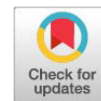


Case Report



Application of Various Diagnostic and Therapeutic Approaches for Detection of a Hemorrhagic Cystitis in a Persian Cat

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Abstract | Billu, a 3 year old male Persian cat weighing approximately 4.9 kg, was presented to the Teaching and Training Pet Hospital and Research Center, Purbachal, Dhaka. Having the complaints of difficulty in urination, hematuria, straining to urinate when peeing, inability to pee about 4 days. Also have weakness, loss of appetite and abnormal body posture. There was no deworming, only rabies vaccination was given. Physical exam revealed that body temperature was 101.2 with mild dehydration. Because of a suspicion of hemorrhagic cystitis, a blood sample was taken and sent to the lab for evaluation of hematological profiles like WBC, platelets etc., as well as biochemical profiles like phosphorus, albumin, BUN, total protein, serum creatinine etc. A urine sample was also taken in order to determine the pH, specific gravity, blood, and whether or not hematuria (red urine) was present. Analysis of the urine reveals pH (7.9), specific gravity (1.01), ketone (-), bilirubin (-), blood (+) report shows that dark color urine have strong odor and blood found in urine. Peripheral lymph-nodes were normal. Ultrasound revealed the thickness of the wall of urinary bladder and increase hyper-tonic contents. In X-ray (**Figure 4**) it was seen distended urinary bladder, ureteral obstruction and vesicoureteral reflux were seen. Biochemical report (**Table 2**) was shows that increase the level of blood urea nitrogen (39 mg/dl) and serum creatinine (1.9 mg/dl) level. Phosphorus (6.7 mg/dl), total protein (7.9 g/dl), albumin level (3.71 g/dl) remain normal. Analysis of urine reveal pH and phosphorus, albumin, creatinine and bilirubin level remain normal. After confirmation of hemorrhagic cystitis treatment was given for this condition were flushing out urine with normal saline. Fluid therapy used as dextrose normal saline (DNS) for maintenance of fluid volume of the body. It can be concluded that hemorrhagic cystitis can be a serious condition requiring prompt veterinary attention to prevent complications like urinary blockage or long-term kidney damage.

Keywords | Hemorrhagic cystitis, Hematuria, Vesicoureteral reflux, Clinical sign, Diagnosis

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INTRODUCTION

Hemorrhagic cystitis is an inflammation of the bladder defined by lower urinary tract symptoms that include dysuria, stranguria, hematuria, periuria (inappropriate elimination), pollakiuria and hemorrhage and is caused by viral or bacterial infection or chemotherapeutic agents

(Widmer *et al.*, 2004). It may be defined as acute or insidious diffuse vesical bleeding (Defauw *et al.*, 2011). At present according to diverse cause, feline lower urinary tract disease (FLUTD) can be classified into feline idiopathic cystitis (FIC), urolithiasis, bacterial urinary tract infection, neoplasia, anatomic malformation, and iatrogenic, behavioral, metabolic, or neurogenic problems (Hostutler

et al., 2005). Hemorrhagic cystitis most often occurs in young to middle aged cats that are less than 5 years old (Lekcharoensuk *et al.*, 2011). Male cats are most prone to this problem, but female can also develop it. Experts believe that stress play a role, as cats who experience sudden changes to their routine or environment and cats that in multi-cat households are more likely to develop hemorrhagic cystitis (Stella *et al.*, 2011). The common causes of hemorrhagic cystitis in cats include urolithiasis, infections, tumors, trauma or obstruction. Some of the most identified risk factors include being overweight, inactive and experiencing several stressful situations (Defauw *et al.*, 2011). Other potential risk factors for evolving hemorrhagic cystitis include dehydration, underlying kidney function and rapid infusion (Forrester and Towell, 2015). Administration of the alkylating agents cyclophosphamide and ifosfamide can cause sterile hemorrhagic cystitis (Korkmaz *et al.*, 2007).

