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Primary extraskeletal duodenal osteosarcoma with peritoneal sarcomatosis in a cat

Fabian Z.X. Lean [a], Benjamin J. Haythornthwaite [a], Sophie E. Broughton [b, c], Jodie R. Green [b], Francisco Llabres-Diaz [b], Balazs Szladovits [a], Henny M. Martineau [a, *]

[a] Department of Pathobiology & Population Sciences, Royal Veterinary College, University of London, Hawkshead Lane, North Mymms, Hatfield, AL9 7TA, UK
[b] Department of Clinical Science and Services, Royal Veterinary College, University of London, Hawkshead Lane, North Mymms, Hatfield, AL9 7TA, UK
[c] Department of Comparative Biomedical Sciences, Royal Veterinary College, University of London, Royal College Street, London, NW1 0TU, UK

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ABSTRACT

This case report describes an extraskeletal intestinal osteosarcoma with sarcomatosis in an 11-year-old female neutered Domestic Longhair cat that presented with a 2-week history of hyporexia, lethargy, vomiting and polydipsia. Clinical examination identified a cranial abdominal mass and ultrasound examination revealed liver nodules and an irregularly shaped, partly mineralized mass around the proximal duodenum and pancreas. Cytological examination of the intestinal and liver lesions identified plump to fusiform to stellate cells with scattered foci of mineralization. Post-mortem examination identified an extraskeletal intestinal osteosarcoma originating in the wall of the duodenum with sarcomatosis on the serosal surface of the liver, gallbladder and omentum. Local infiltration into the pancreas, liver and diaphragm was also present. Increased awareness and reporting of sarcomatosis in cats are important for expanding the knowledge base, guiding clinical management and understanding its impact on survival in such rare cases.

Extraskeletal osteosarcoma (ESOS) is a rare and aggressive malignant tumour that arises in soft tissues without originating from a primary bone tumour. In cats, ESOS accounts for approximately 40% of all OS cases, with neoplasms identified in various anatomical sites including subcutaneous tissues, mammary glands and ocular/orbital regions [1,2]. However, ESOS occurring in the digestive tract, particularly in the stomach and duodenum, is very rare, accounting for less than 2% of feline OS cases [1,2]. The incidence of ESOS in other species, such as dogs and humans, is similarly low [3,4]. Histologically, feline OSs typically have osteoblastic features, with occasional fibroblastic or chondroblastic elements [1]. The metastatic rate of feline OS is relatively low compared to that in the dog [1], and for primary digestive tract ESOS, metastasis has only been reported in the mesenteric lymph nodes [5,6]. Sarcoma dissemination through the peritoneal lining, known as sarcomatosis, has not been documented in ESOS; only two cases of peritoneal spread associated with sarcomas have been reported in cats [7,8].

The prognosis for cats diagnosed with ESOS is generally poor, with a mean survival time of under 13 months [2]. In limited reported cases involving the digestive tract, affected cats are typically euthanized within weeks to months following diagnosis. However, there have been isolated cases in which surgical intervention has extended survival for several months [5,6,9]. For example, cats that underwent only incisional biopsies had a survival time of less than 5 months, while those with excisional biopsies had a mean survival of up to 25 months [2]. In human sarcomatosis, patients receiving curative-intent treatment have a median survival time of 76 months, while those who received palliative treatment had a median survival time of 22 months [10]. Survival data for cats affected by peritoneal sarcomatosis secondary to other sarcomas are limited to individual cases [7,8]. Increased awareness and improved detection of feline peritoneal sarcomatosis is crucial for a better understanding of survival outcomes and evaluating treatment strategies. Here, we document lesions in a cat with extraskeletal intestinal OS and peritoneal sarcomatosis.

An 11-year-old female neutered Domestic Longhair cat was presented to the Emergency and Critical Care referral service of the Royal Veterinary College Queen Mother Hospital for Animals for investigation and management of a 2-week history of hyporexia progressing to anorexia, lethargy, vomiting and polydipsia. The cat had a history of vomiting hairballs, with an increased frequency over the past few months, but had otherwise been well. The cat had been assessed at an out-of-hours provider 5 days prior to

* Corresponding author.
E-mail address: hmartineau@rvc.ac.uk (H.M. Martineau).

