class IV disease can develop laryngospasm, increased airway secretions, and aspiration pneumonia (AP). Respiratory arrest leading to death is a recognized complication (5).

Previously reported respiratory complications in dogs with tetanus include AP, upper airway obstruction (UAO) secondary to laryngospasm, repeated respiratory arrest, and hypoventilation due to spastic muscular rigidity requiring mechanical ventilation (3,4,6). However, the frequency of these respiratory

The Royal Veterinary College Department of Veterinary Clinical Sciences, Hawkshead House Hawkshead Lane North Mymms, Hatfield, Hertfordshire AL9 7TA, United Kingdom (Guedra, Cortellini, Humm); The Royal Veterinary College, London NW1 0TU, United Kingdom (Guedra).

Address all correspondence to Dr. Miriam Guedra; email: mguedraallais@rvc.ac.uk

complications, the need for mechanical ventilation, and the outcome of the affected dogs varies among studies.

Given the variation in previous case series, the aims of this retrospective study were to describe the frequency of respiratory complications in tetanus patients, to further characterize these complications, the treatment administered, and to document patient outcome.

Materials and methods

The medical records of a university teaching hospital were reviewed to detect dogs diagnosed with tetanus between February 2006 and January 2019. A diagnosis of tetanus was based on the presence of compatible clinical signs including *risus sardonicus* and a generalized stiff gait with no obvious evidence of another underlying neuromuscular disease (e.g., muscle wastage, history of exercise intolerance, collapse). All diagnoses were made by an emergency and critical care or neurology boarded clinician.

Age at presentation, breed, sex and neutering status, diagnostic tests, treatment, any adverse reactions to treatments as noted by the attending clinician in the patient record, tetanus score on presentation and at the time of the respiratory complication (either directly assigned by the attending clinician or retrospectively extrapolated from the patient record), day of hospitalization of the respiratory complication, and survival to discharge were recorded.

The clinical notes were searched for evidence of any respiratory complications that occurred during hospitalization. For a patient to be recorded as having a respiratory complication, the clinical notes needed to describe an episode of respiratory distress (tachypnea with a respiratory rate $>$ 40 breaths/min associated with increased inspiratory or expiratory effort) which led to further diagnostics or treatment. The underlying cause of the respiratory complication, as determined by the attending clinician in the patient record, was noted and the investigations and/or treatment of the respiratory complication recorded. Upper airway obstruction was recorded in patients with respiratory distress with characteristic UAO physical examination findings (markedly increased upper respiratory tract noise and increased inspiratory effort) as noted by the attending clinician. Aspiration pneumonia was recorded in patients with respiratory distress associated with either a compatible radiographic pulmonary alveolar-interstitial pattern or a confirmed positive endotracheal lavage culture. If evaluation with pulse oximetry and/or arterial blood gas analysis was performed, this was recorded.

Statistical analyses

Descriptive statistics were used to calculate percentages for categorical data. Normality of continuous data was assessed using the Shapiro-Wilk test. Normally distributed data were reported as mean (± SD), whereas non-normally distributed data were reported as median and range.

Results

A total of 53 canine tetanus patients was presented to the hospital during the study period. Among these dogs, 15.1% (n = 8) were intact females, 30.2% (n = 16) were spayed females, 28.3% (n = 15) were intact males, and 26.4% (n = 14) were neutered males. The mean age was 4.26 y (± 2.78). Twenty-one breeds were represented with crossbreeds (n = 12), Labrador retrievers (n = 11), and border collies (n = 4) being the most reported.

Initial treatment for all patients

Tetanus antitoxin was administered to 23/53 (43.4%) dogs; the dose varied from 70 to 1000 IU/kg body weight (BW) (median: 300 IU/kg BW). It was either given subcutaneously, intramuscularly or intravenously. Three dogs were given chlorpheniramine before administration of the antitoxin. No adverse reactions were reported in any dogs receiving antitoxin.

Most patients (35/53, 66%) were initially treated with metronidazole, 13/53 (24.5%) were treated with metronidazole plus amoxicillin and clavulanic acid, and 3 (5.7%) were treated with amoxicillin and clavulanic acid alone. The antibiotic administered was not recorded for 1 dog and 1 dog died before initiation of antibiotic treatment.

Many dogs (44/53, 83.0%) were treated with sedatives and/or muscle relaxant medications starting with methocarbamol and intermittent acepromazine doses (n = 23). If tetanic spasms continued, treatment was escalated to a midazolam continuous rate infusion (CRI) (n = 18), intermittent diazepam (n = 8) or propofol boluses (n = 3) or a combination of these. Pain was controlled with methadone (n = 6), buprenorphine (n = 4), morphine CRI (n = 1), or a fentanyl CRI (n = 1).

