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CASE REPORT

Companion or pet animals

Concurrent right atrial myxoma with visceral haemangiosarcoma in a dog

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Abstract

A 10-year-old crossbreed (labradoodle) was presented with an acute history of vomiting and diarrhoea, with supraventricular tachycardia and ventricular premature complexes. Physical examination revealed mild tachycardia, but no significant abnormalities otherwise. Investigations with echocardiogram and computed tomography identified a right atrial mass, nodular interstitial lung pattern, multiple nodules throughout the hepatic parenchyma and peritoneal effusion. Abdominocentesis confirmed a haemoabdomen. Treatment was declined and the dog was euthanased the same day. Histopathology of the cardiac mass confirmed a cardiac myxoma, which stained Alcian blue-positive, demonstrating the mucin content of the tumour. The hepatic lesions were factor VIII-positive, consistent with a visceral haemangiosarcoma.

KEYWORDS

cardiology, diagnostic imaging, dogs, emergency medicine, histopathology, oncology

BACKGROUND

Haemangiosarcoma (HSA) is one of the most frequent neoplastic diagnoses in dogs. Primary cardiac myxomas have been rarely reported in dogs, although they are one of the most common cardiac tumours in humans. To the authors' knowledge, this is the first case to describe a concurrent right atrial cardiac myxoma with visceral HSA in a dog with the associated computed tomography (CT) findings. This case highlights the value of extensive investigations with suspected cardiac masses to ensure appropriate diagnosis, prognosis and treatment.

CASE PRESENTATION

A 10-year-old, male, neutered labradoodle dog was referred as an emergency for further investigations after 48 hours of a poor appetite, vomiting, diarrhoea and lethargy. The referring veterinarian had performed an electrocardiogram (ECG), which revealed runs of supraventricular tachycardia and ventricular premature complexes; these were considered secondary to systemic disease. No further investigations were performed. The dog had received maropitant, paracetamol and intravenous fluid therapy before referral.

On physical examination, the dog was bright, alert and responsive. It was of adequate condition (body condition score (BCS) 4/9; muscle condition score (MCS) B) with a bodyweight of 37.0 kg. Mucous membranes were diffusely pigmented. Cardiothoracic auscultation revealed a regular heart rhythm with a heart rate of 100 beats per minute and synchronous moderate quality peripheral pulses. There were no significant abnormalities on abdominal palpation. It was normothermic with a rectal temperature of 39.1°C.

INVESTIGATIONS

Haematology revealed a mild non-regenerative anaemia with red blood cells 5.05×10^{12}/L (reference interval [RI]: 5.67–8.87), hematocrit 0.32 L/L (RI: 0.373–0.617), haemoglobin 119 g/L (RI: 131–205), moderate thrombocytopenia 50×10^{9}/L (RI: 150–400) and lymphopenia 0.69×10^{9}/L (RI: 1.05–5.10). Serum biochemistry identified a mild elevation in alanine transaminase 137 U/L (RI: 10–125). It was normotensive, with a systolic blood pressure of 130 mmHg.

Given the reported supraventricular tachycardia and ventricular premature complexes (ECG documentation provided on referral), a brief focused echocardiographic examination was performed, which revealed a hyperechoic heterogenous mass measuring approximately 2.0 × 4.0 cm in the right atrium positioned on the atrialis side and with apparent proximal attachment to the septal leaflet of the tricuspid valve (Figure 1a–c). The mass was causing mild obstructive trans-tricuspid flow based on colour Doppler, and there was mild tricuspid regurgitation (Figure 2a,b). The myocardium of the right ventricle was subjectively normal. There was no evidence of pericardial effusion to explain the moderate

thrombocytopenia. Simultaneously acquired electrocardiogram revealed sinus rhythm throughout, with no evident ectopy. The dog was considered cardiovascularly stable enough for sedation for advanced imaging.

