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CASE REPORT

Myofibroblastic tumour in the liver of a cat – A case report

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ABSTRACT

This study presents a case of a primary hepatic myofibroblastic tumour in a 15-year-old European Shorthair female cat. The cat showed a gradual increase in liver enzymes (alanine aminotransferase and aspartate aminotransferase), and an abdominal ultrasound revealed a tumour located within the left lateral lobe of the liver. The tumour was surgically excised and sent for histopathology. Histopathological examination showed that the tumour was composed of homogeneous fusiform cells with low mitotic count, crowded within the perisinusoidal, portal and interlobular spaces, and entrapment of hepatocytes and bile ducts. Immunohistochemistry revealed that the tumour cells expressed vimentin and α-SMA, and were negative to desmin and cytokeratins. Based on the histological and immunohistochemical features, as well as some similarities with analogous entities in humans and animals, the tumour was classified as a myofibroblastic neoplasm originating from the liver.

KEYWORDS

liver, hepatic stellate cells, Ito cell tumour, oncology, immunohistochemistry, histopathology

Most of the primary hepatic tumours in cats are cholangiocellular carcinomas and hepatocellular adenomas (van Sprundel et al., 2014). Primary mesenchymal hepatic tumours in cats are rare, and previous studies have reported haemangiosarcoma, fibrosarcoma, leiomyosarcoma and osteosarcoma (Patnaik, 1992; Lawrence et al., 1994; Dhaliwal et al., 2003; Caserto and Almes, 2012).

Myofibroblasts are absent from the normal liver, but under pathological conditions, hepatic stellate cells (Ito cells) and portal mesenchymal cells undergo differentiation towards the myofibroblastic phenotype (Lemoinne et al., 2013). Primary hepatic tumours, derived from myofibroblasts are very rare in animals and have never been reported in cats. Spongiotic pericytoma (or Ito cell tumour), derived from hepatic stellate cells, has been previously observed in rats, mice and occasionally in humans (Stroebel et al., 1995; Tillmann et al., 1999; Kaiserling et Müller, 2005). Moreover, inflammatory myofibroblastic tumour is a well characterised entity in humans (Siemion et al., 2022) and has occasionally been reported also in dogs in various localisations, but not in the liver (Knight et al., 2009; Swinbourne et al., 2014; Romanucci et al., 2019).

In this paper we describe a case of a primary hepatic tumour in a cat. The distinct histological and immunohistochemical features of the surgically removed mass suggested a myofibroblastic origin of the tumour cells.

CASE DESCRIPTION

A 15-year-old European Shorthair female cat with a history of mild, chronic, stable renal insufficiency, manifested by elevated serum creatinine levels for more than two years (mean 2.27 mg dl^{-1}), unexpectedly began to show a gradual increase in alanine aminotransferase

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(ALT; 49.5–490.4 U/l) and aspartate aminotransferase (AST; 23.56–80.4 U/l). The abdominal ultrasound examination (USG) revealed a tumour measuring 39 × 35 mm, located within the left lateral lobe of the liver. Two months later, biphasic computed tomography (CT; with intravenous contrast injection) of the thoracic and abdominal cavity was performed (slice thickness 3 mm). CT confirmed the tumour in the left lateral lobe of the liver with the current dimensions of 50 × 43 × 42 mm. Surgical removal of the tumour was performed with subsequent histopathological examination. The postsurgical period was unremarkable. Six months after surgery, the cat was diagnosed with an unrelated disease (squamous cell carcinoma of the tongue) and finely lost from the follow-up.

Samples for histopathology were immediately fixed in 10% buffered formalin, processed routinely, cut and stained with Mayer's haematoxylin and eosin (HE), Mallory trichrome (Bio-Optica, Milan, Italy), Perl's Prussian blue. Immunohistochemical (IHC) staining was performed using a panel of antibodies for the detection of vimentin (monoclonal mouse anti-bovine, clone VIM 3B4, dilution 1:100; Dako, Glostrup, Denmark), α-smooth muscle actin (α-SMA; monoclonal mouse anti-human, clone 1A4, dilution 1:50, Dako), desmin (monoclonal mouse anti-human, clone D33, dilution 1:50, Dako), cytokeratins (monoclonal mouse anti-human, clone AE1/AE3/PCK26, Anti-Pan Keratin, ready to use antibody cocktail, recognizing most of the acidic and all of the basic cytokeratins, Ventana, Tucson, AZ), major histocompatibility complex class II (MHCII; HLA-DR α chain; clone TAL.1B5, dilution 1:20, Dako). The visualisation system was based on the immunoperoxidase method with 3,3-diaminobenzidine (DAB) as a substrate (EnVision + System-HRP, Mouse, Dako). The slides were counterstained with Mayer's haematoxylin. Positive (including normal feline liver) and negative control slides were processed together with the evaluated slides.

