A rare incidence of Sweating Sickness in a cross-bred Holstein Friesian cow

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Session: 2014-2015

A clinical report submitted in partial satisfaction of the requirements for the degree of
Doctor of Veterinary Medicine (DVM)

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August, 2020

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August, 2020

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LIST OF ABBREVIATIONS

ALT	: Alanine aminotransferase
AST	: Aspartate aminotransferase
BW	: Body weight
CAT	: Clot activating tube
CVASU	: Chattogram Veterinary and Animal Sciences University
DLC	: Differential leukocyte count
EDTA	: Ethylenediaminetetraacetic acid
ESR	: Erythrocyte sedimentation rate
GI	: Gastro-intestinal
Hb	: Hemoglobin
i.m.	: Intramuscularly
MCH	: Mean corpuscular hemoglobin
MCHC	: Mean corpuscular hemoglobin concentration
MCV	: Mean corpuscular volume
MPV	: Mean platelet volume
NSAID	: Non-steroidal anti-inflammatory drug
PCV	: Packed cell volume
RDW	: Red cell distribution width
s.c.	: Subcutaneously
TEC	: Total erythrocyte count
TLC	: Total leukocyte count

ABSTRACT

Sweating sickness is a less-frequent tick-borne toxicosis of cattle characterized by excessive sweating. In this report, a rare incidence of sweating sickness in a cross-bred Holstein Friesian cow was diagnosed. The cow was suffering from recurrent occurrence of vaporization of skin, dehydration, wet hair coat and matting of hairs due to excessive sweating. There were a number of ticks, flies and mosquitoes in tail switch and other parts of the body. We treated the patient successfully with ivermectin as ectoparasite control, ceftiofur sodium to prevent secondary bacterial infections, ketoprofen as analgesics and antipyretics, chlorpheniramine maleate as H_2-blocker, trichlorfon and povidone-iodine skin spray to prevent fly invasion and secondary skin infections. Acyclovir and oil of turpentine was suggested to spray the shed as ectoparasite control. We recommend the prompt diagnosis of patients with sweating sickness by carefully taken clinical history and significant clinical signs, however, blood tests may further aid in diagnosis. We further suggest to follow our treatment procedure for successful management of the patient.

Keywords: Sweating sickness, cross-bred cow, tick control.

INTRODUCTION

Sweating sickness is a tick borne toxicosis characterized by fever, moist eczema and hyperemia of the skin and visible mucous membranes. It affects cattle of all age although young calves are more susceptible (Amstel *et al.* 1987). However, experimental infections in sheep, goat, pigs and dogs were successful (Oberem *et al.* 1985). The disease is caused by an epitheliotropic toxin (27-33 kDA) produced by certain strains of female tick *Hyalomma truncatum* in their salivary gland. The toxin develops in the tick, not in the vertebrate host. The disease is prevalent in hot-humid climate of eastern, central, and southern Africa, Sri Lanka and southern India. Incubation period and severity of the disease is dependent on the length of exposure and dose of toxin. If the exposure is >5 days, severe clinical signs and death may result sometimes. In sub-acute cases, the course is more prolonged and recovery may occur. Mortality in affected calves is 30-70% under natural conditions. Morbidity in endemic areas is ~10%. The severity of infection is influenced by the number of ticks and by the length of time they remain on the host. Recovered animals develop sustained immunity that may last ≥4 years.

Incubation period of sweating sickness takes 4 to 11 days. Sudden onset of hyperthermia, anorexia, listlessness, ocular and nasal discharge, hyperemic mucous membranes, salivation, oral mucosal necrosis, and hyperesthesia are predominant clinical findings. If no care taken, the affected animal may develop blindness due to sticking together of eyelids, hot skin that rapidly worsen to moist dermatitis, matted hair, skin becomes extremely sensitive and emits a sour and foul odor. Most skin lesions appear at the base of the ears, the axillae, groin, and perineum and extend over the entire body. Later, the hair and epidermis can be readily pulled off, exposing red, raw wounds. The tips of the ears and the tail may slough. The skin becomes hard and cracked and predisposed to secondary infection or screwworm infestation at the end of disease course. Affected animals become difficult to handle, show pain when moving, and seek shade. Often, the course is rapid, and death may happen within a few days.