A CT angiogram of the thorax and abdomen was performed to complete tumour staging. Examination of the thorax identified a large right atrial mass at the level of the septal cusp of the tricuspid valve (Figure 3). The mass was iso/slightly hypoattenuating in comparison to the interventricular septum (IVS) on pre-contrast images, contained several pinprick mineral bodies and was hypoenhancing compared to IVS on post-contrast images (venous phase). There was a concurrent nodular interstitial lung pattern and mild sternal lymphadenomegaly. In the abdomen, there was a moderate peritoneal effusion. The liver was small and contained multiple hypoattenuating (compared to surrounding liver parenchyma), variably sized nodules/masses, predominately within the left division of the liver (Figure 4). These lesions were generally poorly enhancing in comparison to the surrounding parenchyma on both arterial and venous phases, although several of the larger lesions had strong irregular rim enhancement. There was enlargement of the hepatic lymph nodes. The spleen was slightly enlarged and contained multiple hypoattenuating nodules, which were predominately poorly enhancing (in comparison to adjacent splenic parenchyma). There were several choleliths visible in the dependent gall bladder lumen. There was incidental coxofemoral and glenohumeral osteoarthrosis, a body wall nodule and spondylosis deformans. The CT findings were concluded to be most consistent with metastatic neoplasia. Abdominocentesis and ultrasound-guided fine-needle aspirates were performed from the peritoneal effusion, hepatic nodules and splenic nodules, respectively. Cytological assessment was non-diagnostic due to sample haemodilution. Fluid analysis of the peritoneal effusion was consistent with recent or active haemorrhage (packed cell volume 27% and total solids 40 g/L). Active haemorrhage therefore likely explained the previously noted thrombocytopenia and anaemia, but these could also be secondary to sequestration and intra tumoural destruction.

Due to the severity of the clinical signs, high clinical suspicion of metastatic neoplasia and the perceived poor prognosis, the owners elected for humane euthanasia. The owners consented to a limited postmortem examination with sampling from the heart and liver allowed. There were multifocal masses within the parenchyma of the liver, which were dark red on the cut surface ranging from 2 to 4 cm in diameter. Histopathological examination of the liver revealed multifocal aggregates of haphazardly arranged mesenchymal cells, which surrounded large areas of haemorrhage and fibrin deposition. The masses were unencapsulated, and infiltrated the surrounding hepatic parenchyma. Neoplastic cells were stellate to spindloid, with small amounts of cytoplasm. Nuclei were small, oval-shaped, with finely stippled chromatin and a single basophilic nucleolus. Mitoses were not observed. Immunohistochemistry was performed to further characterise these cells. Neoplastic cells demonstrated strong expression of factor VIII, consistent with a hepatic HSA.

In the right atrium, adjacent to the tricuspid valve, very close to the base of the valve, there was a dark red botryoid, soft mass, which was strongly adhered to the endocardium (Figure 5a,b,d model). Histopathology revealed a sparsely cellular mass, well demarcated from the adjacent myocardium.

LEARNING POINTS/TAKE-HOME MESSAGES

- A myxoma should be considered a top differential when a primary cardiac mass is found located close to or in close association with the tricuspid valve.
- Aspiration of any cardiac tumours that are not in a typical cardiac haemangiosarcoma location should be attempted where feasibly possible to obtain an antemortem diagnosis, which may change the management and outcome for the dog.
- Staging haemangiosarcoma from advanced imaging alone may not always be accurate. Given the significant change in treatment options and prognosis, further investigations should be considered to confirm disease spread.

There was a focal area of mineralisation at the base of the mass. The mass was composed of spindloid cells, with indistinct cell borders, scant cytoplasm and small, elongated, chromatin dense nuclei; they were often present as single cells, embedded in abundant fibrillar eosinophilic matrix (Figure 6a). Positive staining with Alcian blue revealed this to be consistent with mucin (Figure 6b). Immunohistochemistry revealed neoplastic cells to be vimentin positive (Figure 6c) but negative for factor VIII (Figure 6d). The presence of Alcian blue-positive matrix alongside negative factor VIII expression is consistent with a primary right atrial myxoma rather than representing metastatic or primary HSA.

DIFFERENTIAL DIAGNOSIS

The findings on CT and echocardiogram were supportive of an underlying neoplastic process or, less likely, two possibly independent neoplastic processes. Differentials for the hepatic nodules included primary hepatic neoplasia; nodular to diffuse hepatocellular carcinoma or cholangiocarcinoma, metastatic neuroendocrine tumour, or primary visceral HSA with benign changes including nodular hyperplasia, and extramedullary haematopoiesis considered less likely. An HSA was considered more likely given the concurrent clinicopathological changes seen on haematology.

Differentials for the right atrial mass were considered with right atrial HSA by far the most likely; other less likely differentials in this location included neuroendocrine tumour, myxoma, myxosarcoma, fibrosarcoma, leiomyosarcoma, rhabdomyosarcoma and peripheral nerve sheath tumour. Non-neoplastic possibilities included haematoma or thrombus, but these were considered less likely. Due to the concurrent hepatic nodules, hepatic lymphadenomegaly, suspected pulmonary metastasis and the right atrial mass, a metastatic HSA or disseminated histiocytic disease was favoured rather than two independent neoplastic processes.

