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FELINE UROLOGIC SYNDROME (FUS). I. AETIOLOGICAL ROLE OF NUTRITION AND BACTERIAL INFECTION

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Summary

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The present study was conducted on 46 male intact (uncastrated) cats with clinical signs of FUS (disuria, haematuria and urethral obstruction) admitted in the Surgical Clinic of the Faculty of Veterinary Medicine during the period 1998-2000.

The patient charts yielded information about the following items: breed, age, body weight; recurrence of episodes of symptoms; duration of the last epidose, type of treatment, feeding pattern, brand of the food, duration of feeding with a particular brand, intervals of feeding and water regimen.

Intraoperatively, urine samples were collected (via incision of the urethra before the site of obstruction and after catheterization of the urinary bladder). Immediately after collection, biochemical (pH, protein, glucose, urobilinogen, ketone bodies, blood, specific gravity), microscopical (crystals, red blood cells - RBC, white blood cells - WBC, desquamated epithelial cells), microbiological and parasitological analyses have been performed.

On the basis of obtained data we concluded that the most commonly affected cats were between 3-6 years old, weighing 3-5 kg without a breed predisposition. The primary cause for the development of an obstructive form of FUS was the formation of sterile urinary calculi as a result of feeding dry foods rich in magnesium, phosphorus and proteins and an insufficient water intake. Thus, predominantly strivute uroliths and more rarely, urate and oxalate uroliths were formed. The bacterial infection of the lower urinary tract developed more frequently secondarily. The detected microflora (*Escherichia coli, Proteus spp., Staphylococcus spp.*) was inherent for the urinary tract.

Key words: cats, FUS, FLUTD, struvite, uroliths

INTRODUCTION

Feline urologic syndrome (FUS) is one of the commonest causes of health problems in this animal species (Lung et al., 1999). Osborne et al. (1984) disputed this term and proposed to call all disorders related to the lower urinary tract in cats feline lower urinary tract disease (FLUTD). In the most recent reports, this term is more and more used. Furthermore, some authors divide the separate nosological entities in two groups: obstructive and non-obstructive FLUTD (Osborne et al., 1999). The same author suggests to obtain the most detailed diagnosis wuth regard to the site (urethra, bladder), the pathophysiological mechanisms (obstructive uropathy, dyssynergic reflex), morphological features (inflammation, neoplasm), the primary cause (abnormalities, bacteria,

fungi, viruses, mycoplasmae) (Osborne et al., 1995a).

FUS develops as a result of multiple causes affecting the lower urinary tract: infectious and non-infections inflammation, parasitic invasion (*Capillaria sp.*), uroliths (struvites, calcium oxalate, ammonium urate, calcium phosphate etc.), neoplasms (of the bladder, urethra, prostate, extraurinary), structural abnormalities (persistent urachus, urethral stenoses), traumas, iatroenic and idiopathic disorders (Poltzin and Osborne, 1985). The prinicipal discussion is focused mainly on bacterial infection and the role of the feeding patterns as initiating factors (Kallfelz et al., 1980; Lewis, 1981).

The aim of the present report was to study the roles of bacterial infection and the feeding patterns in FUS aetiology.

MATERIALS AND METHODS

The studies included 46 male intact (uncastrated) cats with disuria, haematuria and urethral obstruction that have been admitted for examination and treatment to the Surgical Clinic of the Faculty of Veterinary Medicine, Trakia University for a 2-year period (1998-2000).

The present article presents a statistics of the patient charts, summarizing all anamnestic data and urinanalysis results. The anamnestic data included the following items:

- Breed, age and body weight;
- Recurrence of episodes of symptoms;
- Duration of the last epidose;
- Treatment;
- Feeding patterns;
- Brand of the food;
- Duration of feeding with a particular brand;
- Intervals of feeding;
- Water regimen.

Urine specimens were collected intraoperatively following incision of the urethra before the site of obstruction and via catheterization of the urinary bladder). The urinalysis was performed immediately after collection. The following parameters have been estimated:

- Biochemical analysis - pH, protein (g/l), glucose (mmol/l), urobilinogen (μmol/l), ketone bodies (mmol/l), blood (RBC/ml), specific gravity - with dry Human-test Combina 9SG tests, Germany;
- Microscopical study of urine sediment - crystals, red blood cells (RBC), white blood cells (WBC), desquamated epithelial cells;
- Microbiological study - 0.01 ml of each specimen was inoculated on a non-selective culture medium - blood agar with 5% sheep RBC and selective medium for enterobacteria: McConkey's agar (National Centre for Infectious and Parasitic Diseases); incubated in aerobic conditions at 37 ^{o}C for 18-24 hours. When a bacterial growth was detected, the microbial colonies were counted; the amouint of microbial cells per 1 ml urine was determined and the bacteruria interpreted according to Lees (1996) as significant or insignificant. The presence of significant bacteriuria was followed by identification of isolates according to routine diagnostic methohds;
- Parasitological study - it was performed on urine sediment for detection of *Capillaria plica* eggs;

All cats, subject of the present study, were submitted to surgical intervention via perineal urethrostomy that is recommended when more than a single FUS episode is observed.

