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Hand-assisted laparoscopic nephrectomy for the treatment of ureterolithiasis and nephrolithiasis in an adult horse

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Summary: An 18-year-old Hanoverian Warmblood gelding was presented with a history of acute haematuria. On rectal examination, a severely dilated right ureter with a concrement was palpated. Transabdominal sonography raised the suspicion of right kidney enlargement and loss of normal architecture. An exploratory laparoscopy was performed to evaluate the diagnostic findings. The tentative plan was to perform a laparoscopic ureterolith removal and a hand-assisted right nephrectomy, as high ureterolith recurrence rates are reported without nephrectomy. Right hand-assisted laparoscopic nephrectomy was performed and confirmed nephrolithiasis. Since the ureteral stone could not be mobilised, it was left in situ. Post-operative pain management proved a major challenge in this case, and was initially insufficient in spite of a multi-modal approach. Applied pain management techniques as used in human donor nephrectomy require further investigation for potential future use in equine patients. The gelding resumed his activity as a leisure horse six weeks after surgery, but was euthanized three months after surgery due to an unrelated cause. Nephrectomy without ureterolith removal provided a successful solution for this case of severe kidney disease.

Keywords: horse, kidney, ureterolith, nephrolith, laparoscopic nephrectomy

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Introduction

Renal disease in horses is uncommon and due to insidious and aspecific clinical signs, often not discovered until the disease process is advanced. Urolithiasis has an estimated prevalence of 0.11%. Nephroliths (12%) and ureteroliths (4%) only constitute a small percentage of uroliths (*Macbeth* 2008, *Saam* 2001). Varied approaches to the treatment of ureterolithiasis in horses have been described, but limited attention has been given to the often-underlying renal problem. This case report is a complete documentation of the history, clinical signs, diagnostic work-up and surgical management of a horse with ureterolithiasis. To our knowledge it is the first described case of successful treatment in which the main ureterolith was left in situ.

Case history

An 18-year-old Hanoverian Warmblood gelding was presented with a history of acute haematuria. Two weeks prior to presentation, haematuria had been noted by the owner for two days, after which urine returned to normal. The horse showed no change in demeanour or stranguria. A urinary examination by the referring veterinarian revealed a negative culture, a clearly increased number of erythrocytes (250/µl), no leukocytes and the presence of calcium oxalate and calcium carbonate crystals. Haematology and biochemistry, including kidney values and electrolytes was deemed unremarkable. Five days before presentation, haematuria reoccurred for one day. At the time considered unrelated, the owner reported that the horse had been treated for lumbar back pain for two years by an osteopath.

Clinical findings

The initial clinical examination was unremarkable, except for mild equine odontoclastic tooth resorption and hypercementosis (EOTRH) as an incidental finding. A rectal examination revealed normal bladder filling, the left kidney was without abnormal findings. On the right paramedian side, a severely dilated, fluid-filled, small intestinal-like tube was detectable, that could be traced back to the bladder. This was presumed to be the right ureter which contained an approximately $10 \times 4 \times 4$ cm rounded, hard concretement. Micturition was normal as was the gross appearance of the voided urine.

Laboratory diagnostics

Clinical laboratory values were as follows PCV 46% (reference range [rr] 32–52%), total protein 68 g/l (rr 54–70 g/l),

leukocytes 5,200/µl (rr 5,000–10,000/µl). Kidney values were within reference range (CREA 166 µmol/L rr 71–194 µmol/L, UREA 4.9 mmol/L rr 3.6–8.9 mmol/L). The free catch urine sample with concurrently collected blood serum was submitted to "Stiftung Tierärztliche Hochschule Hannover", University of Hannover, Germany for renal function assessment. This analysis revealed a slight hypophosphatemia, potentially alimentary in origin. The urinalysis revealed a pH of 7.5, a specific gravity of 1.023. The urine sediment contained small amounts of red blood cells, bacteria and leucocytes and contained high levels of calcium carbonate crystals. These findings were interpretated as being caused by a mild cystitis. Bacteria may have been present due to the nature of the sample collection.