The histopathological examination revealed a poorly circumscribed tumour, with subcapsular location and penetrating deeply into the hepatic parenchyma. At the periphery, the tumour cells were crowded within the perisinusoidal, portal and interlobular areas (Fig. 1A). The tumour was composed of uniform spindle cells, arranged in solid, regular bands, which were separated by scant fibrous stroma (Fig. 1B). The nuclei were oval in shape with finely dispersed chromatin, indistinct nucleoli and moderate amount of slightly eosinophilic, fibrillar cytoplasm, occasionally - vacuolated. Mitotic forms were seldom seen. Within the tumour and in the hepatic parenchyma at the tumour margins, prominent foci of extramedullary haematopoiesis were noted. In the hepatic parenchyma at the tumour periphery, the areas of necrosis, extravasations and multifocal accumulation of haemosiderin were seen. The hepatocytes were swollen, vacuolated and contained intracytoplasmic granules or clumps of haemosiderin (confirmed by Perls' Prussian blue staining). The tumour cells showed cytoplasmic expression of vimentin (Fig. 1C), α-SMA (Fig. 1D), and were negative for desmin (Fig. 1E) and cytokeratins (Fig. 1F). Some tumour cells, randomly distributed within the tumour, showed also cytoplasmic expression of MHCII. Numerous bile ducts, entrapped within the tumour, showed cytoplasmic and membranous expression of cytokeratins (Fig. 1F). Based on these results, a myofibroblastic origin of the tumour cells was strongly suspected.

DISCUSSION

The presented tumour showed unique histological and immunohistochemical features, a case, similar to which has not been reported previously among the feline primary hepatic tumours. The morphology and immunophenotype of tumour cells suggested leiomyoma, however, hepatic leiomyomas are well circumscribed (Omiyale, 2014), while the presented tumour showed an infiltrative growth, with numerous aggregates of the hepatocytes as well as bile ducts entrapped within the tumour parenchyma. In the present study, tumour cells expressed vimentin – a widely used marker of mesenchymal cells (Castro-Muñozledo et al., 2017) and α-SMA - a marker of smooth muscle cells (Zhao et al., 2018). In normal liver, α-SMA is expressed only by the perivascular smooth muscle cells, the pericytes of the portal vessels and in the cells around the bile ducts (Gulubova, 2000). However, during injury, hepatic stellate cells (perisinusoidal, stellate or Ito cells) and portal mesenchymal cells differentiate into myofibroblasts, with *de novo* expression of α-SMA (Lemoinne et al., 2013). Based on the immunophenotype and also the distinct perisinusoidal and portal crowding of the tumour cells at the periphery of the tumour mass, we suggest that the presented tumour was derived most probably from myofibroblasts. In the control liver, the perivascular smooth muscle cells expressed desmin, and therefore were less likely to be the origin of the tumour cells, which were desmin-negative. Desmin expression can also be used to differentiate hepatic myofibroblasts derived from Ito cells and portal mesenchymal cells; desmin expression is upregulated during activation in Ito cells, and shut down in portal fibroblasts (Lemoinne et al., 2013). Therefore, hepatic tumour presented in this study is most probably derived from myofibroblasts of portal origin.

Occurrence of a hepatic tumour, derived from myofibroblasts, has not been reported in cats before. However, the presented tumour shared some similarities with the inflammatory myofibroblastic tumour, a distinctive neoplasm of intermediate biologic potential, diagnosed in the viscera and soft tissues of children and young adults (Siemion et al., 2022), and reported sporadically also in dogs (Knight et al., 2009; Swinbourne et al., 2014; Romanucci et al., 2019). However, this tumour is characterised by a distinct inflammatory component, which was not observed in the present case.

In conclusion, this is the first report of a primary hepatic myofibroblastic tumour in a cat. Based on the histological and immunohistochemical characteristics, portal-derived myofibroblasts are the most likely origin of tumour cells. The biological behaviour of the tumour is unknown, but neither recurrence nor metastasis was observed during a short follow-up period.

