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Clinical and immunohistochemical findings of splenic mast cell tumour in a cat: A case report

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Abstract: A 6-year-old, spayed, female, domestic shorthair cat presented with a 4-month history of chronic intermittent vomiting and anorexia. The haematologic results indicated moderate anaemia and a circulating mast cell population. The abdominal radiography revealed a markedly enlarged spleen. The cytological analysis of the spleen showed a uniform population of mast cells, and a diagnosis of systemic mastocytosis (splenic mast cell tumour with mastocytaemia) was made. This diagnosis was subsequently confirmed by the histopathological examination of the spleen. The immunohistochemistry for KIT showed KIT pattern II (focal cytoplasmic expression). A splenectomy and chemotherapy with vinblastine and prednisolone resulted in remission of the anaemia and other clinical signs. This case report highlights the importance of cytological evaluations of peripheral blood smears and/or aspirates of enlarged spleens for diagnosing splenic mast cell tumours and for quickly initiating the appropriate treatment.

Keywords: KIT; mastocytaemia; prednisolone; spleen; splenectomy; vinblastine

Unlike mast cell tumours (MCTs) in dogs, which are mostly cutaneous/subcutaneous in nature, MCTs in cats can be classified anatomically into cutaneous, splenic, or intestinal forms with some overlap between these variants (Henry and Herrera 2013). A visceral MCT is more common in cats than in dogs, with approximately 50% of feline MCTs occurring at extracutaneous sites. Although a splenic MCT is one of the most common splenic tumours in cats, it is still a relatively rare diagnosis, and

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the literature characterising the disease is sparse, consisting mainly of case reports and small case series (Allan et al. 2000; Evans et al. 2018).

Systemic mastocytosis involves neoplastic mast cell proliferation in multiple visceral organs, especially the spleen and liver, and in the bone marrow. Systemic mastocytosis is rarely observed in cats (Piviani et al. 2013); however, when present, patients commonly suffer from lethargy, anorexia, weight loss, and intermittent vomiting (Allan et al. 2000). These clinical signs are nonspecific, making this diagnosis clinically challenging.

The aetiology of feline MCTs is currently unknown; however, it is evident that cats with MCTs possess somatic activating mutations in the *KIT* (Isotani et al. 2006; Sabattini et al. 2016). The *KIT* proto-oncogene encodes the receptor tyrosine kinase, KIT, which regulates the proliferation, differentiation, and migration of normal mast cells (Okayama and Kawakami 2006). However, the prognostic relevance of aberrant cytoplasmic KIT protein localisation has not yet been clearly elucidated for feline splenic MCTs.

This study aimed at determining the clinical signs and immunohistochemical findings in a cat with a splenic MCT.

Case description

A 6-year-old, spayed, female, domestic shorthair cat (weight: 4.2 kg) was referred to our hospital with a 4-month history of chronic intermittent vomiting, anorexia, and weight loss. Before being admitted to our hospital, the cat was taken to a local hospital, where she was tentatively diagnosed with inflammatory bowel disease and administered prednisolone and antiemetic drugs until her symptoms became more severe.

On physical examination, the cat was lethargic and dehydrated with pale mucous membranes. The abdominal cavity was largely distended with a firm, palpable organ on the left side. The haematological findings included a normal white blood cell count (14.96×10^9/l; reference interval, $2.87–17.02 \times 10^9$/l), a decreased red blood cell count (4.66×10^{12}/l; reference interval, $6.54–12.20 \times 10^{12}$/l), a decreased red blood cell specific volume (24.8%; reference interval, 30.3–52.3%), and decreased platelets (112×10^9/l; reference interval, $151–600 \times 10^9$/l). The serum biochemistry and urinalysis revealed no significant findings. Mast cells were observed in the peripheral blood smears (Figure 1A).

Splenomegaly was detected on the X-ray and sonographic examinations of the abdomen. A computed tomography (CT) scan revealed an enlarged spleen and multiple enlarged lymph nodes in the cranial, mediastinal, sternal, splenic, sub-lumbar, and mesenteric regions (Figure 1B).