Diagnostic imaging

Transrectal sonographic examination could confirm the presence of a dilated right ureter, containing a hyperechoic stone-like structure close to its cranial entrance into the bladder (Fig 1). Ureter diameter on ultrasound was approximately 5 cm proximal to the ureterolith. The bladder was sonographically unremarkable, as was the left kidney. Transabdominal ultrasound raised the suspicion of right renal enlargement, with poorly discernible renal architecture and hyperechoic foci throughout the renal pelvis (Fig 2).

Endoscopy of the urinary tract showed mild haemorrhagic lesions in the urethra and bladder wall. The left ureter opening could be localised and was seen draining urine. The right ureter opening could however not be visualised definitively, potentially the view was obscured by a structure bulging into the bladder wall, thought to be the dilated part of the ureter. Out of cost-benefit considerations, a separate urinary analysis of the left ureter was not performed.

Diagnosis

The tentative diagnosis at this point was obstructive ureterolithiasis with hydroureter on the right. As ureteroliths have been described as a cardinal sign of kidney problems, and the right kidney showed sonographic changes, pathology of the right kidney was suspected. Differential diagnosis included nephrolithiasis, hydronephrosis, renal neoplasia, renal trauma and pyelonephritis of the right kidney. In conjunction with the owner, an exploratory laparoscopy was performed to evaluate the diagnostic findings. The tentative plan was to perform a laparoscopic ureterolith removal and a hand-assisted right nephrectomy upon confirmed abnormality, to eliminate the potential for ureterolith recurrence (*Auer et* al. 2019). In preparation for surgery, feed was withheld for a period of 36 h and the horse was provided with free access to water.

Treatment

Surgery

After placement of an intravenous catheter in the left jugular vein, the horse was premedicated with acepromazine (Tranquisol P® 0.03 mg/kg bwt i.m.)[6], flunixin meglumine (Flunidol® 1.1 mg/kg bwt i.v.)[6], sodium amoxicillin (Belamox® 10 mg/kg bwt i.v.)[3] and gentamicin sulfate (Genta 100 mg/ml 6.6 mg/kg bwt i.v.)[6]. Sedation for surgical preparation was detomidine hydrochloride (Detogesic® 0.01 mg/kg bwt i.v.)[12] and levamethadone hydrochloride (L-Polamivet® 0.06 mg/kg bwt i.v.)[9]. After sterile preparation of the surgical field, sedation was repeated as described and 0.06 mg/kg detomidine hydrochloride[12] was administered diluted in sterile saline to reach a volume of 8 ml as epidural analgesia. Local anaesthesia of the right flank was performed by infiltration with approximately 80 ml lidocaine[3]. Sedation

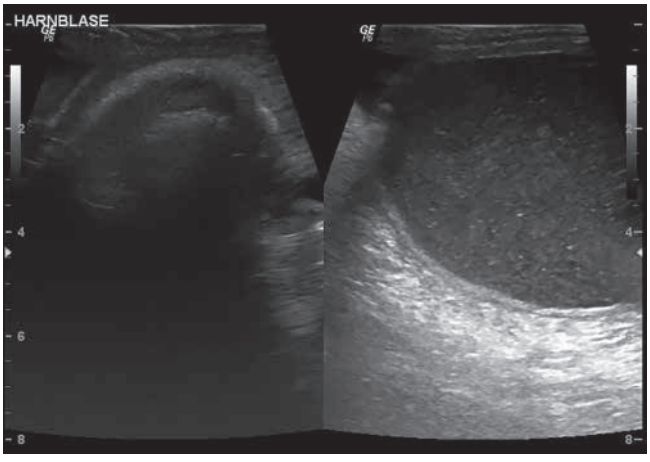

Fig. 1 Transrectal ultrasonographic appearance of the right ureter (right) which was distended and filled with hypoechoic fluid, a large hyperechoic semicircular structure with an acoustic shadow was identified as a cystic calculus (left). The image was obtained with a 8 MHz linear transrectal transducer at a scanning depth of 8 cm. *Transrektale sonographische Bildgebung des rechten Ureters (rechts), dilatiert und gefüllt mit hypoechogener Flüssigkeit. Eine große hyperechogene halbrunde Struktur mit Schallauslöschung wurde als Ureterolith identifiziert (links). Die Bilder wurden mit einem 8 MHz linear transrektal Schallkopf bei einer Eindringtiefe von 8 cm erstellt.*