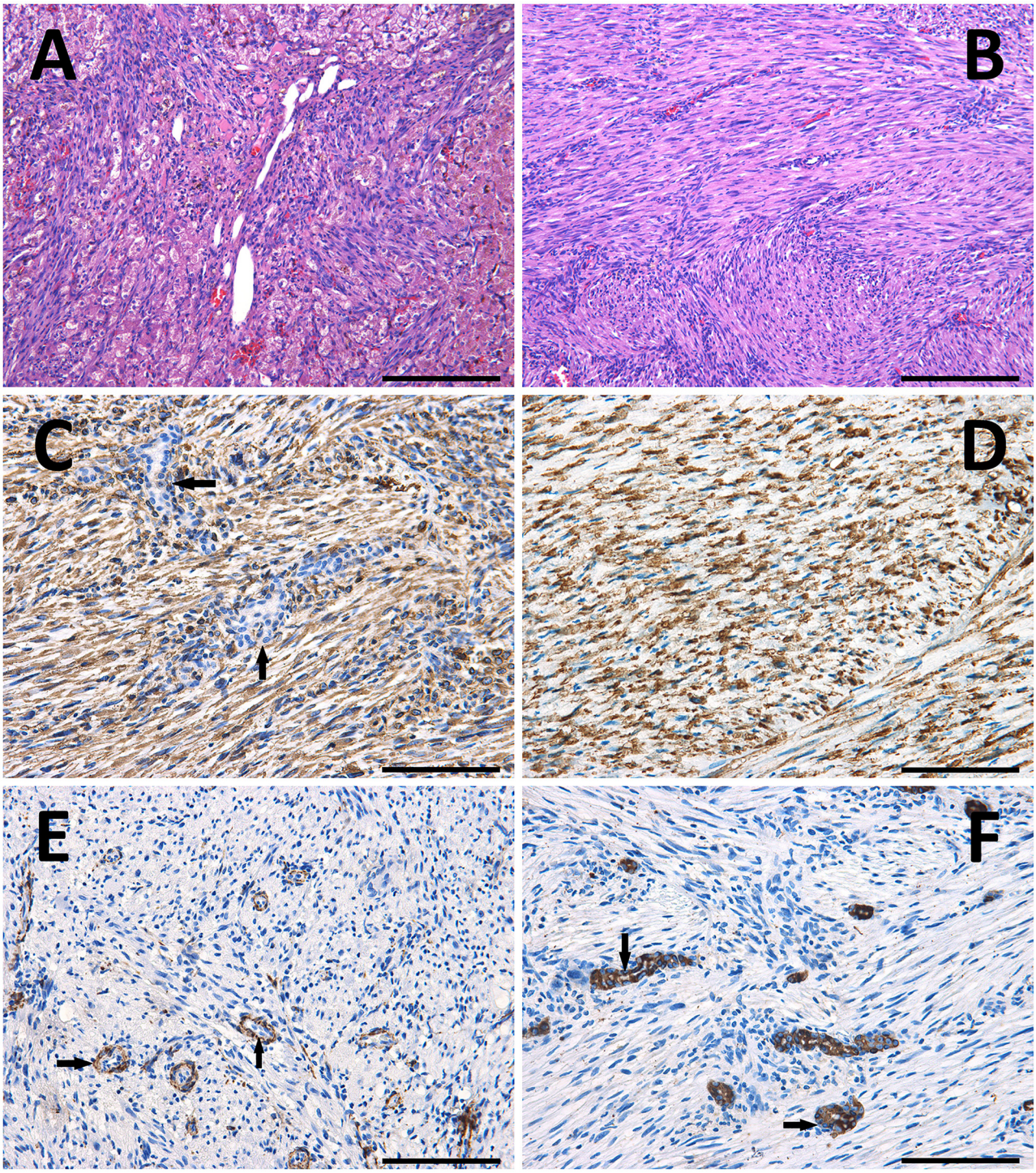

Fig. 1. Myofibroblastic tumour, liver, cat. A: The tumour cells at the tumour periphery were crowded among the trabeculae of hepatocytes, in the portal and interlobular areas. Scale bar: 200 µm. HE. B: Uniformly fusiform tumour cells form regular bands. Scale bar: 200 µm. HE. C: Tumour cells show cytoplasmic expression of vimentin, while the entrapped biliary ducts (arrows) are negative. Scale bar: 100 µm. IHC. D: Tumour cells are positive for α-SMA. Scale bar: 100 µm. IHC. E: Tumour cells are negative for desmin, while the perivascular smooth muscles (arrows) are positive. Scale bar: 100 µm. IHC. F: Within the tumour parenchyma, numerous biliary ducts (arrows) are entrapped, which are positive for cytokeratin antibodies. Scale bar: 100 µm. IHC

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REFERENCES

Caserto, B. G. and Almes, K. A. (2012): Pathology in practice. Primary hepatic chondroblastic osteosarcoma. J. Am. Vet. Med. Assoc. **240**, 1067–1069. https://doi.org/10.2460/javma.240.9.1067.