In addition to the dermal lesions, animal may also suffer from cachexia, dehydration, diphtheroid stomatitis, pharyngitis, laryngitis, esophagitis, vaginitis or posthitis, edema and hyperemia of the lungs, atrophy of the spleen, and congestion of the liver, kidneys, and meninges. Experimentally infected adult cattle develop moist eczema accompanied by a marked leukopenia. Subsequently, desquamation of the superficial layers of the mucous

membranes of the upper respiratory, GI, and external genitalia, and profuse moist dermatitis followed by superficial desquamation of the skin occurs in most cases if left untreated. Identification of toxin in affected cattle is quite difficult. Presence of tick vector and significant clinical findings are the basis to diagnose the disease. Effective treatment typically needs removal of ticks, symptomatic treatment, and good nursing. To check secondary infection non-nephrotoxic antibiotics and anti-inflammatory drugs are recommended. Passive transfer of immune serum may also be effective. Control of vector is the only effective preventive measure. Regular acaricidal medication is suggested.

MATERIALS AND METHODS

A Holstein Friesian crossbred cow was suffering from recurrent episodes of bloody sweating at neck and shoulder region, and was associated with itching and inappetence for about 3-months. The cow was 6-years old and had approximately 350 kg body weight. The patient was from Baluchara region of Hathazari Upazilla, Chattogram and referred to Department of Medicine and Surgery, Chattogram Veterinary and Animal Sciences University (CVASU). The owner complained that the cow was initially suffering from sudden onset of smoky-evaporation from its neck and shoulder region and was associated with sweating tinged with blood. The signs appeared mostly during the evening and night time, and disappeared during daytime. The cow showed signs of anxiety and inappetence while showing sweating signs. There was no history of vaccination, however, anthelmintic medications performed in an irregular basis. The animal was treated with 3rd-generation cephalosporin ceftriaxone @ 30 mg/kg body weight along with antihistamine and NSAID for 5-days but failed to prevent recurrence.

We attended the patient at evening time and observed profuse bloody sweating at neck and shoulder region that made the surface wet (**Figure 1**). There was vapor, skin was hyperemic and the hair coat was rough and stray. The animal was found weak with pale mucous membrane, moderate dehydration, anemia and normal superficial lymph nodes. The rectal temperature was 101.6°F, respiration rate 40/minute with no abnormal sounds, pulse rate 84/minute and rumen motility was 4 per 2-minutes. The defecation and urination was found normal. Further clinical examination observed a huge number of *Haemophysalis* sp. ticks, lice, and mosquitoes on the whole body surface with majority of them observed in the tail switch (**Figure 2**). Ticks and lice were identified by microscopic examination of morphology by experts from the Department of Pathology and Parasitology CVASU. Based on the owner's complaints, detailed clinical history, clinical signs and examination findings we presumptively diagnosed that the cow might have been suffering from sweating sickness.

Figure 1. Sweating sickness of a cow. Arrows represent the area of excessive sweating represented by wet hair coat, glistening on exposure to light, and matting of hairs.

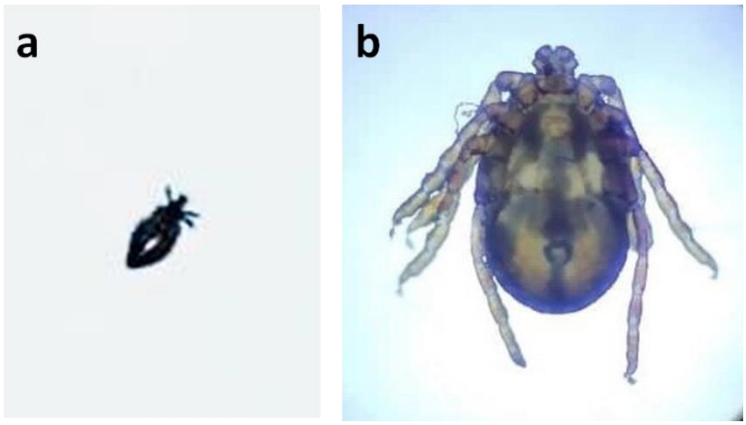

Figure 2. Lice and tick isolated from the cow suffering from sweating sickness. a) *Haematopinus* sp. lice and b) *Haemophysalis* sp. tick were identified by their morphology by parasitologist at CVASU.

