A Brutal Case of Shock

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Introduction

Anaphylaxis is a hypersensitivity reaction with severe, potentially life-threatening consequences that may involve multiple organ systems including, but not limited to the respiratory tract, cardiovascular system, skin, gastrointestinal tract, eyes, and nervous system. It can be triggered by a variety of agents including insect stings or bites, reptile venoms, vaccines, foods, and drugs which results in the activation of mast cells and basophils which release preformed inflammatory mediators. Two immunopathologic mechanisms for anaphylaxis have be identified and will be discussed in depth later in this paper.[2] It is also important to note that the target organs involved in anaphylaxis and shock differ among species. For the purposes of this paper we will focus on the canine patient whose shock organs are the gastrointestinal tract and the liver. In dogs with anaphylaxis dermal and gastrointestinal signs predominate, with hepatic venous congestion and portal hypertension seen in later stages. Presented is a case report involving a canine patient that presented to the Mississippi State College of Veterinary Medicine Emergency Department for treatment of an acute anaphylactic reaction.

History and Presentation

Brutus is an 11-year-old male neutered German Shepherd Dog who presented to the Mississippi State College of Veterinary Medicine Small Animal Emergency Department on July 1, 2018 for respiratory distress and a swollen face. His owners noticed facial swelling approximately two hours prior to presentation. Brutus became acutely dyspneic at home and his owners were unable to get him to rise from a prone position. He was also hypersalivating and gagging at home. Brutus' owner gave him approximately 1 mg of their cat's dexamethasone and brought him in for evaluation. Brutus' current medications at the time included Heartguard monthly and glucosamine.

Upon presentation Brutus was bright, alert and responsive. He weighed 35.8kg (78.8lbs). He had a temperature of 101.7F (99.5-102.5F), an elevated heart rate at 192 beats per minute (60 – 140bpm), and he was panting. His mucous membranes were pink and tacky with a capillary refill time of 2 seconds. He was evaluated to be approximately 7% dehydrated. His ocular exam was unremarkable. Dorsal pedal pulses were palpable and femoral pulses were thready but synchronous. His pinna were erythematous bilaterally. There was no nasal discharge. Cardiothoracic auscultation revealed a sinus tachycardia with no murmurs or arrhythmias and normal lung sounds bilaterally. His abdomen was tense and painful upon palpation. All peripheral lymph nodes palpated normal. Urticaria developed diffusely over his ventral abdomen and thighs during the triage exam. The remainder of his physical examination was normal.

Diagnostic Approach/Considerations

An abdominal focused assessment with sonography for triage (FAST) scan was performed as part of his initial triage which revealed a moderate volume of peritoneal effusion, splenomegaly, and gallbladder wall thickening (i.e., a gallbladder halo sign). His thoracic FAST scan was within normal limits. An abdominocentesis was performed revealing a serosanguinous fluid, which was submitted for analysis. An electrocardiogram (ECG) revealed sinus tachycardia. Brutus was initially hypotensive with a blood pressure via Doppler methodology of 75 mmHg (110-160mmHg). Blood was drawn for a packed cell volume (PCV) and emergency blood gas analysis. Brutus' PCV was elevated at 74% (35-55%). The emergency blood gas analysis revealed hyperlactatemia of 4.9mmol/L (< 2.5mmol/L), hyperbilirubinemia of 1.5mg/dL (0.2-0.6mg/dL), and an unreadable ionized calcium. A venous blood gas analysis was repeated with a second machine in order to confirm the results of the ionized calcium. This second analysis showed a metabolic acidosis with a pH of 7.296 (7.35-7.45) and an ionized calcium within the

normal range at 1.31mmol/L (1.25 to 1.45 mmol/L). Brutus' abdominal fluid analysis revealed a PCV of 5%, a total protein of 6.4 g/dL, and a lactate of 7.4 mmol/L. Cytology of the fluid revealed only red blood cells with no evidence of white blood cells or bacteria.

After stabilization, abdominal radiographs were performed which revealed a loss of serosal detail secondary to peritoneal effusion. They also showed mild hepatomegaly and a large, ingesta-filled stomach with an increased soft-tissue opacity in the region of the pylorus that was round and had some striations. A complete blood count revealed moderate leukocytosis characterized by a mature neutrophilia and a left shift. A serum blood chemistry revealed mild hypernatremia and mild increases in his ALT (148U/L), ALP (324U/L), and total bilirubin (0.9mg/dL). A repeat blood pressure with Doppler after fluid stabilization was 150 mmHg. A prothrombin time and activated partial thromboplastin time were within normal limits.

The following day, a full abdominal ultrasound was performed by the Radiology Department which showed gallbladder sludge, resolution of gall bladder wall edema, multiple splenic nodules, shadowing foreign material in the stomach of unknown clinical significance, and a small volume of peritoneal effusion.

Pathophysiology

A systemic anaphylactic reaction is rapid and can be broken down into three phases: early, mid, and late. The early phase occurs within seconds and consists of antigen binding to high affinity cell receptors and the release of preformed mediators (e.g., histamine) from mast cells and basophils. The mid-phase takes place minutes later and consists of activation of the arachidonic cascade. Arachidonic acid is converted to inflammatory eicosanoids such as prostaglandins, leukotrienes, and thromboxanes. This phase is also responsible for the production

of Lyso-platelet activating factor, which is then converted into platelet activating factor (PAF), one of the key mediators of anaphylaxis. Finally, the late phase can occur over 2-24 hours after initial activation and is the phase in which cytokine production occurs.[2]