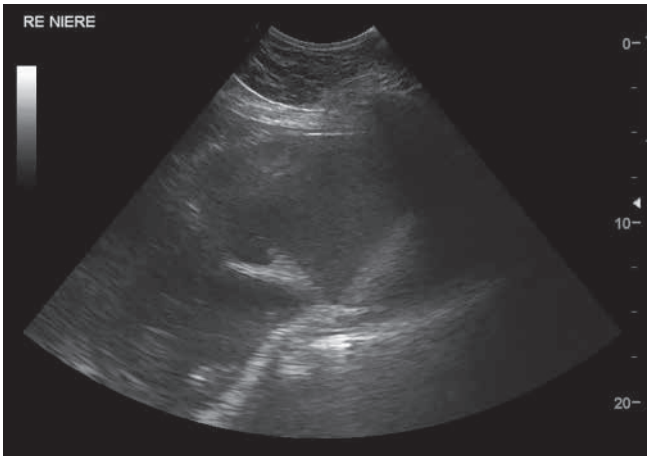

Fig. 2 Transabdominal ultrasonographic image of the right kidney from the right paralumbar fossa showing enlargement and increased echogenicity of the parenchyma and an irregular contour. The image was obtained with a 2.0 MHz curvilinear transducer at a scanning depth of 22 cm. | *Die transabdominale ultrasonographische Bildgebung der rechten Niere über die rechte Fossa paralumbalis zeigt eine Vergrößerung der Niere, eine vermehrte Echogenität des Parenchyms sowie eine unregelmäßige Kontur. Das Bild wurde mit einem konvexen 2.0 MHz Schallkopf bei einer Eindringtiefe von 22 cm erstellt.*

was maintained with an i.v. CRI of detomidine hydrochloride (Detogesic® 6.7 mg/h)[12].

A 20 cm modified grid incision was performed in the right flank, followed by a laparoscopic portal between the last ribs at the level of the ventral margin of the tuber coxae. A 30° 57 cm laparoscope (62032 BPA HOPKINS® Forward-Oblique Telescope)[10] was inserted through a laparoscopic canula in the portal. In the abdominal cavity, the right kidney was identified by palpation, confirmed by laparoscopic view, with a size of approximately 30 × 30 × 25 cm. A nephrolith could be identified on manual palpation and visualised covered by ureteral wall. The right ureter was fluid filled and distended, approximately 5 cm in diameter with a thin wall. The distended ureter could be traced back from kidney to ureteral stone, which was located close to the bladder entrance. The right retroperitoneal space was infiltrated with 20–30 ml 2 per cent lidocainehydrochlorid[3] using a laparoscopic injection needle and bluntly opened. Right ureter, artery and vein were manually freed and triple ligated with extracorporeal knots using 5 metric Polyglactin 910 (Novosyn) under laparoscopic visualisation and transected using a vessel sealing device (Ligasure)[5]. The renal vein and artery could not be separated, as was described in the case of *Röcken* et al. 2005, therefore they were ligated as a bundle. No accessory branches to the renal artery were identified. After separate double ligation and sharp resection, the caudal ureter remnant was oversewn extra-abdominally with 3 metric Polyglactin 910 (Novosyn) in a Cushing pattern. Haemostasis was visually confirmed. Before kidney exteriorisation, intra-abdominal decompression using a metal tip suction canula inserted through the kidney wall was applied to remove approximately 2 L of urine to reduce the size of the organ. The kidney was removed from the abdomen by traction on a large Lahey tissue grasping forceps, enclosed in a sterilised tick plastic storage bag. In the distal right ureter, a ureterolith of approximately 10 × 5 × 5 cm was detectable (Fig 3). As it was impossible to mobilise this part of the ureter towards the incision, the decision was made to leave the ureter stone in situ.

