

Urinary bladder botryoid rhabdomyosarcoma with widespread metastases in an 8-month-old Labrador cross dog

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ABSTRACT

An 8-month-old crossbred Labrador retriever was presented with a history and clinical signs suggestive of lower urinary tract obstruction. Laboratory results revealed azotaemia and hyperphosphataemia. Ultrasonographic evaluation of the urinary tract showed a mass at the bladder trigone, hydronephrosis, hydroureter, and suspected metastases to lymph nodes and the liver. Pulmonary metastasis was identified on thoracic radiographs. A post mortem confirmed metastases to the liver, lungs and regional lymph nodes, as well as to the mesenteric lymph nodes, mediastinum, heart, subcutaneous tissue and several muscle groups. A histopathological diagnosis of metastatic botryoid rhabdomyosarcoma (sarcoma botryoides) was made. A review of the literature shows that, although the bladder trigone is a well documented location for this tumour, this case was unique with its widespread metastases to previously undocumented organs. The incidence, embryology, ultrasonographic appearance and treatment of this tumour are discussed.

Keywords: botryoid, hydronephrosis, metastasis, rhabdomyosarcoma, stranguria, ultrasonography, urinary bladder.

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INTRODUCTION

Tumours of the urinary bladder represent less than 0.5 % of all primary neoplasms in canine patients. Of these tumours, most are of epithelial origin⁶ and most are malignant¹⁶. Tumours of mesenchymal origin occur uncommonly, with those of smooth muscle origin being the most abundant³. Within the urinary tract, the bladder is the organ most frequently afflicted with neoplasia. It is thought that the role of the bladder as a storage organ may result in prolonged exposure to carcinogens voided in the urine. Metastasis to the bladder is rare, since this organ does not provide the right environment for haematogenous or lymphatic tumour embolisation nor does it lend itself to transcoelomic metastasis¹⁶.

Rhabdomyosarcoma is a tumour of striated muscle (skeletal or cardiac) which may also occur in other non-muscle locations²¹. It is a rare primary mesenchymal tumour of the urinary bladder^{6,16} and occurs here more commonly than in other

locations, comprising approximately 2/3 of the reported rhabdomyosarcoma cases in dogs⁷. They occur most commonly at the bladder trigone⁹, although urethral involvement has also been documented¹⁷. Rhabdomyosarcoma can be classified histologically as pleomorphic, embryonal or alveolar. The embryonal and alveolar forms occur in young patients and are known collectively as juvenile rhabdomyosarcoma, whereas the pleomorphic form occurs mainly in adults^{2,10}. Those rhabdomyosarcomas that protrude from the mucous membrane of a hollow organ have been described macroscopically as botryoid (sarcoma botryoides – meaning ‘grape-like’), as they often take a lobulated form resembling a bunch of grapes¹⁰.

Tumours in the bladder occupy space and may cause mucosal ulceration, resulting in signs that mimic cystitis, such as haematuria, dysuria, stranguria, pollakiuria and incontinence. These cases often show a partial response to antibiotic treatment and may be erroneously diagnosed as recurrent cystitis^{3,6,16,18}. A delay in diagnosis often occurs due to the lack of specificity of these signs or due to partial response to treatment of their more common causes. Tumours in this location may result in various complications such as obstruction of urethral outflow result-

ing in bladder distension, infiltration of the bladder’s muscular layer by tumour cells and obstruction of the ureters at the trigone¹⁶. Obstruction of ureteral urine flow increases ureteral pressure and results in hydroureter and hydronephrosis³. Relief of the ureteral obstruction can result in some reversal of renal damage, but chronic obstruction can lead to the obliteration of the entire renal cortex¹³. Rhabdomyosarcoma of the urinary bladder has also been associated with hypertrophic osteopathy (Marie’s disease), even without the presence of pulmonary metastasis^{4,6}.