The prevalence of cats classified as FIC in feline lower urinary tract disease (FLUTD) cats was reported to be 61% in 2001(5) in the Bangladesh and has been estimated to be 57% in Switzerland (8), 55% in Germany (24), 55.5% in Norway (11), 60.7% in Poland (25), 66.4% in Korea (20), 57.7% in Thailand (21) and 56% in Indonesia (26). In Bangladesh the issues of cat health and welfare, including condition like hemorrhagic cystitis and other urinary tract disease, remains under studied and under reported. It leads to significant loss, primarily in the form of veterinary care costs and productivity loss. The costs for treatment are generally affordable in Bangladesh compared to western countries, but they can still be a burden for low-income household.

Symptom of cystitis in cats is straining to pass urine, urinating in unusual places, overgrooming around the genital and lower abdomen, changes in behavior, blood present in the urine, inability to pass urine, licking the urinary opening. In most cases clinical signs of non obstructive feline idiopathic cystitis (FIC) resolve within 7 days without treatment (Defauw *et al.*, 2011). However, recurrence of clinical signs after variable periods of time is very common. Up to 65% of cats with acute FIC will experience one or more recurrences within one year (Defauw *et al.*, 2011). In several published studies, the age, reproductive state, body weight, underlying disease, type of food and environmental stressor have been associated with increased risk for recurrence of FIC (Buffington *et al.*, 1996). Hemorrhagic cystitis can develop in a matter of hours or weeks. Various factors, infection like bacterial, viral or fungal infection of the urinary tract can lead to inflammation and bleeding in the bladder. Common viral causes include Feline herpes virus (FHV-1) and feline calicivirus (FCV). Recurrent hydronephrosis and spontaneous renal rupture also caused by lymphoplasmacytic inflammation in cat (Kim *et al.*, 2021).

Some cat develops hemorrhagic cystitis without an apparent infection or other underlying cause. This is often referred to as idiopathic cystitis and is believed to be related to stress and environmental factors. The presence of bladder stones, also known as uroliths can irritate the bladder lining and cause bleeding (Buffington *et al.*, 1996). With this form of disease, crystals various salts are usually found in the urine, on this basis doctor can make a diagnosis. Blunt trauma to the lower abdomen or pelvic region can lead to hemorrhagic cystitis in cats. It can be initiated by radiation or by chemical agents, such as busulfan, oxazaphosphorines (such as cyclophosphamide and ifosfamide), and occasionally by penicillin's and non-steroidal anti-inflammatory drugs (NSAID) or corticosteroids, can contribute to bladder inflammation and bleeding as side effects

The presence of some toxin, abnormality of some protective factor or presence of microorganism in the urine has been proposed to explain the lower urinary tract sign and symptom in patients' feline idiopathic cystitis. Although less common, bladder tumors in cats can cause hemorrhagic cystitis. The main problems of the urinary tract disease are found feline interstitial cystitis (FIC) of 55-69% and urolithiasis of 13-28% (Hostutler *et al.*, 2005). About 10% may have associated structural abnormality such as urachal diverticulum or urethral stricture, another 10% have what appears to be a behavior disorder, less than 2% of cases will be associated with urinary infection.

Diagnosis of cystitis through anamnesis, abdominal palpation, physical examination, clinical sign, urinalysis, hematology, ultrasonography and radiography (Widmer *et al.*, 2004). It primarily relies on the clinical signs and behavioral history of the affected cats. So, a detailed urinary history of the cat should be recorded, as well as other abnormal beyond the lower urinary tract and a thorough environmental history should be taken. For cats presenting with lower urinary tract system, abdominal palpation is require to test the cat's pain reaction and to roughly figure out the size, texture and inclusions of its bladder based on veterinarians experiences. Complete and comprehensive physical exams should be conducted to detect comorbid abnormalities. Additionally, contrast radiography, including retrograde contrast urethrography, can help to detect small lesions, radiolucent calculi, neoplasia. Abdominal ultrasonography can also assist in identifying urinary calculi and crystals, bladder masses and bladder wall thickness.

