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# HYDRONEPHROSIS, DIABETES AND FELINE UROLOGIC SYNDROME IN A MIXED BREED TOMCAT: CASE REPORT

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***Abstract***

*An 8 years old intact tomcat, was referred with urinary incontinence and polydipsia. After ultrasound examination, the patient was diagnosed with feline urologic syndrome and hydronephrosis. Acute urethral obstruction is the result of a physical or functional obstruction and can be life-threatening due to azotemia, hyperphosphatemia and hyperkalemia. Following the onset of obstruction, regardless of its nature, bilateral hydronephrosis can occur. Biochemistry revealed low serum sodium, serum albumin (ALB), alanine aminotransferase (ALT), blood urea nitrogen (BUN), total proteins (TP) and glucose (GLU) were elevated. On further examination, by determining serum fructosamine concentration, stress hyperglycemia was excluded, and diabetes mellitus was diagnosed. This article brings valuable insights into the complex pathology of feline urologic syndrome, paving the way for enhanced clinical strategies and potential preventive measures.*

***Key words****: hydronephrosis, diabetes mellitus, feline urologic syndrome, serum fructosamine, hyperglycemia.*

## INTRODUCTION

Feline urologic syndrome is a clinical syndrome in cats that encompasses the following typical signs of lower urinary tract disease such as hematuria, periuria, dysuria or anuria, straining to urinate and urethral obstruction with or without polysystemic sign of urethral obstruction (depression, anorexia, vomiting, dehydration, hypothermia) (Willeberg, 1984; Osborne et al., 1984).

Nowadays, the common term used as a synonym for feline urologic syndrome is lower urinary tract disease which also encompasses various disorders with heterogenous causes that can affect the urinary bladder and/or urethra of cats. Feline lower urinary tract disease can be classified into urolithiasis, neoplasia, bacterial urinary tract infection, anatomic malformations, feline idiopathic cystitis and iatrogenic (behavioral, metabolic, neurological). Etiological studies from 1996 found evidence of urethral plugs in 60%, urethral calculi in 20%, stricture or neoplasia with <5% combined, and the rest did not have clear evidence of physical obstruction. In a more recent study, which was carried out in 2008, the incidence of feline idiopathic obstruction was found to be higher than 53%, with 29% urolithiasis, and only 18% urethral plugs. Feline urethral obstruction is associated with 90-95% survival rate, with reported recurrence rates of 15-40% (Cooper, 2015).

The ethiopathogenesis of feline idiopathic cystitis may involve interactions between three main components: environmental factors, neuroendocrine system and urinary bladder of the affected cats (He et al., 2022).

Urethral obstruction can be the result of physical obstruction (due to urolithiasis and formation of struvites, urates, calcium oxalate crystals; mucous plugs) or a functional obstruction (such as idiopathic obstruction) (Bartges et al., 2015).

Urinary tract infection (UTI) refers to the adherence, multiplication and persistence of an infectious agent within the urogenital system that causes an associated inflammatory response and clinical signs. Many felines have asymptomatic or subclinical bacteriuria. UTIs can be classified as complicated (anatomic or functional abnormalities of the urinary tract, comorbidities, recurrent infection or treatment failure, multiple episodes within one year) and uncomplicated (normal urinary tract anatomy