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presentation and routine biochemistry examination (VetScan VS2; Zoetis, www.zoetis.co.uk) identified a mild increase in alkaline phosphatase activity (206 IU/L; reference interval [RI] 10–90 IU/L), a moderate increase in alanine aminotransferase activity (935 IU/mL; RI 20–100 IU/L) and a marked increase in total bilirubin concentration (3.1 mg/dL; RI 0.1–0.6 mg/dL). In-house haematological assessment was unremarkable. The cat was treated supportively with intravenous fluid therapy, maropitant, S-adenosyl-methionine (SAMe), omeprazole, amoxicillin-clavulanate and enteral feeding. The animal was reassessed at the primary care practice due to ongoing clinical signs and referred.

On admission to the referral centre, the cat was bright, alert and responsive, with pink and tacky mucous membranes and a capillary refill time of under 2 s. Conscious oral examination was unremarkable. The cat had a rectal temperature of 39°C, weighed 3.2 kg with a body condition score of 3/9 and a muscle condition score of 2/3. Cardiac auscultation revealed a tachycardia (240 beats per minute) with fair, synchronous pulses, a regular rhythm and a grade 3/6 holosystolic sternal murmur. Abdominal palpation revealed a firm, irregular mass in the cranial abdomen. Blood gas analysis (ABL90 Series; Radiometer, www.radiometer.co.uk) revealed a mild metabolic acidosis (pH 7.297 [RI 7.350–7.470], base excess 4.9, HCO_3 19.2 mmol/L), mild hypernatraemia (157 mmol/L; RI 140–153 mmol/L) and a mild decrease in free calcium (1.26 mmol/L; RI 1.28–1.43 mmol/L). Creatinine and urea concentrations were within reference intervals (148 μmol/L and 8.9 mmol/L, respectively). Packed cell volume was 45%, total protein concentration (refractometric) was 72 g/L and blood film assessment identified adequate platelet concentration.

An abdominal ultrasound, performed by a board-certified diagnostic imaging specialist, revealed a partly mineralized mass (approximately 3.3 cm in diameter) that encircled the cranial duodenal flexure (Fig. 1a). This mass was indistinguishable from the adjacent pancreas and was associated with gastric dilation. In the liver, there were at least two focal, relatively ill-defined lesions measuring between 3.5 and 7.4 mm in width. The gallbladder contained a small volume of non-shadowing sludge and a tortuous, dilated cystic duct, measuring 0.48 cm in width. There was a small volume of free peritoneal effusion. Fine needle aspiration of the duodenal mass and hepatic lesions was performed without complication. Based on the ultrasonography findings, the primary differential diagnosis considered was a pancreatic mass with metastasis.

Fine needle aspirates from the duodenal mass yielded low nucleated cellularity with the predominant nucleated population consisting of individualized and small aggregates of plump to fusiform to stellate cells. Nuclei were round to oval (10–15 μm in diameter) with finely stippled to coarse chromatin, single to multiple prominent nucleoli and moderate amounts of basophilic cytoplasm that frequently contained multiple small vacuoles, low to moderate numbers of small purple granules and, commonly, a lighter staining area away from the nucleus. There was mild to moderate anisocytosis and anisokaryosis, occasional binucleation and multiple nucleoli (Fig. 1b); rare suspected mitotic figures and rare possible erythrophagocytosis were also seen. Scattered rare foci of mineralization and multiple linear pale blue to turquoise material, rarely coiled up at both ends, were also observed (undetermined origin). Cytological examination of the liver nodules revealed rare cells with morphology similar to those described in the duodenal mass and low numbers of similar crystalline and linear material. As no hepatocytes were identified, aspiration of mesenteric fat with likely similar pathology to the abdominal mass was suspected. The overall scant cellularity hindered the assessment, but the major differentials for the mesenchymal cells with moderate atypia that were consistently identified in multiple organs were: reactive fibroblasts; a malignant mesenchymal population; walling off of foreign material; or possibly parasitic larvae given the mineralized and unusual coiled up material present on the smears.

