Primary Ureteral Urothelial (Transitional Cell) Carcinoma in a Boxer dog

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Journal:	*Veterinary Record Case Reports*
Manuscript ID	vetreccr-2018-000607.R1
Manuscript Type:	Companion or pet animals
Species:	Dogs
Date Submitted by the Author:	n/a
Complete List of Authors:	O Cathasaigh, Micheal; Cambridge Veterinary School, Arenas, Carolina; University Complutense Madrid, Small Animal Medicine and Surgery Clinical Sciences Ortiz, Ana; Cambridge Veterinary School, Department of Veterinary Medicine Hall, Jon; University of Edinburgh Royal Dick School of Veterinary Studies, Veterinary medicine Rudorf, Heike; Cambridge Veterinary School, Department of Veterinary Medicine
Keywords:	Primary ureteral urothelial carcinoma, Intravenous urography, Abdominal ultrasound
Topics:	Oncology, Radiology, Imaging, Urology
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TITLE OF CASE ***Do not include "a case report"***

Primary Ureteral Urothelial (Transitional Cell) Carcinoma in a Boxer dog.

SUMMARY ***Up to 150 words summarising the case presentation and outcome (this will be freely available online)***

An eight year old, male entire Boxer dog presented with a 4-week history of haematuria. Abdominal ultrasound identified a moderately dilated left ureter from immediately distal to the renal pelvis to a focal stenosis at the level of L5. Intravenous urography showed a diffusely tortuous proximal left ureter with irregular contrast borders and focal stenosis distally. Left uretero-nephrectomy was performed and histology of the left ureter revealed a primary ureteral urothelial (transitional cell) carcinoma infiltrating the ureteral wall. This is the first imaging description of a primary ureteral urothelial carcinoma and only the second description of a primary ureteral urothelial carcinoma in veterinary literature.

BACKGROUND ***Why you think this case is important – why did you write it up?***

Neoplasms of the urinary tract are commonly encountered, however they only account for 0.5-1%[1] of all canine neoplasms and less than 2% of all malignant canine neoplasms.[1,2] The majority of these tumors originate in the urinary bladder, with primary ureteral neoplasms being quite rare.[1]

A number of primary neoplasms can affect the ureters. Over the past 40 years, 12 individual reports have been published, including fibroepithelial polyps, leiomyoma, transitional cell papilloma, leiomyosarcoma, urothelial (transitional cell) carcinoma, fibropapilloma, spindle cell sarcoma, giant cell sarcoma, mast cell tumour and a poorly differentiated sarcoma.[4, 7-17] It is claimed that urothelial carcinoma is the most common primary ureteral neoplasm,[1] however to the authors knowledge, there has only been one previous "brief communication" from 1980 outlining a primary ureteral urothelial carcinoma.[7] The following discussion details the clinical, imaging and histopathological findings of primary ureteral urothelial carcinoma in a Boxer dog.

CASE PRESENTATION ***Presenting features, clinical and environmental history***

An eight-year-old male entire Boxer dog presented to the University of Cambridge, Queens Veterinary School Hospital (QVSH) with a four-week history of persistent haematuria and lethargy. Abdominal radiographs taken at the referring practice, one week after the onset of clinical signs and four weeks prior to presentation, were normal. Neither cephalexin nor the combination of amoxicillin-clavulanic acid and meloxicam with a urinary diet (Waltham Urinary Diet) had resulted in improvement of the haematuria. The dog was thus referred for the investigation of the haematuria.

INVESTIGATIONS ***If relevant***

On presentation, the dog was bright and alert. There was no pain or discomfort on abdominal palpation. A complete blood count and biochemistry profile were unremarkable. Urine sample collected via cystocentesis revealed haematuria (60 RBC/hpf; reference range 0-5), and a slightly elevated urine protein to creatinine ratio of 0.44 (reference range 0-0.4). No abnormality of the red blood cells and no nucleated cells were seen. There was no growth on urinary culture.

Abdominal ultrasound was performed with a curved-linear (5-8 MHz) as well as a linear (5-12 MHz) transducer (Philips HDI 5000 Sono CT). The left ureter was found to be abnormal (Fig. 1). The changes consisted of an increased size of both the ureteral lumen and the ureteral wall. Changes started immediately distal to the renal pelvis and ended at the level of the caudal lumbar spine. Immediately distal to the kidney, total ureteral luminal diameter measured 13 mm, gradually thinning to 2.5 mm in the distal third of the ureter. The ureteral contents were flocculent, swirling and the ureter followed a tortuous path caudally. The walls were mildly hypoechoic and thickened, particularly proximally, becoming normal in thickness distally. The ureter was actively contracting throughout the study. Left kidney and urinary bladder were normal with normal “jets” of urine entering the bladder.