As previously mentioned, there are two immunopathologic mechanisms for anaphylaxis which have been identified. The classic pathway, otherwise known as a type 1 hypersensitivity reaction, involves IgE receptors, mast cells, basophils, histamine, prostaglandins, leukotrienes, serotonin, and PAF. This pathway occurs when previous exposure to an antigen results in sensitization, which causes the production of IgE. This IgE then binds to the surface of mast cells and basophils by high-affinity receptors. When subsequent exposure to the antigen occurs, cross linkage of two IgE molecules results in the activation of the cells and release of anaphylaxis mediators (histamine, heparin, tryptase, kallikreins, proteases, proteoglycans, eosinophilic chemotactic factor of anaphylaxis, and neutrophil chemotactic factor of anaphylaxis). Non-immunologic stimuli such as extreme heat and cold are capable of activating the classic pathway. The alternative pathway, otherwise known as a type 3 hypersensitivity reaction, involves IgG, Fcγ, macrophages, and PAF. In the IgG-FcγRIII-macrophage pathway, PAF, rather than histamine, is primarily responsible for the development of shock. The alternative pathway requires significantly more antigen and antibody to trigger anaphylaxis relative to the classic pathway. The two pathways may be triggered simultaneously if the amount of challenge antigen exceeds the capacity of IgG to block antigen binding to mast cell associated IgE.[2]

There are four known histamine receptors with H_1, H_2, and H_3 receptors being important in cases of anaphylaxis. Mediation of coronary artery vasoconstriction and cardiac depression is carried out by H_1 receptors. They also result in the activation of rhinitis, pruritus, and bronchoconstriction. When H_1 receptors are stimulated they cause endothelial cells to convert L-

arginine into nitric oxide which is a potent vasodilator that results in decreased venous return. This results in a relative hypovolemia, as up to 50% of the circulating volume is lost into the interstitial space by the sudden increase in vascular permeability. Mediation of gastric acid production is carried out by H_2 receptors. When H_2 receptors are stimulated the resulting effect is coronary artery and systemic vasodilation, an increase in heart rate, and an increase in ventricular contractility. Recently, H_3 receptors have been identified on presynaptic terminals or sympathetic effector nerves that innervate the heart and systemic vasculature. These receptors are responsible for the inhibition of endogenous norepinephrine release from sympathetic nerves. Stimulation of H_3 receptors results in accentuation of the degree of shock due to the blockage of compensatory neural adrenergic stimulation.[6]

Massive histamine release also results in hepatic venous congestion which produces hepatomegaly, gallbladder wall edema that results in gallbladder wall thickening, and peritoneal effusion characterized by a modified transudate. Additionally, anaphylaxis may cause abnormalities in clotting times due to massive mast cell degranulation and subsequent heparin and tryptase release. This can be a contributing factor in the development of hemoabdomen with prolonged PT and aPTT times.[1,4,5]

Treatment and Management

Aggressive fluid resuscitation is recommended for anaphylaxis patients who present with severe hypotension. Isotonic crystalloids should be given rapidly at resuscitative volumes (90mL/kg for dogs and 60mL/kg for cats given in quarter doses over 10-15 minutes). If crystalloids fail to improve hypotension, colloids may be administered at a dose of 5 mL/kg over 15 minutes.[6] Current literature has shown that H_1 blockers and H_2 blockers are not adequate therapies in the acute phases of shock treatment. However, they have proven useful as an

ancillary treatment in reduction of gastric acid secretion and pruritus.[2] No strong evidence exists showing improved outcomes with the use of both H_1 and H_2 blockers with the exception of faster resolution of urticaria.[3]

Do to the fact that Brutus initially presented in a state of shock, an 18-gauge peripheral intravenous (IV) catheter was placed in his left cephalic vein and a shock bolus of 90 mL/kg of PlasmaLyte was administered IV in quarter dose (800mL) increments over 15 minutes. He was then maintained on a higher rate of IV PlasmaLyte at 200 mL/hr in order to address his state of shock and dehydration. He was also administered a 0.1 mg/kg dose of hydromorphone intravenously due to the fact that he was painful in his abdomen. An initial dose of diphenhydramine at 2 mg/kg was administered intramuscularly.

Although epinephrine is often thought to be the treatment of choice for anaphylaxis, it was not used in Brutus' case due to the fact that he responded well to fluid therapy and an antihistamine alone. Epinephrine is often used in anaphylaxis cases for the treatment of shock due to its adrenergic effects which result in vasoconstriction. This leads to increases in blood pressure, peripheral vascular resistance, and coronary artery perfusion. It also decreases mucosal edema in the airways which relieves bronchoconstriction. However, epinephrine administration may result in serious adverse effects such as ventricular arrhythmias, hypertension, and myocardial infarction. Therefore, it is important to evaluate the individual patient in order to decide if the benefits of epinephrine in the treatment of anaphylaxis outweigh the potential adverse effects.[5]

For the remaining two days of his hospitalization, Brutus was maintained on hydromorphone IV every 4-6 hours as needed. Brutus was placed on 1mg/kg famotidine orally every 12 hours for gastroprotection, 1mg/kg maropitant IV every 24 hours for vomiting, and

2mg/kg diphenhydramine intramuscularly every 8 hours as an antihistamine. Physical examinations were performed every 12 hours and he was monitored closely in the ICU for further developing signs of anaphylaxis.

Case Outcome

Brutus was discharged two days later with famotidine, maropitant, diphenhydramine, and acetaminophen with codeine orally. At the time of discharge Brutus was significantly improved, with only a mild amount of erythema in his pinna. The inciting cause of his anaphylaxis remains unknown but his owners were made aware that this type of incident could recur. They were also informed to monitor Brutus for any signs of gastric obstruction which he was not displaying at the time of discharge. It was recommended that they follow up with their primary veterinarian for repeat bloodwork and abdominal radiographs in order to monitor the progression of the foreign material in his stomach.

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