Further investigations were declined and the cat was euthanized due to clinical deterioration and poor quality of life. Necropsy identified a mass involving the proximal duodenum and partially effacing the proximal aspect of the right pancreatic lobe. The mass was multilobulated, firm and white, measured 15 mm in diameter (Fig. 1c and d) and infiltrated the duodenal wall, narrowing the lumen (Fig. 2a) and the distal aspect of the bile duct. The gallbladder was mildly distended with slight resistance on expression, suggestive of partial bile duct obstruction. Multifocally present on the omentum (Fig. 1d), parietal hepatic serosa (Fig. 1e) and serosa of the gallbladder wall were multiple non-infiltrative, white, round, firm nodules, ranging from 3 to 20 mm in diameter. In the diaphragmatic wall there were multiple infiltrative, round, tan, firm masses, measuring 10–30 mm in diameter (Fig. 1f). No visible masses were identified in any other pleural and visceral organs and musculoskeletal structures.

Microscopic examination of the duodenal mass and peritoneal nodules revealed a moderately cellular proliferation of mesenchymal cells resembling osteoblasts or chondrocytes, nested within chondroid and osteoid matrix (Fig. 2a and b). Additionally, numerous multinucleated giant cells resembling osteoclasts were present within Howship's lacunae. There was moderate anisocytosis and mild anisokaryosis, and two mitotic figures were detected in 10 high-power fields (2.37 mm^2). Neoplastic cells were separated by a large amount of extracellular matrix, ranging from dense eosinophilic fibrous material to intense basophilic homogeneous chondroid matrix (confirmed by Safranin O staining; Fig. 2c) or homogeneously eosinophilic osteoid matrix with variable mineralization (confirmed with Von Kossa stain). Occasionally, the neoplasm also exhibited a transition from a chondroid-rich matrix on the external aspect of the nodules towards a mineralized osteoid centre, resembling ossification (Fig. 2d). These findings were consistent with a diagnosis of grade II OS [1].

Immunohistochemical examination was performed on the duodenum and pancreas. The immunophenotyping included the following antibodies on separate sequential histological sections: mouse monoclonal anti-porcine vimentin (1:5000, pH 9 antigen retrieval; Dako, www.agilent.com), mouse monoclonal anti-human desmin (1:25, pH 6 antigen retrieval; Dako), mouse monoclonal anti-human cytokeratin (1:100, proteinase K antigen retrieval; Dako), mouse monoclonal anti-human neuron-specific enolase (1:1000, pH 6 antigen retrieval; Dako) and rabbit polyclonal anti-bovine S100 (1:350, no antigen retrieval; Dako). Approximately 90% of the neoplastic cells had moderate cytoplasmic immunolabelling for vimentin (not shown). There was no immunolabelling for cytokeratin, desmin, neuron-specific enolase or S100.

This report documents a case of feline ESOS with peritoneal sarcomatosis. Sarcomatosis refers to the widespread dissemination of a primary soft tissue sarcoma to serosal surfaces. Peritoneal sarcomatosis is extremely rare in cats, with only two previously documented cases, one associated with fibrosarcoma and the other with splenic haemangiosarcoma [7,8]. In humans, sarcomatosis is most commonly linked to gastrointestinal stromal tumours (GISTs), liposarcoma and leiomyosarcoma, all of which are associated with a poor prognosis [11,12]. In the dog, a small case series found sarcomatosis occurred secondarily to primary splenic haemangiosarcoma (n = 5), soft tissue haemangiosarcoma (n = 1) and scapular OS (n = 1). All of these dogs presented with peritoneal nodules, and one case also had pleural nodules [13].

The pathogenesis of sarcomatosis has not been investigated in any species. In carcinomatosis, peritoneal spread of the neoplasm involves implantation of epithelial cancer cells via adhesion molecules, such as ICAM, VCAM and integrins, transformation of mesothelial cells into cancer-associated fibroblasts and modulation of immunosuppressive tissue-resident macrophages over the neoplastic cells [14]. Being a mesenchymal neoplasm, OS may exhibit mesenchymal–epithelial transition (MET), characterized by upregulation of adhesion molecules such as E-cadherin [15]. In this case the implantation of neoplastic mesenchymal cells onto the mesothelium suggests a potential role for upregulated adhesion molecules. In human skeletal OS, overexpression of E-cadherin (epithelial marker) or knockout of N-cadherin/vimentin (mesenchymal markers) has been associated with a loss of metastatic potential [16]. Considering the absence of vascular or lymphatic metastasis of ESOS and the minimal invasion of neoplastic foci into surrounding tissues, it is plausible that the neoplastic cells in this case may have exhibited a MET phenotype, but further research, including molecular analyses, would be required for confirmation.

