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AZOTEMIA AND METABOLIC ALKALOSIS IN CALVES WITH UROLITHIASIS ASSOCIATED WITH URINARY BLADDER AND URETHRAL RUPTURE

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ABSTRACT

Obstructive urolithiasis (OU) with ruptured bladder and urethra is one of common life-threatening diseases affecting male calves. The present study was undertaken to clinically evaluate and determine the changes of acid-base balance and levels of non protein nitrogenous compounds (BUN and serum creatinine) associated with ruptured bladder and urethra in calves. Seventeen cases with ruptured bladder and urethra were prospectively examined in the Veterinary Teaching Hospital (VTH) at Assiut University-Egypt. Diagnosis was based on anuria, abdominal distension and abdominocentesis. Complete blood count, status of acid-base balance, and levels of BUN and serum creatinine were determined. Ruptured bladder was confirmed in 11 cases while ruptured urethra was diagnosed in 6 cases. Results of this study showed that both cases had significant ($P < 0.05$) increases in the total count of RBCs, WBCs and granulocytes, Hb concentration, PCV%, and the levels of BUN and serum creatinine. Only cases of ruptured bladder exhibited significant ($P < 0.05$) increase in their blood pH value, bicarbonate ion, and base excess concentrations. In conclusion, cases of ruptured bladder and urethra were associated with leucocytosis, granulocytosis and azotemia suggesting state of stress and uremia while a state of progressive metabolic alkalosis accompanied by azotemia was only evident in ruptured bladder.

Key Words: *Urinary Bladder, Urethra, Azotemia, Alkalosis*

INTRODUCTION

Obstructive urolithiasis (OU) is a common life-threatening problem in ruminants. It has been attributed to be the fifth most prevalent cause of death in feedlots (Singh *et al.,* 1981). The condition causes significant economic losses due to rupture of the bladder and urethra with subsequent azotemia and death. Mortality rate, susceptibility and economic impact of urolithiasis have been reported in field and slaughter-house studies in many countries (Gasthuys *et al.,* 1993; Radostits *et al.,* 2007). Up to 10 % of male cattle could be affected annually with 100% mortality rates in untreated cases (Hay, 1990; Kimbeling and Arnold 1983). Both sexes appear to be affected with urolithiasis, however males are more susceptible because of the anatomical conformation of their urinary tract (Larson, 1996; Radostits *et al.,* 2007). The nature of urinary calculi (uroliths) is usually mineral stones formed by the precipitation or crystallisation of mineral salts in the urine. A combination of predisposing factors including physiologic, nutritional and managemental play an important role in the genesis of urinary calculi. Excessive or imbalanced intake of minerals is a major contributing factor (Larson, 1996; Radostits *et al.,* 2007). Numerous additional factors like heavy concentrate-low roughage diets, limited water intake, deprivation of water, urine alkalinity, mineralized artesian water, alkaline water supplies, excess of sodium bicarbonate in the diet, vitamin imbalances (hypo vitaminosis A and hyper vitaminosis D) and high-protein rations have been incriminated as contributing causes for the development of OU (Radostits *et al.,* 2007).

Despite sophisticated clinical approach, prognosis of OU in bovine still remains unpredictable (Honeck *et al.,* 2009; Sharma *et al.,* 2009). Animals with OU usually undergo different disease conditions including ruptured bladder and urethra, with potential fatal outcomes from building-up of toxic substances of non protein nitrogenous compounds, BUN and creatinine, (azotemia) and derangement of acid-base balance. The purpose of the present study is to clinically evaluate and determine the primary change in the acid-base balance and levels of BUN and serum creatinine in OU associated with ruptured bladder or urethra in ruminant calves.

MATERIALS and METHODS

Animals

A total of 17 clinical cases of non castrated male calves of 5-14 months age suffered from anuria and abdominal distension with a history of colic of varying duration were admitted to the Veterinary Teaching Hospital (VTH) at Assiut University- Egypt during the period of Sept, 2010 to Dec, 2012. Ruptured lower urinary tract was diagnosed after a careful clinical examination and abdominocentesis. Five healthy calves were taken as a control in this study.