CASE HISTORY

An 8-month-old entire male crossbred Labrador presented with stranguria and dysuria of 1 month’s duration and anorexia and depression of 2-day duration. The owner reported that the dog would attempt to urinate, which only resulted in urine dripping from the prepuce. On clinical examination he was depressed and slightly underweight. Temperature, pulse and respiration were within normal limits. Multiple hard, mobile subcutaneous masses of 2–3 cm in diameter were palpable over the trunk and hindlimbs, as well as enlarged superficial inguinal lymph nodes. Abdominal palpation revealed a grossly distended urinary bladder occupying most of the caudal abdomen. The kidneys appeared considerably enlarged and even visible as bulges of the abdominal wall when the dog was placed in dorsal recumbency. He was unable to urinate spontaneously and small amounts of urine dripped from the penile urethra when mild pressure was applied to the bladder. He could, however, be easily catheterised. The dog was a unilateral cryptorchid with the retained testicle palpable subcutaneously in the inguinal area.

Urine obtained by catheterisation was dark orange in colour. Results of a urinalysis were as follows: isosthenuria (specific gravity 1.012), pH 6, moderate proteinuria (2+) and severe haematuria. Examination of the urine sediment, stained initially with Sternheimer-Malbin and then with Diffquick, revealed erythrocytes, some

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leukocytes and several anaplastic spindle-shaped cells. No parasites were observed on blood smear.

The dog was admitted and stabilised overnight. Initial therapy included urinary catheterisation to facilitate bladder emptying and intravenous isotonic crystalline fluids (IntraMed Ringer's lactate, Fresenius Kabi) to compensate for the expected post-obstructive diuresis.

On day 2, haematology revealed a degenerative left shift neutrophilia with a mild thrombocytopenia. Serum sodium and calcium were within reference ranges; serum potassium was at the high end of the normal range (4.95 mmol/l; reference 3.6–5.1 mmol/l); serum globulin was mildly elevated (39.9 g/l; reference 20–37 g/l); serum inorganic phosphate was mildly elevated (2.37 mmol/l; reference 0.9–1.6 mmol/l), and serum urea (44.2 mmol/l; reference 3.6–8.9 mmol/l) and creatinine (674 μ l/l; reference 40–133 μ l/l) concentrations were markedly raised.

Abdominal ultrasound showed gross enlargement of the left kidney, measuring 12.5 \times 6.7 cm in sagittal view. The pelvis was dilated and filled with anechoic fluid and a thin rim of renal cortical tissue could be discerned (hydronephrosis) (Figs 1a and 1b). Blood flow was demonstrated in the cortical tissue using colour Doppler. The bladder was grossly distended and contained a mass measuring 5.1 \times 3.2 cm in the trigone area (Fig. 2). Dilated ureters could be seen entering the bladder in this area. The prostate appeared normal, but was surrounded by multiple small nodules (most likely superficial inguinal lymph nodes). The right kidney was also grossly enlarged and hypoechoic due to severe pelvic dilation and hydronephrosis and measured 15 \times 9 cm in sagittal view. No remaining cortical tissue could be visualised (Fig. 3). A hypoechoic mass measuring 3 \times 3 cm could be seen at the caudal edge of the right liver lobe. (Fig. 4) The sublumbar lymph nodes were enlarged. Ultrasound-guided fine needle aspirates of the trigone mass, the liver nodule and the caudal epigastric and internal iliac lymph nodes revealed anaplastic spindle-shaped cells consistent with a tumour of mesenchymal origin. Results of aspirates of the subcutaneous masses were similar. No specific diagnosis could, however, be made on the basis of cytology.

Thoracic radiographs revealed a diffuse nodular lung pattern, suggesting extensive pulmonary metastasis (Fig. 5).