The following day, the dog was anesthetised for an intravenous urogram (IVU). Survey abdominal radiographs were normal. A Foley catheter was inserted into the urinary bladder. The urine was removed and 2 mls/kg of room air was instilled via the Foley catheter. A bolus of 2 mls/kg Iohexol – 240 contrast medium (Omnipaque 240 mgI/mL, GE healthcare, Oslo, Norway) was injected intravenously. The resulting nephrogram phase of the IVU showed a normal, homogenous enhancement of both kidneys. The pyelogram was normal. The ureterogram and cystogram phases showed a markedly abnormal left ureter (Fig. 2 & Fig. 3). The ureteral lumen was moderately dilated (8-11 mm) starting immediately distal to the renal pelvis and extending to the level of the caudal aspect of the 5th lumbar vertebra (L5). Multiple filling defects were present in the contrast column giving it a highly irregular contrast outline. At the level of caudal L5, the contrast column showed focal narrowing (1.3 mm). The ureteral wall was markedly thickened at this level. Distal to this narrowing, the ureter continued a tortuous path with an irregular contrast column and dilated lumen (6.5 mm) to the level of L6. Caudal to this, the ureter remained dilated (2 mm), but the lumen appeared smooth all the way to the trigone with no further abnormalities seen in the ureteral wall. This corresponded to the ultrasonographic findings of a slightly dilated lumen distally but with the ureteral wall appearing normal. The right ureter and trigone of the bladder were normal. A retrograde urethrocystogram, which was performed 30 minutes after the initial IVU procedure, was normal. Based on the imaging findings, the irregularly thickened ureteral wall appeared to be the reason for the haematuria.

DIFFERENTIAL DIAGNOSIS ***If relevant***

There are multiple differential diagnoses for the haematuria this dog presented for. Prior to ultrasound, these included urinary calculi, neoplastic disease, idiopathic renal haematuria and pyelonephritis (as these can sometimes have a negative result on urinalysis and no growth on culture). Other causes which had been ruled out or thought much less likely due to initial bloodwork, urinalysis and history included a coagulopathy (normal complete blood count), traumatic injury (no history of this), pharmaceuticals (no history of use of drugs such as cyclophosphamide, the haematuria had commenced prior to the use of NSAIDs). A lower urinary tract infection was also thought unlikely due to the benign sediment and lack of growth of any bacteria on culture.

Post abdominal ultrasound and IVU/retrograde urethrogram, our primary differential diagnosis was neoplasia of the ureter. No evidence of calculi or mineralisation was found in any section of the urinary system. When coupled with the fact that no evidence of renal pelvic enlargement was found, benign complete obstruction was considered unlikely.

TREATMENT ***If relevant***

The dog was re-admitted for left uretero-nephrectomy seven days after initial presentation. Haematuria had been present consistently. A ventral midline coeliotomy requiring a left parapreputial incision was performed and the abdomen was thoroughly explored. The left kidney appeared normal. The left ureter was thickened and tapered as it progressed caudally. The remainder of the abdomen was unremarkable. A standard complete left ureteronephrectomy was performed. The patient recovered uneventfully and was discharged on a five day course of meloxicam (Metacam®), 0.1 mg/kg, PO, SID. The left kidney and ureter were submitted for histopathological examination.

Macroscopically, the left ureter had a pale pink and smooth serosal surface and was soft to the touch. Proximally it measured 14 mm, from serosa to serosa, with the lumen being irregularly dilated up to 13 mm, distally. The ureteral mucosa was cream coloured, soft, markedly thickened in the areas of luminal dilation (5 to 9.5 mm thick microscopically), and had an irregular and oedematous appearance (Fig. 4). The distal ureter, at the level of the surgical margin, did not show gross changes. The left kidney and its renal pelvis were normal.

Representative histopathological samples showed the urothelium of the ureter to be effaced by a non-papillary and locally infiltrative urothelial carcinoma extending to the subjacent lamina propria (Fig. 5). Most neoplastic cells exhibited moderately sized to large intracytoplasmic vacuoles and eccentric nuclei or formed pseudoacini containing eosinophilic homogeneous material, which stained positively with PAS and alcian blue stains (acid polysaccharides), both classically associated with urothelial carcinomas. Microscopically, neoplasic cells were present at the surgical margin of the distal ureter. Samples from the left kidney demonstrated mild chronic membranous glomerulonephritis. There was no evidence of neoplastic disease in the renal tissues.

OUTCOME AND FOLLOW-UP

The owners elected not to proceed with chemotherapy and the dog was discharged on NSAIDs (meloxicam, Metacam®) for five days, 0.1 mg/kg, PO, SID. After initially declining follow up appointments, the dog represented 23 months post operatively, for episodes of collapse. There had been no further episodes of haematuria or any other clinical sign related to the urinary system.

On abdominal ultrasound, the bladder was unaffected. Unfortunately, a number of masses were found in the abdominal cavity; One, focal, echogenic mass measuring 0.8 cm x 1.6 cm, was seen in the retroperitoneal space in the region of the removed left

kidney. It was felt that this most likely represented a local re-occurrence of the primary tumour removed during surgery. The second was a large, rounded mass of mixed echogenicity associated with the tail of the spleen, measuring at least 3 cm x 3 cm. The third was a focal hyperechoic mass in the mid jejunum with a complete loss of layering of the associated intestinal wall. Metastatic disease was considered the most likely differential diagnosis for the second and third mass. However, other differential diagnoses for the splenic mass include other primary neoplasms (haemangioma, haemangiosarcoma, histiocystic sarcoma, mast cell tumour) and less likely, extramedullary haemoatopoesis, lymphoid hyperplasia and a haematoma. The intestinal mass was thought to be most likely neoplastic in origin due to the focal thickening and loss of layering, though an inflammatory cause can not be ruled out. Neoplastic differential diagnoses other than a metastatic cause include adenocarcinoma, mast cell tumour and lymphoma.