Esophagostomy tubes were placed in 28 dogs (52.8%) 2 of which received parenteral nutrition as well. Gastrostomy tubes were placed in 5 dogs (9.4%), 1 dog (1.9%) had a nasoesophageal tube placed, whereas parenteral nutrition alone was used in 2 dogs (3.8%). The rest of the population (n = 17, 32.1%) did not require assisted feeding.

Toe amputation was performed in 10 dogs to remove the source of infection, with samples submitted for histopathology and microbiology for 4 cases. None of the samples was positive for *Clostridium tetani,* 1 was positive for *Enterococcus faecium,* and the other 3 were reported as a neutrophilic inflammation with no evidence of micro-organisms.

The frequency of respiratory complications in this population was 26.4% (n = 14) with 9 dogs developing AP and 6 developing UAO (with 1 dog developing both complications and therefore being in both groups). Among the UAO population, 50% (3/6) were brachycephalic (2 boxers and 1 English bulldog), whereas in the no complications population, only 2.6% (1/39) were brachycephalic. There were no brachycephalic dogs in the aspiration pneumonia group. The mean tetanus severity score for the dogs that developed respiratory complications was 2 (± 1.25) on admission and 3.2 (± 0.61) at the time of the complication. In the no complication population, the median severity score on admission was 2 (range: 1 to 3). At the time of the complication, 7.1% (1/14) were classified as a Class II on the tetanus severity scale, 57.2% (8/14) were Class III, and 35.7% (5/14) were Class IV. The mean day of hospitalization when the complication occurred was 4.4 d (± 3.69).

Aspiration pneumonia was diagnosed with thoracic radiographs interpreted by a diagnostic imaging boarded clinician (n = 4) or with endotracheal or bronchoalveolar lavage cytology and culture (n = 4). One dog with AP also developed pyothorax.

Table 1. Culture and sensitivity results of airway samples of 5 of the 9 dogs with aspiration pneumonia.

	Case 1	Case 2	Case 3	Case 4	Case 5
Sample method	BAL	BAL	TTW	TTW	ET tube swab
Isolates cultured	1. *Streptococcus canis* 2. *Escherichia coli* 3. *Klebsiella pneumoniae* ssp. *pneumonia* 4. *Staphylococcus pseudintermedius*	1. *Escherichia coli,* mucoid colony type 2. *Escherichia coli,* non-mucoid colony type	1. Profuse growth of *Pseudomonas aeruginosa* 2. *Klebsiella pneumoniae* subsp. *pneumoniae* 3. *Enterococcus faecium* 4. Coagulase negative *Staphylococcus* spp.	1. Beta hemolitic *Escherichia coli* 2. Scant growth of *Proteus* spp. 3. *Enterococcus faecalis* 4. *Streptococcus equi* subsp. *zooepidemicus*	Moderate growth of *Escherichia coli*
MDR	*Escherichia coli, Streptococcus canis, Klebsiella pneumoniae* ssp. *pneumonia*	*Escherichia coli* (both types)	*Pseudomonas aeruginosa* *Klebsiella pneumoniae* subsp. *pneumoniae, Enterococcus faecium, Staphylococcus* spp.	Nil	*Escherichia coli*

MDR — Multi Drug Resistant; BAL — bronchoalveolar lavage; TTW — transtracheal wash; ET — endotracheal tube.

The dog with both complications (AP and UAO) had both radiographic and microbiological evidence of AP. Culture and sensitivity results of the isolated organisms are shown (Table 1).

Treatment of respiratory complication patients

Dogs diagnosed with AP (n = 8) and both AP and UAO (n = 1) were empirically treated with amoxicillin and clavulanic acid while results for culture and sensitivities were pending. Oxygen supplementation was provided either *via* nasal prongs or cannulas. If oxygen supplementation alone did not resolve the dog's hypoxemia (3/9) and/or if the dog developed hypercapnia (1/9), and/or appeared to be fatiguing (7/9), mechanical ventilation was offered to the owners. If mechanical ventilation was declined, the dogs either died from cardiopulmonary arrest (3/4) or were euthanized (1/4).

A total of 4/9 dogs diagnosed with AP were mechanically ventilated. Among the 9 dogs with AP, 4 had airways sampled and 3 were from the mechanically ventilated group. When necessary, the antimicrobial regimen was escalated and either enrofloxacin, marbofloxacin, cephalexin, or imipenem were initiated in addition to amoxicillin clavulanic acid or metronidazole.

All 6 dogs with UAO were treated with supplementary flow by oxygen therapy. Three were treated with a temporary tracheostomy. Another dog presented to the hospital with UAO, hypoventilation, hyperthermia, and coma and was euthanized shortly after mechanical ventilation was instituted. Of the 2 other dogs with UAO, 1 was euthanized due to further complications and recurrent obstructions, whereas the other survived to discharge.

