CASE REPORT

Management of Bee Sting Induced Anaphylaxis and Acute Kidney Injury in a Husky Dog

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Apidae (bees), Vespidae (hornets, wasps, and yellow jackets), and Formicidae (fire ants) the three genera of Hymenoptera are most responsible for physical symptoms associated with allergic reactions seen in veterinary facilities (Casale and Burks, 2014). The venom in the sting can produce conditions ranging from minor local lesions to life-threatening systemic reactions. It is worth mentioning here that the honeybees can only sting once in their lifetime as their barbed stinger snags in the victim's skin, ripping the stinging mechanism from the bee's body and killing the bee. The venom sac keeps contracting outside the body of the bee, and 100% of its venom is delivered over 60 seconds. Honeybee venom is a clear acidic substance consisting of several enzymes, proteins, and amines that can cause poisonous and adverse reactions in the bodies of those who are exposed to it. Melittin and phospholipase A_2 are the primary components of bee venom, however several additional chemicals are also present. These compounds cause haemolysis, rhabdomyolysis, renal tubule degradation, and necrosis, ultimately leading to failure of the organs (Almeida *et al*., 2011). Melittin, in collaboration with phospholipase A_2, breaks cell membranes in certain mammals, resulting in lysis of erythrocytes, leukocytes, platelets, myocytes, and vascular endothelium. Hyaluronidase, often known as "spreading factor" in venom, is responsible for modifying the permeability of cell membranes and thus allowing other venom components to permeate into the tissues of the host. Melittin has the potential to adhere to and generate transitory holes on the surface of red blood cells, which can range from minor to severe depending on weather conditions, age, and the types of flowers used by bees for honey production. The deadly dose for humans and mammals is believed to be 500 stings per adult and 20 stings per kilogram, respectively (Vetter *et al*., 1999). Intravascular haemolysis, rhabdomyolysis, hepatopathy, cardiac injury, acute kidney injury, immune-mediated haemolytic anaemia (IMHA), immune-mediated thrombocytopenia (IMTP), and disseminative intravascular coagulopathy (DIC) are all side consequences of severe envenomation and anaphylaxis. This document reports successful management of bee sting induced anaphylaxis and acute kidney injury in a Husky dog.

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Case History and Observations

A 2-year-old male Husky dog weighing 17.8 kg was presented to Referral Veterinary Polyclinic-Teaching Veterinary Clinical Complex, ICAR-Indian Veterinary Research Institute, Izatnagar (UP, India) with the history of bloody diarrhea, anorexia, haematuria and oliguria for last 3 days. Further history revealed that dog had multiple bee sting 3 days before being presented to the clinics. Animal was previously treated by local veterinarian for haemorrhagic gastroenteritis but no improvement was noticed.

On clinical examination, the animal was found to be dull, dehydrated (8%), recumbent and temperature was within normal range with heart rate 130 bpm and respiratory rate 60 breaths per minute. The conjunctiva was severely congested with hyphema. Furthermore, multiple haemorrhages were observed during preparation of the dog for abdominal ultrasonography. All these findings along with presence of bloody diarrhea and haematuria were suggestive for disseminative vascular coagulopathy.

The laboratory investigation included complete blood count and serum biochemistry (liver and renal function tests), which revealed leukocytosis, severe thrombocytopenia, reduced haemoglobin concentration, haematocrit and total erythrocyte count. The serum biochemistry showed elevated levels of SGOT, whereas the SGPT was within normal range which is more liver specific in canines. Among renal parameters, both BUN and creatinine were elevated notably (Table 1).

The ultrasonographical examination revealed gastritis and splenic enlargement with mild peritoneal effusion

which might be due to haemoperitoneum. Based on clinical, laboratory and ultrasonographical findings, the dog was diagnosed with anaphylaxis induced immune mediated haemolysis and acute kidney injury and treatment was initiated accordingly.