Further investigation was declined by the owner and the dog was taken home with a view to euthanasia when clinical symptoms became too severe.

DISCUSSION ***Include a very brief review of similar published cases***

It has been suggested that the cause of primary ureteral neoplasia is invariably a urothelial carcinoma.[1] This is rather curious, as other than the brief communication from 1980[7], the authors could not find another report of primary ureteral urothelial carcinoma. In the past 40 years, 17 cases of a primary ureteral tumor have been described in 12 case reports, including: fibroepithelial polyps (7) leiomyoma (2), transitional cell papilloma (2) leiomyosarcoma (1), fibropapilloma (1), spindle cell sarcoma (1), giant cell sarcoma (1), mast cell tumor (1) and a poorly differentiated sarcoma (1).[4, 7-17] This poses the question if primary ureteral transitional carcinomas are as common as is claimed [1] or are simply under reported.

Ultrasound was the initial imaging modality used in this case. It has been previously documented that ultrasound is a sensitive method of diagnosing renal lesions and ureteral dilation,[3] and indeed ultrasound confirmed the presence of a focal ureteral dilation with an abnormally thickened wall. The IVU complimented the ultrasonographic findings. It demonstrated that the proximal and mid ureter was diffusely abnormal with marked intraluminal protrusions from the wall, that the ureter was tortuous and that there was stenosis distally. In particular, it demonstrated the intraluminal filling defects clearly, which can often be difficult to demonstrate in both humans and animals.[4, 5] This does not mean, however, that an IVU should always be used in isolation. Complete ureteral obstruction, which has been described in the majority of primary ureteral neoplasms, can cause severe hydronephrosis and result in poor or no urinary excretion. In such cases it has been reported that percutaneous pyelography may improve the diagnostic yield of the study.[4] Computed tomography has also been shown to demonstrate the ureters clearly on both non-contrast and contrast studies.[6]

The ureteral urothelial carcinoma reported here presented not as a discrete mass as previously reported,[7] but as a generalised thickening of the ureteral wall. This thickening caused by infiltration with neoplastic cells was most evident in the mid and proximal sections of the ureter, with the distal infiltrative changes only identified microscopically. This is in contrast to the urothelial carcinoma communication from 1980, in which there was marked hydronephrosis and hydroureter due to a discreet mass present in the distal ureter causing complete obstruction.
This ureteral urothelial carcinoma also presented differently to the cases of primary ureteral neoplasia in the literature. The majority of these tumors were found to have either a discreet mass or polyps, emanating from the ureter, causing subsequent obstruction.[4, 7-10,12-17] Thus the majority showed evidence of secondary hydronephrosis and hydroureter[15, 17] both clinically and/or grossly/histologically. In our case however,

there was no evidence of hydronephrosis or pyelectasia, and only a moderate hydroureter. The most likely reason is the infiltrative nature of the tumor that did not result in focal, luminal occlusion, as opposed to the discreet mass seen in the majority of the other cases. This difference also likely accounts for the fact that the only clinical signs seen in this case were hematuria and lethargy. Interestingly, hematuria has only been seen in three other cases.[10, 14-15] Anorexia, lethargy, abnormal urination and abdominal pain were far more common in the reported literature.[4, 7, 9-10, 7-14]

On repeat abdominal ultrasound 23 months after initial presentation, there were no abnormalities seen in the bladder or the remaining urinary tract. This was surprising as microscopically, neoplastic cells were found at the surgical margin of the distal ureter as it entered the urinary bladder. This is a common problem as the majority of urothelial cell carcinomas are intermediate to high-grade papillary infiltrative tumours,[22-24] thus surgical resection is often not possible.[22] In the case of urothelial carcinomas of the bladder, complete surgical resection is further complicated by the fact that they are often located in the trigonal region and also that they may have spread to the urethra. Additionally, some dogs can develop multifocal urothelial carcinomata in the bladder. This is thought to be consistent with the "field effect" seen in humans, where malignant change occurs of the entire mucosal lining in response to carcinogens in the urine.[24] Therefore, it is important to strive for as wide a surgical margin as is possible in the effort to achieve clean margins, reducing the likelihood of recurrence; however, this can be challenging to achieve in cases of urothelial carcinoma.

Finally, urinary bladder/urethral urothelial carcinomas in general carry a poor prognosis, with a reported median survival time with combined treatment (surgery, traditional chemotherapy or metronomic chemotherapy) ranging from 5 to 7 months.[18-21] Although in this case surgery was unlikely to have been curative, the survival time of 23 months and good quality of life after surgery is encouraging and much higher than previously reported for urothelial carcinoma of the urinary tract.

LEARNING POINTS/TAKE HOME MESSAGES ***3 to 5 bullet points – this is a required field***

- Primary ureteral tumours can present in a variety of ways, and should be included in the differentials list for haematuria.
- Ultrasound and intravenous urogram can be utilised in the diagnosis of a ureteral tumour.
- Surgical resection may be a first choice of treatment for instant relief from clinical symptoms and, possibly, longer survival.