RESULTS

The analysis of anamnestic data (Table 1) showed that the incidence of FUS was the greastest among European Shorthair and Siamese breeds – 43.75% and 31.25% of all patients respectively. The age allocation showed an increased morbidity rate between 3 and 6 years – 69.44%. Cats weighing 3-5 kg were the most affected as well.

Recurrence of the disease was frequently observed: in 76.4%, the clinical signs occurred for the second time, and in 23.6% - multiple episodes with intermediate periods of remission occured. The duration of the last episode was 2-3 days in 41.9% of cats, up to 7 days - in 29.1% and more than a week - in 29% of cases. The major part of the cases were referred to the clinic after being treated with medications (78.1%) as followed: 46.8%

Table 1. Data from the anamnesis, obtained from the charts of feline FUS patients

Indices	Status	Percentage of all patients
Breed	European Shorthair	43.75
	Siamese	31.25
	Other	25.00
Age	under 3 years	22.26
	3-6 years	69.44
	over 6 years	8.30
Body weight	under 3 kg	3.20
	3-5 kg	83.80
	over 5 kg	13.00
Recurrence of symptoms	2 times	76.40
	more than 2 times	23.60
Duration of last episode	2-3 days	41.90
	up to 7 days	29.10
	more than 7 days	29.00
Treatment	Yes	78.10
	No	21.90
Type of consumed food	only dry food	83.00
	dry and other type of food	14.28
	other type of food	2.72
Brand of the food	Kitekat	21.40
	Whiskas	7.10
	Bosh	10.50
	other	61.00
Duration of feeding a particular brand	under 1 year	30.00
	over 1 year	70.00
Frequency of feeding	under 3 times	47.00
	more than 3 times	53.00
Water regimen	at intervals of 12-18 hours	64.80
	free access	35.20

treated with antibiotics; 24.4% - with uro-antiseptics; 14.6% with analgetics and 14.2% with spasmolytics. In 83.9% of patients, a bladder catheterization was performed.

With respect to the feeding patterns, the majority of cats were given exclusively dry (granulated) cat food – 83% compared to animals fed periodically dry food (14.28%) and kitchen wastes (2.72%). The brand of dry food was different in 61% of cases. In 21.4%, Kitekat was used, others were given Whiskas (7.1%), Bosh (10.5%). The duration of feeding with the mentioned foods was under one year in 30% of cats and more than an year in the other 70%. Analysing ing the intervals of feeding, it was noticed that the frequence of feeding in 53% of cats was more than three times daily. The majority of this group had a free access to food. The other 47% were fed less than three times daily. The water intake was at 12-18 hour intervals in 64.8% of cats, while the other 35.2% had a free access to water.

The urinalyses showed deviations in the chemical, morphological and microbiological composition. All studied animals were with weak to moderate prote-inuria (0.3–3 g/l) and significant haematuria (>250 RBC/ml). In 28.6%, the urine specific gravity was increased (>1.060). Only 13% of cats had elevated urine glucose levels (6 mmol/l) (Table 2).

The most significant changes were observed in urine sediment (Table 3). In all studied cases, there were plenty of RBC, desquamated epithelial cells, various crystals and single WBC. In 3 cases (5.36%) , more than 15 WBC per observation field were present. Epithelial cell originating from the urinary tract were observed in 60% of cats, from the bladder – in 30% and from the renal pelvis - in 10%.

Table 2. Biochemical analysis of urine in FUS patients (n=46)

Parameter	Value	Percentage*
PH	6	68.0
	6.5	8.0
	7	8.0
	7.5	16.0
Specific gravity	>1.060	28.6
Protein, g/l	0.3	63.0
	3	47.0
Glucose, mmol/l	6	13.0
Blood, RBC/ml	>250	100.0
Ketone bodies, mmol/l	n.d.	-
Urobilinogen, μmol/l	n.d.	-

* of all patients; n.d. – not detected

Table 3. Results of the analysis of urine sediment in FUS patients (n=46)

Parameter	Status	Percentage*
Erythrocytes	multiple	100.0
	single	-
Leukocytes	single	94.64
	>15/observation field	5.36
Epithelial cells originating from	bladder	30
	renal pelvis	10
	urinary tract	60
Calculi	struvites	45
	urates	35
	oxalates	20

* of all patients

The observed calculi were from 3 types: struvites (45%), urates (35%) and oxalates (20%). The type of crystals corresponded to urine pH. In 68% of cats, pH was 6, in 16% - 7.5; in 8% - 7 and in 8% 6.5. The cats with struvite uroliths had an urine pH between 6.5-7.5 while those with urate and oxalate crystals – pH of 6-6.5.

