



Successful Medical Treatment of Haemorrhagic Cystitis in a Dog

Chigozie S. Ukwueze^{1*}

¹Department of Veterinary Medicine, Michael Okpara University of Agriculture, Umudike, Abia State, Nigeria.

Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

Article Information

DOI: 10.9734/IJMPCR/2015/17004

Editor(s):

(1) Abdelwahab Omri, Department of Chemistry and Biochemistry and Departments of Biomolecular Sciences, Laurentian University, Canada.

Reviewers:

(1) A. Papazafiropoulou, Department of Internal Medicine and Diabetes Center, Tzaneio General Hospital of Piraeus, Greece.

(2) Anonymous, India.

Complete Peer review History: <http://www.sciencedomain.org/review-history.php?iid=995&id=38&aid=8813>

Case Report

Received 22nd February 2015

Accepted 23rd March 2015

Published 15th April 2015

ABSTRACT

Aims: To evaluate the aetiology and medical treatment of haemorrhagic cystitis in a nine-month-old Caucasian dog.

Place and Duration of Study: The study was carried out in the Veterinary Teaching Hospital, Michael Okpara University of Agriculture, Umudike for a period of 3 weeks.

Methodology: In this study, clinical examination revealed blood in urine (haematuria), painful urination (dysuria), hyperaemic mucus membrane, ocular discharges, mild tick infestation and evidence of pain on the bladder on palpation. Blood sample was collected to determine the haematological changes and to check for haemoparasites. Urine was also collected with the aid of a catheter for urinalysis and culture.

Results: No haemoparasite was seen in the thin smear stained with giemsa. The result of the haematology were as follows; packed cell volume (PCV) 22%, Haemoglobin concentration (HB) 8.0 g/dl, total leucocyte count 9500 (103/ μ L) and differential leucocyte counts were; neutrophils 52%, lymphocyte 36%, eosinophil 7%, monocytes 3% and basophils 2%. The urinalysis revealed the presence of oxalate crystals, nitrate, proteinuria, urine PH (6.0), bloody and turbid urine. The culture showed pure growth of Streptococcus species sensitive to gentamicin. Based on the case history, clinical examination and laboratory diagnosis, the condition was diagnosed to be canine

*Corresponding author: E-mail: chynet2006@yahoo.com;

haemorrhagic cystitis. Intravenous infusion of 5% dextrose saline was first administered followed by furosemide at a dose of 3 mg/kg BW, dexamethasone 0.2 mg/kg BW, gentamicin 5 mg/kg BW and 3 ml of vitamin B-complex. The animal was monitored and supportive therapy continued for 5 days before discharging.

Conclusion: Uncomplicated haemorrhagic cystitis can be successfully treated medically.

Keywords: Haemorrhagic; cystitis; cyclophosphamide; haematuria; dysuria.

1. INTRODUCTION

Haemorrhagic cystitis is an inflammatory disease of the bladder caused by infectious and non-infectious agents resulting in the bleeding from the bladder mucosa [1]. The disease is characterized by presence of blood in urine (haematuria), painful urination (dysuria) and abnormal frequent urination (pollakiuria). The most common infectious agent is bacterial and usually responds promptly to treatment. The bacteria commonly known to cause haemorrhagic cystitis are *Escherichia coli*, *Staphylococcus saprophyticus*, *Proteus mirabilis* and *Klebsiella* species [2]. The fungal organisms associated with haemorrhagic cystitis are *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus* and *Torulopsis glabrata*. The polyoma virus, adenovirus and herpes virus have also been implicated in haemorrhagic cystitis in pediatrics and immunocompromised patients [3,4]. Polyoma virus has been reported to cause haemorrhagic cystitis in 5.7-7.7% of bone marrow transplant recipient [5]. *Echinococcus granulosus* infections can also lead to calcified cysts formation that may penetrate the bladder wall resulting in haematuria and cystitis [1].

Chronic and recurrent haemorrhagic cystitis usually result due to cancer chemotherapy or exposure to radiation when undergoing treatment for pelvic malignancies. A wide range of chemotherapeutic agents are known to predispose dogs to haemorrhagic cystitis. Oxazaphosphorine compounds such as cyclophosphamide and ifosfamide are the most important among the group because of its regular use in managing cancers patients. Urinary tract toxicity with these agents is usually associated with dose administered. Haemorrhagic cystitis has been reported in dogs treated with cyclophosphamide [6]. Cyclophosphamide is an immunosuppressive drug and is used in dogs for treating lymphosarcoma, mastocytoma, transmissible venereal tumor, bladder carcinoma, macroglobulinemia, multiple myeloma, and

autoimmune diseases. It can cause bone marrow depression and cystitis, which may be associated with induction of transitional cell carcinoma [7]. In humans, adverse effects of cyclophosphamide ingestion can be leukopenia, anorexia, nausea, sterile haemorrhagic cystitis, which often can be fatal, and nephrotoxicity with haemorrhage and clot formation in the renal pelvis. Haematuria can persist for several months after drug withdrawal [8].