The initial diagnostic evaluation included an ultrasound-guided fine-needle aspiration (FNA) of the spleen for the cytological examination. Diff-Quik-stained smears of the spleen contained numerous, well-differentiated mast cells covering the entire specimen, with basophilic granules

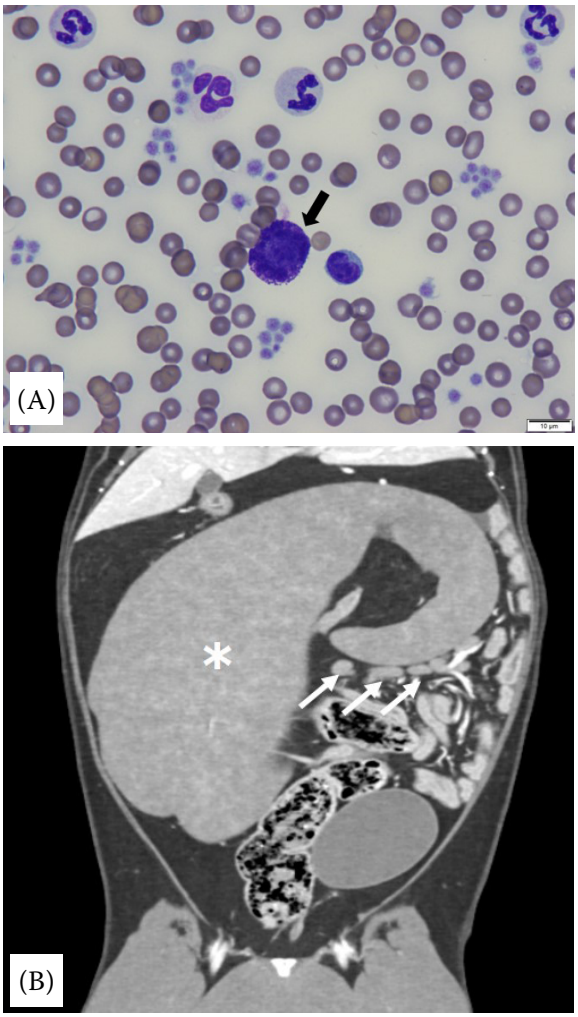

Figure 1. Light microscopy findings of the peripheral blood smear (A) and post-contrast computed tomography (CT) findings (B)

(A) A mast cell (black arrow) was observed in the peripheral blood smear (Diff-Quik, scale bar = 10 µm). (B) CT images revealed an enlarged spleen (white asterisk) and multiple enlarged mesenteric lymph nodes (white arrows)

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in the background (Figure 2A). Based on these findings, a tentative diagnosis of a splenic MCT was made, and the cat underwent a total splenectomy within a few days (Figure 2B).

The histopathological analysis showed that the native parenchyma of the spleen had largely been replaced by sheets of neoplastic mast cells (Figure 3A–B). These cells were round with distinct

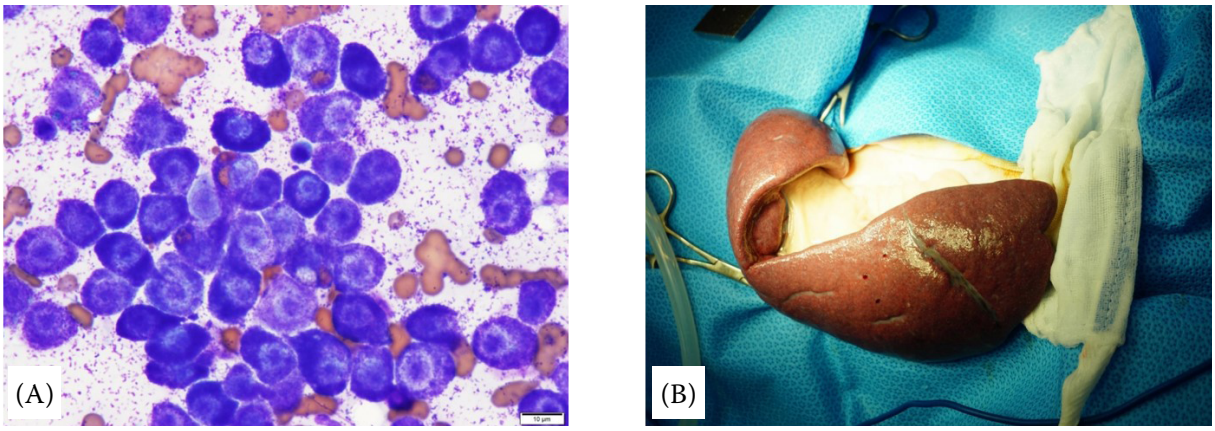

Figure 2. Light microscopy findings of the splenic aspirate (A) and the enlarged and firm spleen (B) of a cat with a splenic mast cell tumour

(A) Cells in the splenic aspirate were almost entirely composed of well-differentiated mast cells (Diff-Quik, scale bar = 10 µm). (B) A markedly enlarged spleen in a cat with a splenic mast cell tumour