Treatment and Discussion

Therapeutic protocol consisted of Inj. Ringer's lactate @ 10 mL/kg body weight IV, BID, Inj. DNS @ 10 mL/kg body weight IV, BID, Inj. Ceftriaxone-tazobactam @ 25 mg/kg body weight IV, OD, Inj. Pantoprazole @ 1 mg/ kg IV, BID, Inj. Eldervit-c™ 2.5 mL IV, BID, Inj. Etamsylate @ 2 mL IM, BID, Inj. Avil™ @ 0.2 mg/ kg IM, BID, Inj. Lasilactone™ @ 1.1 mg/kg body weight BID, IV, along with tablet Caripill™ ½, Syrup LIV-52™ @ 5 mL and Syp. Dextrose @ 5 mL BID, PO. Adrenaline was also administered to counter the effects of anaphylaxis, but the animal developed tachycardia and administration was stopped. The patient was monitored closely on daily basis until recovery.

A urethral catheter was placed to measure glomerular filtrate rate simultaneously. First day urine output was 250 mL and it increased to 650 mL after 5 days of treatment. The animal started showing improvement after 2nd day of treatment and gradually started consuming liquid food. On 4th day, the animal developed severe anaemia and thus, blood transfusion was done after major and minor cross match. Prior to blood transfusion Inj. Erythropoietin @1000 IU subcutaneously was given to stimulate bone marrow cell production. Effect of therapy was assessed based on the improvement in haematological and biochemical parameters on days 3 and 6 post-therapy. On 6th day the animal was fully active, eating normally and the urine output was also normal. Kidney and liver function tests were within normal reference range as given in Table 1. Haematological parameters also improved on day 6 and as per the owner, the animal was in healthy condition following the treatment.

There are numerous reports of bee sting induced anaphylaxis in humans, however such reports in veterinary medicine are scarce. Bee stings may lead to development of severe systemic reactions including immune reactions (Pucca *et al.,* 2019). This dog had thrombocytopenia and anaemia, this might be immune-mediated caused by the bee's venom leading to type 2 hypersensitivity reaction, also it causes direct damage to the vascular endothelium leading to disseminated intravascular coagulation (DIC). Acute IV hemolysis is thought to be due to melittin and phospholipase A_2 (PLA_2) and has been reported in other studies (Nair *et al*., 2019). This was evident clinically by various haemorrhages on abdomen of the dog while shaving and also during intravenous catheter placement. However, no coagulation tests like prolonged partial thromboplastin time, prolonged prothrombin time were performed and haemorrhages resolved along the course of treatment. Nakamura *et al.* (2013) have also reported development of thrombocytopenia in response to bee stings. Among serum biochemical parameters, BUN, creatinine and SGOT were elevated 3 days following the bee attack. However, SGPT was within normal range which is liver specific enzyme in canines. Clinically the dog had haematuria and decreased urine output, which might be caused by acute tubular necrosis leading to decreased GFR. Other studies have also reported polycythemia, leukocytosis and azotemia in dogs attacked by bees (Buckley *et al.,* 2017; Silva *et al.,* 2022). Anaphylaxis caused by bee's venom is a type-1 hypersensitivity reaction which causes degranulation of mast cells leading to release of inflammatory mediators like serotonin, histamine, PGs, LTs, PFA etc (Casale and Burks, 2014).

In management of anaphylaxis, epinephrine is the most important drug as it prevents degranulation of mast cells, causes constriction of blood vessels, bronchodilation etc. however, in this case administration of epinephrine was stopped due to worsening tachycardia. The dog

Table 1: Haemato-biochemical values of dog on 1st, 3rd day and 6th day of treatment

Parameters	1st day	3rd day	6th day	Reference values
Red blood cells ($\times10^6$/µL)	3.38	2.03	3.25	4.95-7.87 $\times10^6$/µL
White blood cells ($\times10^3$/µL)	34.9	20.2	7	5-14 $\times10^3$/µL
Haemoglobin (g/dL)	8	4.5	6.2	11.9-18.9 g/dL
Packed cell volume (%)	22	13.7	18	35-57 %
Platelets ($\times10^3$/µL)	32	55	70	211-621 $\times10^3$/µL
Neutrophils (%)	74	74	75	58-85 %
Lymphocytes (%)	21	17	17	8-21 %
Monocytes (%)	05	09	08	2-10%
Eosinophils (%)	03	00	00	0-9%
SGPT (U/L)	73.7	44.38	42.5	10-109 U/L
SGOT (U/L	404.9	86.81	88.38	78-132 U/L
Creatinine (mg/dL)	3.22	8.37	1.5	0.5-1.7 mg/dL
BUN (mg/dL)	143.7	162.2	18	8-28 mg/dL