Treatment of hemorrhagic cystitis is symptomatic and includes continuous bladder irrigations, analgesia, forced diuresis and transfusion to maintain blood level above 50,000 cell /mm and. The most effective way to treat and manage cystitis in cats is usually environmental changes (to

reduce stress) combined with dietary changes (to increase fluid intake).

Research gaps regarding hemorrhagic cystitis in cats in our country such as lack of detailed studies on the prevalence and incidence of hemorrhagic cystitis in cats, particularly specific regions or demographics. Insufficient research on causes specific to the local feline population such as infectious agents, stress, or toxin exposure. Lack of advanced diagnostic tools or laboratories, limited awareness among veterinarians about differentiating hemorrhagic cystitis from other urinary tract disorders, lack of access to advanced treatments or diagnostic tools, limited exploration of alternative therapies. The objective of the research to outline the diagnostic process, including laboratory tests, imaging and differential diagnoses, that led to identifying hemorrhagic cystitis, to illustrate the therapeutic interventions used, such as medications, supportive care or dietary modifications and their outcomes.

CASE PRESENTATION

CASE DESCRIPTION

A 2.6 year old male persian cat weighted 5.4 kg attended at Teaching and Training Pet Hospital and Research Center, Purbachal, Dhaka with the history of weakness, loss of appetite, vomiting, lameness, defective posture, inability to pee, blood mixture urine for last 3 days on 23 September 2024. Only rabies vaccination was given, deworming was not given regularly. Diet includes boiled chicken, boiled fish, pumpkin, milk, egg as well dry food.

CLINICAL EXAMINATION

Rectal temperature was 101.2 F. Physical examination revealed that mild dehydration and mucous membrane was pale in color. Abdominal palpation showed distended abdomen with abdominal pain. The cat was unable to pee. Blood containing urine were found (Figure 1). The cat was dehydrated, Respiration rate was 25 per minute and heart rate was 150 bpm which is normal. Peripheral lymph nodes were normal and hair coat was shiny.

BLOOD COLLECTION

Based on clinical history and observations we collected blood and urine from the cat. Meanwhile blood sample was drawn from the cephalic vein (Figure 2). These sample was sent to lab of Teaching and Training Pet Hospital, Purbachal, Dhaka following appropriate procedure.

Diagnosis of hemorrhagic cystitis in a cat should be based on through veterinary examination including clinical signs, blood test, urine analysis, ultrasonography and potentially imaging. Patient information like breed, age, gender etc. are also important to diagnose possible disease condition.

Clinical history includes hematuria, straining to urinate any other relevant clinical signs. Physical examination such as abdominal pain or abnormal palpation of the bladder. Knowing the bladder and urinary tract radiographs and ultrasound are recommended. According to anamnesis and clinical history Billu was affected by urinary tract infection. The clinical history also indicative to urinary infection. In X-ray report it was seen distended urinary bladder full of urine. Ultrasound indicated that a clear thickness of urinary bladder.



Figure 1: Bloody Urine excrete out from a cat with feline lower urinary tract disease.



Figure 2: Blood collection from cephalic vein of cat.

HEMATOLOGICAL AND BIOCHEMICAL TEST OF BLOOD

The laboratory examination results for hematology (Table 1) shows that lymphocytosis was found in the complete blood count, with 17,500 white blood cell/mcl. The remaining parameters such as monocytes, eosinophil, basophils, MCV, MCH, MCHC, and platelets are essentially typical.

Table 1: Complete blood count of hemorrhagic cystitis in cat.

Parameter	Test Result	Reference value
Hemoglobin (Hb%)	9.8 g/dl	9.0-15.0 g/dl
Total WBC Count	17,500/mcl	5,000-19,000/mcl
Neutrophils	48%	40-70%
Lymphocytes	48%	10-45%
Monocytes	06%	2-8%
Eosinophil	02%	01-04%
Basophiles	00%	00-01%
RBC Count	6.01m/ μ l	6.00-10.00m/ μ l
PCV	30.9%	32.0-55.0%
MCV	45.7fl	39.0-55.0fl
MCH	13.8pg	13.0-18.0pg
MCHC	27.7 g/dl	30.0-36.0g/dl
Platelet Count	161,000/mcl	150000-500000/mcl

Table 2: Biochemical analysis of the blood of hemorrhagic cystitis in cat.

