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Platzierung eines subkutanen Ureterbypasses bei einem Zwergpinscher mit vermuteter Xanthin-Urolithiasis infolge einer Allopurinol-Behandlung

Der vorliegende Fallbericht beschreibt die langfristig erfolgreiche Behandlung einer Ureterobstruktion mittels eines subkutanen Ureterbypasses bei einem Hund. Die Verdachtsdiagnose einer Xanthin-Urolithiasis wurde aufgrund einer Behandlung mit Allopurinol gegen Leishmaniose gestellt. Klinisch zeigte der Hund eine Lethargie, Anurie und Abdominalschmerzen. Bei der biochemischen Analyse wurde eine leichte Azotämie festgestellt, und die Abdomen-Ultraschalluntersuchung ergab eine beidseitige Ureterobstruktion. Therapeutisch wurde mit einer standardmässigen chirurgischen Technik ein subkutaner Ureterbypass gelegt. Der Hund erholte sich ereignislos und die Azotämie verschwand innerhalb weniger Tage. Nachuntersuchungen wurden in jedem Trimester über einen Zeitraum von mehr als drei Jahren durchgeführt, während dieser Nachbeobachtungszeit wurden keine Komplikationen, wie eine Obstruktion des Bypasses, Harnwegsinfektionen oder eine Azotämie, festgestellt. Als Langzeitbehandlung gegen Leishmaniose wurde Allopurinol durch Domperidon ersetzt, was zeitweise zu einem leichten Anstieg des Serum-Antikörpertiters gegen Leishmanien führte. Die Platzierung des subkutanen Ureterbypasses war bei diesem Hund erfolgreich und stellt daher bei Hunden eine geeignete Alternative bei Ureterobstruktion dar.

Schlüsselwörter: Nebenwirkungen, Hund, Leishmaniose, Uretersteine, Ureterobstruktion

Summary

This case report describes the long-term success of a subcutaneous ureteral bypass device in a dog for treatment of a ureteral obstruction. The suspected xanthine urolithiasis was secondary to treatment with allopurinol for leishmaniasis. The dog presented initially with lethargy, anuria and abdominal pain. Mild azotemia was found on biochemical analysis and abdominal ultrasound revealed bilateral ureteral obstruction. A subcutaneous ureteral bypass was subsequently placed using a standard surgical technique. The dog recovered uneventfully and the azotemia resolved within days. Follow-up examinations were performed every trimester for over three years and no complications like obstruction of the bypass tubes, urinary tract infection or azotemia were recognized during this follow-up period. Allopurinol was replaced with domperidone as long-term treatment against Leishmaniasis which resulted in a mild increase of the leishmania serum antibody titer. The subcutaneous ureteral bypass placement was successful and safe in this dog and is a valuable alternative in cases of ureteral obstruction also in dogs.

Keywords: adverse effect, dog, leishmaniasis, ureteral calculi, ureteral obstruction

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Introduction

Canine leishmaniasis is a common and life-threatening vector-borne disease caused by leishmania infantum. Most current treatment protocols include allopurinol as monotherapy or in combination with other drugs.^{2,7,18} Allopurinol is a xanthine oxidase inhibitor, interfering with purine metabolism and leading to accumulation of xanthine and hypoxanthine instead of their further metabolization to uric acid. This can result in xanthine urolith formation, a possible side effect of allopurinol treatment in dogs.28 Subcutaneous ureteral bypass (SUB) placement in cats is a surgical technique for treatment of ureteral obstructions, which gained popularity in the last decade.3 This case report describes the case of a Miniature Pinscher diagnosed with ureteral obstruction due to suspected xanthine urolithiasis, secondary to allopurinol treatment for canine leishmaniasis, treated surgically with a unilateral SUB.

Case history

A 4-year old male castrated Miniature Pinscher (2,5 kg) was referred to the Small Animal Clinic of the University of Berne for evaluation of anuria, anorexia and progressive weight loss. The dog had been treated with allopurinol 10 mg/kg PO twice daily over nearly two years for canine

Table 1: Blood chemistry profile in a 4-year old male

 castrated Miniature Pinscher at time of presentation

Sodium	mmol/l	142–154	149
Potassium	mmol/l	4,22–5,43	3,78
Chloride	mmol/l	106–135	105
Calcium	mmol/l	2,42–2,85	2,42
Phosphorus	mmol/l	0,91–1,90	2,45
Glucose	mmol/l	4,16-6,69	5,5
Total protein	g/l	56–73	62,6
Albumin	g/l	30-40,5	30,8
Urea	mmol/l	3,30–10,83	56,83
Creatinine	µmol/l	52–117	232
Canine CRP	mg/l	<10,7	45,4



Figure 1: Abdominal ultrasound in a 4-year old male castrated Miniature Pinscher showed severe distention of the left renal pelvis (1,72 cm diameter, blue dotted line) on transverse view.