An ante-mortem diagnosis of sarcomatosis was not reached. Ultrasonography did not identify serosal nodules, probably due to

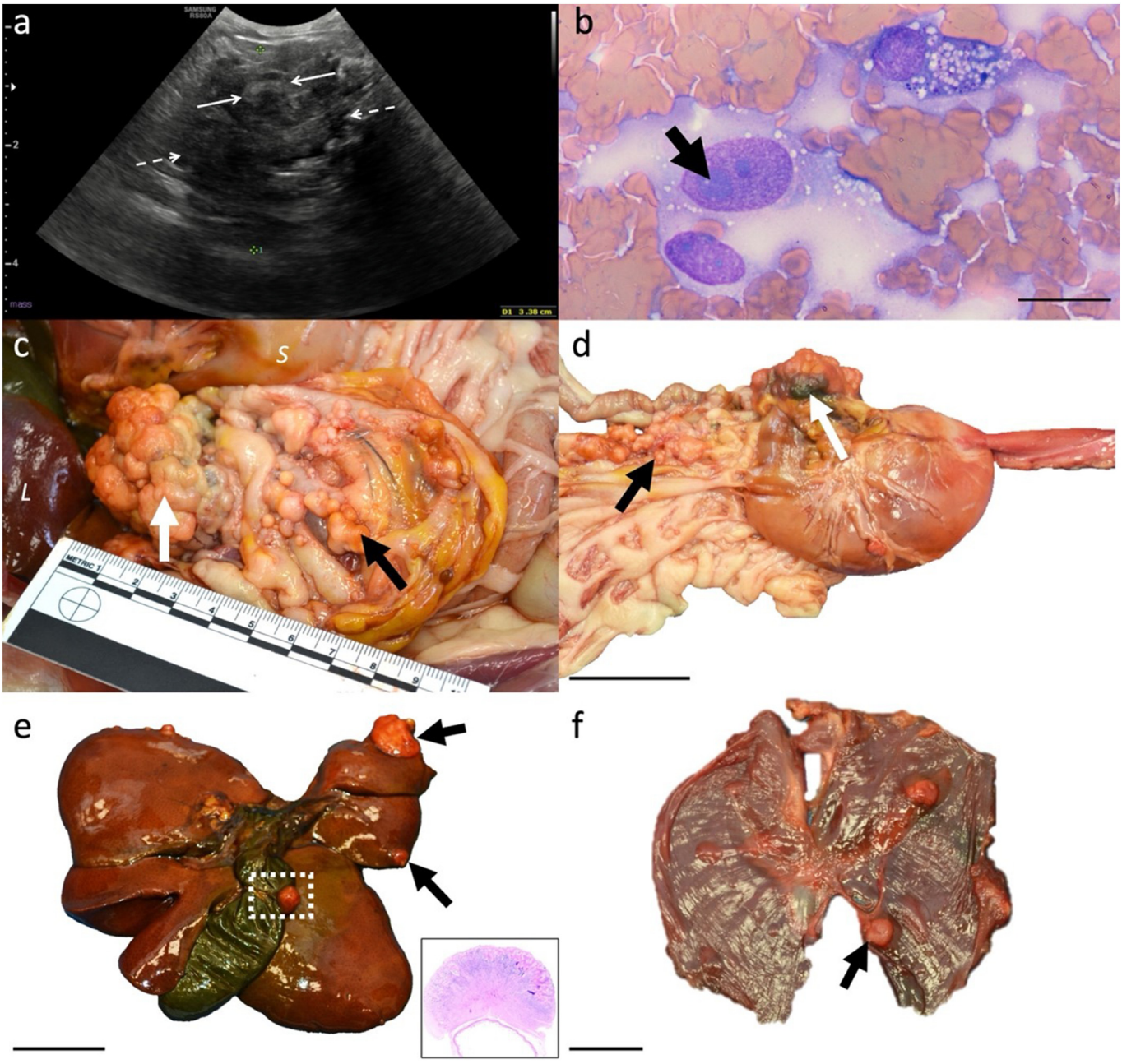

Fig. 1. Peritoneal sarcomatosis, primary intestinal osteosarcoma, cat. (**a**) Abdominal ultrasonography. Mass (dashed arrows) encircling proximal duodenum (arrows). (**b**) Aspirate of abdominal mass. Large plump mesenchymal cells with moderate to marked anisocytosis and anisokaryosis, macrokaryosis, and multiple variably sized nucleoli (arrow). Modified Wright's stain. (**c, d**) Multilobulated firm masses expand proximal duodenal wall (white arrows) and are present on omentum (black arrows). L, liver; S, stomach. (**e, f**) Multiple white, firm, well-demarcated, non-invasive masses (arrows) on hepatic capsule (**e**), gallbladder serosa (dotted box; inset: gallbladder. HE) and visceral aspect of diaphragm (**f**). Bars, 40 μm (**b**); 5 cm (**d**); 2.5 cm (**e,f**).