Clinical assessment

All animals were subjected to thorough clinical examination according to the method of Radostits *et al.* (2007). General condition of the animal, heart rate, respiratory rate, rectal temperature and abdominal distension were examined. Diagnosis of ruptured urethra and urinary bladder was confirmed by exploratory puncture and abdominocentesis using biopsy needle, respectively.

Samples

1. ***Heparinized whole blood samples***

   Blood samples were collected from jugular vein using lithium heparinized BD vacutainer tubes and used for analysis of blood gases and acid-base balance immediately and then used for complete blood count (CBC).

2. ***Serum sample***

   Blood samples were collected in clean, dry centrifuge tubes without anticoagulant for serum collection. The obtained clear non hemolyzed sera were stored at -20 ^{o}C for determination of BUN and serum creatinine.

Bioassays

1. **Blood Gases and acid-base balance**

   Blood gases and acid-base balance parameters including blood pH value, partial tension of carbon dioxide (PCO_2), partial tension of oxygen (PO_2), concentration of bicarbonate ion (HCO_3), total carbon dioxide (tCO_2) and base excess (BE), were measured using ABL5 Blood Gas Analyser (Radiometer, Denmark). The machine was calibrated and subjected to test of quality control before assay.

2. **Complete blood count (CBC) assessment**

   Total red blood cell count (RBCs), hemoglobin concentration (Hb), packed cell volume (PCV), total white blood cell (WBCs) and differential leuckocytic counts were determined using a fully automated blood cell counter machine, Medonic CA620 Veterinary Hematology Analyzer -Sweden.

3. **Biochemical assays**

   BUN and creatinine were determined spectrophotometrically using Phillips Pye Unicam spectrophotometer (U.V. visible Mod. 800). Kits and reagents were obtained from Spectrum (Egyptian Company for Biotechnology, Cairo, Egypt).

Surgical techniques

Cystorraphe, urothrostomy and penile transection techniques were applied for surgical correction of OU associated with ruptured bladder or urethra according to Van Metre, (2004). Briefly, the animal was restraint in right lateral recumbency and the skin above the scrotum was incised at the midline of the perineal region after application of linear infiltration anesthesia. The penis was grasped, released, severed and fixed to the skin keeping the dorsal neurovascular bundle intact. The urethra was spatulated using straight scissor. The distal portion of the penis was placed to normal position and the incised wound was co-apitated. After that, trans-abdominal cystorraphe was performed for correction of ruptured bladder. The animal was positioned in dorsal recumbency and prepared for post umbilical laparotomy. Deep paramedian incision at the distance between the preputial orifice and the scrotum (8-10 cm) was performed. The urine was removed gradually to avoid the animal's shock. The ruptured bladder was allocated and sutured. In case of ruptured urethra, urothrostomy and penile transection were performed as previous, in addition to scarification of the infiltrated tissue.

Statistical analysis

Data were analyzed using the packaged SPSS program for windows version 10.0.1 (SPSS Inc., Chicago, IL). All data were presented as mean ± standard error (mean ± SE). Differences between affected and healthy animals were determined by analysis of variance (ANOVA). Significance level was set at $P \leq 0.05$.

RESULTS

Clinical findings

A total of 17 cases of urolithiasis in calves were presented to the VTH, Assiut-Egypt from Sept, 2010 to Dec, 2012. All affected animals were admitted to the clinic during winter season with a history of abdominal colic, anuria and abdominal distention. Affected animals with ruptured bladder (n = 11) showed symmetrically distention of the ventral part of the abdomen (Water belly appearance) (Fig.1). On ballottement, fluid thrill was obvious in the abdominal cavity and presence of fluid was confirmed by abdominocentesis, which yielded large quantity of straw colored fluid (Fig. 2). Signs of dehydration were evident in animals with ruptured bladder (Fig. 3). Cases with ruptured urethral (n = 6) were also presented with the same history however they showed asymmetrical, non-painful swelling extending from the base of scrotum to the prepuce in the ventral part of the abdomen (Frog belly appearance) (Fig. 4). Exploratory puncture with

biopsy needle revealed dribbling of straw colored fluid. Both cases were presented in standing position with good reflexes however they showed signs of restlessness, swishing elevated tail (Fig, 5), increased respiratory and heart rates but the rectal temperature was either normal or slightly below the normal range.