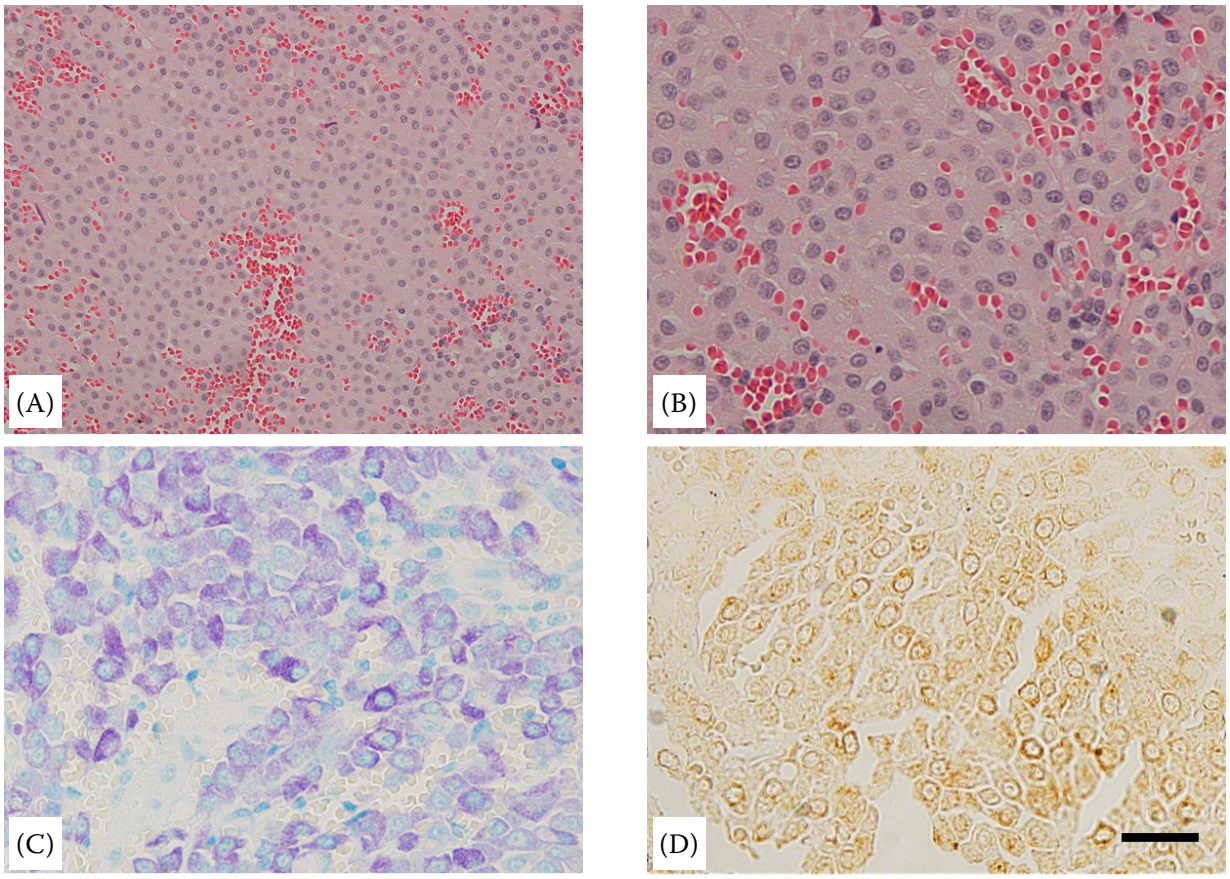

Figure 3. Histopathological (A–C) and immunohistochemical (D) images of a feline splenic mast cell tumour

(A, B) Histopathology of the splenic mast cell tumour showed well-differentiated mast cells on haematoxylin and eosin staining. (C) Granulated mast cells interspersed in the splenic parenchyma on toluidine blue staining. (D) Immunohistochemistry for c-KIT in a feline splenic mast cell tumour. Scale bar: A = 50 µm, B–D = 20 µm

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cell borders and an abundant, poorly granulated, basophilic cytoplasm. Mild anisocytosis and anisokaryosis were observed. The nuclei were round with coarsely clumped chromatin and prominent nucleoli. Toluidine blue staining revealed large round cells with characteristic metachromatic granules of mast cells (Figure 3C). An immunohistochemical staining for KIT was performed on sections of the spleen [Dako rabbit polyclonal anti-CD117 (KIT) antibody diluted 1 : 150; Dako North America, Inc., Carpinteria, CA, USA]. The KIT protein expression was classified based on the patterns described for canine MCTs (Kiupel et al. 2004). The immunohistochemistry for KIT showed positive dark brown staining in the mast cells, mostly with a focal cytoplasmic expression (KIT pattern II) (Figure 3D).

