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Thrombocytosis in cats: a retrospective study of 51 cases (2000–2005)

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Feline haematology profiles of patients presented to the University of Bristol Small Animal Hospital from January 2000 to October 2005 were evaluated for thrombocytosis (defined as a platelets count of $>700 \times 10^9$/l and confirmed on smear evaluation). Thrombocytosis was found in 79 cats (4.64% of the hospital feline population), with values ranging from 703 to 1895×10^9/l. Signalment, clinical presentation, concurrence of other haematological abnormalities, diagnoses and outcome were evaluated in 51 cases in which complete medical records were available. Other variables (feline immunodeficiency virus/feline leukaemia virus status, thyroxine level, haemoplasma PCR, toxoplasma antibody titres) were also evaluated. No association was found between the presence of thrombocytosis and breed or gender. Gastrointestinal signs were the most common clinical presentation. Lymphopenia was the most common concurrent haematological abnormality. Based on final diagnosis reached, cats were grouped both according to the DAMNITV classification and according to the body system affected. Amongst the DAMNITV classification, inflammatory/infectious conditions were most commonly associated with thrombocytosis. According to body systems, gastrointestinal involvement was most represented, followed by endocrine cases. No association was found between the severity of thrombocytosis and outcome.

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Thrombocytosis is an uncommon haematological disorder in dogs and cats (Davenport et al 1982). An increase in circulating platelets can arise due to either increased bone marrow production or increased release of platelets from storage sites. Increased platelet production can occur in myeloproliferative diseases, such as essential or primary thrombocythaemia, or can arise as the part of the bone marrow's response to a wide variety of surgical and medical conditions known as reactive (secondary) thrombocytosis. Platelets are stored in the spleen and lungs and can be released in response to a number of stimuli including exercise and drugs such as vincristine and epinephrine (Feldman et al 1988, Chisholm-Chait 1999), resulting in a physiological thrombocytosis.

To the authors' knowledge little literature has been published regarding thrombocytosis in cats, although isolated case reports exist (Hammer et al 1990, Beale et al, 1992, Hogan et al 1999). The clinical significance of thrombocytosis also remains largely unclear as the relationship between clinical signs, diagnosis and increased platelet numbers is unknown. The purpose of this retrospective study was to investigate thrombocytosis in cats presenting to a referral hospital. Cases were evaluated in order to identify possible relationships between signalment, clinical presentation, diagnosis and outcome.

Materials and methods

Cases with thrombocytosis were identified from the feline haematology profiles of patients presented to the University of Bristol Small Animal Hospital between January 2000 and October 2005. Blood samples were collected from

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hospitalised patients by jugular venepuncture and placed in standard ethylenediaminetetraacetic acid tubes. Samples were analysed in most cases within 2–4 h (maximum of 24 h) using the Cell-Dyn 3700 (Abbott Limited Diagnostics, Maidenhead, UK) calibrated to enumerate feline platelets according to the manufacturer's instructions. A diagnosis of thrombocytosis was made based on an automated blood platelet count of $>700 \times 10^9$/l which was confirmed by performance of a manual count by microscopic blood smear evaluation. The latter was performed on a Wrights-stained smear using a standard method with each platelet visible per standard $\times$ 100 field being equivalent to 20×10^9/l in the circulation (Tasker et al 1999). Samples where platelet clumps were detected or where the count was not accurately manually confirmed were not further evaluated. A platelet count of $>700 \times 10^9$/l was chosen as a cut off as this represents the upper end of the reference interval used in our diagnostic laboratory, the reference interval being derived from the mean $\pm$ 2 standard deviations of the platelet counts of 52 healthy adult cats (data not shown). Medical records of those cases with thrombocytosis were retrieved if available. These medical records were evaluated for signalment (breed, gender, age), clinical presentation, platelet count and the presence of concurrent haematological abnormalities at the time of detection of thrombocytosis. Cases were evaluated for feline immunodeficiency (PetCheck FIV enzyme-linked immunosorbent assay (ELISA) test kit, IDEXX Laboratories, ME, USA) and feline leukaemia virus (FeLV PetCheck FeLV ELISA test kit, IDEXX Laboratories, ME, USA) status, thyroxine levels (Total T4 Immunofluorescence, Axiom Veterinary Laboratories, UK) haemoplasma PCR (Langford Veterinary Diagnostic Laboratories, University of Bristol, UK), toxoplasma titres (Toxoplasma IgG and IgM IFA titres, Biobest Laboratories, UK) and blood iron profile results. The final diagnoses reached for each case were grouped according to the DAMNITV classification (Garosi 2004) and according to body system involved (gastrointestinal, endocrine, cardiovascular, urinary, respiratory, haematological, musculoskeletal, nervous system, pleural or peritoneal cavity). The outcome, where stated, was also recorded. Sex and breed data were also obtained for the hospital feline population over the same time period during which a total of 1703 cats presented to the University of Bristol Small Animal Hospital. Our study population was compared with these data using χ^2 analysis, with significance taken as $P < 0.05$.