Some topical agents can also cause haemorrhagic cystitis through direct contact on bladder mucosa. Intraurethral insertion of nonoxynol-9 has also been reported to cause haemorrhagic cystitis [1]. Other agents that may lead to development of haemorrhagic cystitis include allopurinol [9], methaqualone [10], methenamine mandelate [11], gentian violet [12] and insertion of acetic acid on the bladder mucosa [13]. Contact with chemicals such as aniline and toluidine are known to cause haemorrhagic cystitis besides predisposing to development of urothelial cancer. Ingestion, inhalation or direct skin contact with the pesticide chlorodimeform, commonly used on cotton plants and fruit trees productions, can also lead to haemorrhagic cystitis which is due to its metabolite 2-methylaniline, which is an aniline derivative. In most cases, the haematuria is self-limiting once exposure to the offending chemical agent is eliminated [14].

Cases of haemorrhagic cystitis could be challenging and frustrating problem to the clinician or urologist and could lead to unthriftiness and even death in some patients. This work therefore presents a case of haemorrhagic cystitis in a dog and the management procedures employed.

2. CASE HISTORY

A nine-month-old male Caucasian dog weighing 30 kg was presented to Veterinary Teaching Hospital, Michael Okpara University of Agriculture, Umudike with a history of blood in urine (haematuria) and painful urination (dysuria)

for the past three months. On clinical examination the rectal temperature was high (40.8°C), mucus membrane was hyperaemic, ocular discharges, mild tick infestation and evidence of pain on the bladder on palpation. Blood sample was collected from the cephalic vein into EDTA bottles to analyze for haemoparasites and haematological changes. Urine sample was also collected with the aid of a catheter for urinalysis and culture.

3. RESULTS

No haemoparasite was seen in the thin smear stained with giemsa. The haematology revealed; packed cell volume (PCV) 22%, Haemoglobin concentration (HB) 8.0 g/dl, total leucocyte count 9500 ($10^3/\mu\text{L}$) and differential leucocyte counts were as follows; neutrophils 52%, lymphocyte 36%, eosinophil 7%, monocytes 3% and basophils 2%. The urinalysis revealed the presence of oxalate crystals, nitrate, proteinuria, urine (PH 6.0), bloody and turbid urine. Pure growth of *Streptococcus* species sensitive to gentamicin was isolated from the culture.

4. DISCUSSION

Based on the case history, clinical examination and laboratory diagnosis the condition was diagnosed to be canine haemorrhagic cystitis. Intravenous infusion of 5% dextrose saline was first administered followed by furosemide at a dose of 3 mg/kg BW, dexamethasone 0.2 mg/kg BW, gentamicin 5mg/kg BW and 3 ml of vitamin B-complex. The animal was monitored and supportive therapy continued for 5 days before discharging. Marked improvements were observed following this medication, the haematuria and dysuria reduced gradually. After one week the dog was represented in the clinic with no observable signs of haemorrhagic cystitis. Manikandan et al., [1] recommended hydration and forced diuresis as measure of alleviating haemorrhagic cystitis. Intravenous administration of saline and whole blood have been used successful to treat sever haemorrhagic cystitis in dog [6].

Continuous bladder irrigation, mesna and intravenous hydration are commonly employed as prophylactic measures for alleviation of haemorrhagic cystitis [15,16]. The disease can reoccur after prophylactic measures and could be more severe, causing pain, prolonged hospitalization and increased rate of morbidity

and mortality. Severe haemorrhagic cystitis presents with gross haematuria, blood clots and life threatening complications. Several methods have been advocated in the treatment of complications arising from severe haemorrhagic cystitis. These methods include procedures such as local bladder instillation of aluminum, formalin, phenol, silver nitrate and prostaglandin or surgical interventions such as cystoscopy, suprapubic cystotomy, and open cystotomy with simultaneous urinary diversion [17,18]. Patients who are treated surgically are at more risk of death or mortality than patients whose haemorrhagic cystitis resolves with medical management only [18]. Drug induced haemorrhagic cystitis is managed by withdrawing the drug or lowering the drug dosage. Continuous bladder irrigation (CBI) is also useful in these patients, because it reduces the length of exposure of the urothelium to acrolein there by lowering the toxicity. Mensa (sodium 2-mercaptoethane sulfonate) has also been indicated in the prevention of haemorrhagic cystitis associated with ifosfamide and cyclophosphamide [19].

Radiation induced haemorrhagic cystitis is often difficult to treat due to the ischemic nature of the disease and lack of well-known and controlled clinical trials comparing the existing treatment options and guidelines [20]. Attempts have been made towards relieving radiation induced haemorrhagic cystitis using various oral agents such as steroids, vitamin E, trypsin and orgotein with no positive result. However, focusing the irradiation field and limiting the radiation dose to the bladder have been employed in reducing the incidence of haematuria and blood clots [1]. Hyperbaric oxygen (HBO) therapy has also been indicated in the management of radiation induced injuries [21].