After physical and clinical examination, blood, feces and urine samples were collected for further tests. Ten milliliter of blood was collected from the jugular vein with 18G needle and half was transferred to CAT vial to separate serum and the rest to purple capped vacutainer having K2-EDTA in it. Five hundred milliliter of midstream urine sample was collected in a sterile container. Using sterile hand gloves 100 gm fecal sample was collected directly from rectum. The samples were transported to physiology, parasitology and clinical laboratories of CVASU using a sample carrying ice-box.

In the meantime, the animal was treated with ivermectin @ 0.2 mg/kg BW subcutaneously (s.c.) 3-days interval for 4 times, ceftiofur sodium @ 2.85 mg/kg BW intramuscularly (i.m.)

once-daily for 5-days, ketoprofen @ 3 mg/kg BW i.m. once-daily for 4-days as specific anti-toxin was not available. Chlorpheniramine maleate was injected to prevent unwanted immune reaction against ceftiofur, trichlorfon was suggested to bath the animal once-daily for 10-days, povidone-iodine spray was suggested onto the wet skin once-daily for 10-days. Acyclovir and oil of turpentine was suggested to sprinkle the shed to prevent fly and tick. After a-week, the animal was treated with Ringer's acetate 1000ml intravenous along with amino acid and iron preparations once-daily for 3-days as anemia was diagnosed. All the samples were collected and tested a second time after completion of treatment provided.

The whole blood sample was tested using a blood analyzer for Hb level, ESR, PCV, TEC, TLC and DLC values etc. using established protocols (Feldman *et al.* 2000). Using a serum analyzer, the serum sample was analyzed to measure Ca, P, Mg, glucose, total protein, and hepatic enzyme AST and ALT following protocols previously described (Elitok *et al.* 2006). To detect any blood protozoa, Giemsa staining of thin, thick and wet smear of blood was performed and examined under microscope following the procedures described elsewhere (Özbilgin 2018). Coproscopy was performed following standard procedures of direct smear, floatation and sedimentation techniques to detect GI worm load in the affected cow (Mirzaei and Fooladi 2013). Using a urine analyzer, urine pH, glucose, protein, ketone, creatinine etc. were measured following standard procedures (Herman *et al.* 2019).

RESULTS

It was observed that the animal was suffering from anemia as lower Hb, TEC, MCV and RDW values were observed (**Table 1**). Leukocytosis was also observed and represented by higher TLC, neutrophilia, eosinophilia and monocytosis. The parasitological examination of blood and feces was negative (results not shown).

Table 1. Whole blood test values before and after treatment

Name of test	Normal ranges	Before treatment	After treatment
Hb (g/dL)	8-15	**7.7**	**9.3**
ESR (mm/h)	0-3	0	0
TEC (million/cmm)	4-12	**6.05**	**8**
TLC (thousand/cmm)	5-10	**8.7**	**7.5**
Neutrophils (%)	15-33	**55**	**35**
Eosinophils (%)	0-20	**5**	**3**
Lymphocytes (%)	45-75	35	43
Monocytes (%)	0-8	**5**	**3**
Basophils (%)	0-2	0	0
Platelets (lakhs/cmm)	1-8	4.63	5.35
MCV (fL)	40-60	**36.2**	**46.03**
MCH (pg)	5.2-8	12.7	7.7
MCHC (g/dL)	31-38.5	35.2	36.3
RDW (%)	0-99.9	**16.4**	**48.5**
MPV (fL)	3.5-6.5	5.2	5.6

Hb: hemoglobin, ESR: erythrocyte sedimentation rate, TEC: total erythrocyte count, TLC: total leukocyte count, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, RDW: red cell distribution width, MPV: mean platelet volume

Serum analysis of the cow was demonstrated with lower levels of calcium and higher levels of phosphorus (**Table 2**). The glucose and total protein levels were remain normal before and after treatment. Surprisingly, there was elevated level of AST in blood although the ALT level was normal. There was no an enteric worm or worm eggs observed in coproscopy and neither blood protozoa observed in blood smears (results not shown).