Figure 2: Abdominal ultrasound in a 4-year old male castrated Miniature Pinscher showed proximal ureteral dilation (0,44 cm, blue dotted line) with a hyperechoic structure with distal shadowing in the median part of the left ureter.



Figure 3: Ultrasonic picture of a left-sided ureteral dilation with multiple hyperechoic uroliths with distal shadowing over a distance of 1,5cm (blue dotted line) in a 4-year old male castrated Miniature Pinscher.

Placement of a subcutaneous ureteral bypass in a Miniature Pinscher with presumed xanthine urolithiasis as a result of allopurinol treatment

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leishmaniasis manifested as alopecia and ulcerative dermatitis. Additionally, the dog had been intermittently treated with amoxicillin-clavulanic acid 25 mg/kg q 12 h for pyoderma. Relevant clinical findings on presentation included lethargy, decreased body condition score (2/9), dehydration estimated as 7 % and diffuse abdominal pain.

A complete blood count showed neutrophilia without left shift (19,98×10⁹/l segmented neutrophils, ref. 3,0–11,5×10⁹/ l). A serum biochemical profile showed moderate azotemia and a moderately increased canine C-reactive protein (table 1). The leishmania serum antibody titer was negative. The urine specific gravity was 1,014, urine pH 6,0. A urine sediment examination (for crystalluria) could not be performed due to small sample size. A urine bacteriological examination was negative with a positive antibiotic inhibitor test. Radiographs of the abdomen showed reduced abdominal serosal detail, attributed to cachexia, but no urolithiasis was visible. Abdominal ultrasound revealed bilateral hydronephrosis with dilation of the renal pelvis of 1,7 cm on the left, and 1 cm on the right side, respectively. Moderate left-sided nephromegaly (4,35 cm length) with proximal ureteral dilation (0,44 cm) was noted with a hyperechoic structure with distal shadowing in the median part of the left ureter (Figure 1 - 3). The right ureter was moderately dilated (0,40 cm) due to two hyperechoic structures.

Treatment

Based on these findings, the azotemia was diagnosed as of postrenal origin, and it was decided to treat the dog with a left-sided surgically placed SUB. This decision was based on the size of the dog and its very small ureters and the risk of post-surgical stricture formation in case of ureterotomy.¹⁶ Only unilateral placement was decided in view of the ultrasonographic absence of a urolith in the right ureter and visualization of urine flow from this ureter after initial therapy; the clinical assumption was a previous obstruction on this side causing similar renal pelvis dilation, but that the obstruction had spontaneously resolved. Pre-anaesthetic medication included intravenous dexmedetomidine (0,003 mg / kg), ketamine (1 mg / kg) and midazolam (0,1 mg / kg). Anesthesia was induced with propofol (3 mg



Figure 4: Laterolateral abdominal radiograph of a 4-year old male castrated Miniature Pinscher after surgical subcutaneous ureteral bypass (SUB) placement to check position of the device.

/ kg) and maintained with isoflurane (1-2%) and oxygen. Systemic analgesia was provided with fentanyl constant rate infusion 3–5 µg / kg / h. Intravenous fluid therapy consisted of Plasmalyte-A (Baxter) solution administered at a rate of 5 ml/kg/h during surgery. Preoperatively, intravenous ampicillin-sulbactam (30 mg / kg) was administered for antimicrobial coverage. A standard midline laparotomy was performed and a left-sided nephrostomy tube and a cystostomy tube from the SUB device (Norfolk Vet Products (SUB version 1.0)) placed with fluoroscopic assistance using the Seldinger technique, as described in the manual.²¹ Briefly, the left renal pelvis was punctured from the caudal pole with an 18 gauge catheter. A 0,035" J-tip guide wire was advanced through the catheter and coiled inside the renal pelvis. The 18-ga. catheter was removed and the pigtail nephrostomy tube advanced over the guide wire into the renal parenchyma. The Dacron cuff was glued to the renal capsule. Then, before placing the multi-fenestrated cystotomy catheter, a purse string suture pattern was made at the apex of the bladder. In the center of this purse string, the bladder wall was punctured and the cystostomy catheter advanced through the incision into the urinary bladder lumen. The

purse-string suture was secured and tied, the Dacron cuff was sutured to the bladder wall and in addition glued to the serosal surface of the urinary bladder. Once the catheters were placed, both were passed through the body wall and the tubes were connected with a special subcutaneous port which was fixed to the equilateral ventral abdominal wall. Under fluoroscopic guidance, the system was rinsed with contrast medium to ensure patency and absence of leakage.