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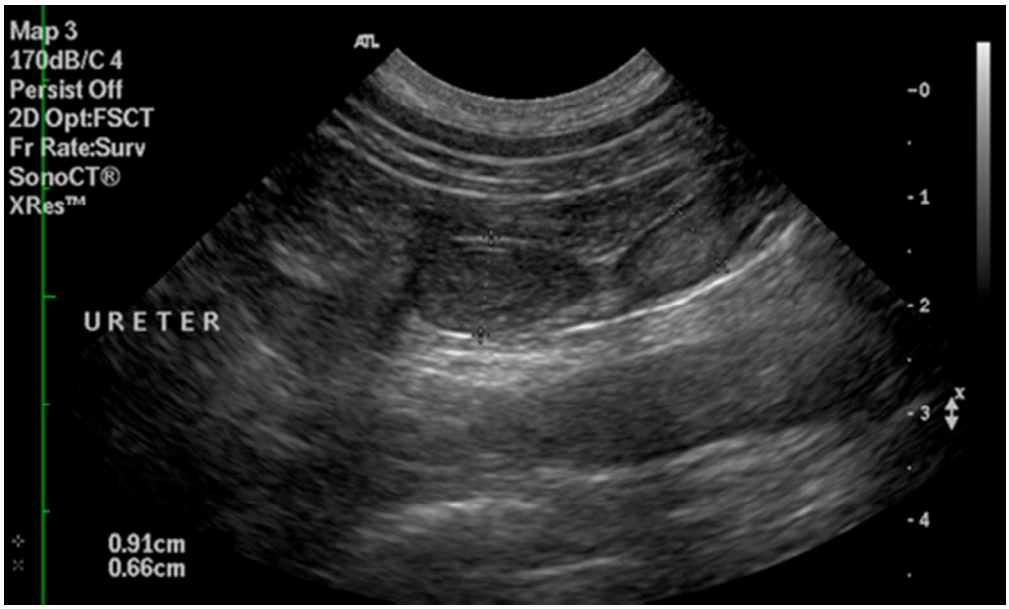

Fig. 1: Left ureter: Ultrasound demonstrated a moderately distended ureteral lumen with a hyperechoic, swirling material. Ureteral walls are mildly thickened in this image.

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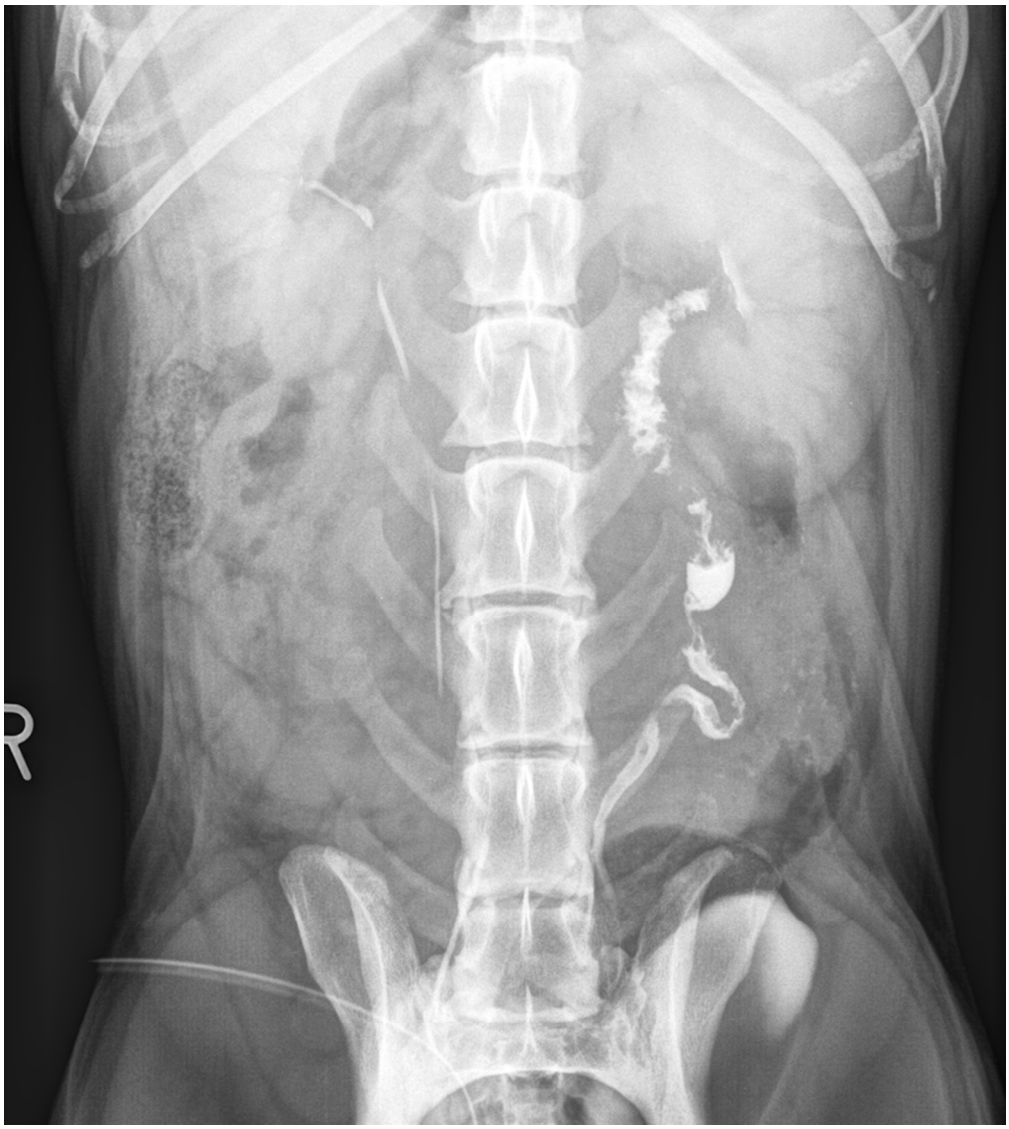

Fig. 2: Intravenous urography, ventrodorsal radiograph: This radiograph demonstrated a moderately dilated ureter from the level just distal to the renal pelvis to the level of caudal L5, with a funnel shaped narrowing at the level of caudal L5. Within this region of moderately dilated ureter, there are multiple filling defects present in the contrast column with a highly irregular contrast outline.