Peritoneum in the laparotomy incision was not closed, abdominal muscles were closed in three layers in a continuous pattern with 7 metric breaded polyglycolic acid (Safil). The subcutis was closed in a simple continuous pattern with 3.5 metric glyconate (Monosyn) and the skin was closed with interrupted horizontal matrass sutures, 3.5 metric polyamid (Dafilon).

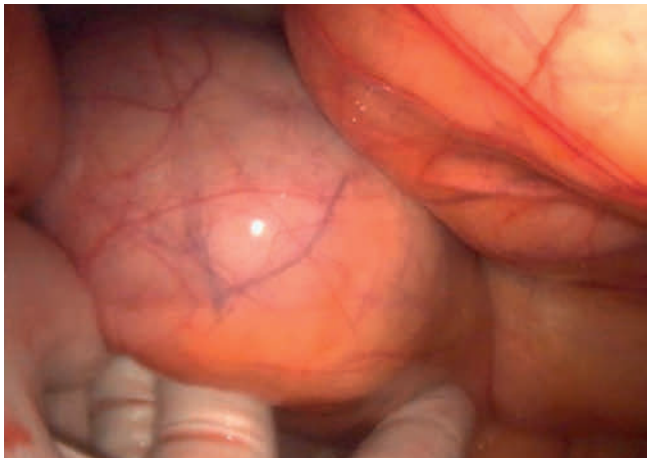

Fig. 3 Hand assisted laparoscopy image, the ureterolith was palpable and visualized in the right distal ureter. | *Bild der hand-assistierten Laparoskopie, der Ureterolith war spürbar und darstellbar im rechten distalen Ureter.*

Histopathological findings

Parts of the right kidney were submitted for histopathological examination. The right kidney measured 30 × 25 × 20 cm after intra-abdominal fluid aspiration. The renal pelvis contained calcium rich, cement coloured detritus in large amounts of variable consistency (sand-stone like) (Fig 4). The kidney showed medium-high levels of interstitial fibrosis with numerous highly dilated kidney tubules and atrophy of the renal medulla with an interstitial nephritis and suburothelial fibrosis. Similar findings are reported in hydronephroses as a consequence of blockage of the urinary tract. A bacterial culture of a swab of the detritus in the right kidney was negative.

Post-operative care

The horse was maintained on procaine penicillin (Procain-penicillin-G ad. us. vet. 15,000 IE/kg bwt i.m.)[1] and gentamicine sulfate (Genta 100 mg/ml 6.6 mg/kg bwt i.v.)[6] SID for five days following surgery. The horse was offered free choice water and progressively reintroduced to food (offering gras hay, grazing and hay cobs). As described for other cases (*Hilton et* al. 2008), the horse was in considerable pain starting 12 h post-operatively. Initial analgesia consisted of flunixin meglumine (Flunidol® 1.1 mg/kg bwt twice daily i.v.), as well as metamizole (Novaminsulfon 500 mg/ml 50 mg/kg bwt q 6h)[3]. At 27 h post-surgery, a lidocaine continuous rate infusion (CRI, loading dose 1.3 mg/kg bwt for 15 min, followed by 0.05 mg/kg/min)[3] was given for 15 hours. During this period, significant discomfort was observed to be present (trem-

Fig. 4 Macroscopic image of the right kidney after removal. A large amount of sand-stone like detritus was present throughout the dilated renal pelvis. | *Makroskopisches Bild der rechten Niere nach Entfernung. Eine große Menge sandsteinartiger Detritus füllte das dilatierte Nierenbecken.*