Blood gases and acid-base balance findings

Venous blood gas and acid-base balance data are listed in Table 1. Cases of OU associated with ruptured bladder showed significant increase ($P< 0.05$) in their blood pH value, and concentrations of HCO_3 and BE (7.48 ± 0.01, 35.9 ± 2.81 mmol/l, and 11.25 ± 2.26 mmol/l, respectively) compared to control healthy ones (7.37 ± 0.01, 24.33 ± 0.41mmol/l, 1.4 ± 0.21mmol/l, respectively). PCO_2 showed overall non significant change (48.13 ± 2.8 mmHg) suggesting a case of primary metabolic alkalosis without compensation. Within this group, 3 animals that presented after 4 days of the onset of illness showed severe degree of metabolic alkalosis (7.49-7.53 pH value, 12-25 mmol/l BE). On the other hand, none of the admitted calves with ruptured urethra had the problem of metabolic alkalosis and they tended to maintain a normal acid-base status.

Hematological findings

Mean values of CBC of healthy and affected calves were presented in Table 2. Both cases of ruptured bladder and urethra had significant increase ($P<0.05$) in the total RBCs, PCV% and Hb concentration, however the degree of elevation of erythrocytic indices in ruptured bladder was higher than those of ruptured urethra. Significant increase ($P<0.05$) in the WBCs count (leucocytosis) and granulocytes (granulocytosis) was also recorded in both cases.

Biochemical findings

Levels of BUN were found to be significantly elevated in confirmed cases of OU associated with ruptured bladder and urethra (183.40 ± 5.56 and 61.47 ± 4.3mg/dl, respectively) compared to healthy group (15.80 ± 0.62 mg/dl) (Table 2). On the other hand, serum creatinine levels showed significant increase in ruptured bladder (4.82 ± 0.25mg/dl) compared to healthy group (1.27 ± 0.21 mg/dl).

Surgical correction

Surgical approach was of great help in correction as well as determination of the underlying cause of ruptured bladder and urethra. Correction was performed by cystoraphe and urthrostomy successfully and one or more urethral calculi were identified as the major cause (Fig. 6). A Foley catheter was placed intra-abdominally to remove urine residual post-operatively. The animals were discharged in a good mental status after application of fluid therapy (0.9% NaCl).

Table 1: Mean ± SE of blood gases and acid-base balance in healthy control and affected calves with obstructive urolithiasis associated with ruptured bladder or urethra.

Parameter	Control (n = 5)	Obstructive urolithiasis (n = 17)	
		Ruptured bladder (n = 11)	Ruptured urethra (n = 6)
pH	7.37 ± 0.01	7.48 ± 0.01*	7.36 ± 0.01
PCO_2 (mmHg)	44.67 ± 0.42	48.13 ± 2.8	46.75 ± 0.75
PO_2 (mmHg)	39.50 ± 0.43	43 ± 1.74	39.00 ± 0.41
HCO_3 (mmol/l)	24.33 ± 0.41	35.9 ± 2.82*	25.15 ± 0.42
tCO_2 (mmol/l)	26.38 ± 0.12	37.4 ± 2.90*	27.33 ± 0.39
BE (mmol/l)	1.4 ± 0.21	11.25 ± 2.26*	1.25 ± 2.29

Table 2: Mean ± SE of complete blood count and BUN and serum creatinine in healthy control and affected calves with obstructive urolithiasis associated with ruptured bladder or urethra.

Parameter	Control (n = 5)	Obstructive urolithiasis (n = 17)	
		Ruptured bladder (n = 11)	Ruptured urethra (n = 6)
RBCs ($\times10^6$/mm^3)	6.40 ± 0.25	10.97 ± 0.33*	7.40 ± 0.29*
Hb (g/dl)	10.9 ± 0.33	14.28 ± 0.71*	12.67 ± 0.51*
PCV (%)	29.80 ± 0.7	42.40 ± 1.123*	33.43 ± 0.97*
WBCs ($\times10^3$/mm^3)	6.79 ± 0.63	10.57 ± 0.55*	8.89 ± 0.33*
Lymph ($\times10^3$/mm^3)	4.78 ± 0.33	2.51 ± 0.22	2.00 ± 0.51
Gran ($\times10^3$/mm^3)	1.04 ± 0.12	7.10 ± 0.42*	5.96 ± 0.32*
MID ($\times10^3$/mm^3)	0.9 ± 0.10	0.81 ± 0.12	0.90 ± 0.18
BUN (mg/dl)	15.80 ± 0.62	183.40 ± 5.56*	61.47 ± 4.3*
Creatinine (mg/dl)	1.27 ± 0.21	4.82 ± 0.25*	2.81 ± 0.22*