74x82mm (300 x 300 DPI)

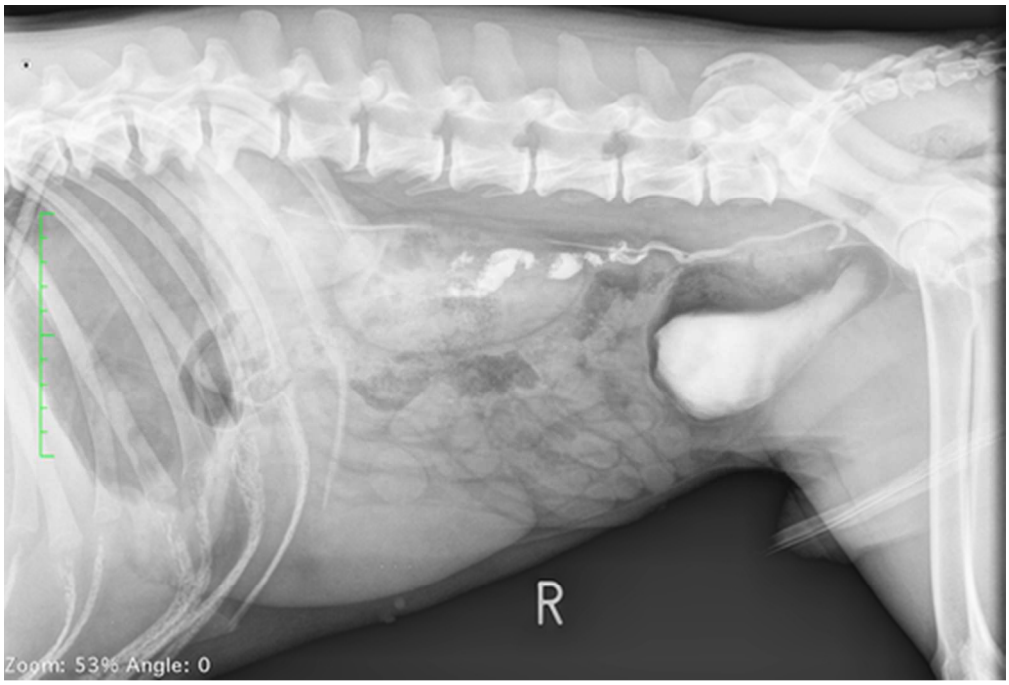

Fig 3: Intravenous urography right lateral radiograph: A highly irregular ureter is visible, extending from the level just distal to the renal pelvis to the level of cranial L6. The distal third of the ureter is visualised more clearly than on the VD. It is very mildly thickened, but there are no irregularities of the wall, or filling defects seen.

42x28mm (300 x 300 DPI)