Parameters	Test results	Reference value
Phosphorus	6.7 mg/dl	2.4-8.2 mg/dl
Total protein	7.9 g/dl	5.2-8.8 g/dl
Albumin	3.71 g/dl	2.5-3.9 g/dl
Blood Urea Nitrogen	39 mg/dl	14-36 mg/dl
Serum Creatinine	1.9 mg/dl	0.6- 1.6mg/dl

The Serum biochemistry (Table 2) evaluation revealed elevated blood urea nitrogen (39 mg/dl) which reference value was 14-36 mg/dl. Serum creatinine level also elevated (1.9mg/dl) levels possibly resulted from urethral obstruction which reference value was 0.6-1.6 mg/dl. Phosphorus level was (6.7mg/dl), total protein was (7.9mg/dl) and albumin level was (3.71 mg/dl) remain in normal range.

URINALYSIS

In cats with hemorrhagic cystitis, urinalysis is a key diagnostic tool to identify potential causes and assess the severity of the condition. The color of urine appeared dark red color due to the presence of blood. A foul smell indicate bacterial infection. Decreased specific gravity indicate may have other disease condition. Positive result of blood indicate hematuria (Table 3).

Table 3: Biochemical analysis of urine of cat.

Parameters	Result	Reference value
Color	Darker	Yellow
Turbidity	Cloudy	Clear
Odor	Strong odor	Slightly acidic
Blood	Present	Absent
pH	7.9	6.0-7.5
Specific gravity	1.01	1.036-1.060



Figure 3: Collection of urine sample.

RADIOGRAPHY

The radiological appearance of kidney was normal. Figure 4 shows that slightly radiopaque area in bladder which indicated the presence of structure or materials within the urinary tract that appear faintly denser than the surrounding soft tissues on the X-ray. Some stone (e.g., struvite, calcium oxalate) may appear as faintly visible areas of increased density on X-rays



Figure 4: The radiographs of the urinary tract shows slightly radiopaque areas in bladder.

Ultrasound revealed in bladder wall having irregular and considerably increased thickness indicating the presence of a marked widespread inflammatory conditions (Figure 5). Bacterial infections may cause inflammation and thickening of the bladder wall, often irregular in distribution. Often associated with debris, sediment, or sludge in the bladder lumen.



Figure 5: Irregular thickness indicating the presence of inflammation in bladder a marked inflammatory condition.

DISCUSSION

Cystitis is an inflammation of the bladder which signed pain in the abdomen, dysuria and hematuria. Additional clinical symptoms: depression, weakness, vomiting, decreased appetite, usually accompanied bottom urinary tract infection, severe blockage (debris and crystals), uremia, hematuria, often licking the genital area and maturation when urination due to illness (Widmer *et al.*, 2004). Billu showed weakness, dehydrated, pee problem, blood containing urine which indicates that infection in urinary tract. Vomiting in case of cystitis caused by stimulation of the chemoreceptor trigger zone (CTZ) by ureum's toxin, a decrease in gastric secretion and increased gastric acid secretion, and gastrointestinal irritation by toxins of urea (Elliot and Grauer, 2007). The increasing of urea in the blood can cause uremic gastropathy at the gastric mucosa, that makes gastric hormone to initiate production of stomach acid increased (Elliot and Grauer, 2007). Dysuria is caused by debris or crystals (struvite) which inhibits the flow of urine expenditure which have direct relation with distention of urinary bladder which result urine in the bladder cannot be removed outside normally. The kidney eliminates creatinine, a waste product of muscle metabolism and its retention is caused by a significant reduction in the glomerular filtering rate (Ramsey, 2008). Hemorrhagic cystitis is similar to feline idiopathic cystitis but often more severe hematuria, systemic sign (fever, lethargy) found in hemorrhagic cystitis. Urine culture result is negative