* Significant at ($P < 0.05$) compared with control healthy animals

Fig. 1: Six-month-old of native cow's calf suffered from ruptured bladder (Water belly appearance)

Fig. 2: Abdominocentesis in 6-month-old of native cow's calf suffered from ruptured bladder

Fig. 3: Abdominocentesis and signs of moderate dehydration (Tenting skin and sunken eye) in 6-month- old of native cow's calf suffered from ruptured bladder

Fig. 4: Four-month-old of native cow's calf with ruptured urethra (Frog belly appearance)

Fig. 5: Four-month-old of native cow's calf with ruptured urethra showed sign of mild dehydration, restlessness and swishing elevated tail

Fig. 6: Six-month-old of native cow's calf suffered from ruptured bladder due to OU. Two large urethral calculi were located on peins traction

DISCUSSION

Rupture of urinary bladder and subsequent uroperitoneum is a common life-threatening problem in ruminants. Obstructive urolithiasis in males is the major underlying cause. The diagnosis of uroperitoneum can be suspected on the basis of the history and the clinical signs (Radostits *et al.,* 2007). In the present study, history of anuria and demonstration of fluid thrill on abdominal ballottement was helpful to formulate a tentative diagnosis; however the diagnosis was confirmed by the presence of straw colored fluid of characteristic odor by abdominocentesis. Clinical presentation in most of the affected calves was typically associated with anuria, anoroxia, cessation of rumination, depression, lethargy and abdominal distention. The clinical course of the disease initiated 2-5 days before admission according to case history. During this time, animals expressed painful attempts of urination, colic, and weight shifting, and grinding of teeth (Radostits *et al.,* 2007). Colic was relieved upon urinary bladder or urtheral rupture (Buchholz *et al.,* 2010); however signs of restlessness were still recorded and animal had an arched stance, tread their feet and wring the tail, especially in urethral rupture. As the disease progress, bilateral fluctuating abdominal distention or patchy edematous ventral abdominal swelling was recorded in ruptured bladder or urethra, respectively. Uremic odor to the breath was not obvious in most cases. Systemic reaction including tachycardia and tachypnea were recorded in ruptured bladder probably due to retention of metabolic wastes and their reabsorption results in toxaemia (Radostits *et al.,* 2007).

The major underlying cause of ruptured bladder or urethra in all admitted cases was found to be the presence of one or more calculi blocking the pathway of urine outflow in the urethra (Fig 6). Formation of calculi and development of urolithiasis is a complex process and occurs in a series of phases from formation of nidus, concentration of urine and lastly the precipitation of various salts from urine (Radostits *et al.,* 2007).

In an attempt towards in-depth understanding of the pathophysiological changes associated with the complications of OU, ruptured bladder and urethra, the present study was designed to know much about the most common disorders of blood gas and acid-base balance in such cases. Our results showed derangement of acid-base balance with presence of primary metabolic alkalosis in all examined cases with ruptured bladder. This finding was in agreement with George *et al.* (2007). The authors examined 107 goats with uroliths and rupture in the urinary tract and found that hypochloremic metabolic alkalosis was the most common acid-base disorder in these cases. On contrary, Kinjavdekar *et al.* (2005) examined 25 goats with uroliths, four of them had ruptured urinary bladder. The authors reported that the affected animals within 2- 3 days of the onset of illness had no acid-base disturbances, however metabolic acidosis were recorded in three goats. Thus, our study could strongly suggest that there is derangement of acid-base balance with the majority of the complicated OU develop metabolic alkalosis in ruminant animals (Singh and Singh 1990). Metabolic alkalosis seems to be multifactorial. A consequent digestive disorder, anorexia and cessation of rumination, associated with ruptured bladder results in sequestration of chloride ions in the digestive tract with the development of hypochloraemia and metabolic alkalosis (Sastry 1985; Socket *et al.,* 1992). Moreover, the ability of ruminants to recyle urea may also account for the development of metabolic alkalosis. This might also explain the ability of ruminant animals to withstand the condition of ruptured bladder in comparison with simple stomach animals. Other animal species usually suffer from severe outcomes of ruptured bladder because they could not reuse BUN, rapidly develop metabolic acidosis and are more vulnerable to diffuse peritonitis. In case of ruptured urethra, animals showed no change in the acid-base balance. Trapping of the urine in the subcutaneous tissue seems to have no detrimental change on blood pH.