OUTCOME AND FOLLOW-UP

Treatment options were considered limited, with palliative emergency surgery and excisional biopsy provided as the only option to control the active haemorrhage. Due to the high

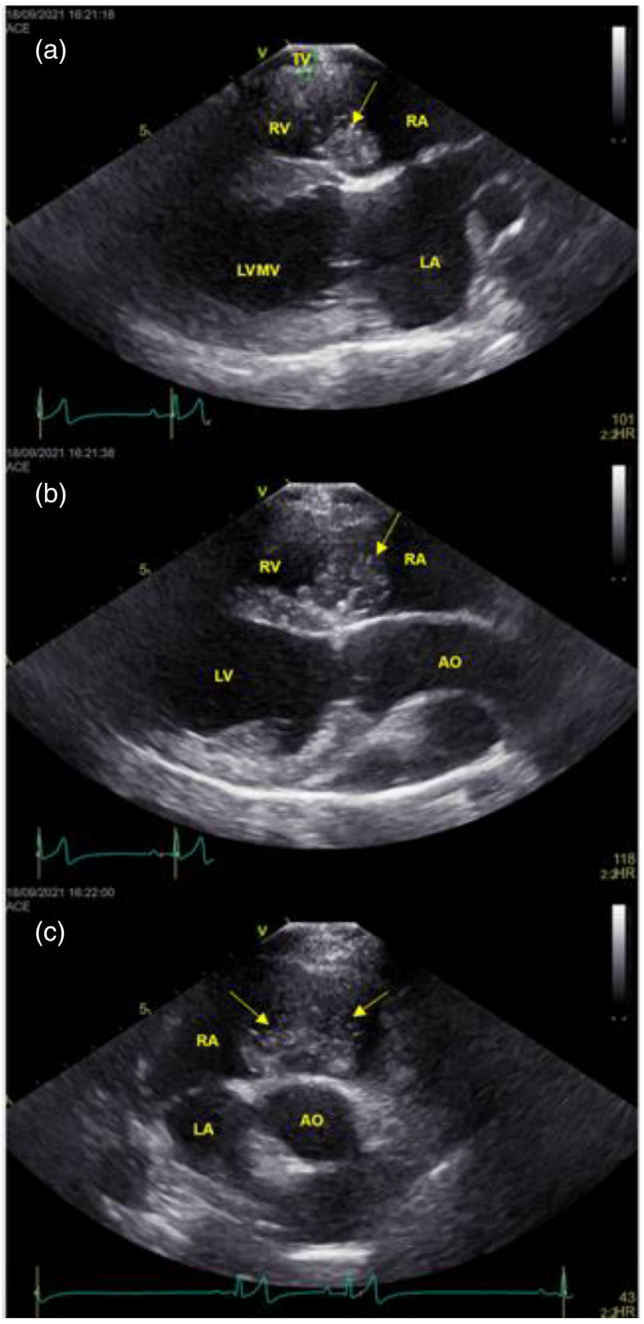


FIGURE 1 Two-dimensional echocardiographic images from the thoracic point-of-care ultrasound. Right atrial mass indicated by the yellow arrow in each image. It appeared attached to the atrialis side of the tricuspid valve. (a) Right parasternal long axis 4 chamber view. (b) Right parasternal long axis 5 chamber view. (c) Right parasternal short axis view, at level of aortic valves. Abbreviations: Ao: aorta, LA: left atrium, LV: left ventricle, RA: right atrium, RV: right ventricle, TV: tricuspid valve (open green arrow)

suspicion of multifocal neoplasms in multiple organs and likely poor long-term survival, the owners elected in favour of euthanasia.

DISCUSSION

This report describes a case of a dog with visceral metastatic HSA, with a concurrent right atrial myxoma.

Canine visceral HSA is a biologically aggressive tumour derived from vascular endothelial cells or bone marrow-derived endothelial progenitors.[1] HSA can develop in any