On the strength of these findings the prognosis was considered poor, and the dog was euthanased. *Post mortem* examination confirmed the ultrasonographic

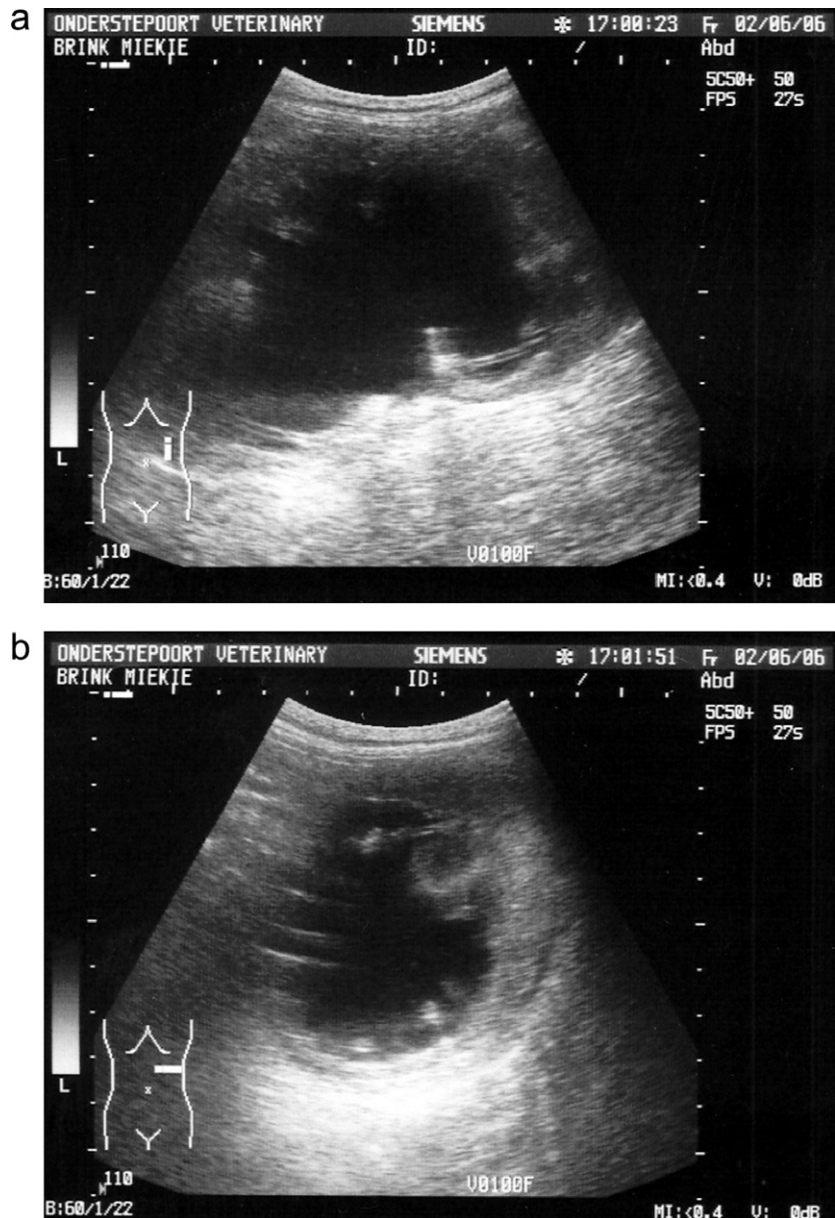


Fig. 1: Sagittal (a) and transverse (b) views of the left kidney showing severe hydronephrosis.



Fig. 2: Sagittal view of the urinary bladder showing a mass at the trigone area.

findings. A yellowish grapelike mass was found in the bladder lumen at the trigone, obliterating the prostate and occluding the ureters. There was severe bilateral hydronephrotic and hydronephrosis. The right kidney cortex was completely obliterated and the organ reduced to a fluid-filled sac (Figs 6 and 7). The superficial inguinal lymph nodes were enlarged and there were nodules in the mesentery. The liver contained a mass in the right lobe with a necrotic, fluid centre consistent with the ultrasonographic observations (Fig. 4). Tumours were also found in the lungs, mediastinum, abdominal muscles, intercostal muscles, cervical and quadriceps muscle groups and the papillary muscles of the heart. Rhabdomyosarcoma was confirmed by histopathology in all the macroscopic lesions.