Regarding haematobio-chemical alterations during the phase of OU, there was increase in RBCs, and WBCs counts and PCV% as well as Hb concentration (Jadon *et al.,* 1989; Gangwar *et al.,* 1990). Accumulation of urine in the peritoneum with its hyperosmolarity nature leads to fluid leakage across peritoneum with subsequent hemoconcentration and some degree of dehydration (Singh *et al.,* 1981; Jadon *et al.,* 1989). An increase in nuetrophil count and leuckocytosis could be attributed due to stress, which causes release of adrenaline that reduces stickiness of neutrophils with erythrocytes causing increase in neutrophil pool. Similar trend was observed in several studies (Socket *et al.,* 1992; Berkow 1998; Sharma *et al.,* 2005).

The most prominent and descriptive measure of complicated OU is BUN and serum creatinine. BUN can be used as an index of azotemia because of its simplicity in assessment (Radostits *et al.,* 2007). In this study, there is rising trend of BUN and serum creatinine during the course of ruptured bladder. This is in agreement with Makhdoomi and Marudwar (1992) and Socket *et al.* (1992). The authors found that there has been a progressive increase in BUN levels at the rate of 53 mg/dl per day in an induced urethral obstruction in Bullocks.

CONCLUSION

In conclusion, OU associated with ruptured bladder is a serious medical problem in calves and thorough understanding to the hemato-biochemical and acid-base balance derangement is essential. Azotemia and metabolic alkalosis are major systemic abnormalities in ruptured bladder and their correction should be of high priority before and after initiating surgical correction to accomplish good disease outcome.

Conflict of interest

None of the authors have any conflict of interest to declare.

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الازوتيميا والقلوية الايضية في العجول التي تعاني من تحص البولي ألانسدادي مع تمزق المثانة والإحليل

نصر الدين محمد عارف ، محمد حمدي عبد الحكيم

تعتبر حالات تحص البولي الانسدادي مع تمزق المثانة والإحليل هو واحد من الأمراض الاكثر شيوعا والتي تهدد الحياة في العجول الذكور. أستهدفت هذه الدراسة التقييم السريري وتحديد التغيرات في التوازن الحمضي القاعدي ومستويات المركبات النيتروجينية غير البروتينية (اليوريا والكرياتينين في مصل الدم) المرتبطة بتمزق المثانة ومجرى البول في العجول البقر ي. تم فحص عدد سبعة عشر حالة تمزق مثانة ومجرى البول في المستشفى البيطري التعليمي - جامعة أسيوط، مصر. أستند التشخيص على انقطاع البول، انتفاخ وبزل البطن. تم تحديد صورة الدم ومؤشرات التوازن الحمضي القاعدي، ومستويات اليوريا والكرياتينين في مصل الدم لهذه الحيوانات. اوجدت الدراسة اصابة عدد 11 حالة بتمزق المثانة في حين تم تشخيص تمزق مجرى البول في عدد 6 حالات. أظهرت نتائج هذه الدراسة زيادة معنوية في إجمالي عدد كريات الدم الحمراء والبيضاء والمحببة، وتركيز الهيموغلوبين وحجم الدم المضغوط ومستويات اليوريا والكرياتينين في مصل الدم في الحيوانات التي تعاني من تمزق في المثانة ومجرى البول. أظهرت الحالات التي تعاني فقط من تمزق المثانة زيادة معنوية في قيمة الاس الهيدروجيني ، أيون البيكربونات، وتركيزات الشق القاعدي. استنتجت الدراسة ان حالات تمزق المثانة ومجرى البول تعاني من حالات اجهاد ويوريميا في حين أن حالة القلوية الأيضية في الدم كانت واضحة فقط في تمزق المثانة.