The microbiological studies of urine

samples showed a bacterial growth only in 6 urocultures (13.04%). Four of them were determined as significant because the number of colonies were over the threshold of 10^3 colony forming units (CFU)/ml. In the other 2 samples, the finding was determined as contamination (single or few colonies). The negative findings were 86.96% of all samples. The bacteria belonged to the following genera: *Acinetobacter spp., Proteus spp., Staphylococcus spp., Escherichia coli*. The identification of significant bacteriurias in our sudies evidenced uropathogenic *E. coli* (UREC) in 2 samples, a coagulase-negative stahylococcus in one sample and *Proteus mirabilis* in another one. The insignificant bacteriurias were caused by *Acinetobacter sp*. and *E.coli*. It is important to notice that in cases, where *Proteus* and *Staphylococcus* isolates were found out, a leukocyturia was also present (5.36%).

The parasitological tests of all specimens were negative.

DISCUSSION

The causes involved in FLUTD with clinical manifestation of haematuria, disuria and urethral obstruction are multiple. Some of them, as neurogenic disorders, neoplasms, abnormalities, viral, mycoplasmic or mycotic infections and parasitic invasions are rarely encountered and do not correspond to the high incidence of the disease. Thus, the bacterial infection and the improper diet are considered as the most probable initiating factors (Kallfelz et al., 1980; Lewis, 1981).

The results of our study confirm the opinions of Gaskell et al. (1979), Kruger et al. (1991) etc. that bacterial infection of the urinary tract is not the primary cause of FUS.

According to our data, the highest incidence of the disease is observed in cats aged 3-6 years, weighing 3-5 kg from the European Shorthair or Siamese breeds, that could be explained by the widest distribution of those breeds in our country. In all patients the episodes were recurrent althogh in 78.1% some treatment have been initiated. This could be due to the administration of inadequate medications and to the absence of a calculytic diet.

The anamnestic data obtained by us confirm the relapse of the disease, as reported by other authors too (Osborne et al., 1995a; Osborne et al., 1999; Senior, 1999).

The issue of the disease correlates with the duration of the epidose (Senior, 1999). The majority of the cases suffered from FUS since 2-3 days that evidenced the acute development of the disease.

The data about the feeding patterns are the most informative. The predominant part of cats were fed dry diets (83%). The peak of disease occurrence during the last years is related to the extensive distribution of dry foods on our market. Osborne et al. (1989), Osborne et al. (1995b) that have followed the epidemiology of FUS from 1984 to 1995 have expressed the same opinion. The brand of dry food could not be specified with respect to disease incidence because of the lack of data for the use of a particular brand.

The results of urine sediment analysis are indicative for the presence of lower urinary tract inflammation. This statement is supported by the presence of epithelial cells originating from the urinary bladder and urinary tract (90%) while those coming from the renal pelvis were only 10% as well by the limited leukocyturia, the weak proteinuria and the significant haematuria. Those data confirm the opinion of Kruger (1991) that most cases of urethral obstruction are caused by mineral

precipitates leading to aseptic inflammation while the bacterial urinary tract infection is involved in less than 10% of FUS cases.

The small amounts of urine glucose, found out in 13% of cats could be interpreted as insignificant because the circadial variations in urine glucose have not been determined. The glucosuria present in those cases could be due to the stress and the release of catecholamines and cortisol in blood that enhance and increase the glycolysis.

Our data about the crystaluria with prevalence of struvite uroliths (45%) correspond to those of Polzin and Osborne (1985). Those authors consider that struvites are the most frequently encountered in cats (68%) while urates and oxalates are rarely encountered (20% and 3% respectively). Similar data are reported by Osborne (1996) who observed the same pattern of distribution but in a different ratio.

Struvite uroliths could be formed in urethral infections with urease-producing organisms as well as without infection (Osborne et al., 1999). In our study, 86.96% of urocultures were negative. Those data deserve further attention at the background of urine sediment changes, indicative for lower urinary tract disease (presence of crystals, desquamated epithelial cells coming from urinary tract and the bladder, RBC and WBC) and support the assumption for the alimentary origin of the disease.