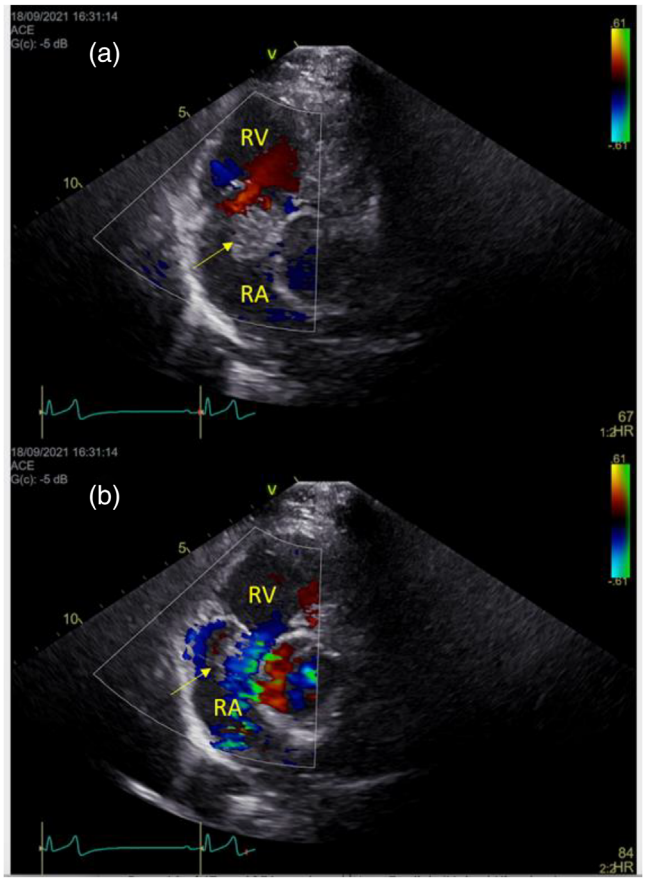


FIGURE 2 Colour flow Doppler echocardiography of the tricuspid valve, assessing the impact of the mass (yellow arrow) on tricuspid flow. Left parasternal cranial view, optimising the right heart. (a) Diastolic image, showing trans-tricuspid flow (red) bypassing the mass. (b) Systolic frame, showing mild tricuspid regurgitation (blue/greens on velocity variance map) around the mass. Abbreviations: RA: right atrium, RV: right ventricle neoplasia

location with a vascular supply, with the spleen being by far the most common primary site. Other well-reported primary visceral sites include the heart, usually the right atrium, liver and retroperitoneum.[1–3] The liver, lung and omentum are the most common sites of metastasis.[2,3]

Canine HSA is staged according to World Health Organization classification as follows: stage I confined to primary tissue and less than 5 cm in size; stage II, the tumour is greater than 5 cm or has ruptured; and stage III with gross distant metastatic disease.[4] For this reason, identifying the site of the primary in stage III HSA is not always certain. In this case, histopathology confirmed a primary liver HSA with pulmonary metastasis highly suspected from CT, with a peripheral nodular lung pattern consistent with stage III HSA. Before the histopathology results, the right atrial mass was incorrectly assumed to represent part of the same multifocal neoplastic disease process (i.e., presumed right atrial HSA). The histopathology unexpectedly confirmed a primary cardiac myxoma.

Cardiac tumours in dogs are uncommon to rare, with the most extensive retrospective study documenting an incidence rate of 0.19%.[5] Tumours can be either primary or secondary. Two studies investigating the proportion of primary and secondary neoplasms in dogs reported disparate results; with one reporting 84% to be primary and 16% metastatic,[5] while a retrospective postmortem examination study reported

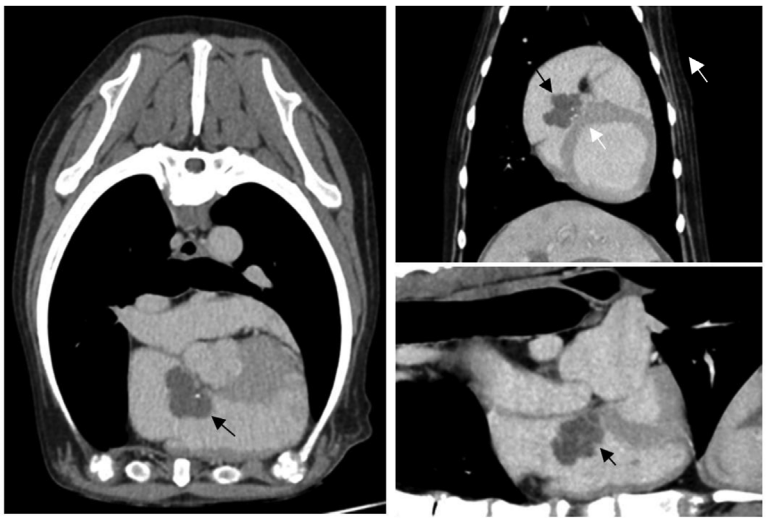


FIGURE 3 Computed tomography angiogram (soft tissue window) showing the right atrial mass (black arrow) at the level of the septal cusp of the tricuspid valve. The mass was hypoenhancing in comparison to the adjacent interventricular septum (white arrow).