Table 2. Serum analysis for minerals, glucose, total protein and liver function test

Serum components	Normal ranges	Before treatment	After treatment
Calcium (mg/dL)	8-11.4	**6.9**	**8.21**
Phosphorous (mg/dL)	5.5-8	**6.85**	**5.22**
Magnesium (mg/dL)	1.5-2.9	**2.66**	**1.79**
Glucose (mg/dL)	40-100	61.79	45.42
Total protein (g/dL)	6.7-7.5	5.5	4.7
AST (U/L)	11-40	**96.9**	**8.82**
ALT (U/L)	60-125	**45.09**	**28.40**

AST: aspartate aminotransferase, ALT: alanine aminotransferase

Urinalysis of the cow revealed that there was increased creatinine level and acidity of urine when the disease was in clinical form. However, the creatinine level came back to below normal range and pH became basic following treatment (**Table 3**).

Table 3. Urinalysis of cow before and after treatment

Name of test	Normal ranges	Before treatment	After treatment
Specific gravity	1.02-1.05	1.05	1.03
Odor	Aromatic	Aromatic	Aromatic
Color	Straw	straw	straw
Urobilinogen (mg/dL)	Negative	2	2
Glucose (mg/dL)	Negative	Negative	Negative
Bilirubin	Negative	+ (low)	+ (low)
Ketone	Negative	Negative	Negative
Ph	7-8.4	6	8
Protein	Negative	Negative	Negative
Creatinine (mg/dL)	45-75	**100**	**10**
Nitrate	Negative	Negative	Negative
Leukocyte (…/µl)	Negative	>25	>25

DISCUSSION

Sweating sickness is a rare tick-borne illness in cattle and possibly other ruminants that is reported sometimes in southern India and African countries. The disease is extremely infrequent in Bangladesh, and there is no reported case till today. Although the disease is caused by the toxin produced by *Hyalomma* tick, we identified *Haemophysalis* sp. from the cow. It is suggested to study whether *Haemophysalis* sp. tick can produce toxin(s) causing similar disease in cattle. Anemia and leukocytosis observed in the affected cow was might be due to chronic infections (Weiss 2002). The anemia of chronic disease occurs as part of a chronic inflammatory disorder, most often chronic infection. In the current study the cow had been suffering for more than two months. Chronic illness might have contributed to the anemia by either due to increased hemophagocytosis by macrophages, occurs in patients with inflammatory diseases. Alternatively, erythropoiesis might have impaired because of decreases in both erythropoietin production and marrow responsiveness to erythropoietin. Alteration of iron metabolism due to an increase in hepcidin, which inhibits iron absorption and recycling, might also have lead to iron sequestration in the cow. However, following treatment the blood values became within normal range.

Neutrophils are host's first line of immune defense cells that are among the first to migrate into the skin in response to invading pathogens followed by monocytes. These cells respond to chemotactic signals present at the site of infection. Among the roles played by neutrophils in inflammatory and immune responses are phagocytosis and killing of bacteria or toxin via the generation of reactive oxygen intermediates and the release of lytic enzymes stored in granules (Mölne *et al.* 2000; He and Liang 2015). In this case study, we observed neutrophilia and monocytosis might be due to the toxemia of the patient.

Changes in the skin are frequently found in patients with chronic hypocalcemia and hyperphosphatemia (Plantinga *et al.* 2008; Schafer and Shoback 2000). Skin lesions reported in patients with hypocalcemia include atopic eczema, exfoliative dermatitis, impetigo herpetiformis, and psoriasis. Restoration of normocalcemia is reported to improve these skin disorders (Schafer and Shoback 2000). Chronic skin lesions or toxemia of the cow might have contributed to the hypocalcemia and hyperphosphatemia observed. Furthermore, hypoproteinemia occurs when blood proteins particularly albumin and globulin levels are very low. Albumin makes up a significant portion of the blood plasma.

