Neurology
Case Log 3
10/05/2022
15930 Nala

Signalment:

Nala, 6.6 year, Female Entire, Canine, Staffordshire Bull Terrier

History:

Nala presented with a 6-day history of rapidly progressive generalised muscle rigidity, developing over 2-3 weeks following a wound to one of the digits on her left pelvic limb. The owners reported that exposure to toxins was unlikely. Nala has been in the owner's possession since a puppy, with no history of concurrent conditions nor ongoing medication.

Patient status on presentation:

Nala was alert, with an unremarkable general examination. Neurological examination revealed facial muscle contraction (risus sardonicus) including a narrowed palpebral fissure, drawing back of the lips, and wrinkling of the forehead. Alongside there was a mild to moderate degree of trismus and severe ambulatory extensor rigidity of all limbs, giving her a sawhorse appearance. Hypersensitivity to light sound and touch was also noted. All other aspects of the neurological examination were normal. Body weight was 21.3kg. Vital signs: Temperature 38.8 degrees Celsius; Pulse 80 bpm, no murmurs or arrythmias auscultated, good pulse quality with no deficits; Respiration 52 rpm, lung auscultation clear, but tachypnoea potentially due to stress or discomfort. The primary body systems affected were the nervous system and muscular system.

Problem list:

Risus sardonicus, moderate trismus, severe ambulatory extensor muscle rigidity, hypersensitivity to light, sound, and touch.

Veterinarian's differential diagnosis:

The DVM's presumed diagnosis was generalized tetanus, based on the characteristic pathognomonic appearance of the dog and the patient history. The following differential diagnoses can resemble tetanus but would be very unlikely; hypocalcaemic tetany, strychnine toxicity, and masticatory muscle myositis (if the clinical signs were limited to the head) (de Lahunta et al., 2015; Penderis, 2012).

Veterinarian's initial assessment of prognosis:

Prognosis of generalized tetanus is dependent on the severity at presentation and disease progression, with a wide reported survival rate ranging between 50-92% in dogs (Adamantos et al., 2007; Bandt et al., 2007). As Nala's clinical presentation was moderate and had so far not demonstrated signs of disease progression, initial prognosis was guarded to good dependant on the response to treatment and intensive supportive care.

Interventions:

Serum biochemistry and CBC were performed and were normal. The DVM considered performing electromyography to confirm the presence of sustained muscle depolarization, however due to the requirement for general anesthesia, the risk to Nala was considered too great. Difficulty intubating or extubating Nala due to trismus was the primary concern. In most animals the muscle contraction reduces with general anesthesia, but usually does not completely resolve. Due to the characteristic clinical presentation and history, the DVM felt confident in the presumptive diagnosis of generalized tetanus; no further diagnostics were performed.

Case Management:

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An intravenous canula was placed in the right cephalic vein, enabling administration of medications and intravenous fluid therapy. Balanced crystalloid solution was provided at maintenance rate 2ml/kg/hr (43.2ml/hr). Fluid inputs, outputs and indications of hydration such as capillary refill time were monitored Q12hr.

Antimicrobial therapy was commenced with amoxicillin-clavulanic acid 100mg/ml, 22mg/kg (468.6mg) IV Q8hr and metronidazole 5mg/ml, 10mg/kg (213mg) IV Q12hr.

Diazepam 5mg/ml, 1mg/kg (213mg) IV Q8hr was given to provide muscle relaxation, anti-epileptic therapy, and anxiolysis. As diazepam is short acting, the DVM also prescribed a medetomidine 1mg/ml CRI at 3mcg/kg/hr (63.9mcg/hr) IV to provide a constant plane of sedation. Methocarbamol 750mg, 35.21mg/kg PO Q8hr was given in addition to this to provide further muscle relaxation. Analgesia was administered in the form of methadone 10mg/ml, 0.2mg/kg (4.26 mg) IV Q4hr.

Respiration rate, pattern and effort was monitored and recorded every hour by observing Nala from a distance. Axillary temperature and heart rate readings were taken Q8hr at the same time as Nala was due treatment, to reduce handling. Blood pressure readings were taken Q24hr for the initial 3-days of hospitalization. Nala was monitored including for evidence of epileptic activity using a small camera, allowing constant observation while enabling Nala to remain in a quiet and dark environment with minimal disturbance.