and function). Lower UTI have signs that are non-specific and can be seen in any disease of the lower urinary tract (Dorsch et al., 2019).
Hydronephrosis can be unilateral or bilateral and results from partial or complete obstruction of the ureters. Obstruction of urine flow causes a progressive dilation of the renal pelvis. As bilateral hydronephrosis presents with acute azotemia, rapid diagnosis and urgent therapy are required if renal function is to be re-established (Elliot et al., 2017).
Feline diabetes is one of the most common endocrinopathies in cats. Most affected cats are older than 8 years old, with a peak of incidence between 10 and 13 years. Protracted hyperglycemia and glucosuria cand lead to the classic clinical signs of polyuria, polydipsia, polyphagia and weight loss. If left untreated or inadequately controlled, ketoacidosis can occur. It is important to differentiate patients with clinical diabetes mellitus from those with transient hyperglycemia or mildly increased blood glucose (BG). In felines, when BG concentration exceeds 250-300 mg/dL, glycosuria will typically develop (Behrend et al., 2018).
Marked hyperglycemia in cats is shown in acute stress associated with blood sampling, and therefore this will not ensure a reliable result. Fructosamine is a glycated serum protein (albumin and other plasma proteins) that reflect glycemic control over the previous 2 to 3 weeks. Its concentration directly depends on the plasma glucose concentration (Lutz et al., 1995; Kaneko et al., 1992; Crenshaw et al., 1996).
Felines with transitory hyperglycemia and diabetes mellitus cand be differentiated based on fructosamine concentrations. Fructosamine is a valuable parameter in the diagnosis and metabolic control of diabetes mellitus in cats (Reusch et al., 1993).

## MATERIALS AND METHODS

An 8 years old, intact tomcat with a body weight of 4.8 kilograms was referred for a second opinion nephrology consult on 13$^{th}$ of September, 2023. Owner reported that the patient presented one episode of urinary incontinence the previous day and is polydipsic. The patient did not present any signs of feline urologic syndrome (FUS) such as: stranguria, dysuria, lethargy, anorexia, vocalization and excessive grooming of the perineum. Patient did not express any inappetence or lack of appetite. The patient usually consumed dry and wet food. During clinical examination, the following findings were noted: body temperature of 38.6°C, 5% dehydration, dry mucous membranes and painful sensitivity and defensive reaction to deep palpation of the abdomen.
The complete blood count (CBC) was performed on Vetscan HM5 Hematology (5-part Differential) and determined: white blood cells (WBC), lymphocytes (LYM), monocytes (MON), neutrophils (NEU), eosinophils (EOS), basophils (BAS), LYM%, MON%, NEU%, EOS%, BAS%, red blood cells (RBC), hemoglobin (HGB), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red blood cell distribution width-coefficient of variation (RDWc), red blood cell distribution width-standard deviation (RDWs), platelet (PLT), mean platelet volume (MPV), plateletcrit (PCT), platelet distribution width-coefficient of variation (PDWc) and platelet distribution width-standard deviation (PDWs).
Serum biochemistry was performed on Vetscan VS2 Chemistry Analyzer with a comprehensive diagnostic panel that determined: albumin (ALB), alkaline phosphatase (ALP), alanine aminotransferase (ALT), amylase (AMY), total bilirubin (TBIL), blood urea nitrogen (BUN), calcium (CA), phosphorus (PHOS), creatinine (CRE), glucose (GLU), sodium ($NA^+$), potassium ($K^+$), total proteins (TP) and globulin (GLOB).
Urinalysis was performed on Vetscan UA Urine Analyzer and determined leukocytes, ketones, nitrites, urobilinogen, bilirubin, glucose, protein, specific gravity, pH, blood, ascorbic acid, microalbumin, calcium, creatinine and protein/creatinine.
Abdominal ultrasound with a major focus on the kidneys is essential in the diagnosis and management of kidney-related diseases. The kidneys are easily examined in longitudinal and transverse scan planes, and most pathological changes in the kidneys are distinguishable by ultrasound. The exam was initiated in the

longitudinal scan plane, parallel to the long diameter of the kidney (Hansen et al., 2015).

Decompressive cystocentesis, prior to urethral catheterization, was done to lower intraluminal bladder pressure in order to facilitate retropulsion and improve catheterization. No complications emerged following this procedure.

Ultrasound guided cystocentesis was performed using a 21-gauge needle attached to a 10 milliliters syringe, which was inserted percutaneously at a 45 degrees angle. The needle was attached to an IV extension tubing, three-way stopcock and a 20 milliliters syringe.

Urethral catheterization was performed using an open-end tomcat catheter (3.5 Fr, 14 cm) and retrograde urohydropropulsion. After decompression, a closed-end urinary catheter was placed. The urinary catheter was maintained in place for the next 48 hours of hospitalization.