Castro-Muñozledo, F., Meza-Aguilar, D. G., Domínguez-Castillo, R., Hernández-Zequinely, V. and Sánchez-Guzmán, E. (2017): Vimentin as a marker of early differentiating, highly motile corneal epithelial cells. J. Cell. Physiol. **232**, 818–830. https://doi.org/10.1002/jcp.25487.

Dhaliwal, R. S., Johnson, T. O. and Kitchell, B. E. (2003): Primary extraskeletal hepatic osteosarcoma in a cat. J. Am. Vet. Med. Assoc. **222**, 340–342. https://doi.org/10.2460/javma.2003.222.340.

Gulubova, M. V. (2000): Ito cell morphology, alpha-smooth muscle actin and collagen type IV expression in the liver of patients with gastric and colorectal tumors. Histochem. J. **32**, 151–164. https://doi.org/10.1023/a:1004043206422.

Kaiserling, E. and Müller, H. (2005): Neoplasm of hepatic stellate cells (spongiotic pericytoma): a new tumor entity in human liver. Pathol. Res. Pract. **201**, 733–743. https://doi.org/10.1016/j.prp.2005.08.008.

Knight, C., Fan, E., Riis, R. and McDonough, S. (2009): Inflammatory myofibroblastic tumors in two dogs. Vet. Pathol. **46**, 273–276. https://doi.org/10.1354/vp.46-2-273.

Lawrence, H. J., Erb, H. N. and Harvey, H. J. (1994): Non-lymphomatous hepatobiliary masses in cats: 41 cases (1972 to 1991). Vet. Surg. **23**, 365–368. https://doi.org/10.1111/j.1532-950x.1994.tb00496.x.

Lemoinne, S., Cadoret, A., El Mourabit, H., Thabut, D. and Housset, C. (2013): Origins and functions of liver myofibroblasts. Biochim. Biophys. Acta. **1832**, 948–954. https://doi.org/10.1016/j.bbadis.2013.02.019.

Omiyale, A. O. (2014): Primary leiomyoma of the liver: a review of a rare tumour. HPB Surg. 2014, 959202. https://doi.org/10.1155/2014/959202.

Patnaik, A. K. (1992): A morphologic and immunocytochemical study of hepatic neoplasms in cats. Vet. Pathol. **29**, 405–415. https://doi.org/10.1177/030098589202900506.

Romanucci, M., Defourny, S., Massimini, M., Bongiovanni, L., Aste, G., Vignoli, M., Febo, E., Boari, A. and Della Salda, L. (2019): Inflammatory myofibroblastic tumor of the pancreas in a dog. J. Vet. Diagn. Invest. **31**, 879–882. https://doi.org/10.1177/1040638719879737.

Siemion, K., Reszec-Gielazyn, J., Kisluk, J., Roszkowiak, L., Zak, J. and Korzynska, A. (2022): What do we know about inflammatory myofibroblastic tumors? – a systematic review. Adv. Med. Sci. **67**, 129–138. https://doi.org/10.1016/j.advms.2022.02.002.

Stroebel, P., Mayer, F., Zerban, H. and Bannasch, P. (1995): Spongiotic pericytoma: a benign neoplasm deriving from the perisinusoidal (Ito) cells in rat liver. Am. J. Pathol. **146**, 903–913.

Swinbourne, F., Kulendra, E., Smith, K., Leo, C. and Ter Haar, G. (2014): Inflammatory myofibroblastic tumour in the nasal cavity of a dog. J. Small Anim. Pract. **55**, 121–124. https://doi.org/10.1111/jsap.12140.

Tillmann, T., Kamino, K., Dasenbrock, C., Germann, P. G., Kohler, M., Morawietz, G., Campo, E., Cardesa, A., Tomatis, L. and Mohr, U. (1999): Ito cell tumor: immunohistochemical investigations of a rare lesion in the liver of mice. Toxicol. Pathol. **27**, 364–369. https://doi.org/10.1177/019262339902700314.

van Sprundel, R. G., van den Ingh, T. S., Guscetti, F., Kershaw, O., van Wolferen, M. E., Rothuizen, J. and Spee, B. (2014): Classification of primary hepatic tumours in the cat. Vet. J. **202**, 255–266. https://doi.org/10.1016/j.tvjl.2014.07.002.

Zhao, W., Wang, X., Sun, K. H. and Zhou, L. (2018): α-smooth muscle actin is not a marker of fibrogenic cell activity in skeletal muscle fibrosis. PLoS One **13**, e0191031. https://doi.org/10.1371/journal.pone.0191031.