Cats need more proteins and relatively more phosphorus in their diet compared to magnesium (Girginov and Kallfeltz, 1997) that is why their urine contains enough ammonia and phosphate ions while the magnesium content depends entirely on the amount ingested with food. Therefore, the high magnesium content in cat foods is a prerequisite for the formation of struvite uroliths. Commercial brands of cat foods contain averagely 0.16% magnesium (on a dry matter basis) that is 4-18 times more than feline requirements (0.016% of dry matter) (Girginov and Kallfeltz, 1997). This is due to the high magnesium content of cat food components. Furthermore, the lower the energy content of food is, the higher ingested amounts are (especially when the animal is fed *ad libitum*) and respectively, the ingested amount of magnesium is higher (Buffington, 1992).

When urease-producing bacteria are involved in an urethral bacterial infection, they lead to saturation of urine with ammonia, hydrogen carbonates and carbon dioxide and could initiate a struvite urolithiasis (Rosenstein et al., 1984; Wong et al., 1996). Under the action of bacterial urease, the urine urea is hydrolyzed and an hyperammoniuria occurs. The formed ammonia is conjugated to hydrogen ions from the tubular lumen thus forming ammonia ions that are not fat-soluble and could not pass through the tubular wall (the so-called ion-trapping occurs). Thus, the urine is alkalized and the ammonia ions are combined to magnesium and phosphate forming magnesium ammonium phosphate crystals. The ammonia ions could adhere to sulphate groups of protective glycosaminoglycane layers on urinary tract mucosa and thus favour the desquamation of epithelial cells, the nucleation and growth of struvite crystals (Osborne et al., 1995b; Osborne, 1996).

It is considered that the principal predisposing factor for the formation of ammonia urate crystals is the high content of purine precursors in food, especially liver (Hesse and Sanders, 1985; Osborne et al., 1995b) that provide additional urea for obtaining ammonia within the renal tubules and glutamate for its transformation

to ammonia ions. The aciduria contributes to the formation of calcium oxalate crystals as well via mobilization of calcium from bones and inhibition of its reabsorption from renal tubules. Our data confirm the significance of urinary pH for crystal formation revealing a predilection for formation of urates and oxalates in acid pH (6-6.5) and struvites in pH 6.5-7.5.

The water defficiency contributes for the onset of urolithiasis because it leads to decreased intravasal, respectively urine volume and to urine retention. Thus, the urine is oversaturated with minerals from one side and more time for uroliths formation is allowed on the other (Osborne, 1996).

The analysis of microbiological results shows clearly that the primary cause of FUS is impaired mineral homeostasis while the relative part of urinary bacterial infections is smaller and they develop secondarily.

The low percentage of positive urocultures correlates with the data of Schecter (1970), Barsanti (1982), Martens (1984) and Lees (1996) reporting that the total percentage of positive urocultures in FLUTD was between 5% and 43%. The comparatively big differences are related to the presence, respectively the absence of an urethral obstruction. In FUS, obstruction is rather preceding the bacterial infection (Osborne et al., 1989; Kruger et al., 1991).

The species composition of microbiological finding could not be determined as unusual. Feline urocultures, caused by the same bacteria are found by Schechter (1970); Hirsh (1973); Wooley and Blue (1976) in cases of miscellaneous urinary tract inflammations – pyelitis, cystitis and non-obstructive urethritis. The positive bacteriurias in FUS are generally aetiologically related to the resident microflora in the distal part of the urethra and/or are coming from an invasion (catheterization). In those cases, the contamination and the consecutive colonization occur via an ascendent route. The species composition is determined also by the usual for this topographic region species as *Escherichia coli, Proteus spp., Klebsiella spp., Staphylococcus spp., Corynebacterium spp*. etc. (Hirsh, 1973; Lees, 1996).

Nevertheless, the analysis of urocultures is an obligatory diagnostical technique because of the necesity of aetiotropic therapy and with regard to the high resistance of microbial agents to usually applied chemotherapeutics.

CONCLUSIONS

The primary cause for the development of obstructive form of FUS in male cats is struvite, urate or oxalate urolithiasis that favours the secondary bacterial infection.

The bacterial infection of the feline lower urinary tract is most commonly caused by the usual for this topographic region microflora (*E. coli, Proteus spp., Staphylococcus spp.*).

The formation of sterile urinary calculi occurs after improper feeding with dry granulated cat foods, containing more proteins, magnesium and phosphorus, in restricted access to water and deviations in urine pH.

The most affected group of cats is that of young animals (3-6 years) weighing 3-5 kg, without a breed predisposition.

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