The sedation protocol included alfaxalone 3 mg/kg IM with ketamine with a dose of 2 mg/kg IV and midazolam with a dose of 0.3 mg/kg IV. Lidocaine gel was applied topically to the glans penis of the patient in order to achieve a topical anesthesia.

Rehydration and electrolyte rebalancing were initiated by continuous rate of infusion (CRI) with Ringer solution (rate and dosage 7 ml/kg/h) and partial parenteral nutrition based on levo-amino acids was administered (rate and dosage: 0.6-0.8 g amino acids/kg/24 h). The active ingredients in the levo-amino acids solution are: L-isoleucine, L-leucine, L-lysine monoacetate, L-lysine, L-methionine, L-phenylalanine, L-threonine, L-tryptophan, L-valine, L-arginine, L-histidine, L-alanine, N-acetyl-L-cysteine, L-cysteine, Glycine, L-proline, L-serine, L-tyrosine, N-glycine-L-tyrosine dehydrate, N-glycine/L-tyrosine. It contains a total of 100g/L amino acids and Enteric dialysis supplements based on *Streptococcus thermophiles, Lactobacillus acidophilus, Bifidobacterium longum* and *Lactobacillus casei*, nutritional supplements based on amino acids combined with a peptide that supports kidney functions and supplements that help maintain and support the urinary tract (based on DL-methionine) were introduced as adjuvants in the therapy.

The initial approach in managing diabetes mellitus was to initiate the administration of insulin glargine at a starting dose of 0.5 units (U) per kilogram every 12 hours. Blood glucose was monitored hourly for the first 48 hours of hospitalization. For the next 72 hours of hospitalization BG was determined every 3-4 hours. The patient was given a low carbohydrate diet.

## RESULTS AND DISCUSSIONS

On the 13$^{th}$ of September 2023, the patient had the following serum biochemistry modifications: $Na^+$ 118 mmol/L (RR = 142-164 mmol/L), ALB 4.7 g/dL (RR = 2.2-4.4 g/dL), ALT 121 U/L (RR = 20-100 U/L), BUN 41 mg/dL (RR = 10-30 mg/dL), TP 8.4 g/dL (RR = 5.4-8.2 g/dL) and GLU 627 mg/dL (RR = 70-150 mg/dL). There were no changes regarding the CBC. Urine sediment did not present any crystals. Urinalysis was carried out from urine obtained through ultrasound guided cystocentesis and showed leukocytes +3500 cell/uL, glucose +328 mmol/L with a specific gravity of 1.020 and a pH of 5.0. A urine culture sample was submitted to a microbiology laboratory and the result was negative (0 colony-forming unit - CFU).

Following the elevated result of the BG, quantification of serum fructosamine concentration was performed and the following result was obtained: 772.60 µmol/L (RR = 190-365 µmol/L). Abdominal ultrasound was performed and the following changes were observed: over distension of the urinary bladder with moderate parietal reaction with no corpuscular elements detected with tendency of sedimentation. The left kidney with a diameter of 5.83/3.3 centimeters had a regular contour with a slightly globular appearance, suitable cortico-medullar ratio and hydronephrosis of grade 1-2 without urolithiasis. The right kidney had a diameter of 5.3/3.2 centimeters and revealed the same aspects. Hydronephrosis is typically graded visually and can be divided into five categories going from a slight expansion of the renal pelvis to end-stage hydronephrosis with cortical thinning (Hansen et al., 2015).

Medical management of urethral obstruction consists of maintaining adequate renal

perfusion, reversing life threatening electrolyte disturbances, minimizing visceral pain and alleviating the urethral obstruction (Hall et al., 2015).

By performing retrograde urohydropropulsion, the patient was catheterized and 395 milliliters of yellow colored urine were eliminated. Urinary bladder lavage was performed twice daily with NaCl 0.9% (Tsuruta et al., 2022).

The patient was hospitalized and submitted to intravenous fluid therapy for electrolyte rebalancing and partial parenteral nutrition based on levo-amino acids (rate and dosage: 0.6-0.8 g amino acids/kg/24 h).

Alfaxalone provided induction of anesthesia with stable respiratory and cardiovascular effect (Warne et al, 2015).