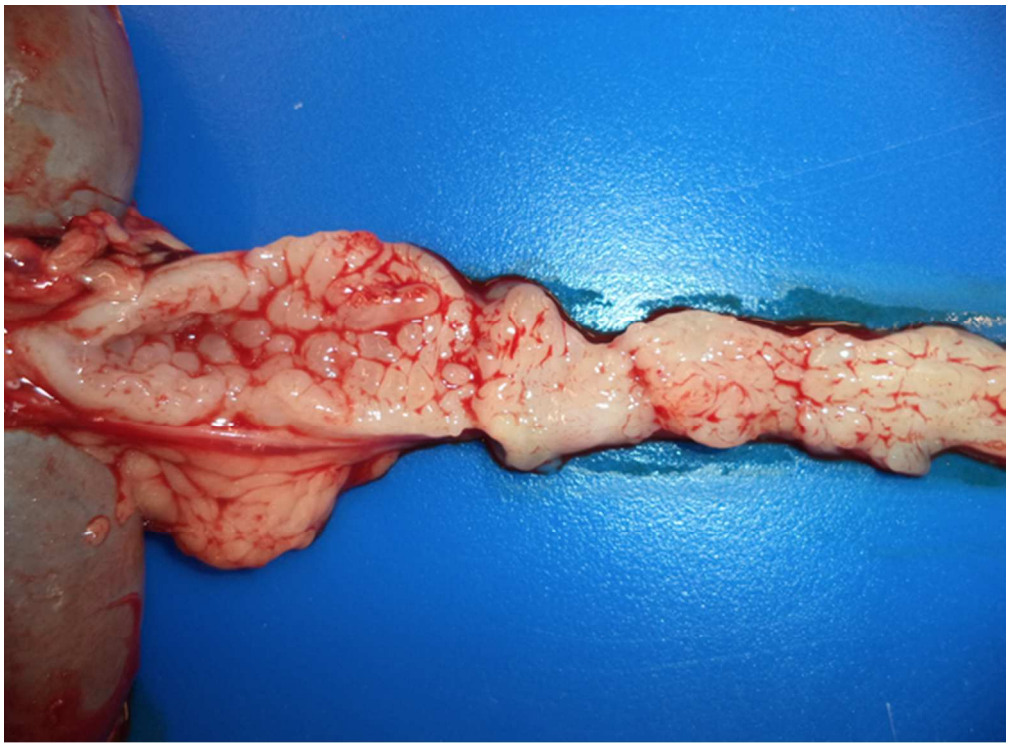

Fig. 4: Left ureter. Macroscopic appearance of the ureteral urothelial carcinoma, where the ureter has been longitudinally dissected. Areas of the ureteral mucosa containing the tumour were markedly thickened and irregular.

52x38mm (300 x 300 DPI)

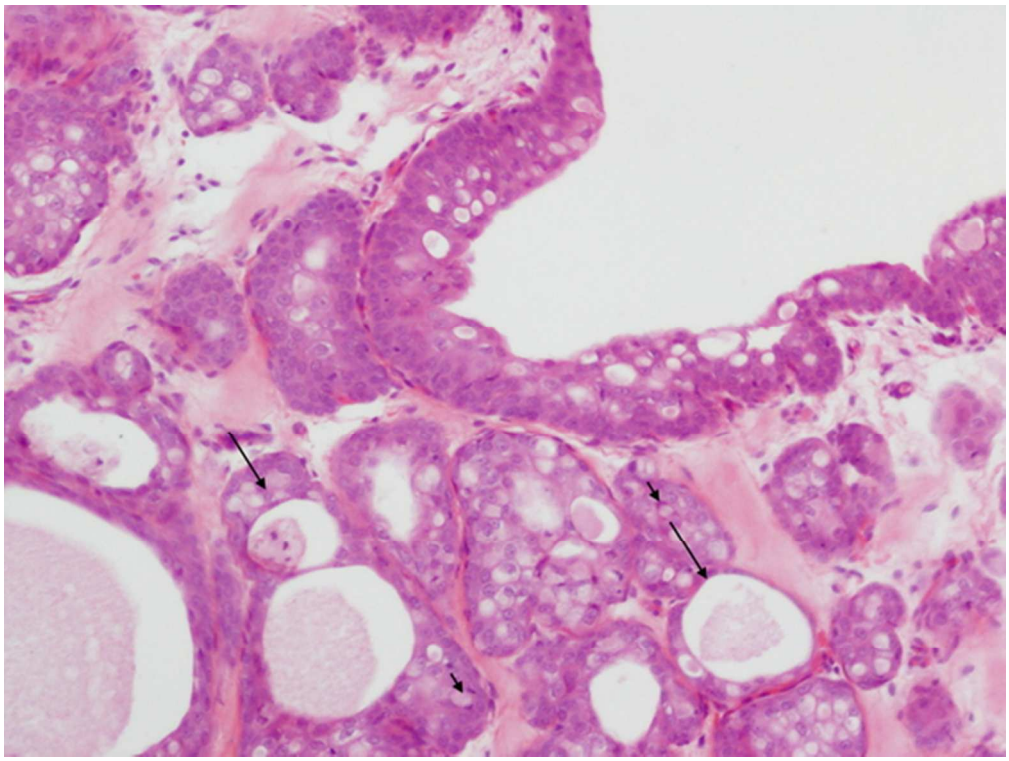

Fig. 5: Histological section of the ureteral urothelial carcinoma (haematoxylin and eosin stain). Pseudoacini containing mucinous material (long arrows) and signet ring-like cells (short arrows) are visible. 100x.

50x38mm (300 x 300 DPI)

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On presentation, the dog was bright and alert. There was no pain or discomfort on abdominal palpation. A complete blood count and biochemistry profile were unremarkable. Urine sample collected via cystocentesis revealed haematuria (60 RBC/hpf; reference range 0-5), and a slightly elevated urine protein to creatinine ratio of 0.44 (reference range 0-0.4). No abnormality of the red blood cells and no nucleated cells were seen. There was no growth on urinary culture.

Abdominal ultrasound was performed with a curved-linear (5-8 MHz) as well as a linear (5-12 MHz) transducer (Philips HDI 5000 Sono CT). The left ureter was found to be abnormal (Fig. 1). The changes consisted of an increased size of both the ureteral lumen and the ureteral wall. Changes started immediately distal to the renal pelvis and ended at the level of the caudal lumbar spine. Immediately distal to the kidney, total ureteral luminal diameter measured 13 mm, gradually thinning to 2.5 mm in the distal third of the ureter. The ureteral contents were flocculent, swirling and the ureter followed a tortuous path caudally. The walls were mildly hypoechoic and thickened, particularly proximally, becoming normal in thickness distally. The ureter was actively contracting throughout the study. Left kidney and urinary bladder were normal with normal “jets” of urine entering the bladder.

