COMpanion OR PET ANIMALS

Suspected haemorrhagic cystitis in a dog as delayed complication after contrast-enhanced computed tomography

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SUMMARY
A 10-month-old female intact Australian shepherd dog was diagnosed with an intrapelvic mass. Blood and urinanalyses were unremarkable. A contrast-enhanced CT scan was performed to define the extent of the mass. A large, expansile, heterogeneous mass, extending from the ventral aspect of the last lumbar vertebra until the second caudate vertebra and invading the vertebral canal at the lumbosacral junction with displacement of all organs in the caudal abdomen, was diagnosed. Two days after the CT scan, the dog was euthanised because of deterioration of clinical signs despite the start of multimodal analgesia. Necropsy and subsequent histology and immunohistochemistry revealed the presence of a plasmacytoma and haemorrhagic cystitis. The haemorrhagic cystitis was most likely caused by the contrast agent used for the CT scan that remained in the bladder for a prolonged time, secondary to subobstruction of the urethra.

BACKGROUND
CT is a commonly used imaging technique to visualise masses, to determine their invasiveness and tissue of origin and to perform staging. Contrast-enhanced CT can help to further characterise masses and to determine their degree of vascularisation. 2 Contrast agents used for contrast-enhanced CT scans can be divided in high-osmolar ionic and low-osmolar non-ionic agents. Ionic agents have a higher tendency to interact with biological structures such as cell membranes. 2 A lower rate of serious adverse reactions is reported for non-ionic contrast agents but they are considerably more expensive than ionic contrast agents. 3 Most common reported side effects are haemodynamic changes and anaphylactoid reactions. 4 Side effects can be classified according to severity (mild, moderate or severe) or according to time of onset (acute or delayed). 5 It has been shown that up to 79 per cent of dogs and cats that undergo retrograde contrast urethrography using an ionic contrast agent develop urinary bladder lesions, varying from focal haemorrhagic to diffuse transmural fibrinonecrotic cystitis. 6

This case report describes a dog with an intrapelvic mass that developed haemorrhagic cystitis as a delayed complication after a contrast-enhanced CT scan using a non-ionic contrast agent. Awareness of the risk for this adverse reaction is important, not only because it is a painful condition, but also because this complication can easily be avoided by prompt removal of the contrast agent after imaging, especially in dogs that cannot empty the bladder (completely) by themselves.

CASE PRESENTATION
A 10-month-old female intact Australian shepherd dog was referred for investigation of a mass in the caudal abdomen. One month before referral, the dog developed partial anorexia, lethargy and tenesmus. According to the owner, urination was normal. The dog had swollen mammary glands containing a small amount of milk and the referring veterinarian started a three-day course of cabergoline for suspected pseudopregnancy, which did not give significant improvement. Seven days after the start of the first clinical signs, the dog developed pain at the level of the left hindlimb and refused to walk more than a few steps at a time, abdominal radiographs were taken two days later. These revealed the presence of a large mass in the caudal abdomen, displacing the colon ventrally. Subsequently, the dog was referred.

INVESTIGATIONS
At presentation, the dog was very calm and reluctant to move for her age but general physical examination was within normal limits. The dog would try to sit down immediately whenever possible. When encouraged, she was able to walk 100 m, mildly limping on the left hindlimb. No abnormalities were present on general orthopaedic and neurological examination. On rectal examination, a mass was palpable in the craniodorsal part of the pelvis, which was hard and not painful on palpation. General blood analysis was within normal limits. Abdominal ultrasound (US) revealed a large multilobulated heterogeneous echogenic mass dorsal to the urinary bladder neck, considered to be in close association with the uterine body, and displacing the colon ventrally and to the left. The mass was markedly vascularised on colour Doppler examination. The urinary bladder was largely filled with anechoic urine, and had normal wall layering. The remainder of the abdominal organs was within normal limits. Abdominal radiographs were taken two days later. These revealed the presence of a large mass in the caudal abdomen, displacing the colon ventrally. Subsequently, the dog was referred.

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Received 4 November 2019
Revised 6 January 2020
Accepted 3 February 2020

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normal limits. US-guided cystocentesis and fine-needle aspirates of the mass were performed without complications. Urinalysis was within normal limits. The fine-needle aspirates were not diagnostic.

The following morning, an abdominal CT scan was performed. The dog was premedicated with dexmedetomidine (5 µg/kg intravenous, Dextdomitor, Orion) and induced with propofol (up to 6 mg/kg to effect, Propovet, Abbott Logistics). Anaesthesia was maintained with isoflurane (up to 2 per cent to effect, Isoflo, Abbott Logistics) vapourised in oxygen. Ringer lactate solution was administered throughout anaesthesia (3 ml/kg, Vetivex, Dechra). A four-slice helical CT device (Lightspeed OX/I, General Electric Medical Systems) was used and 1.25 mm thick contiguous slices were obtained (120 kVp, 140 mAs, image matrix 512×512). The dog was placed in ventral recumbency. The CT scan revealed a large, expansive, heterogeneous mass (9.1 cm in length×6.4 cm in height×5.5 cm in width) extending from the ventral aspect of the last lumbar vertebra until the second caudate vertebra and invading the vertebral canal at the lumbosacral junction (*). The colon is displaced ventrally (arrows) and the urinary bladder is largely filled and has a normal wall (§).

DIFFERENTIAL DIAGNOSIS
Based on the CT scan, the most likely differential diagnoses for the intrapelvic mass were haemangiosarcoma, haemangioma, soft tissue sarcoma and nerve sheath tumour.