Midazolam produces reliable muscle relaxation and is often administered with other anesthetic drugs that do not provide sufficient muscle relaxation alone (Riviere et al. 2018).

Muscle tone is reduced because of the effects on the dorsal horn of the spinal cord (Smith et al., 2009).

Ketamine is a rapid acting general anesthetic that also has significant analgesic activity and a lack of cardiopulmonary depressant effects. Effects on muscle tone are described as being variable, but ketamine generally either causes no changes in muscle tone or increases tone (Plumb, 2018). The patient was preoxygenated and oxygen was delivered by mask. During the urethral catheterization, the patient was continuously monitored (body temperature, blood pressure [BP], pulse oximetry - $SpO_2$). The following values were noted: body temperature 38.2-38.5°C, mean arterial BP 83-95 mmHg and $SpO_2$ 95-97%. The patient did not present any complications following this protocol (Grubb et al., 2020).

The use of an indwelling urinary catheter for the measurement of urine output allowed for a personalized patient fluid therapy. During the first night of hospitalization, rehydration was established by CRI with Ringer solution (rate and dosage 5 ml/kg/h) and urinary output was 10 ml/kg/h. For the next 24 hours, urinary output was approximately 9.53-9.64 ml/kg/h with a CRI of 7 ml/kg/h during the day and 5 ml/kg/h over the night. After 48 hours, the indwelling urinary catheter was removed. Urethral obstruction did not reoccur (Cosford et al., 2020; Hall et al., 2015).

Blood glucose curves were initiated and maintained over a period of five days and monitored hourly in the first 48 hours (Figures 1 and 2). In the following days of hospitalization, the BG levels were monitored every 3-4 hours until the day of discharge from the clinic (Figures 3-5) (Rand et al., 2005).

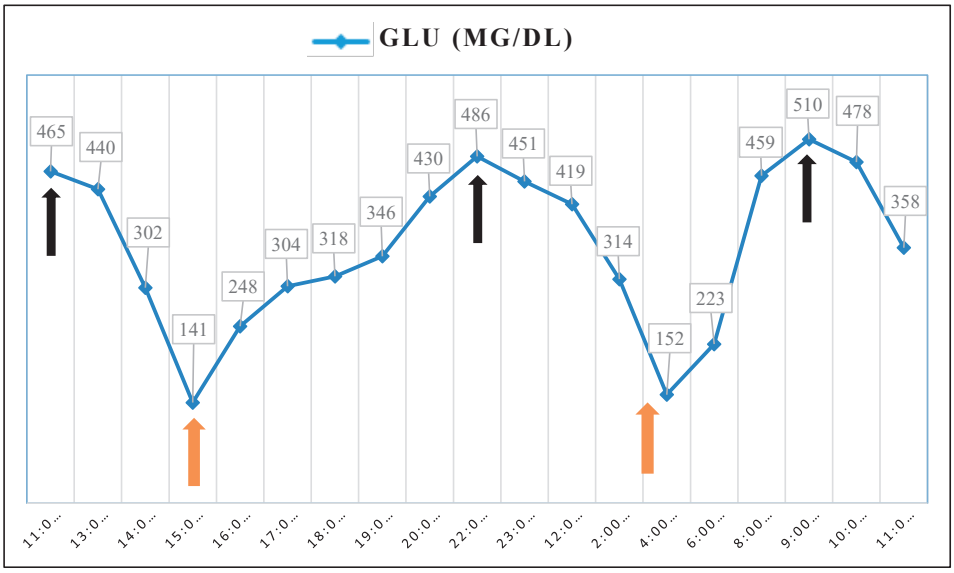


Figure 1. Evolution of GLU in the first 24 hours of hospitalization (original)
Black arrows - administration of insulin glargine, orange arrows - food administration