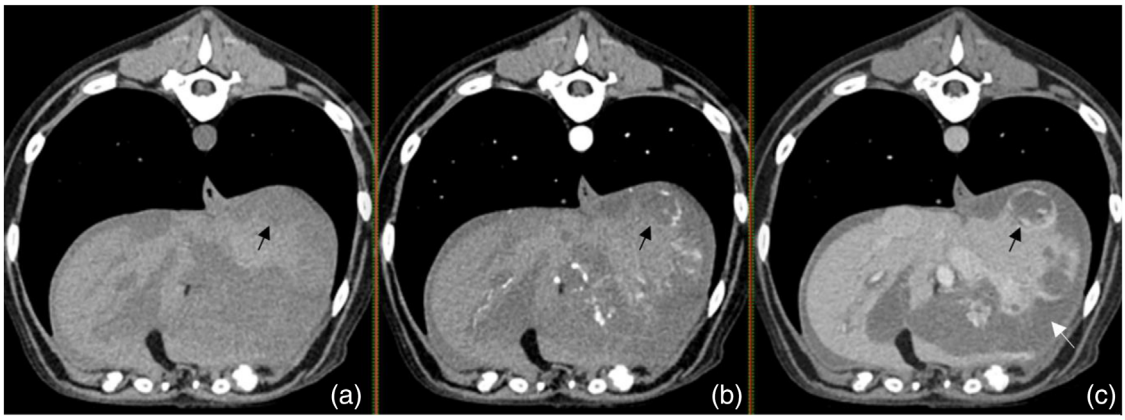


FIGURE 4 Contrast computed tomography of the liver (soft tissue window a: pre-contrast, b: arterial phase, c: venous phase) demonstrating a hypoattenuating hepatic mass with strong rim enhancement (black arrow). A moderate volume of free fluid is also visible within the abdomen (white arrow).

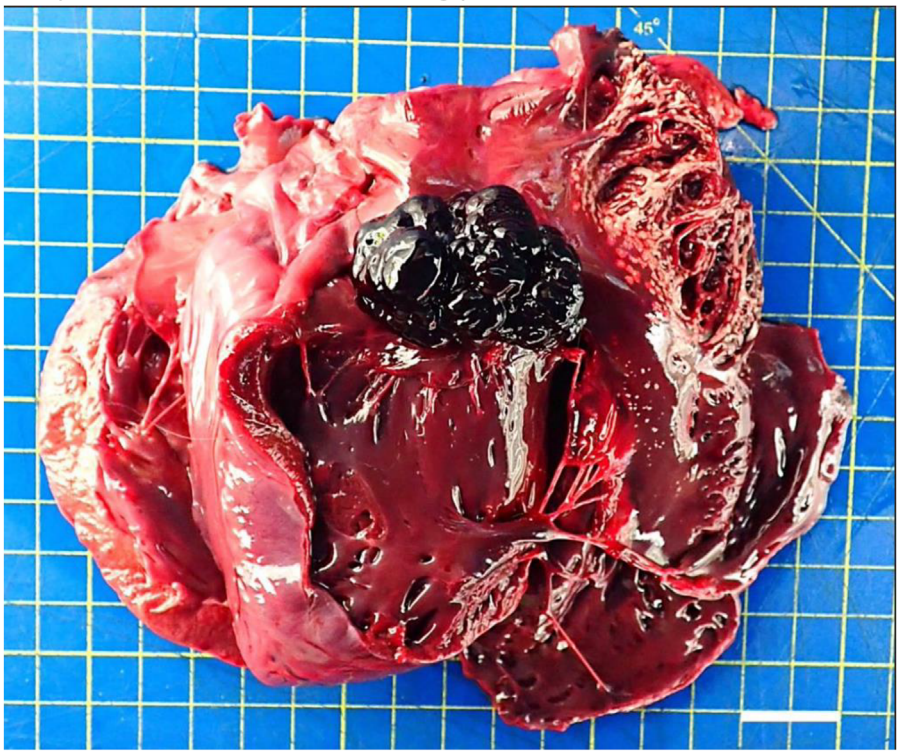
finding primary tumours in 31% of cases and metastatic lesions in 69% of cases—more consistent with findings in humans.[6] The higher reported rate of metastatic cardiac tumours found at postmortem examination may be because cardiac tumours can be clinically silent, and antemortem echocardiography may not be performed.[7] Of all cardiac tumours, HSA make up the largest proportion, around 70%, with the majority found in the right atrium and right auricular appendage.[7,8] While in humans, cardiac myxoma is the most common neoplasm,[9] in dogs they are considered rare.[8] These have been previously described in several case reports, the first of which was in 1959.[10–15] As with this case, myxomas have mostly been reported to involve the right atrioventricular valve,[10–13] with only one reported to involve the left ventricles.[14]