TREATMENT
Awaiting the results of histology, a combination of meloxicam (0.1 mg/kg orally once daily, Metacam 1.5 mg/ml, Boehringer Ingelheim), tramadol (5 mg/kg orally three times daily, Tramadol EG, Eurogenerics) and gabapentin (10 mg/kg orally three times daily, Neurontin, Pfizer) was started.

OUTCOME AND FOLLOW-UP
Despite medical treatment, the condition of the dog deteriorated over the next two days. She became again partially anorectic, developed urinary incontinence and urine was reported to be odorous. The dog was euthanised by the referring veterinarian two days after the CT scan.

Necropsy was performed the next day. The intrapelvic mass had an irregular surface and had a cystic aspect containing a white mucinous content. There was no clear connection with any abdominal organ. The colon was impacted with faecal material and the urinary bladder was largely filled with macroscopically normal urine. Ulcerated fibronecrotic plaques were present on the mucosa at the trigonum of the bladder. On histology, the main mass consisted of dense sheets of neoplastic cells moderate in size with a varying amount of granular pale eosinophilic cytoplasm and small oval nuclei with dens chromatin. There was moderate anisokaryosis and anisocytosis with areas of lytic necrosis. Based on these findings, a round cell tumour was suspected and further immunohistochemical examination was performed in order to identify the tissue of origin. Immunohistochemical stains of CD3, CD18, CD20, CD45RA, CK, desmin, MHCII, S100 and vimentin were negative, whereas staining for Lambda light chain was positive, making a plasmacytoma the most likely diagnosis. The bladder mucosa was multifocally disrupted by extensive haemorrhage in a network of fibrin containing several degenerated neutrophils mixed with cellular and karyorrhectic debris, indicative of haemorrhagic cystitis (figure 2).

DISCUSSION
Cystitis is a relative common disease, with uncomplicated bacterial cystitis being most prevalent. 8 Haemorrhagic cystitis is a well-known side effect of cyclophosphamide, which is caused by acrolein, a toxic metabolite of cyclophosphamide. 9 Other possible causes of non-infectious haemorrhagic cystitis are radiation therapy, traumatic catheterisation, thrombocytopenia or coagulation disorders. 8 9 Although coagulation profiles were not performed in the current case, this would have been a very unlikely cause of the haemorrhagic cystitis, as no other signs of bleeding tendencies were observed in any other organ during necropsy.

Since US-guided cystocentesis before the CT scan revealed a completely normal urine sample, the most likely cause of the haemorrhagic cystitis in this dog is the contrast agent used for the CT scan that remained for a prolonged time in the bladder, causing chemical cystitis. The contrast medium used in this case was a non-ionic iodinated contrast agent that has a low osmolality, a low viscosity and a high water solubility. 10 Contrast agents are known to cause dose-dependent and time-dependent endothelial and smooth muscle damage. In vitro, a 32.5 per cent reduction of endothelial cells and 68.1 per cent reduction of smooth muscle cells is seen after one day exposure to a non-ionic contrast agent. 11 Cell death might have occurred secondary to a combination of an overstretched bladder and the presence of the contrast agent. Subsequent exposure of the detrusor smooth muscle and blood vessels to urine might have caused further damage, resulting in haemorrhagic cystitis. 8 Abnormalities seen in this case were very similar to changes described in a previous
study in which ionic contrast was used to perform retrograde contrast urethrographies.  

Even though the owners did not report any problems with urination during initial presentation, the dog had a large bladder at all occasions (US, CT scan and during necropsy). Probably, the dog developed bladder atony secondary to subobstruction, resulting in incomplete emptying of the bladder during urination. The bladder wall was thin with a normal layering on both US and CT scan, and urinanalysis was within normal limits. The dog only developed urinary complaints after the CT scan. Urinary incontinence was most likely caused by a combination of an overfilled bladder and the presence of pollakisuria secondary to cystitis, even though the presence of lower motor neuron bladder dysfunction due to the location of the tumour that only started to cause clinical signs after the CT scan cannot be completely ruled out. Although it is possible that the dog developed a urinary tract infection after the CT scan, the causative agent of the haemorrhagic cystitis is most likely the contrast agent used for the CT scan. In human medicine, haemorrhagic cystitis is known to be very painful and to cause severe clinical signs. The reported dog clinically deteriorated the day after the CT scan despite the multimodal analgesia. 

Based on this case, it is advisable to always empty the bladder after contrast-enhanced CT in patients who might have difficulties in emptying the bladder completely, such as patients with urinary (sub)obstruction, detrusor atony or micturition disorders associated with either upper or lower motor neuron lesions. Veterinarians must be aware of the potential risk of development of haemorrhagic cystitis as a delayed complication following contrast-enhanced CT scan, especially as this imaging technique is a routinely performed part of diagnosing and staging multiple (neoplastic) diseases.

Learning points

► Haemorrhagic cystitis is a possible delayed complication after contrast-enhanced CT.
► It is advisable to always empty the bladder after contrast-enhanced CT in patients who might have difficulties in emptying the bladder completely.
► Haemorrhagic cystitis is painful and should be treated immediately.

Figure 2  Histopathology of the urinary bladder of a dog that developed haemorrhagic cystitis after contrast-enhanced CT. The bladder mucosa is multifocally disrupted by extensive haemorrhage ($) in a network of fibrin containing several degenerated neutrophils (*) mixed with cellular and karyorrhectic debris (x), indicative of haemorrhagic cystitis (bar=100 μm, haematoxylin and eosin staining).

REFERENCES