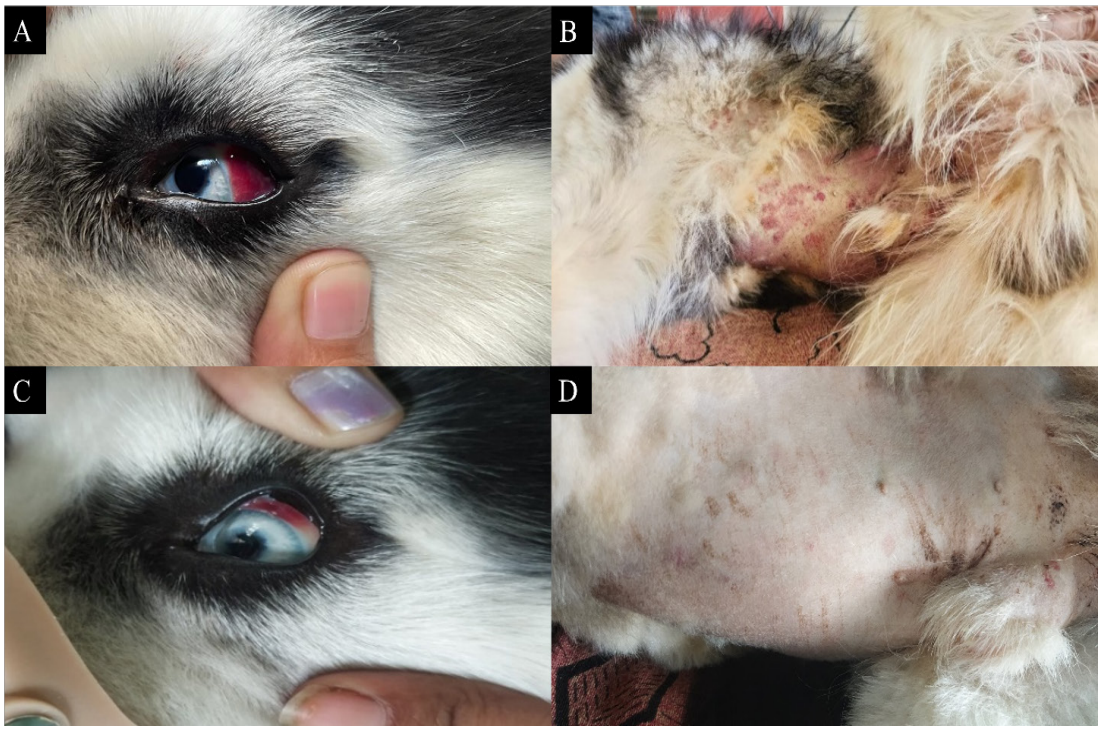

Fig. 1: Bee sting induced anaphylaxis and acute kidney injury in a husky dog: A- Congested conjunctiva with hyphema; B- Haemorrhagic spots around abdominal area; C- Improvement in mucosal congestion post-treatment; D- Reduction in haemorrhage around abdominal area post-treatment.

was administered fluid therapy to counter dehydration, antibiotics were given to prevent any secondary infections, diuretics were given to increase the urine output as there was oliguria on presentation. Haemostatic (Etamsylate) was given to prevent excessive haemorrhages and blood loss along with pantoprazole and other supportive drugs like multivitamins. Erythropoietin was also administered to stimulate the bone marrow and finally blood transfusion was done. The patient started showing improvement in condition from 2nd day of treatment and by 6th day all the biochemical parameters were within normal range, leukocyte count also decreased to normal, however, anaemia and thrombocytopenia still persisted. After 2 months of the treatment, the dog was in apparently healthy condition as reported by the owner.

This is a rare but important case in Veterinary Medicine especially for the animals with pre-existing renal, hepatic or cardiac diseases. Further investigations like urine examination and coagulation tests might have helped in better understanding of the pathogenesis of bee envenomation, however, this case report describes the clinical signs and potential complications which can be associated with bee stings in dogs and their management. Unfortunately, bee antivenoms, anti-melittin antibodies or melittin binder are not yet available in Veterinary Medicine, thus it is an area of significance for researchers in Veterinary Medicine.

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