Cardiac myxomas are thought to arise from multipotent vasoformative cells.[15] Their gross appearance is typically described to be white and gelatinous,[13,14] which contrasts with this case in which the mass had a dark red colour. This unusual appearance was considered most likely secondary to autolysis; however, there was also evidence of acute and chronic haemorrhage (siderophages) within the mass, which also likely contributed to this colour. Histological appearance and immunohistochemistry were typical for a myxoma with spindloid fibroblast-like cells with elongated nuclei and stellate cells, which are both vimentin-positive (i.e., of mesenchymal origin) and abundant Alcian blue-positive mucinous extracellular matrix.[15]

Associated clinical signs of cardiac myxoma reported in previous case studies include syncope, exertional syncope, ascites or sudden death.[12–15] In this case, the dog presented without any of these clinical signs. The dog did have an arrhythmia described by the referring veterinarian, with both supraventricular tachycardia and ventricular premature complexes, although had no clinical signs attributable to the arrhythmia. The arrhythmia had not persisted during the time of referral. Primary cardiac tumours have been previously associated with arrhythmias, but most commonly bradyarrhythmias such as atrioventricular block.[16,17] As presented in this case, supraventricular tachycardia has been previously reported in association with a right atrial mass, but a causal relationship between tumour and arrhythmia could not be confirmed.[18] Furthermore, a primary endocardial pleomorphic sarcoma was reported to cause a left ventricular outflow obstruction, with a complex arrythmia, involving sinus arrest, junctional escape rhythm and periods of ventricular tachcardia.[19] The tricuspid valve origin of myxoma has been reported previously in the dog,[15] but association with the tricuspid valve would be less likely with right atrium HSA.[15]

While these tumours are benign, intracardiac blood flow may be interrupted by these space-occupying intercavitary

Heart after dissection showing opened right ventricle and atrium, exposing the right atrioventricular valve. In the right atrium, and adjacent to the valve there was a dark red, botryoid, soft mass which was strongly adhered to the endocardium. Scale bar = 2 cm



(b) Heart after dissection showing opened right ventricle and atrium, exposing the right atrioventricular valve. In the right atrium, and adjacent to the valve there was a dark red, botryoid, soft mass which was strongly adhered to the endocardium. Scale bar = 3 cm

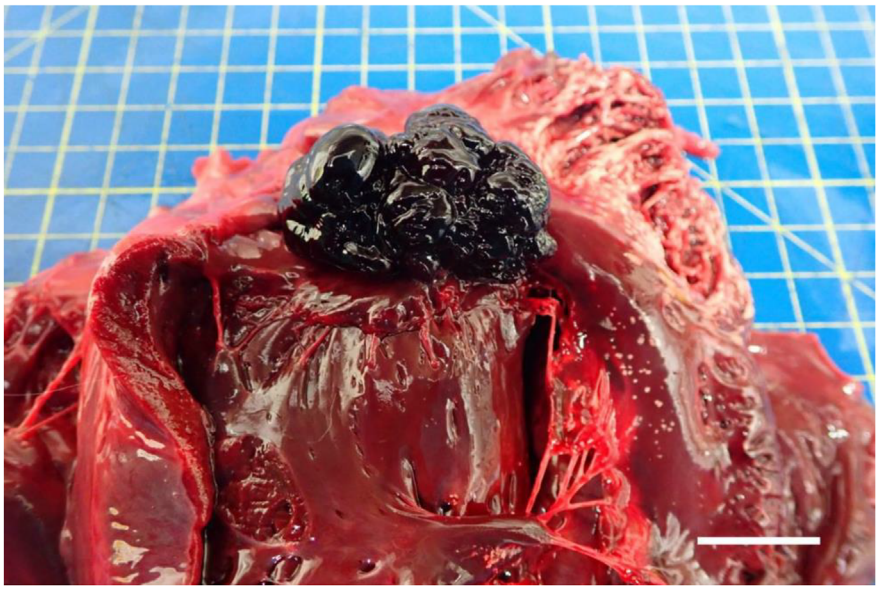


FIGURE 5 Path figures. Heart after dissection showing opened right ventricle and atrium, exposing the right atrioventricular valve. In the right atrium and adjacent to the valve, there was a dark red, botryoid, soft mass, which was strongly adhered to the endocardium. (a) Scale bar = 2 cm. (b) Scale bar = 3 cm. Three-dimensional model link: https://sketchfab.com/3d-models/cardiac-myxoma-093202156e274ce8a42d72a3af9f9b7a

masses, and although they do not metastasise, they can generate emboli.[15] In this dog, the echocardiogram did not indicate significant obstructive flow despite its close association with the tricuspid valve. Although a nodular interstitial lung pattern was identified on CT, it was not considered to be consistent with underlying embolic disease. Unfortunately, histopathology of the pulmonary parenchyma was not performed at postmortem examination due to the owners' personal request. In this case, given the lack of clinical signs of emboli, the dog's right atrial myxoma was likely to have been an incidental diagnosis and not contributing to the clinical signs.