bling, inappetence, tachypnea, tachycardia), warranting further multimodal analgesia including the use of levamethadone hydrochloride (L-Polamivet® 0.06 mg/kg bwt i.v.)[9], butorphanol (Torbugesic® 0.03 mg/kg bwt i.v.)[12] and xylazine (Xylariem® 0.66 mg/kg bwt i.v.)[8]. As the horse was still considerably painful, a ketamine CRI (Ursotamin® 0.4 mg/kg/h)[11] was started in an attempt to make the horse more comfortable the second evening after surgery. This unfortunately resulted in adverse effects, including pronounced ataxia, and was therefore discontinued after 20 minutes. Not until five days post-operatively, the horse was judged to be pain free under flunixin meglumine (Flunidol® 1.1 mg/kg bwt twice daily i.v.)[6]. Because of reduced feacal output the gelding received water, salt and dextrose via a nasogastric tube on several occasions. Normal micturition was observed on multiple occasions but no faeces were passed spontaneously, presumably due to discomfort in active defecation. The rectum was manually evacuated for four days following surgery before spontaneous defaecation returned. To compensate for reduced food uptake parenteral nutrition (Nutriflex 13 ml/kg bwt in 24 hrs)[2] and polyionic fluids (Ringers solution 30 ml/kg bwt in 24 hrs)[2] were administered from 24 h until 7 days post-operatively. According to standard clinic procedures, the horse was maintained on low dose heparin (Heparin-Natrium-25000-ratiopharm®)[7] treatment for the duration of jugular vein catheterisation. Omeprazole (Gastrogard 4 mg/kg bwt once daily p.o.)[4] was given in the period of reduced food uptake and NSAID treatment. Kidney values were within normal limits (CREA 128 µmol/L, UREA 4.6 mmol/L) two and eight days post-operatively, as were electrolyte values. Wound healing was uneventful, though a pronounced ventral edema developed after a week (TP 65 g/L, ALB 25 g/L rr 19–32 g/L). The horse was discharged from the hospital 13 days after surgery without further medication. Stall rest and hand-walking for 15–30 min for four weeks was recommended.

Outcome

Follow-up by telephone conversations with the owner revealed that the horse was comfortable and symptom-free for six weeks after surgery. The gelding resumed his activity as a leisure horse six weeks after surgery. Twelve weeks after the surgery, the horse was presented for an acute colic episode. A strangulating small intestinal lesion was diagnosed and as the owners opted against surgical intervention, the horse was humanely euthanised.

Post-mortem findings

Upon post-mortem examination, a mesenterial rent causing ileal strangulation was diagnosed, with extensive jejunal congestion. A small adhesion between the colon descendens and the surgical site, the right kidney bed, was seen. The left kidney was macroscopically unremarkable. The right ureter was identified with the remaining concretement.

Discussion

Urolithiasis is an uncommon disease in the horse, with an estimated prevalence of 0.11 %. Nephroliths (12 %) and ureteroliths (4 %) only constitute a small percentage of uroliths (*Macbeth* 2008, *Saam* 2001). Ten per cent of the diseased horses have calculi in more than one location. Since signs are usually mild and aspecific, the disease is often unrecognised until advanced stages are reached (*Macbeth* 2008). Occasionally lumbar back pain is reported (*DeBowes* 1988, *Divers* 1989), as was recognised in the presented gelding after osteopathic examination of rideability issues. Haematuria with the passing of blood clots, as in the current case, has also been reported in mere nephrolithiasis and is thus not always a consequence of secondary urinary tract trauma (*Juzwiak et* al.1988). Dysuria, pollakuria and stranguria are uncommon and likewise not present in the current case (*DeBowes* 1988). As in most described cases of kidney disease, the general examination was unremarkable in this case and the transrectal and sonographic examination were most important in achieving the diagnosis. Multiple reports have underlined the prevalence of bilateral ureterolithiasis and or nephrolithiasis, therefore bilateral kidney disease must always be excluded before advising nephrectomy and could have been more conclusive in this case (*Divers* 1989, *Hope et* al. 1989, *Macbeth* 2008). For welfare reasons, nephrectomy should not be pursued if the prognosis for successful long-term outcome is poor (*Ferguson et* al. 2007). Blood and urine analysis are an insensitive way of analysing the remnant kidney function. A loss of at least 50% of nephrons is required to cause pathologic changes in serum urea, creatinine or urine specific gravity (*Ferguson et* al. 2007). Therefore, a functional assessment of mixed urine from both kidneys is often unremarkable in unilateral disease (*Röcken et* al. 2005). Although a urine analysis was performed in this case, evaluation of split renal function would have been more valuable. This can confirm unilateral kidney disease, while at the same time checking the health of the contralateral kidney (*Röcken et* al. 2005). In this case, identification of the right ureteral opening to the bladder on endoscopy was problematic. In case of complete obstruction of the ureter, peristaltic evacuation of urine from the distal ureteral openings is not observed on fibreoptic evaluation (*DeBowes* 1988). To improve visibility of urine outflow, the administration of intravenous sodium fluorescein could have been used, which was unfortunately not available at the time of examination (*Sullins et* al.1988). Additionally, an ultrasound guided kidney biopsy could have been used to determine the degree of renal damage and establish a more reliable prognosis (*Hope et* al. 1989, *Rijkenhuizen* 2008). The role of urinary tract infection in the aetiology of calculus formation is subject of discussion. Although concurrent pyelonephritis and nephrolithiasis have been described, 90% of horses have negative urinary culture results at the time of stone removal, as was true for the culture of the described case performed by the referring vet. Transient urinary tract infection may however have an important role in calculus initiation, as 63% of cases record positive bacteriologic culture of stone nuclei (*Macbeth* 2008, *Saam* 2001). In this case, the renal debris has been cultured negative.