Outcome

Overall survival to discharge for the whole patient population was 39/53 (73.5%). For the dogs that did not have respiratory complications, survival to discharge was 37/39 (94.8%). Of the 2 dogs without respiratory complications that did not survive, 1 was a Labrador retriever that presented with Class II tetanus but acutely deteriorated on day 8 of hospitalization and suffered cardiopulmonary arrest (CPA). No prior respiratory distress was noted. Cardiopulmonary resuscitation was performed but was unsuccessful and the cause for the CPA was unknown. The other patient was an American bulldog became severely tachycardic, hypotensive, and developed severe hyperthermia; the owners elected euthanasia.

Among the dogs that developed respiratory complications, only 2/14 (14.2%) survived. Survival was 12.5% (1/8) in dogs with AP and 20% (1/5) in dogs with UAO. The dog with both complications died. None of the dogs that underwent mechanical ventilation survived and only 1 dog that had a tracheostomy tube placed survived. Of the dogs that died, 5/12 (41.6%) were euthanized due to poor response to medical therapy, perceived a poor prognosis, or for financial reasons. Three of these 5 dogs (60.0%) were diagnosed with AP; and 2/5 (40.0%) were diagnosed with UAO. The other 7/12 (58.3%) died naturally, with 4/7 (57.1%) diagnosed with AP, 2/7 (28.6%) with UAO, and 1/7 (14.3%) with both AP and UAO. A summary of the treatment and the outcome in each population is provided (Table 2).

Discussion

In this retrospective study, respiratory complications were frequent in dogs with tetanus, affecting ~25% of the population. This was consistent with previous veterinary studies reporting frequencies of respiratory complications from 18 to 50% (2,4,6). Respiratory complications are also a recognized complication of human tetanus (ranging from 43 to 50%) and respiratory failure was the leading cause of death in human tetanus patients before the introduction of mechanical ventilation (7).

The most common respiratory complication in this study was AP. In previous veterinary studies, AP was reported in 15.7 to 45% dogs, compared to 16.6% cases in this study (3,4,6). Tetanus increases the risk of regurgitation and aspiration due to dysphagia, prolonged recumbency, changes in cardiac sphincter tone, and the sedative drugs administered to control tetanic spasms (1). It was not possible to determine the cause of aspiration in the individual dogs in this study, but we speculated a multifactorial origin. When sedating tetanus patients, care should be taken to prevent excessive sedation and limit the risk of aspiration.

Table 2. Summary of treatments and outcomes of dogs with tetanus.

	Received antitoxin	Antibiotic treatment	Nutrition	Outcome
AP	Yes 4/8 (50%) No 3/8 (37.5%) N/A 1/8 (12.5%)	Co-amoxiclav 1/8 (12.5%) Metronidazole 4/8 (50.0%) Co-amoxiclav + metronidazole 1/8 (12.5%) Metronidazole + other 1/8 (12.5%) Co-amoxiclav + metronidazole + other 1/8 (12.5%)	Oral 1/8 (12.5%) NE 1/8 (12.5%) E-tube 4/8 (50.0%) TPN only 2/8 (25.0%)	Died 7/8 (87.5%) Survived 1/8 (12.5%)
UAO	Yes 0/5 (0%) No 5/5 (100%)	Metronidazole 2/5 (40.0%) Metronidazole + other 1/5 (20.0%) Not reported 1/5 (20.0%) None 1/5 (20.0%)	Oral 1/5 (20.0%) E-tube 4/5 (80.0%)	Died 4/5 (80%) Survived 1/5 (20%)
Both	Yes 1/1 (100%) No 0/1 (0%)	Co-amoxiclav + metronidazole 1/1 (100%)	E-tube 1/1 (100%)	Died 1/1 (100%) Survived 0/1 (0%)
None	Yes 18/39 (46.2%) No 21/39 (53.8%)	Co-amoxiclav 1/39 (2.6%) Metronidazole 26/39 (66.7%) Co-amoxiclav + metronidazole 10/39 (25.5%) Metronidazole + other 1/39 (2.6%) Co-amoxiclav + metronidazole + other 1/39 (2.6%)	Oral 16/39 (41.0%) E-tube 17/39 (43.6%) G-tube 4/39 (10.2%) TPN + E-tube 2/39 (5.1%)	Died 2/39 (5.1%) Survived 37/39 (94.9%)

AP — aspiration pneumonia; UAO — upper airway obstruction; E-tube — esophageal tube; NE — nasoesophageal tube; TPN — total parenteral nutrition; G-tube — gastrostomy tube; N/A — not available. Other antibiotics included ampicillin, imipenem, enrofloxacin, marbofloxacin.