DISCUSSION

Rhabdomyosarcoma is a rare tumour most commonly occurring in large-breed dogs under 2 years of age, particularly Saint Bernards^{2,6,7,10,12}, although several cases have been reported in Retriever-type dogs^{1,2,17}. It is similar to embryonal rhabdomyosarcoma in humans¹⁹, the most common soft tissue tumour in children under 15 years of age.¹⁰ Whereas rhabdomyosarcoma arising in skeletal muscle metastasises early (to other skeletal muscle sites)⁸, the type occurring in the bladder metastasises more rarely and later in the course of the disease.^{6,19} Metastases have been reported previously in the liver, lungs, mesentery, kidneys, adrenal glands, spleen and regional lymph nodes^{2,6,17,19}. There have also been reports of post-operative metastasis within the peritoneal cavity after attempted resection of the primary lesion, most likely as a result of tumour seeding during surgery⁶. The extensive metastases seen in this case, most notably those to various striated muscle groups and the papillary muscles of the heart, sets it apart from previously documented cases. It is difficult to explain the presence of the subcutaneous nodules in this patient. They may represent widespread contemporary neoplastic transformation of subcutaneous pleuripotent mesenchymal stem cells, as opposed to metastatic foci.

The location and macroscopic appearance of the tumour, as well as the patient's clinical picture, are very similar to previously reported cases. The mass in the bladder was most likely the primary lesion. This mass occluded the patient's urethral outflow, resulting in bladder distension and stranguria. The blockage of the ureters resulted in the severe hydronephrosis and hydronephrotic and the decreased functional renal mass and urinary obstruction



Fig. 3: Right parasagittal image of a fluid-filled sac thought to represent the right kidney, suggesting severe hydronephrosis.



Fig. 4: Right parasagittal view of the caudal liver margin showing a 3 cm x 3 cm mass with distal acoustic enhancement.



Fig. 5: Left lateral radiograph of the thorax showing multiple pulmonary nodules of varying sizes.

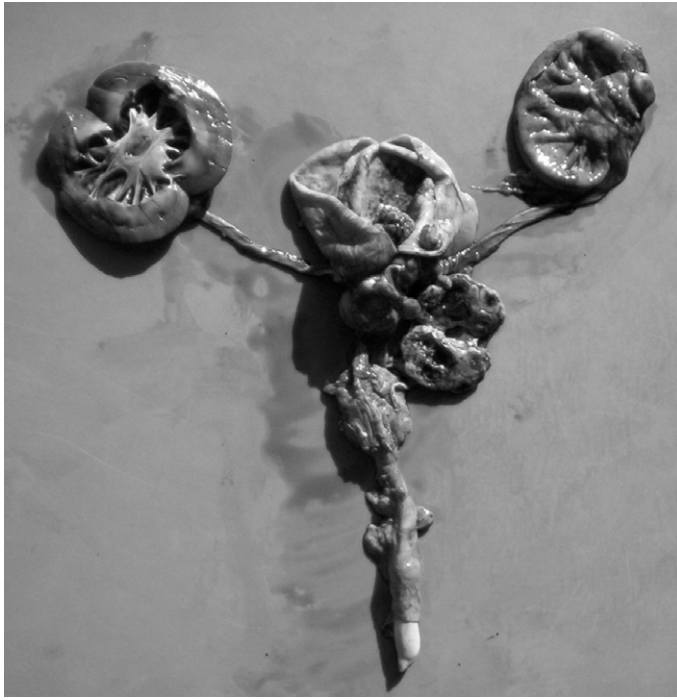


Fig. 6: Botryoid mass at the bladder trigone with severe bilateral hydroureter and hydroureterosis.

resulted in severe renal and post-renal azotaemia, high normal serum potassium and mild hyperphosphataemia.