Follow-up

The dog recovered uneventfully from surgery and the renal parameters returned to reference intervals within three days. An abdominal ultrasound examination was repeated. The left-sided dilation of the renal pelvis had markedly decreased to a diameter of 4 mm. The SUB tubes were correctly positioned in the left renal pelvis and the urinary bladder. Pyelectasia of the right kidney (7 mm) and proximal dilation of the right ureter (3 mm) had slightly decreased. The dog was discharged from the hospital after 7 days with amoxicillin-clavulanic acid 62,5 mg PO q12h for



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Figure 5: Course of creatinine and phosphorus in a 4-year old male castrated Miniature Pinscher after the placement of the subcutaneous ureteral bypass (SUB) device. X: Time since placement of the SUB device (in days). Y left: Creatinine (in μ mol/I). Y right: phosphorus (in mmol/I)

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3 weeks. The allopurinol treatment was replaced with intermittent administration of domperidone 1 mg/kg PO q24 for a month followed by a 3-month break. The dog was presented for flushing of the SUB device and a routine urinalysis and bacteriological examination every trimester. Renal parameters remained within reference intervals and no SUB-related complications like blockage or dislocation of the device or urinary tract infections had occurred (figure 5). The leishmania serum antibody titer slightly increased under exclusive treatment with domperidone, but without development of clinical signs seven and 25 months after SUB placement (figure 6). Therefore, miltefosin 2 mg/kg PO q 24 h over 28 days was added to the treatment which again lowered the serum titer (figure 6). Forty months after SUB placement, the dog is clinically asymptomatic regarding leishmaniasis and the SUB, normal regarding serum renal parameters and without evidence of urinary tract infection.

Discussion

Various studies and review articles report an increased incidence of ureteral obstructions in cats in the past decades.^{1,16} Compared to cats, urolithiasis in dogs is rare and has been estimated at 0,5-1 %.6,13,22 Globally, the predominant uroliths in dogs are calcium oxalate and struvite, which is also true for nephrolithiasis. ^{6,15,22,25,26,27} Xanthine urolithiasis is rare in dogs and most commonly associated with allopurinol treatment.²³ In a recent study, 42 of 320 dogs (13%) trseated for leishmaniasis developed xanthinuria as a consequence of allopurinol treatment, but no all xanthinuria resulted in urolith formation as suspected in this dog. ²⁸ To decrease the risk of xanthine urolithiasis low purine diet is recommended for dogs on allopurinol treatment.²⁸ Finally, domperidone is considered a safe and effective alternative to allopurinol¹¹, which was the approach in our dog for the continued treatment of his leishmaniasis.



Figure 6: Course of Leishmania serum antibody ELISA in a 4-year old male castrated Miniature Pinscher with the subcutaneous ureteral bypass (SUB) placement at month 0. Due to the slight increase in antibody titer two additional treatments with miltefosin to the treatment with domperidone were performed at month 7 and 25 (*).

Ureteral obstruction may be approached by medical management, traditional surgery (e.g. ureterotomy) or with newer less invasive techniques like stent or SUB implantation. Suggested medical treatment options include medical management, involving intravenous fluid therapy, mannitol continuous rate infusions and alpha-adrenergic blockage, however, only rarely are successful for relieve of the obstruction. As clinical patients presenting with partial or complete obstruction usually have pre-existing kidney damage, prompt aggressive treatment is currently recommended. ^{8,10,17,19,29,30}

Stent and SUB techniques adapted to the feline small ureter size (0,4 cm) have been gaining popularity with the increasing incidence of ureteral obstructions.^{3,14} Potential complications with both can occur, particularly obstruction of the device with a stone and recurrent urinary tract infection. In retrospective case series of successful stent placement in 75 out of 79 feline ureters, stent exchange was required in 27 % of the cases.⁴ Another retrospective study compared double-pigtail stent (n = 30) to subcutaneous ureteral bypass (n = 30) placement in cats with ureteral obstruction. Stent placement performed inferior to SUB essentially in all respects, i.e. longer surgery time, higher perioperative mortality, longer hospitalization, more often signs of lower urinary tract disease or device occlusion with necessity for additional procedures, and shorter survival time.9 Nevertheless, in another retrospective study including 44 cats stent placement was not associated with longer hospitalization lengths or worse outcome when compared to a SUB device.14 An important aspect when considering an interventional procedure is the mentioned pre-existing renal damage. Likewise, azotemia will persist in a high percentage of cases, even though the degree may decrease.³ There is no pre-interventional parameter that can predict the outcome.14

Whereas in veterinary medicine the SUB placement technique has been initially developed in a canine experimental model as a short - term palliative treatment for ureteral obstructions in which other solutions are unsuitable, e.g. presence of retroperitoneal metastases,¹² until recently it has only been described in cats with mostly benign causes of ureteral obstruction and therefore a longer life expectancy. In a retrospective study, cats tolerated well long-term SUB placement (up to 6,5 years).⁵ Ureteral stent placement has been previously described in dogs. While this technique has been successfully performed in dogs as small as 1,3 kg, the small diameter of the ureters represents a challenge.²⁴ A SUB placement was therefore considered the better option in our patient.