Conjugated estrogens are useful and have been advocated for the treatment of viral and radiation induced haemorrhagic cystitis. Estrogens are thought to act by stabilization of the microvasculature. Several studies have reported the use of oral and intravenous administration of conjugated estrogens with a varying degree of success ranging from 60% to 86% [22]. Sodium pentosan polysulfates have been suggested due to its uroprotective qualities that aids in the reduction of inflammatory response of the urothelium [23]. This compound enhances the surface glycosaminoglycans that have been disrupted by the inciting agents, thereby reducing the rate of bacterial colonization. This

thus reduces the risk of infection which is associated with haematuria.

5. CONCLUSION

Reports of canine haemorrhagic cystitis are infrequently reported in this part of the world, which could be attributed to the ignorant of some pet owners. It was concluded from the study that medical treatment should be considered in uncomplicated form of haemorrhagic cystitis and clinicians or urologists should properly evaluate the condition to determine the aetiological agent and the predisposing factors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

REFERENCES

1. Manikandan R, Kumar S, Dorarrirajan LN. Haemorrhagic cystitis: A challenge to the urologist. *Indian Journal of Urology*. 2010; 26(2):159-166.
2. Krane DM, Levine LA. Haemorrhagic cystitis AUA update series XI: lesson 31. 1992
3. Storver B, Corey L, Nolkamper J, Hauang ML, et al. BK virus infection in haemopoietic system stem cell transplant recipient: frequency, risk and association with post engraftment. *Haemorrhagic Infectious Disease*. 2004;39:1861-5.
4. Hatland C.A, Eron LJ, Waschcka RM. Haemorrhagic adenovirus after renal transplantation. *Transplantation procedure*. 2004;36:325-7.
5. Paduch DA. Viral lower urinary tract infections. *Current Urology Reproduction*. 2007;8:324-35.
6. Marin P, Samson RJL, Jackson ER. Haemorrhagic cystitis in a dog. *Canadian Veterinary Journal*. 1996;37:240.
7. Allen D. *Small Animal Medicine*. Philadelphia: JB Lippincott. 1991;1132-1133.
8. Krogh CME. *Compendium of Pharmaceuticals and Specialties*. 27th ed. Ottawa, Ontario: Canadian Pharmaceutical Association. 1992;272-273.
9. Bramble EJ, Morley R1. Cystitis associated with alloupurinol. *Brit J of Uro*. 1997;79: 817.
10. Goldfarb M, Finnelli F. Necrotizing cystitis. *Secondary Bootleg Methaqualone Urology*. 1974;3:54-5.
11. Ross RR Jr, Conway GF. Haemorrhagic cystitis following overdose of methenamine mandealate. *American Journal of Disease Child*. 1970;119:86-7.
12. Kim SJ, Koh DH, Park JS, Ahn HS, et al. Haemorrhagic cystitis due to intravesical instillation of gentian violet recovered with constructive therapy. *Yonsi Medical Journal*. 2003;44:163-5.
13. Osorio AV, Simickes AM, Hellerstein S. Haemorrhagic cystitis caused by acetic acid installation. *J Urol*. 1996;155:685.
14. Follad DS, Kimbourgh RD, Cline RE, et al. Acute haemorrhagic cystitis: Industrial exposure to the pesticide chlorodimeform. *JAMA*. 1991;1052-5.
15. Shepered JD, Pringle LE, Barneth MJ, et al. Mensa versus hyperhydration for prevention of cyclophosphamide-induced haemorrhagic cystitis in bone marrow transplantation. *Journal of Clinical Oncology*. 1991;9(11):216-20.
16. Vose JM, Reed EC, Pippert GC, et al. Mesna compared with continuous bladder irrigation as uroprotection during high dose chemotherapy and transplantation: a randomized trial. *J Clin Oncol*. 1993; 7:1306–1310.
17. Andriole GL, Tuan JJJ, Catalona WJ. Cystotomy, temporary urinary diversion and bladder packing in the management of severe cyclophosphamide-induced hemorrhagic cystitis. *J Urol*. 1990; 143:1006–1007.
18. Baronciani D, Angelucci E, Erer B, et al. Suprapubic cystotomy as treatment for severe hemorrhagic cystitis after bone marrow transplantation. *Bone Marrow Transplant*. 1995;16:267–270.
19. Schoneike SE, Dana WJ. Ifosamide and mensa. *Clinical Pharmacology*. 1990; 9:179-91.
20. Denton AS, Clarke NW, Maher EJ. Non-surgical interventions for late radiation cystitis in patient who have received radical radiotherapy to pelvis. *Chrono Data Base System*. 2002;3:CD001773.

21. Max RE, Ehier W, Tayapongsak JP, Pierce LW. Relationship oxygen dose to angiogenesis induction in irradiated tissue. American Journal of Surgery. 1990;160: 519-24.
22. Health JA, Mishr S, Mitchells S, Waters KD. Estrogen as a treatment of haemorrhagic cystitis in children and adolescent undergoing bone marrow transplantation. Bone Marrow Transplant. 2006;37(5):523-6.
23. Hampson S, Woohouse C. Sodium pentosan polysulphate in management of haemorrhagic cystitis: Experience in 14 patients. Eurp J Urol. 1994;25:40-2.

© 2015 Ukwueze; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

The peer review history for this paper can be accessed here:
<http://www.sciencedomain.org/review-history.php?iid=995&id=38&aid=8813>