The following day, the dog was anesthetised for an intravenous urogram (IVU). Survey abdominal radiographs were normal. A Foley catheter was inserted into the urinary bladder. The urine was removed and 2 mls/kg of room air was instilled via the Foley catheter. A bolus of 2 mls/kg Iohexol – 240 contrast medium (Omnipaque 240 mgI/mL, GE healthcare, Oslo, Norway) was injected intravenously. The resulting nephrogram phase of the IVU showed a normal, homogenous enhancement of both kidneys. The pyelogram was normal. The ureterogram and cystogram phases showed a markedly abnormal left ureter (Fig. 2 & Fig. 3). The ureteral lumen was moderately dilated (8-11 mm) starting immediately distal to the renal pelvis and extending to the level of the caudal aspect of the 5th lumbar vertebra (L5). Multiple filling defects were present in the contrast column giving it a highly irregular contrast outline. At the level of caudal L5, the contrast column showed focal narrowing (1.3 mm). The ureteral wall was markedly thickened at this level. Distal to this narrowing, the ureter continued a tortuous path with an irregular contrast column and dilated lumen (6.5 mm) to the level of L6. Caudal to this, the ureter remained dilated (2 mm), but the lumen appeared smooth all the way to the trigone with no further abnormalities seen in the ureteral wall. This corresponded to the ultrasonographic findings of a slightly dilated lumen distally but with the ureteral wall appearing normal. The right ureter and trigone of the bladder were normal. A retrograde urethrocystogram, which was performed 30 minutes after the initial IVU procedure, was normal. Based on the imaging findings, the irregularly thickened ureteral wall appeared to be the reason for the haematuria.

DIFFERENTIAL DIAGNOSIS ***If relevant***

There are multiple differential diagnoses for the haematuria this dog presented for. Prior to ultrasound, these included urinary calculi, neoplastic disease, idiopathic renal haematuria and pyelonephritis (as these can sometimes have a negative result on urinalysis and no growth on culture). Other causes which had been ruled out or thought much less likely due to initial bloodwork, urinalysis and history included a coagulopathy (normal complete blood count), traumatic injury (no history of this), pharmaceuticals (no history of use of drugs such as cyclophosphamide, the haematuria had commenced prior to the use of NSAIDs). A lower urinary tract infection was also thought unlikely due to the benign sediment and lack of growth of any bacteria on culture.

Post abdominal ultrasound and IVU/retrograde urethrogram, our primary differential diagnosis was neoplasia of the ureter. No evidence of calculi or mineralisation was found in any section of the urinary system. When coupled with the fact that no evidence of renal pelvic enlargement was found, benign complete obstruction was considered unlikely.

TREATMENT ***If relevant***

The dog was re-admitted for left uretero-nephrectomy seven days after initial presentation. Haematuria had been present consistently. A ventral midline coeliotomy requiring a left parapreputial incision was performed and the abdomen was thoroughly explored. The left kidney appeared normal. The left ureter was thickened and tapered as it progressed caudally. The remainder of the abdomen was unremarkable. A standard complete left ureteronephrectomy was performed. The patient recovered uneventfully and was discharged on a five day course of meloxicam (Metacam®), 0.1 mg/kg, PO, SID. The left kidney and ureter were submitted for histopathological examination.

Macroscopically, the left ureter had a pale pink and smooth serosal surface and was soft to the touch. Proximally it measured 14 mm, from serosa to serosa, with the lumen being irregularly dilated up to 13 mm, distally. The ureteral mucosa was cream coloured, soft, markedly thickened in the areas of luminal dilation (5 to 9.5 mm thick microscopically), and had an irregular and oedematous appearance (Fig. 4). The distal ureter, at the level of the surgical margin, did not show gross changes. The left kidney and its renal pelvis were normal.

Representative histopathological samples showed the urothelium of the ureter to be effaced by a non-papillary and locally infiltrative urothelial carcinoma extending to the subjacent lamina propria (Fig. 5). Most neoplastic cells exhibited moderately sized to large intracytoplasmic vacuoles and eccentric nuclei or formed pseudoacini containing eosinophilic homogeneous material, which stained positively with PAS and alcian blue stains (acid polysaccharides), both classically associated with urothelial carcinomas. Microscopically, neoplasic cells were present at the surgical margin of the distal ureter. Samples from the left kidney demonstrated mild chronic membranous glomerulonephritis. There was no evidence of neoplastic disease in the renal tissues.

OUTCOME AND FOLLOW-UP

The owners elected not to proceed with chemotherapy and the dog was discharged on NSAIDs (meloxicam, Metacam®) for five days, 0.1 mg/kg, PO, SID. After initially declining follow up appointments, the dog represented 23 months post operatively, for episodes of collapse. There had been no further episodes of haematuria or any other clinical sign related to the urinary system.

On abdominal ultrasound, the bladder was unaffected. Unfortunately, a number of masses were found in the abdominal cavity; One, focal, echogenic mass measuring 0.8 cm x 1.6 cm, was seen in the retroperitoneal space in the region of the removed left

kidney. It was felt that this most likely represented a local re-occurrence of the primary tumour removed during surgery. The second was a large, rounded mass of mixed echogenicity associated with the tail of the spleen, measuring at least 3 cm x 3 cm. The third was a focal hyperechoic mass in the mid jejunum with a complete loss of layering of the associated intestinal wall. Metastatic disease was considered the most likely differential diagnosis for the second and third mass. However, other differential diagnoses for the splenic mass include other primary neoplasms (haemangioma, haemangiosarcoma, histiocystic sarcoma, mast cell tumour) and less likely, extramedullary haemoatopoesis, lymphoid hyperplasia and a haematoma. The intestinal mass was thought to be most likely neoplastic in origin due to the focal thickening and loss of layering, though an inflammatory cause can not be ruled out. Neoplastic differential diagnoses other than a metastatic cause include adenocarcinoma, mast cell tumour and lymphoma.