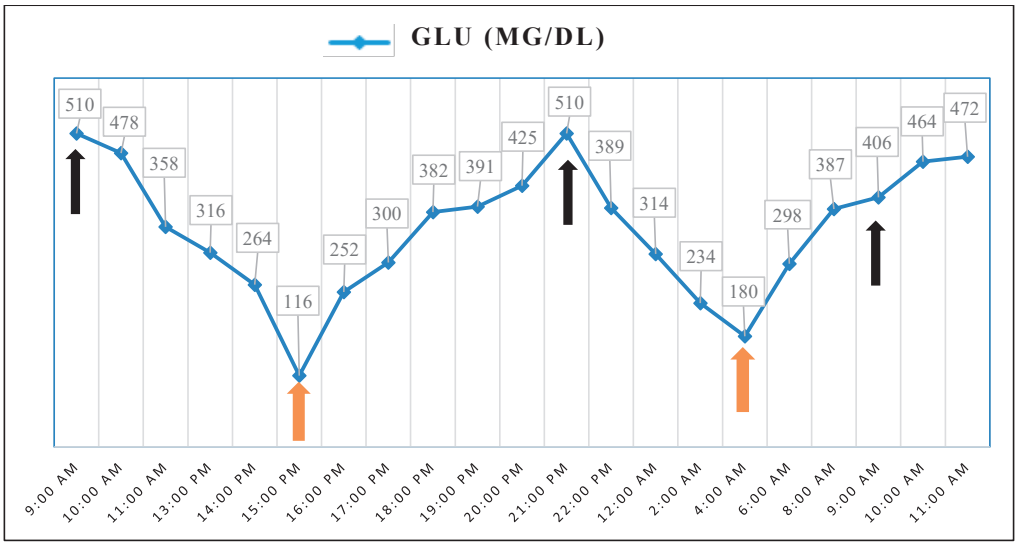


Figure 2. Evolution of GLU in the next 24 hours of hospitalization (original)
Black arrows - administration of insulin glargine, orange arrows - food administration

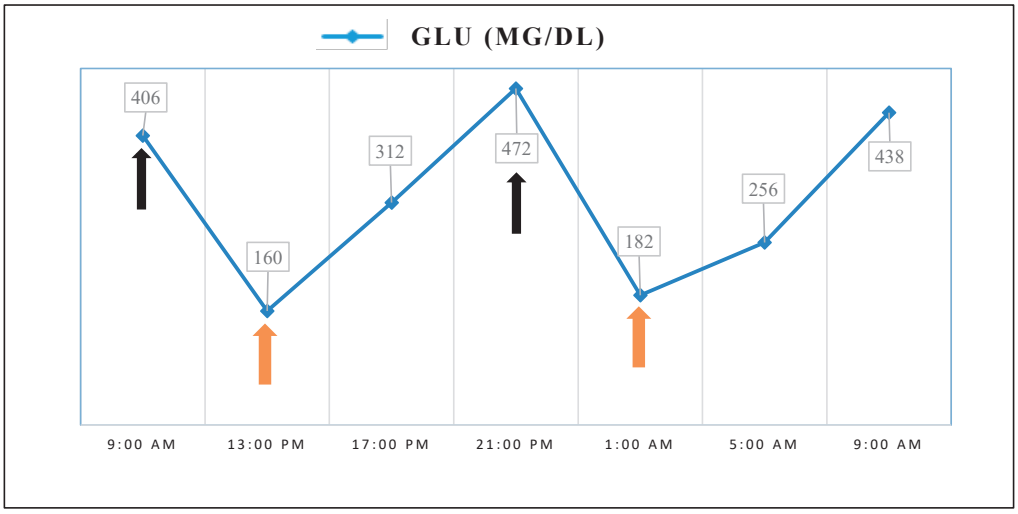


Figure 3. Evolution of GLU on the third day of hospitalization (original)
Black arrows - administration of insulin glargine, orange arrows - food administration