Nephrolithiasis is presumed to be associated with renal pathology and literature suggests that the occurrence of lower urinary tract calculi as a consequence of upper urinary tract disease may be underestimated (*Saam* 2001). Since renal pathology was suspected, nephrectomy was the chosen treatment in this case in agreement with the owner. The standing laparoscopic technique has the advantage of avoidance of

general anaesthesia and rib resection and provides a superior anatomic overview with visual control of ligation and transection of the renal vessels and is therefore preferred over a laparotomy approach under general anaesthesia (*Cockelaere* et al. 2007, *Röcken et* al. 2007). Moreover, the hand-assisted laparoscopy allows surgeons to perform the surgery more efficiently (*Keoughan et* al. 2003). During evisceration of the kidney, manipulation can cause trauma to the abdominal wall and the kidney, and therefore contamination of the abdomen and incisional complications like seroma formation (*Röcken et* al. 2005). In human surgery, renal morcellation before abdominal retrieval is described to significantly reduce post-operative pain and clearly reduce incisional complications (*Rijkenhuizen* 2008). This technique could therefore have contributed to post-operative pain reduction, as significant manipulation was needed to remove the enlarged kidney in the current case.

In this case, the ureter could not be mobilised far enough to allow extracorporeal removal of the ureterolith by standing laparotomy. Incision of the ureter under laparoscopic vision followed by suturing was weighed against the potential abdominal contamination risk and prolonged surgery time and rejected. Alternatively, the removal of ureteroliths by ureterolithectomy over a ventral midline approach or through a vestibulourethral approach with a Dormia basket stone dislodger have been described (*DeBowes* 1988, *Macharg et* al. 1984). Since the ureteral stone was large, the only viable alternative would have been a parainguinal approach following the laparascopic nephrectomy. Risks of general anaesthesia and an additional surgery were weight against the retention of the ureteral stone. In this case, as no propulsive force was expected on the ureteral calculus after nephrectomy, it was decided to leave the ureterolith in situ.