The origin of a skeletal muscle tumour within the urinary bladder appears to be linked to the embryology of this organ. In the embryo the urinary bladder is formed when mesodermal folds grow medially to divide the cloaca (endoderm) into the rectum dorsally and the bladder ventrally. Most of the bladder is derived from the ventral portion of the cloaca and is therefore of endodermal origin, with part of the dorsal wall (the area forming the trigone) being formed by mesodermal

tissue¹⁴. It is postulated that these tumours develop from pleuripotential mesodermal cells that have the potential for skeletal muscle differentiation. Such cells are believed to reside in this area, particularly around the Mullerian and Wolffian ducts^{10,12,19} that are incorporated into the dorsal bladder wall¹⁴. The fact that leiomyosarcomas and teratomas also arise from this region supports the notion that pleuripotential cells reside at the trigone⁸.

Diagnosis and prognostication was greatly aided in this case by the use of ultrasound. Assessment of the urinary tract by diagnostic ultrasound is convenient as this is a non-invasive modality in which the internal architecture of relatively superficially situated structures can be studied^{5,11}. Evaluation is further aided by the presence of urine, which provides a good acoustic window, allowing better assessment of the bladder wall. Masses in the bladder may be confused with those caused by other non-neoplastic conditions such as polypoid cystitis, adherent blood clots or mural haematomas. Thorough examination, together with the use of ultrasound-guided fine needle aspiration and careful consideration of the ultrasonographic characteristics of each condition, can allow a fairly confident diagnosis of neoplasia¹¹. As well as its diagnostic uses, ultrasound is a suitable medium for monitoring of treatment or detection of tumour recurrence²².

Tumours of the urinary bladder may be treated successfully by partial cystectomy if the tumour can be excised completely along with a 1 to 2 cm border of grossly

normal tissue.¹⁸ Over 75 % of the bladder can be removed without complications, provided the trigone remains intact.¹⁶ The typical location and infiltrative nature of rhabdomyosarcoma at the trigone implies a poor prognosis¹². A technique involving *en-bloc* removal of the bladder neck and proximal urethra has recently been described for dogs with invasive tumours causing urinary tract obstruction and although technically challenging, may be indicated in some cases in the future.¹⁵ Complete cystectomy with surgical diversion of the ureters into the colon has been described as treatment for tumours with trigone involvement,¹⁸ but the associated complications (including loss of continence) make it an undesirable choice.¹⁶ Surgical treatment alone is often unrewarding due to recurrence and post-operative metastasis.⁷ In general, the more invasive a tumour is, the more likely it is to recur and metastasise.^{17,16} Chemotherapy is critical to success and remission post-operatively.¹⁷ Treatment should follow as soon as possible after surgery to prevent recurrence²⁰, especially if the tumour margins were incomplete, and to prevent possible tumour seeding in the abdomen as a result of surgical manipulation of the tumour.¹⁷ Chemotherapy protocols such as a combination of vincristine, doxorubicin and cyclophosphamide²⁰ or doxorubicin with cyclophosphamide have been used. In addition, antibiotic treatment should be initiated if the patient has concurrent cystitis.¹⁷

Almost all reported cases of rhabdomyosarcoma have been euthanased at diagnosis, or soon after attempted surgery.^{2,17,19} For treatment to be successful, the whole tumour must be removed relatively early in the course of the disease.¹⁹ There is only 1 report of prolonged remission in a dog with urinary bladder rhabdomyosarcoma. This is thought to have been a slower growing, less infiltrative tumour diagnosed relatively early and treated aggressively with surgery and post-operative chemotherapy.¹⁷ The presence of hydronephrosis and/or hydroureter worsens the prognosis in these patients as this indicates likely trigonal involvement as well as the possibility of compromised renal function.¹⁶ In the case reported here the prognosis was deemed to be extremely poor due to the location of the tumour, the severity of the hydroureterosis, the compromised renal function and the extent of metastasis.

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Fig. 7: Close-up view of the bladder showing the mass and additional nodules surrounding the bladder neck area.

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