Nala was ambulatory and was therefore able to be walked. Nala was also able to urinate consciously, however urination frequency and effort was closely monitored. Due to confinement in the kennel for long periods of time often lying down, an orthopedic mattress was provided for patient comfort and to reduce the risk of decubital ulcers (Dewey & Talerico, 2016; Penderis,

2012). As Nala could not maintain normal lubrication of her eyes and mouth, synthetic tears were applied Q4hr to her eye, and her mouth was cleaned and damped with a wet swab Q12hr. Nala was initially able to prehend wet food, which was hand fed as meatballs whilst Nala was sat up right to reduce regurgitation and the risk of aspiration pneumonia. Food was provided 1 hour after the administration of diazepam to allow optimal muscle relaxation (Dewey & Talerico, 2016). Daily Energy Requirement (DER) of 709Kcal was calculated (DER = 30 x 21.3kg +70) however the aim was to exceed this due to the increased metabolic demands of prolonged muscle contraction. There is limited literature on the exact requirements of these patients, so the nursing team monitored weight and body condition closely (Chad., 2020; Eirmann., 2015).

Nala was kept in an isolation kennel away from other patients and traffic to reduce stimulation. The light intensity was kept as low as possible and cotton wool was placed into each of Nala's ears to limit auditory stimulation; this was removed daily to allow cleaning. A plastic water bowl, rather than a metal one was used to reduce noise. Treatment and monitoring were coordinated to limit disturbance of Nala (Dewey & Talerico, 2016; Penderis, 2012).

Serum biochemistry was repeated after 10-days to monitor for evidence of acute kidney injury caused by rhabdomyolysis as a result of the uncontrolled muscle spasms, but was normal (Dewey, & Talerico, 2016; Penderis, 2012).

On day 2 of hospitalization the applicant noticed that Nala was straining to urinate and informed the DVM. The DVM prescribed prazosin 1mg, 0.05mg/kg PO BID to reduce internal urethral sphincter tone. This allowed Nala to urinate normally again the following day and prevented the need for an indwelling urinary catheter.

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On day 3 of hospitalization, the applicant noticed that Nala had become anorexic and the DVM elected to place an eosophagstomy tube under general anesthesia. Nala was premedicated with methadone 10mg/ml, 0.2mg/kg (4.26mg) and induced with propofol 10mg/ml 8ml (3.75mg/kg, 80mg) to effect. Despite Nala's trismus, a small endotracheal tube was successfully placed. Recovery was uneventful. An assisted feeding plan was devised with liquid feed (1kcal/ml), split into 6-10 feeds, initially meeting 1/3 of the Nala's daily caloric requirements on day 1, 2/3 on day 2 and full caloric requirements from day 3 onwards (Chan, 2020; Eirmann, 2015). The area around the stoma was cleaned Q24hr and a new dressing applied at such time. Tube patency and placement was checked with sterile water before each feed and flushed thereafter.

On day 8 of hospitalization, the applicant noticed that Nala was straining to defecate. The applicant informed the DVM, who prescribed lactulose 667mg/ml, 667mg/kg (14.21g) PO BID, which allowed easier passage of faeces.

Nala showed mild improvement after 8-days of treatment with some relaxation of the appendicular muscles. After 12 days of treatment, mild relaxation of the facial muscles was observed alongside there was improvement of the trismus. Nala's appetite and ability to prehend food improved, permitting the return of feeding by mouth.

Final Outcome:

After 14-days of hospitalization, Nala was discharged into the owners' care. The eosophagstomy tube was left in situ as a backup feeding strategy should Nala deteriorate or re-experience anorexia. The DVM dispensed oral antibiotics, amoxicillin-clavulanic acid 500mg (23.47mg/kg) PO BID and metronidazole 250mg (1.741mg/kg) PO BID. Muscle relaxants, including diazepam 20mg (0.94mg/kg) PO TID, and methocarbamol 750mg (35.21mg/kg) PO TID. The applicant

demonstrated how to clean and care for the stoma site and safely check for correct tube placement before administration of a feed, if assisted feeding was required. The owners were advised to continue to keep Nala in a quiet, dark environment to minimize stimulation. The applicant also explained the signs of Rapid Eye Movement (REM) sleep disorder which may be observed during and after recovery (Shea et al., 2018).

At 2-week follow-up after discharge from the hospital. Nala had continued to improve, although a mild degree of facial muscle contraction was still apparent. The eosophagstomy tube was removed at this point. At 1 month follow-up after discharge from the hospital. Nala had returned to normal.