A major challenge in the management of this patient was the post-operative period. As described in the study by *Keoughan et* al. no pain was registered in the immediate post-operative period in our patient (*Keoughan et* al. 2003). This may be related to the intra-operative use of local anaesthesia, epidural analgesia and latent effects of the standing sedation. However, severe pain developed about 12 h postoperatively, an aspect that has not been adequately described in the equine literature. In humans, significant postoperative pain is described after laparoscopic donor nephrectomy (*Kumar et* al. 2019). This pain has a multifactorial origin, encompassing port pain, pelvic organ nociception, pain from residual pneumoperitoneum and neuropathic pain. Inadequate acute pain management, mainly of movement evoked pain, can lead to central sensitisation and persistent chronic pain in people (*Mathuram* et *al*. 2012). In the kidney donor patient, various multimodal analgesic techniques have been studied and proven superior for pain relief compared to unimodal approaches (*Mathuram* et *al*. 2012). NSAIDs, as were used in this case, are described to provide moderate analgesia in humans, and are used critically because of the potential nephrotoxic effect (*Mathuram* et *al*. 2012). Morphine and other opioids are effective at the pain transmission level, and are used standardly, usually systemically in a patient-controlled analgesia system (*Capdevila et* al. 2017). As in horses, side effects such as bowel dysfunction, are limiting opioid benefits for systemic use (*Mathuram* et *al*. 2012). Therefore, alternatives to reduce opioid systemic use have been studied intensively (*Capdevila et* al. 2017, *Mathuram* et *al*. 2012). Epidural analgesia over CRI is meanwhile considered one of the mainstays for optimal postoperative analgesia and the most effective technique for dynamic pain release (*Capdevila et* al. 2017, *Mathuram* et *al*. 2012). In humans, thoracic epidural analgesia is considered superior to lumbar epidural analgesia (*Mathuram* et *al*. 2012). In the current case, implantation of an epidural catheter was considered. This was not implemented, due to regulational difficulties in the use of morphine in Germany, which is the only medication reported to reach a dermatome far enough cranially (*Natalini* and *Robinson* 2000). The use of epidural local anaesthetics, as in humans, can lead to severe ataxia and recumbency upon motor blockage of the pelvic limbs and was therefore not considered a valuable option. The systemic sedative effects of epidural administration of α2 agonists were also undesired. Alternative techniques in human patients use local anaesthetics, which prevent conduction of nociceptive stimuli and central sensitisation (*Mathuram* et *al*. 2012). Implantation of catheters for continuous surgical site analgesia have been described with good results, with use up to 72 hours post-surgery (*Capdevila et* al. 2017). Also, neuraxial techniques are used in which local anaesthetics are injected into the neurofacial plane to block sensory nerves before they perforate the musculature to innervate the abdominal wall. The poor vascularisation locally is thought to be responsible for the prolonged analgesic effect of this procedure (*Mathuram* et *al*. 2012). Lately, intraperitoneal nebulisation of local anaesthetics was described for post-operative pain release and may in future be a possibility in equine patients (*Kumar et* al. 2019). The latter techniques require further investigation in equine patients. In our patient, a low dose ketamine CRI was implemented in an attempt to improve multimodal analgesia, with adverse effects. These could be explained by altered post-operative pharmacokinetics and pharmacodynamics of renally metabolised and excreted drugs (*Ferguson et* al. 2007). Horses with renal dysfunction are described to show prolonged recovery times after ketamine anaesthesia (*Lin et* al.2014). Frequent monitoring of serum drug levels may thus be required, although unlikely feasible in a clinical setting (*Ferguson et* al. 2007). Despite the initial five days in which pain management was suboptimal, nephrectomy without ureterolith removal provided a successful solution for this case of severe kidney disease.

Manufacturers' addresses

1 aniMedica GmbH, Senden-Bösensell, Germany
2 B. Braun Vet Care GmbH, Tuttlingen, Germany
3 Bela-pharm, Vechta, Germany
4 Boehringer Ingelheim Vetmedica GmbH, Ingelheim am Rhein, Germany
5 COVIDIEN Deutschland GmbH, Neustadt a. d. Donau, Germany
6 CP-Pharma, Burgdorf, Germany
7 Dechra Veterinary Products Deutschland GmbH, Aulendorf, Germany
8 Ecuphar GmbH, Greifswald, Germany
9 Intervet Deutschland GmbH, Unterschleißheim, Germany
10 KARL STORZ SE & Co. KG, Tuttlingen, Germany
11 Serumwerk Bernburg AG, Bernburg, Germany
12 Zoetis Deutschland GmbH, Berlin, Germany

Conflict of interest statement

No conflicts of interest have been declared.

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