The use of mechanical ventilation was less frequent in previous studies, being only used in 2 of the cumulative 71 patients described compared to 6/53 cases in this study (3,4). The increased use of mechanical ventilation in this study may have been due to the increasing use in veterinary critical care over time, given that this is a more recent study. In this study population, mechanical ventilation was offered once less invasive medical management failed and was only pursued if the owner could afford it. In comparison, in human medicine, most patients affected with generalized tetanus will undergo long-term positive pressure mechanical ventilation *via* a tracheostomy tube, whether signs of respiratory failure are present or not (5,8). This control of the patient's airway should decrease the risk of AP, but obviously hugely increases the cost of treatment and is associated with many other morbidities including the risk of ventilation-associated pneumonia; therefore, this proactive approach is likely not feasible or appropriate in canine patients.

Upper airway obstruction was the other respiratory complication reported in 6/53 (11%) cases. This compared to reported frequencies of 23 to 55% in previous studies, although tracheostomy tube use was rare compared to 3/6 (50%) of UAO patients having tracheostomy tube placement in this study (3,4,6). The variation in occurrence of UAO was likely due to differences in definition and the severity of disease present in patients. It is worth noting that brachycephalic dogs represented 50% of the population that developed UAO in this study and comprised 2/3 patients treated with a tracheostomy tube. Brachycephalic obstructive airway syndrome is a well-documented problem in dogs such as English bulldogs and the ventilatory dysfunction and tendency to hyperthermia induced by tetanus could easily exacerbate the anatomical tendency to UAO already present.

Survival to discharge overall was similar to that previously reported at 73.5%, ranging from 50 to 92% in previous studies (3,4,6). Dogs with respiratory complications had a far lower chance of survival to discharge. It is important for clinicians to realize that respiratory complications are often perceived to have a poorer prognosis and should allow a more informed discussion of risks with clients. Perhaps, even more importantly, this study should raise awareness of the risk of AP and UAO in canine tetanus patients. Further studies should investigate whether the use of oral care to decrease and manage secretions, the avoidance of inappropriate oral feeding, the appropriate positioning of patients when administering enteral feeds, and careful titration of sedation could decrease the risk of AP. Also, it would be worth investigating whether appropriate titration of sedation level, minimization of hyperthermia, and increased monitoring of susceptible breeds (e.g., brachycephalic) decreases risk of UAO.

There were several limitations in this retrospective study. Firstly, the diagnosis of UAO was subjective, based on the attending clinician's opinion and the patient's clinical signs that were recorded. Upper airway obstruction is an umbrella term for various processes that can lead to a partial or complete blockage of the upper airway. More objective assessment for UAO involving obtaining expiratory and inspiratory flow-volume curves is not readily available in the clinical setting. Also, treatment choices were often financially driven. Indeed, cost of mechanical ventilation was prohibitive for some owners and euthanasia was then offered, which consequently negatively affected survival rate in the respiratory complications population. However, these financial limitations make these clinical findings even more relevant as positive pressure ventilation might not be widely affordable. Also, more subtle respiratory pathology could have been missed, meaning that dogs with less severe respiratory complications could have a better prognosis. This study was also performed over a long interval (13 y) during which patient care was likely to have changed; this was not evaluated. Finally, being a single-institution study, treatment decisions could differ in different settings.

In conclusion, based on this retrospective study, we inferred that dogs with tetanus that develop respiratory complications have a higher mortality rate. This could guide the clinician regarding the prognosis of dogs with tetanus and raise awareness of these issues, hopefully enabling clinicians to make proactive decisions to decrease their incidence. CVJ

References

1. Sykes JE, Greene CE. Tetanus. In: Infectious Diseases of the Dog and the Cat. 4th ed, St. Louis, Missouri: Elsevier, 2011:423–431.
2. Popoff MR. Tetanus in animals. J Vet Diag Investig 2020;32:184–191.
3. Adamantos S, Boag A. Thirteen cases of tetanus in dogs. Vet Rec 2007; 161:298–302.
4. Burkitt JM, Sturges BK, Jandrey KE, Kass PH. Risk factors associated with outcome in dogs with tetanus: 38 cases (1987–2005). J Amer Vet Med Assoc 2007;230:76–83.
5. Cook TM, Protheroe RT, Handel JM. Tetanus: A review of the literature. Brit J Anaes 2001;87:477–487.
6. Bandt C, Rozanski EA, Steinberg T, Shaw SP. Retrospective study of tetanus in 20 dogs: 1988–2004. J Amer Anim Hosp Assoc 2007;43:143–148.
7. Farrar JJ, Yen LM, Cook T, et al. Tetanus. J Neurol Neurosurg Psych 2000;69:292–301.
8. Hsu SS, Groleau G. Tetanus in the emergency department: A current review. J Emerg Med 2001;20:357–365.