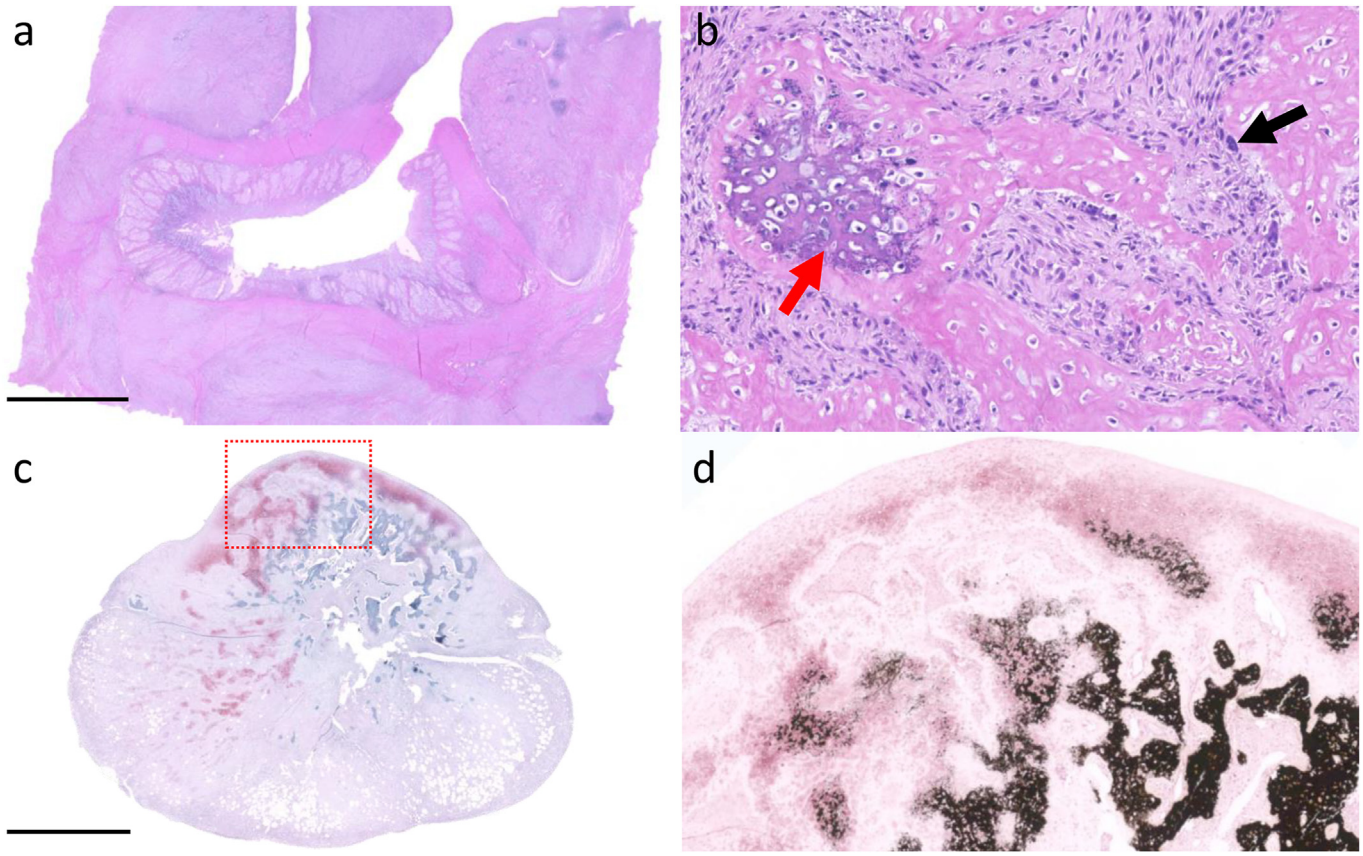

Fig. 2. Peritoneal sarcomatosis, primary intestinal osteosarcoma, cat. (**a**) Duodenal tunica muscularis circumferentially expanded and replaced by mesenchymal neoplasm. HE. (**b**) Duodenal mass comprised of variably mineralized osteoid matrix (red arrow), interspersed with neoplastic osteoblasts and occasional osteoclasts (black arrow). HE. (**c, d**) Neoplastic mass on omentum composed of chondroid-rich matrix (**c**; Safranin O histochemical stain; omental nodule) transitioning towards a mineralized osteoid centre, resembling ossification (**d**; red box in **c**; Von Kossa histochemical stain). Bars, 2.5 mm (**a, c**).

the limited extent of peritoneal spread, similarities in echogenicity to surrounding tissues and the deep location of some of the lesions at the time of examination. Despite the lack of ultrasound identification in this case, peritoneal or omental spread can be detected in some cases as nodules or plaque-like deposits [7,17,18]. However, in this instance, ultrasonography detected a small volume of abdominal effusion. In a separate report of a cat with abdominal fibrosarcoma and sarcomatosis, peritoneal fluid was not observed [8], and in canine sarcomatosis peritoneal effusion is infrequent ($n = 2/7$). This contrasts with carcinomatosis, where it was present in all seven cases in dogs [13]. Although sarcomatosis in humans and dogs typically presents with minimal to no ascites, in contrast to carcinomatosis [13,19], whether a similar trend exists in cats is unclear due to the rarity of feline sarcomatosis.

Although contrast-enhanced computed tomography (CT) scans were considered but not performed in our case, sarcomatosis is typically characterized by well-defined nodules with heterogeneous contrast enhancement, differing from the homogeneous enhancement and infiltrative foci seen in carcinomatosis, as observed in dogs and