The association of visceral HSA and ventricular arrhythmias has been well described.[19–21] The arrhythmias and lethargy reported in this case may be attributed to volume depletion with the haemoabdomen. Thrombocytopenia is a

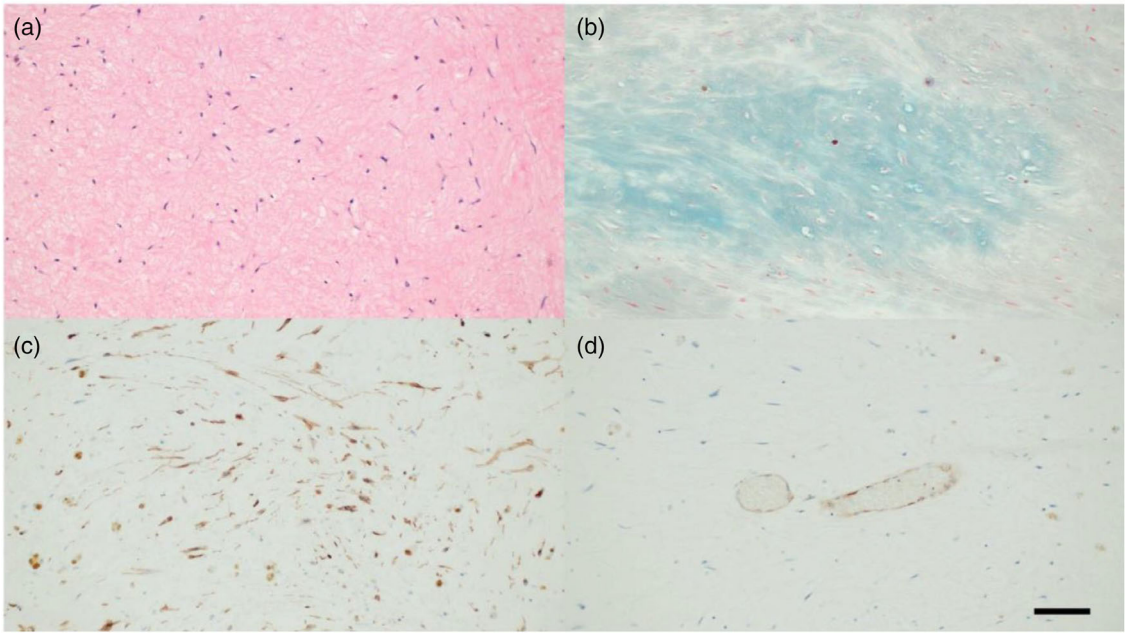


FIGURE 6 Histological and immunohistological images of the tricuspid valvular mass; scale bar = 50 μm. (a) Section showing a paucicellular mass, with spindloid cells within an abundant eosinophilic matrix (20× magnification, haematoxylin and eosin stain). (b) Similar section stained with Alcian blue, to illustrate the myxomatous nature of the matrix (20× magnification, Alcian blue stain). (c) Immunohistological staining with vimentin antibody; the neoplastic cells are positive (20× magnification). (d) Immunohistological staining with factor VIII antibody; the neoplastic cells are negative, and the endothelial cells lining blood vessels in the centre of the image are positive (20× magnification).

common finding in HSA and has been reported specifically with hepatic HSA, although the cause is multifactorial in this dog's case likely due to acute haemorrhage, sequestration within the tumour, intratumoural destruction and coagulopathic consumption.[22] Vomiting is considered a non-specific clinical sign. In this case, in the absence of clinicopathologic changes, it was considered most likely secondary to the advanced abdominal neoplasia. Despite the underlying disease processes, the clinical signs of this patient had largely resolved with supportive symptomatic care provided before referral.