Further investigation was declined by the owner and the dog was taken home with a view to euthanasia when clinical symptoms became too severe.

DISCUSSION ***Include a very brief review of similar published cases***

It has been suggested that the cause of primary ureteral neoplasia is invariably a urothelial carcinoma.[1] This is rather curious, as other than the brief communication from 1980[7], the authors could not find another report of primary ureteral urothelial carcinoma. In the past 40 years, 17 cases of a primary ureteral tumor have been described in 12 case reports, including: fibroepithelial polyps (7) leiomyoma (2), transitional cell papilloma (2) leiomyosarcoma (1), fibropapilloma (1), spindle cell sarcoma (1), giant cell sarcoma (1), mast cell tumor (1) and a poorly differentiated sarcoma (1).[4, 7-17] This poses the question if primary ureteral transitional carcinomas are as common as is claimed [1] or are simply under reported.

Ultrasound was the initial imaging modality used in this case. It has been previously documented that ultrasound is a sensitive method of diagnosing renal lesions and ureteral dilation,[3] and indeed ultrasound confirmed the presence of a focal ureteral dilation with an abnormally thickened wall. The IVU complimented the ultrasonographic findings. It demonstrated that the proximal and mid ureter was diffusely abnormal with marked intraluminal protrusions from the wall, that the ureter was tortuous and that there was stenosis distally. In particular, it demonstrated the intraluminal filling defects clearly, which can often be difficult to demonstrate in both humans and animals.[4, 5] This does not mean, however, that an IVU should always be used in isolation. Complete ureteral obstruction, which has been described in the majority of primary ureteral neoplasms, can cause severe hydronephrosis and result in poor or no urinary excretion. In such cases it has been reported that percutaneous pyelography may improve the diagnostic yield of the study.[4] Computed tomography has also been shown to demonstrate the ureters clearly on both non-contrast and contrast studies.[6]

The ureteral urothelial carcinoma reported here presented not as a discrete mass as previously reported,[7] but as a generalised thickening of the ureteral wall. This thickening caused by infiltration with neoplastic cells was most evident in the mid and proximal sections of the ureter, with the distal infiltrative changes only identified microscopically. This is in contrast to the urothelial carcinoma communication from 1980, in which there was marked hydronephrosis and hydroureter due to a discreet mass present in the distal ureter causing complete obstruction.

This ureteral urothelial carcinoma also presented differently to the cases of primary ureteral neoplasia in the literature. The majority of these tumors were found to have either a discreet mass or polyps, emanating from the ureter, causing subsequent obstruction.[4, 7-10,12-17] Thus the majority showed evidence of secondary hydronephrosis

and hydroureter[15, 17] both clinically and/or grossly/histologically. In our case however, there was no evidence of hydronephrosis or pyelectasia, and only a moderate hydroureter. The most likely reason is the infiltrative nature of the tumor that did not result in focal, luminal occlusion, as opposed to the discreet mass seen in the majority of the other cases. This difference also likely accounts for the fact that the only clinical signs seen in this case were hematuria and lethargy. Interestingly, hematuria has only been seen in three other cases.[10, 14-15] Anorexia, lethargy, abnormal urination and abdominal pain were far more common in the reported literature.[4, 7, 9-10, 7-14]

On repeat abdominal ultrasound 23 months after initial presentation, there were no abnormalities seen in the bladder or the remaining urinary tract. This was surprising as microscopically, neoplastic cells were found at the surgical margin of the distal ureter as it entered the urinary bladder. This is a common problem as the majority of urothelial cell carcinomas are intermediate to high-grade papillary infiltrative tumours,[22-24] thus surgical resection is often not possible.[22] In the case of urothelial carcinomas of the bladder, complete surgical resection is further complicated by the fact that they are often located in the trigonal region and also that they may have spread to the urethra. Additionally, some dogs can develop multifocal urothelial carcinomata in the bladder. This is thought to be consistent with the "field effect" seen in humans, where malignant change occurs of the entire mucosal lining in response to carcinogens in the urine.[24] Therefore, it is important to strive for as wide a surgical margin as is possible in the effort to achieve clean margins, reducing the likelihood of recurrence; however, this can be challenging to achieve in cases of urothelial carcinoma.

Finally, urinary bladder/urethral urothelial carcinomas in general carry a poor prognosis, with a reported median survival time with combined treatment (surgery, traditional chemotherapy or metronomic chemotherapy) ranging from 5 to 7 months.[18-21] Although in this case surgery was unlikely to have been curative, the survival time of 23 months and good quality of life after surgery is encouraging and much higher than previously reported for urothelial carcinoma of the urinary tract.

LEARNING POINTS/TAKE HOME MESSAGES ***3 to 5 bullet points – this is a required field***

- Primary ureteral tumours can present in a variety of ways, and should be included in the differentials list for haematuria.
- Ultrasound and intravenous urogram can be utilised in the diagnosis of a ureteral tumour.
- Surgical resection may be a first choice of treatment for instant relief from clinical symptoms and, possibly, longer survival.

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OWNER'S PERSPECTIVE ***Optional***

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