humans [13,19]. Cytological evaluation of the duodenal mass *ante mortem* identified cells resembling osteoblasts; however, a definitive differentiation from fibroblasts was not possible due to the poor cell yield. Erythrophagocytosis, a feature that has been reported in OS cells but is not specific to OS alone, was also seen [20]. The presence of mineralized material, for which a reaction to foreign material was considered, complicated the diagnosis.

This report highlights a case of peritoneal sarcomatosis secondary to an extraskeletal intestinal OS in a cat, a condition not previously reported in this species. The diagnostic challenges associated with ultrasonography and cytology emphasize the need for more advanced ante-mortem imaging modalities, such as contrast-enhanced CT, to enhance detection of primary and disseminated neoplasms. While minimal peritoneal effusion was observed in this case, its diagnostic significance in differentiating sarcomatosis from conditions such as carcinomatosis remains unclear and warrants further investigation as more cases of sarcomatosis are described.

Institutional Animal Care and Use Committee (IACUC) or other approval declaration

The authors declared no IACUC or other approval was needed. The diagnostic investigation was conducted in accordance with The Veterinary Surgeons Act 1966.

Statement of author contributions

FZXL, HMM: contributed to the conception and design of the article. **FLD, BJH, FZXL:** involved in the acquisition of images. **FZXL, BJH, HMM, BS, SEB:** drafted and reviewed the manuscript. All authors contributed to the article and approved the final version for publication.

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Declaration of competing interests

The authors declared no conflicts of interest in relation to the research, authorship or publication of this article.

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