Inflammatory diseases are reflected by reduced serum protein levels in patients with chronic skin diseases (Phillips *et al.* 2014). The sickness in the cow of the present study was chronic recurrent type that might be responsible for the hypoproteinemia.

Aspartate aminotransferase (AST or SGOT) and alanine aminotransferase (ALT or SGPT) are the most sensitive and widely used liver enzymes to detect liver function. These enzymes are normally predominantly contained within liver cells and to a lesser degree in the muscle cells. If the liver is injured or damaged, the liver cells spill these enzymes into the blood, raising the AST and ALT enzyme blood levels and signaling liver disease (McGovern *et al.* 2015; Yadav *et al.* 2016). We observed higher levels of AST in the cow that came back to normal following treatment. High AST level might be due to the toxin having hepatic injury. No blood and intestinal parasites were observed in the current case that might be due to the routine treatment with anthelmintics. Furthermore, urinalysis of the cow revealed almost double the creatinine level than the normal cow. Skin care is essential in preventing skin diseases, or it may leads to several chronic complications such as kidney dysfunction (Kuypers 2009). Several other diseases that ended up with toxemia may cause a higher serum creatinine level greater than or equal to 1.5 times the normal (Yu *et al.* 2015).

We provided treatment with antibiotics, antihistamines, analgesics, Ringer's acetate to dilute the toxin, and ectoparasite control. Surprisingly, the cow started to back to normal upon progression of treatment indicating that the treatment was highly effective. We suggest to rapid management of the sweating sickness following our provided treatment schedule.

LIMITATIONS

Confirmatory diagnosis of sweating sickness is only possible following laboratory identification of the toxin produced by *Hyalomma* tick. Although we identified *Haymophysalis* tick from the cow further studies are suggested to detect toxin(s) produced by this tick causing sweating sickness. Specific etiologic treatment with anti-toxin immunotherapy is only suggested following confirmatory diagnosis of toxin. However, in the current case report, specific identification of toxin and treatment with anti-toxin was not possible due to lack of laboratory support and unavailability of anti-toxin.

CONCLUSION

Sweating sickness in cattle is a rare disease in Bangladesh. Cattle with signs of sudden onset of excessive sweating can pose a diagnostic and therapeutic challenge. Prompt identification of signs, making the diagnosis, and offering effective treatment can dramatically improve the quality of life.

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ACKNOWLEDGEMENT

The author feels proud in expressing his deepest sense of gratitude, sincere appreciations, indebtedness to respected teacher and supervisor **Dr Suchandan Sikder**, Associate Professor, Department of Medicine and Surgery, Chattogram Veterinary and Animal Sciences University (CVASU), for his ingenuous and scholastic supervision, constant inspiration, providing valuable suggestions, necessary corrections to report writing and for his affectionate help in completion of this report. The author would like to express his deepest sense of respect and affection to the honorable Dean **Professor Dr Abdul Ahad**, Faculty of Veterinary Medicine, CVASU, Khulshi, Chattogram.

The author also expresses sincere gratefulness and thanks to **Professor Dr. AKM Saifuddin**, Director of External Affairs (CVASU) for his valuable suggestions for completion of this report. He also acknowledge the farmer for allowing him to write a clinical case report on his animal, and the persons of parasitology lab, biochemistry lab, physiology lab and medicine lab of CVASU for their support.

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August, 20

BIOGRAPHY

I am Omar Faruq, son of Md. Atar Ali and Mrs. Ajiba Begum. I passed Secondary School Certificate (SSC) in 2012 with GPA-5.00 and Higher Secondary Certificate (HSC) Examination in 2014 with GPA-5.00. Now I am an intern veterinarian under the Faculty of Veterinary Medicine in Chattogram Veterinary and Animal Sciences University (CVASU). In the future, I would like to work as a veterinary practitioner and do research on animal diseases to improve animal health and production in Bangladesh.