A month after the splenectomy, the cat's symptoms, including the anaemia, vomiting, and anorexia, had almost completely disappeared, and the cat was in an overall better clinical condition. However, mast cells were still found in the peripheral blood smear; therefore, chemotherapy with vinblastine and prednisolone was initiated. The patient received vinblastine (Vinblastine; Teva-Handok, Seoul, Republic of Korea) 10 mg/m^2 intravenously every two weeks and prednisolone (Solondo; Yuhan, Seoul, Republic of Korea) 5 mg/cat orally once a day. Two weeks after the chemotherapy, the mast cells in the peripheral blood smears had disappeared without evidence of myelosuppression. After the fourth chemotherapy session, the owner reported that the cat appeared to be in good overall health. At the last follow-up, the cat was doing well without recurrence of MCT after treatment (for 22 months).

DISCUSSION AND CONCLUSIONS

This case involved a cat with a splenic MCT and mastocytaemia. In cats, systemic mastocytosis is almost exclusively associated with visceral MCTs and is frequently associated with splenic MCTs (Allan et al. 2000; Woldemeskel et al. 2017). When mast cells are identified in the peripheral blood of a cat, an MCT, and especially a splenic MCT with systemic mastocytosis, should be considered (Skeldon et al. 2010). Because splenic MCTs in cats can present with nonspecific clinical signs of a systemic illness, this disease may not be recognised in the absence of apparent splenomegaly or if fine-needle aspirates of the affected internal organs are not examined (Woldemeskel et al. 2017). Mastocytaemia can be detected by examination of a peripheral blood smear or the buffy coat (Piviani et al. 2013). A cytological evaluation of the peripheral blood smear or the buffy coat should be performed in cats with weight loss and vomiting of unknown aetiology to rule out mastocytaemia.

In the current case, there was mild anisocytosis and anisokaryosis, the mitotic rate was low, and neither uninucleated nor multinucleated neoplastic giant cells were observed, which is most consistent with the well-differentiated form of MCT in cats. Staging procedures for feline MCTs are far less standardised than for dogs, and their utility is still being debated, probably due to the lower frequency of MCTs in cats and because the biological behaviour of these tumours is considered less aggressive (Sabattini et al. 2017).

In canine MCTs, juxtamembrane domain *KIT* mutations and aberrant cytoplasmic KIT protein localisation have been associated with increased cellular proliferation and reduced progression-free and overall survival (Webster et al. 2006). However, the prognostic relevance of aberrant cytoplasmic KIT protein localisation in feline MCTs has not yet been clearly elucidated. Aberrant cytoplasmic KIT immunohistochemical expression has been reported in 29–67% of feline cutaneous MCTs, and a higher frequency has been observed in tumours with unfavourable outcomes (Sabattini and Bettini 2010; Mallett et al. 2013). Previous studies have reported that aberrant cytoplasmic KIT protein localisation does not appear to be strictly correlated with the biological behaviour or prognostic relevance (Sabattini et al. 2013; Sabattini et al. 2017).

In this case, the symptoms almost completely disappeared and the clinical signs became more stable after the patient underwent splenectomy. Though there is a lack of a standardised treatment approach for this disease, a splenectomy is considered the treatment of choice for splenic MCTs, even in cats with systemic involvement (Evans et al. 2018). Although the role of chemotherapy is not yet certain, it is known that prednisolone and vinblastine multi-agent protocols can partially confer a high treatment response in dogs and cats with mast cell disease. Furthermore, some partial responses have been observed with vinblastine treatment in cats with splenic MCTs (Kraus et al. 2015). After our

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patient's first chemotherapy session, her mastocytaemia disappeared and was well maintained. Following treatment, intermittent restaging, which involves monitoring of the enlarged lymph nodes and mastocytaemia, is required to identify any disease recurrence or progression (Piviani et al. 2013).

This case report highlights the importance of cytological evaluations of peripheral blood smears and/or aspirates of enlarged spleens for diagnosing splenic MCT-associated systemic mastocytosis in cats and for initiating appropriate treatment in a timely manner. Twenty-two months after treatment, this cat was doing well without any recurrence of an MCT. In this case, no prognostic value was associated with the KIT staining pattern; therefore, further studies are necessary to assess the utility of the immunohistochemical analysis of the KIT protein in cats with a splenic MCT.

Conflict of interest

The authors declare no conflict of interest.

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