Only recently, SUB placement has been reported in clinical dogs.²⁰ At the time of placing the SUB in our dog, there was thus no experience in this species. Whereas in the dog of this report no complication was recognized, the most com-

mon reported long-term complication was mineralization in half of the placed devices.²⁰

Since June 2014, 151 cats and 7 dogs with unilateral or bilateral ureteral obstructions have been treated at the Small Animal Hospital at the University in Bern with a SUB device. Most of them showed a good outcome depending on the degree of residual kidney damage from the ureteral obstruction (unpublished data).

In summary this case report describes the successful placement and long-term management of a SUB device in a small-breed dog. The SUB technique developed for cats seems to be useful for managing ureteral obstruction a in dogs as well. Placement of a subcutaneous ureteral bypass in a Miniature Pinscher with presumed xanthine urolithiasis as a result of allopurinol treatment

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Mise en place d'une dérivation urétérale sous-cutanée (SUB) chez un Pinscher miniature présentant une urolithiase présumée à la xanthine à la suite d'un traitement à l'allopurinol.

Ce rapport de cas décrit le succès à long terme d'une dérivation urétérale sous-cutanée chez un chien pour le traitement d'une obstruction urétérale. L'urolithiase xanthique suspectée était secondaire à un traitement à l'allopurinol contre la leishmaniose. Le chien a d'abord présenté une léthargie, une anurie et des douleurs abdominales. L'analyse biochimique a révélé une légère azotémie et l'échographie abdominale a révélé une obstruction urétérale bilatérale. Une dérivation urétérale sous-cutanée a été mise en place selon une technique chirurgicale standard. Le chien s'est rétabli sans incident et l'azotémie a disparu en quelques jours. Des examens de suivi ont été effectués tous les trimestres pendant plus de trois ans et aucune complication telle qu'une obstruction du tube de dérivation, une infection urinaire ou une azotémie n'a été constatée au cours de cette période de suivi. L'allopurinol a été remplacé par de la dompéridone dans le cadre d'un traitement à long terme contre la leishmaniose, ce qui a entraîné une légère augmentation du titre des anticorps sériques contre la leishmaniose. La mise en place d'une dérivation urétérale sous-cutanée s'est avérée efficace et sûre chez ce chien et constitue une alternative intéressante en cas d'obstruction urétérale, y compris chez les chiens.

Mots clés: effet indésirable, chien, leishmaniose, calculs urétéraux, obstruction urétérale

Posizionamento di un bypass ureterale sottocutaneo (SUB) in un Pinscher nano con presunta urolitiasi da xantina a seguito di trattamento con allopurinolo

Questo caso clinico descrive il successo a lungo termine di un dispositivo di bypass ureterale sottocutaneo per il trattamento di un'ostruzione ureterale in un cane. La presunta urolitiasi xantinica era secondaria al trattamento con allopurinolo per la leishmaniosi. Il cane clinicamente presentava letargia, anuria e dolore addominale. Un'azotemia lieve è stata riscontrata nell'analisi biochimica e l'ecografia addominale ha rivelato un'ostruzione ureterale bilaterale. Successivamente è stato posizionato un bypass ureterale sottocutaneo utilizzando una tecnica chirurgica standard. Il cane si è ripreso senza complicazioni e l'azotemia si è risolta entro pochi giorni. Esami di follow-up sono stati eseguiti ogni trimestre per oltre tre anni e durante questo periodo di follow-up non sono state riscontrate complicazioni come l'occlusione dei tubi di bypass, infezione del tratto urinario o azotemia. L'allopurinolo è stato ora sostituito con domperidone come trattamento a lungo termine contro la leishmaniosi, il che ha comportato un lieve aumento del titolo degli anticorpi sierici contro la leishmania. Il posizionamento del bypass ureterale sottocutaneo è stato efficace e sicuro in questo cane e risulta essere un'alternativa preziosa nei casi di ostruzione ureterale.

Parole chiave: effetti collaterali, cane, leishmaniosi, calcoli ureterali, ostruzione ureterale

Placement of a subcuta-

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