in case of FIC. Hematuria on cystitis condition can also associated with bladder inflammation and the trauma it caused by struvite (urolithiasis). According to the case the cat was unable to pee normally for about 4 days with very little amount of bloody urine. Bladder stone and infection - induced cystitis both affect the urinary bladder but have different causes, symptoms and treatment. Bladder stones are physical Obstruction, while cystitis is inflammatory/infectious. Bladder stones may be asymptomatic until they cause irritation or obstruction, cystitis typically presents with classic urinary tract sign. Stones require removal or dissolution, while cystitis is treated with antibiotics and supportive care.

Blood test for a cat with hemorrhagic cystitis is usually part of a diagnostic workup to determine the cause of the condition and assess the overall health of the cat. Table 1 shows that increased the % of lymphocytes which indicate that may occurred some viral infection (e.g., feline leukemia virus feline immunodeficiency virus) which may lead to lymphocytosis (Stella *et al.*, 2011), while red blood cells (RBCs) are indicative of bleeding disorders, injuries, and other conditions (Piech and Wyscilo, 2019). Hemorrhagic cystitis can trigger localized or even systemic inflammation, leading to a rise in white blood cell (17500/mcl). Other parameters like hemoglobin, neutrophil, monocytes, eosinophil, basophile remained in normal range. Red blood cell count and packed cell volume remained normal which is most common in cystitis, unless severe bleeding present.

Biochemical report (Table 2) of Billu shows that elevated blood urea nitrogen (BUN) level which indicates possible secondary kidney involvement (e.g., from ascending infection or concurrent urinary obstruction). If cystitis leads to urinary obstruction, urine cannot flow out properly. This can cause buildup of waste products, including creatinine in the blood. Creatinine and BUN may normalize with proper rehydration (e.g., IV or subcutaneous fluids). Others parameter like phosphorus, albumin, total protein remained in normal level. In case of chronic inflammation albumin, protein level may increased. As it was acute cystitis so albumin, protein level remained normal range.

Urinalysis examination (Table 3) shows urine pH 7.9 was an alkaline urine (normal 6.5 to 7.0). Alkaline condition of urine which cause the formation of crystals, such as struvite. This is consistent with the results of microscopic examination were found struvite crystals. MgO_2 ions and $MgSO_4$ ions on dry cat food will make the urine alkaline. Alkaline urine will make Mg ions, and ammonium phosphate will be crystallizing to struvite crystals forms. Crystals will make obstruction of the bladder, urethra and ureter. Bacterial infections can increase the formation of struvite because the bacteria that infect will produce urease, it will make increasing of urine pH becomes alkaline.

Macroscopic examination of the urine shows presence of red color urine or blood mixed urine gives indication of inflammation of bladder wall contains hemoglobin (Stella *et al.*, 2011). Turbid, strong odor urine can be caused by a nidus, bacteria, sediment such as epithelial, leukocytes and erythrocytes in large quantities.

Billu also showed distend urinary bladder indicator of blocking urinary passage. Hematuria on cystitis condition that also associated with bladder inflammation. Removed urine by flushing out it was blood containing urine indicative to hematuria. As blood mixed urine was also found in this case which clearly indicates the hemorrhage in bladder wall. Thickening of the walls of the bladder can be caused by an inflammation reaction due to pathological causes. This is having the same correlation with (Widmer *et al.*, 2004) cystitis can make thickening of the bladder. Hemorrhagic cystitis is similar to feline idiopathic cystitis but often more severe hematuria, systemic sign (fever, lethargy) found in hemorrhagic cystitis.

Radiography can play a vital role in the diagnosis and management of hemorrhagic cystitis in cats by helping identify causes such as bladder stone, tumors, or anatomical abnormalities. Figure 4 shows that slightly radiopaque area in bladder which indicated the presence of structure or materials within the urinary tract that appear faintly denser than the surrounding soft tissues on the X-ray. Some stone (e.g., struvite, calcium oxalate) may appear as faintly visible areas of increased density on X-rays.