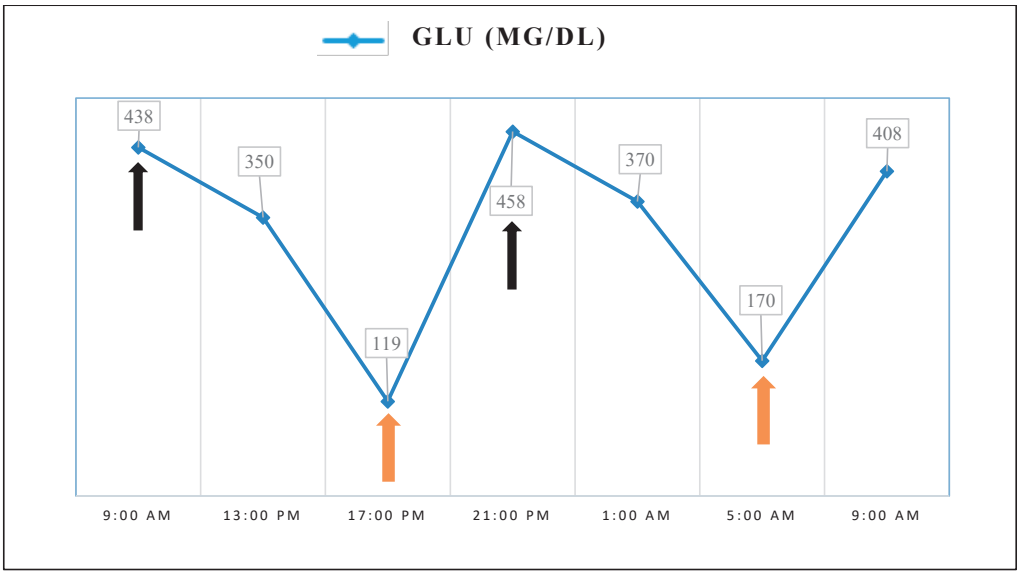


Figure 4. Evolution of GLU on the fourth day of hospitalization (original)
Black arrows - administration of insulin glargine, orange arrows - food administration

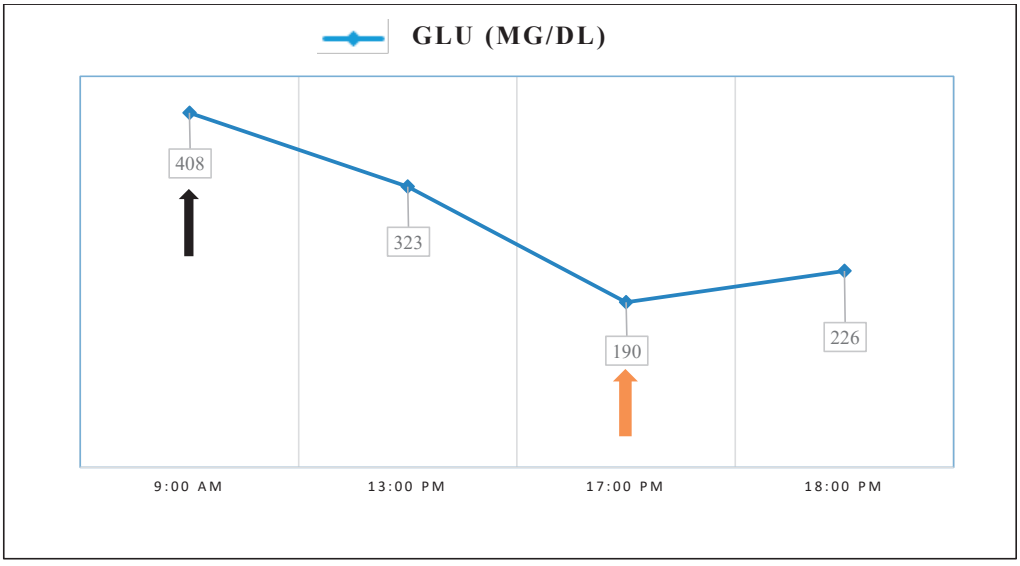


Figure 5. Evolution of GLU on the final day of hospitalization (original)
Black arrow - administration of insulin glargine, orange arrow - food administration

On discharge day, serum biochemistry values were in normal ranges, except BG, which was elevated (226 mg/dL; RR = 70-150 mg/dL). Serum fructosamine concentration was 412.1 µmol/L (RR = 190-365 µmol/L). The patient was discharged with the following recommendations:

- determination of BG before food administration at 9:00AM; if BG is >400 mg/dl, insulin glargine will be administered with a dose of 0.5 UI/kg;
- insulin glargine will be administered every 12 hours (9:00 AM and 21:00 PM);
- BG will be tested at 9:00 AM, 17:00 PM and 21:00 PM;
- food will be administered at 9:30 AM, 17:30 PM and 21:30 PM;
- nutritional supplements based on amino acids combined with a peptide (300 mg every 12 hours) and supplements that help maintain and support the urinary tract (based on DL-methionine - 250 mg TID);
- low carbohydrate diet.