Discussion:

Tetanus is an infectious disease caused by the neurotoxin tetanospasmin, produced by the bacteria Clostridium tetani which is a gram-positive, obligate anaerobe, rod-shaped bacteria. This bacterium produces hardy spores which are ubiquitous in the environment in soil, faeces, and dust. When the bacteria enter the body under anaerobic conditions, such as a penetrating wound to the paw in Nala's case, the spores germinate becoming the vegetative form. This vegetative form of the bacteria produces the neurotoxin tetanospasmin which enters the systemic circulation and eventually binds and penetrates the local and distant motor nerve endings at the neuromuscular junction. The neurotoxin ascends the motor neuron through retrogrades axonal transport, eventually crossing the synaptic junction, reaching the inhibitory interneurons located in the spinal cord and brainstem. Here it acts as a zinc dependant endopeptidase preventing the release of inhibitory neurotransmitters such as glycine and gamma aminobutyric acid (Penderis, 2012). Deficiency of these inhibitory neurotransmitters causes sustained and uncontrolled

skeletal muscle contraction resulting in the characteristic clinical signs seen observed in Nala. This includes risus sardonicus as a result of the contraction of the facial muscles, trismus as a result of the contraction of the masticatory muscles and severe ambulatory extensors rigidity of all limbs due to contraction of the appendicular muscles. Straining to urinate was observed due to increased internal and external urethral sphincter tone, as well as straining to pass feces due to increased external anal sphincter tone.

The onset of Nala's clinical signs 14-days after sustaining a wound, is consistent with the reported onset ranging between 3-18 days (Dewey & Talerico, 2016). Head and neck musculature are usually affected first causing trismus and risus sardonicus, followed by the body and limbs producing a ridged sawhorse stance (Penderis, 2012). Given Nala's pathognomonic history and clinical presentation, generalised tetanus was the primary differential diagnosis. Diagnosis of tetanus is most commonly based upon the pathognomonic clinical presentation as well as recent history of a wound.

The DVM performed a minimum database to investigate the possibility of hypercalcaemic tetany, which was normal. Increased creatine kinase activity has been reported in some tetanus cases because of prolonged muscle contraction, but this was not observed in Nala's case (Dewey & Talerico, 2016). The following tests were contemplated by the DVM but not pursued. The reasons for this are discussed below. Electromyography was avoided due to the potential general anaesthetic risk as previously discussed. Clostridium tetani cultures were not performed as positive growths are uncommon due to the difficulty of collecting a sample anaerobically, and as in many cases, such as Nala's, it is not possible as the wound has healed or cannot be found. An immunoglobulin G ELISA that can detect tetanospasmin toxin is available, however sensitivity

is low as the tetanospasmin toxin is able to cause disease well below the titre level detected by this test, hence this test has low diagnostic ability.

The goals of therapy are twofold. The first involves stopping toxin production as well as neutralising the neurotoxin. This involves identifying, debriding and flushing any wounds. Additionally, hydrogen peroxide increase oxygen saturation of the wound making the environment more aerobic. However, in cases such a Nala's this was not possible as the wound had already healed. Alongside, antimicrobial therapy effective against the clostridium tetani bacteria (amoxicillin-clavulanic acid and metronidazole) should be administered as described in Nala's case. Neutralisation of tetanospasmin can be achieved through the administration of tetanus antitoxin. However, tetanus antitoxin can cause anaphylaxis and it is not reported to improve outcome (Dewey & Talerico, 2016). Therefore, this was not administered in Nala's case. The second aspect of treatment involves intensive supportive care (O'Dwyer, 2017). This entails providing muscle relaxation to counteract the muscle rigidity and sedation to counteract the hypersensitivity. In Nala's case this was achieved by administering diazepam and methocarbamol. Sedation was achieved through a medetomidine CRI IV (Dewey & Talerico, 2016; Penderis, 2012). The applicant monitored Nala closely for associated complications including autonomic instability, respiratory spasm, seizure activity, dysphagia, regurgitation, hyperthermia and hypertonicity of the urethral and anal sphincter (Dewey & Talerico, 2016; Penderis, 2012). Where the latter was identified by the applicant, the DVM was able to provide treatment. Maintaining adequate nutrition is important in these patients due to increased metabolic demands. This involved handfeeding techniques initially, followed by placement and management of an eosophagstomy tube (Chan, 2020; Eirmann, 2015). Additional considerations

to increase patient comfort such as regular eye lubrication, and reducing patient hypersensitivity by minimising auditory, visual and tactile stimuli were employed (O'Dwyer, 2017).

The applicant had a positive impact on the outcome of Nala's case, as they were able to provide exemplary intensive supportive care. The applicant's advanced knowledge of the disease pathophysiology and clinical presentation allowed the applicant to anticipate, monitor and identify potential complications allowing timely treatment. Advanced clinical skills were demonstrated, when assisting to place the eosophagstomy tube, devising a feeding plan, calculating medetomidine CRIs and providing the owners with appropriate information and support at discharge.

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