Ultrasonography (Figure 5) of urinary bladder was taken which showed thickness of bladder wall that surely indicative to inflammation of bladder wall showing pain in abdominal palpation of the cat. Hyperechoic mass in the urinary bladder shows the presence of crystals in the urinary bladder. The cat showed rare hyperechoic mass which not surely shows any crystals in urinary bladder. The ultrasound revealed of the case that clear thickness of the urinary bladder wall which indicates cystitis of the cat (Voros *et al.*, 2000). Above all the clinical signs, radiographs and ultrasound indicates that Billu has hemorrhagic cystitis.

There is no proven effective therapy for treatment of idiopathic cystitis. The disease resolves spontaneously over 5–7 days in non-obstructed cats. While several treatments have been suggested for idiopathic cystitis, none are more proven to be more effective than a placebo. As Billu showed distended urinary bladder with urine so flushing out of urine is necessary to empty the bladder relieving from pain. The list of the drugs that are used for cystitis in cats is very wide, and specific regimens depends on the cause of the disease. But there are groups of drugs that are always prescribed. We inject Amoxicillin @ 10mg/kg body weight whose task to fight the growth of microflora

in urinary tract (Ramsey, 2008). Dextrose normal saline @ 80 ml, daily 2 times administered through intravenously which is necessary to activate the natural flushing of the bladder. Hemostat as Tranexamic acid @ 10 mg/kg BW as hemostatic to help manage significant bleeding. Non-steroidal anti-inflammatory drug like meloxicam @ 0.2 mg/kg to reduce inflammation in urinary tract. Corticosteroids have been suggested to reduce inflammation in idiopathic cystitis, but a double-blind clinical trial showed no improvement with steroids compared to a placebo. Prednisone did not reduce inflammation in an experimental model of idiopathic cystitis and predisposed the cats to pyelonephritis. Steroids can also predispose cats to UTI. Dexamethasone @ 0.2mg/kg BW was given to reduce severe bladder wall inflammation and swelling. Urinary supplement also given to support urinary health in cat and it is often composed of ingredients like cranberry extract, glucosamine, methylsulfonyl methane etc. Vitamin B complex concerns about nerve related dysfunctions to bladder dysfunction. Inflammation in urinary bladder wall here vitamin A will helpful for growing of epithelial cell (Ramsey, 2008). It was advised that to keep the litter box clean to encourage frequent urination and reduce the risk of bacterial infection. It also necessary to keep track of food and water consumption of the cat and should be offer urinary care food, canned food. Uncontrolled clinical trials suggest that dietary therapy designed to prevent crystalluria, such as a canned dietary therapy, may reduce the incidence of recurrent FIC episodes and urethral obstruction. Adding water to the diet and/or feeding canned diets is the main treatment that appears to reduce recurrence of hemorrhagic cystitis.

LIMITATION

The limitation of the case study was Advanced diagnostic tools like cystoscopy, or biopsy not be available, lack of long term follow up, absence of bacterial culture, limited efficacy of antibiotics, small sample size, lack of specific biomarkers, incomplete diagnostic workup etc leading to incomplete data or assumption about the cause of the condition. Catheterization would need to flushing the urine. As the time was short, follow up of the case was not possible.

CONCLUSIONS AND RECOMMENDATIONS

Hemorrhagic cystitis in the cat characterized by inflammation and bleeding in the bladder which highlights the importance of early diagnosis, appropriate management and diligent follow up in feline medicine. This condition can be challenging to address, but with prompt intervention, a tailored treatment plan, maintaining a stress free environment ensuring proper hydration it is possible to improve the cats quality of life and minimize the recurrence of hemorrhagic cystitis. Close collaboration

between veterinarians and pet owners is essential to ensure the best possible outcome of the affected cat.

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NOVELTY STATEMENT

Most of the cats in Bangladesh are dying from the disease but there was no research paper on it before.

AUTHOR'S CONTRIBUTION

All the authors contributed to research and manuscript writing.

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CONFLICT OF INTEREST

The authors have declared no conflicts of interest.

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