Five days after discharge a CBC, serum biochemistry, urinalysis, abdominal ultrasound and serum fructosamine were reassessed. The owner was informed to administer the dose of insulin the day of the reexamination. There were no abnormalities on the CBC. Serum biochemistry revealed a mild elevation of blood glucose 190 mg/dL (RR = 70-150 mg/dL) with a serum fructosamine concentration of 382.5 µmol/L (RR = 190-365 µmol/L). The urine sample was obtained by ultrasound guided cystocentesis and urinalysis showed a decrease in leukocytes, glucose +105 mmol/L with a specific gravity of 1.029 and a pH of 6.0. Abdominal ultrasound showed an improvement of the morphology of the kidneys.

There was no sign of obstructive uropathy (hydronephrosis), except a mild dilation of the renal pelvis.

The evolution of BG and serum fructosamine is presented in Figure 6.

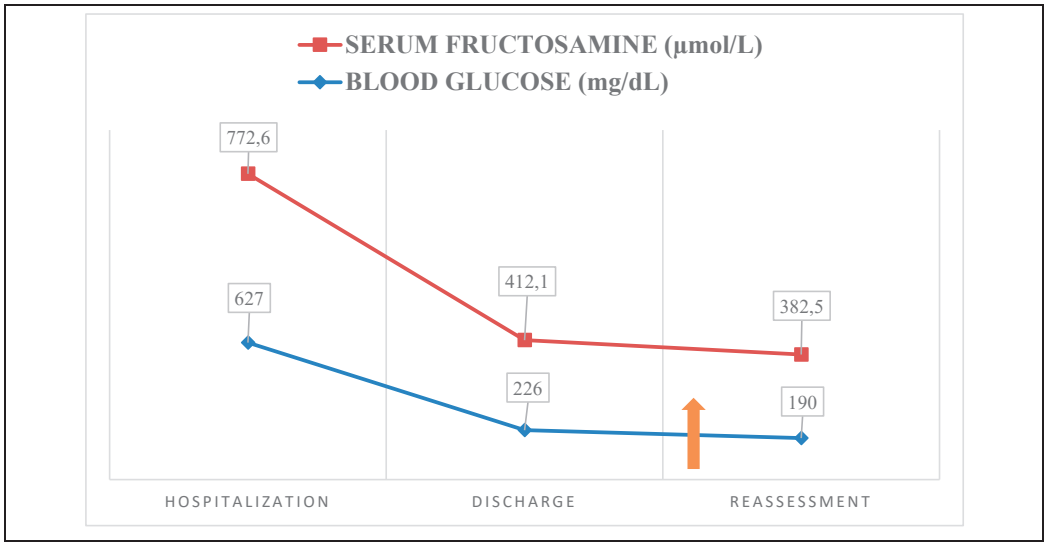


Figure 6. Evolution of BG and serum fructosamine of the patient during hospitalization, at the time of discharge and reassessment

## CONCLUSIONS

Serum fructosamine concentration is a valuable parameter for the diagnosis and metabolic control of diabetes mellitus.

Understanding the effects of diabetes and hyperglycemia, acid-base status is paramount to safely anesthetize and sedate diabetic patients.

Alfaxalone provides induction of anesthesia with stable respiratory and cardiovascular effect. Each patient requires an individualized treatment plan with frequent reassessmen and tempering depending on the patient's response.

In this study, the administration of insulin glargine resulted in no reported clinical signs of hypoglycemic episodes.

An accurate management of feline lower urinary tract disease can lead to remission of hydronephrosis and full recovery.

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