Antemortem diagnosis of cardiac tumours is challenging due to their location. The most widely used imaging tool for diagnosis of cardiac tumours is echocardiography, with a reported sensitivity and specificity of 82% and 100%, respectively.[7] Tumour location is often used to infer the type of cardiac tumour, with right atrial tumours often assumed to be haemangiosarcoma in dogs, given their high incident rate for this location. However, tumour location has been shown to be only moderately predictive for correctly identifying tumour type.[23] Indeed, in cases of splenic HSA, a concurrent right atrial lesion has been reported to occur in only 9% of cases.[24] Similarly in this case, the tumours were not related, and further antemortem diagnostics were not performed to distinguish the cardiac tumour type. When diagnostic confusion exists following echocardiogram in humans, CT or cardiac magnetic resonance imaging (MRI) are employed, with CT allowing extensive anatomical assessment of calcified lesions and evaluation of extracardiac involvement, and cardiac MRI allowing excellent soft tissue characterisation and identification of tissue invasion.[9]

To the authors' knowledge, this is the first paper to describe the associated CT changes of a cardiac myxoma in a dog. The cardiac myxoma identified several pinprick mineral bodies on pre-contrast images, with the mass hypoenhancing on post-contrast images compared to the IVS. There is a paucity of knowledge regarding the CT findings of cardiac masses in dogs; primarily as they are more commonly diagnosed by echocardiography.[7] In humans, calcified lesions are identified in around 50% of cardiac myxomas.[25] Mineralisation of a right atrial tumour on CT may therefore be beneficial in helping distinguish at antemortem, cardiac myxomas from primary or metastatic cardiac HSA. To confirm this finding, further investigation of mineralisation as a pathognomonic feature should be considered.

Although not assayed in this case, cardiac troponin I (cTnI) has been shown to be a useful marker for confirming or ruling out cardiac HSA. Dogs with cardiac HSA had significantly higher TnI values than dogs with HSA at other sites or with other neoplasms.[26] Fine-needle aspiration of cardiac tumours has been shown in a small case series to be highly successful in obtaining a diagnostic cytology sample, with five out of the six dogs having a neoplastic diagnosis confirmed and two dogs having only mild complications.[27] In most cases when a primary right atrial or appendicular cardiac mass is identified, further imaging (usually with CT) is advised to identify if there is metastasis in secondary locations.[4] Despite the previous evidence discussed, sampling of distant lesions is often implemented to provide a suspected diagnosis of the primary cardiac mass.[4] Furthermore, cardiac tumours continue to be managed and treated based on anatomic location in veterinary medicine.[4]

The prognosis and treatment for stage III HSA following emergency surgery is generally regarded as grave.[27,28] Although maximum tolerated chemotherapy with anthracycline-based protocols can prolong survival, this only achieves palliation.[19] In comparison, stage I and II disease with both surgery and adjunctive maximum tolerated chemotherapy with anthracycline-based protocols and/or metronomic chemotherapy have more favourable

outcomes, with median survival times of 239–355[29] and 120–145 days,[30] respectively, with around 15% of dogs still alive after 1 year.[31] This demonstrates accurate staging is vital for appropriate owner communication regarding treatment options and prognosis. In humans, treatment of cardiac myxomas is surgical via either traditional sternotomy or minimally invasive cardiac surgery, both with similar outcomes. Surgery is generally considered curative, with a low recurrence rate of 1%–3%.[9] Successful right auricular mass removal of cardiac HSA in dogs is well described.[32] Surgical excision of cardiac myxomas has been described in one dog; unfortunately, this was not successful with the dog arresting 2 days after the procedure.[15] This may be due to their intracardiac location, increasing the likelihood of potential complications.[15]

This case report is the first to describe the concurrent diagnosis of a primary right atrial myxoma with visceral HSA. This case highlights the value of appropriate diagnostic tests for cardiac tumours, and additionally, the potential pitfalls in using tumour location and clinical presentation to assume the diagnosis of the primary tumour type.

AUTHOR CONTRIBUTIONS

David John Brewer wrote most of the case report and was the primary clinician on the case discussed, with Joanna Dukes-McEwen the senior clinician. David John Brewer and Joanna Dukes-McEwen conceived and designed the project. Lorenzo Ressel and Gail Leeming analysed the histopathology and produced the figures. Rachel Marlow analysed and reviewed the CT images. Joanna Dukes McEwen analysed and reviewed the focused echocardiogram. All authors contributed and edited the case report.

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CONFLICT OF INTEREST

The authors declare they have no conflicts of interest.

FUNDING INFORMATION

The authors received no specific funding for this study.

ETHICS STATEMENT

Ethical approval was not required, and emergency care received was deemed appropriate according to the attending clinicians in this case. Further the animal herein discussed was euthanased on humane grounds. Permission to perform a postmortem was granted and performed according to the owners' wishes.

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