Results

Of the 1703 cats presented to Small Animal Hospital, 79 cases (4.64%) were found to have thrombocytosis. Medical records were available for 51 of the 79 thrombocytosis cases. Recorded automated platelet counts for these 51 cases ranged from 703 to 1895×10^9/l (median 801×10^9/l). Thirty-three of the 51 cats were domestic shorthair (64.7%), 4/51 were domestic longhair (7.8%), 4/51 were Maine Coon (7.8%), 2/51 were Abyssinian (3.9%) and 2/51 were Siamese (3.9%). Other breeds (Bengal, Burmese, Persian, Devon Rex, Ragdoll, Exotic) were represented with one case each. These breeds were similar to those seen in the overall hospital population over the same time period. The 51 cases comprised 33 males (64.7%) and 18 females (35.3%); comparable to the sex distribution of the overall hospital population over the same period. Thus, breed and sex distribution did not highlight any predispositions (χ^2 analysis, data not shown). The ages of the 51 thrombocytosis cases ranged between 10 weeks and 16 years, with a median of 6 years. Age analysis of the overall hospital population was not available, therefore comparison between the two groups for this variable was not possible.

Clinical presentation details were available for the 51 cases for which medical records were available; these were grouped according to major presenting signs (Table 1). Gastrointestinal signs were reported in 26 cats, 10 cats had neurological signs, seven had respiratory signs, four cats had lower urinary tract signs and two cats presented with skin disease. Of the 51 cases, six cats (11.7%) had clinical signs of bleeding; three of these had haematuria, two had gastrointestinal bleeding and one had a seroma with chronic minimal bleeding. Two further cases were suspected of having gastrointestinal bleeding (based on the presence of gastrointestinal signs and concurrent unexplained regenerative anaemia), but this could not be confirmed. Seven cats were referred for investigation of hyperthyroidism. Five of these seven cats had signs associated with hyperthyroidism (which are listed in various categories), whilst two were asymptomatic as a result of pre-referral medical treatment with methimazole. (Felimazole; Arnolds Veterinary Products, UK)

Forty-six of the 51 cats were tested for FIV and FeLV and all were negative. Thyroxine levels were tested in 13/51 cats; seven cats had elevated thyroxine concentrations. Toxoplasma IgG and IgM titres were negative in the nine

Table 1. Presenting signs (some cases are listed under more than one category and some cases had more than one sign at the same time)

Category	Presenting signs
Gastrointestinal (26)	Vomiting (9), anorexia (8), weight loss (4), polyphagia (2), dyschezia (1), regurgitation (1), intestinal foreign body (1), jaundice (1)
Neurological (10)	Seizures (4), hind limbs ataxia (2), ataxia (1), abnormal behaviour (1), listlessness (1), hind limbs paresis (1)
Respiratory (7)	Tachypnoea (3), coughing (2), sneezing (2), dyspnoea (2), hyperpnoea (1)
Bleeding (6)	Haematuria (3), haematochezia (2), melena (1), seroma (1)
Urinary (4)	Haematuria (3), dysuria (1), pollakiuria (1), stranguria (1),
Dermatological (2)	Pruritus (1), exfoliation (1)
Other (2)	2 cats were referred for treatment of hyperthyroidism; these cats were euthyroid at the time of presentation and did not show any clinical signs

cases in which they were performed. Haemoplasma PCR was negative in the three cases in which it was performed. Blood iron profiles were not performed in any of the cases. Concurrent haematological abnormalities were present in 39/51 cases with thrombocytosis. These included lymphopaenia (17 cats), neutrophilia (14), monocytosis (11), leukocytosis (nine), erythrocytosis (seven), anaemia (six), eosinopaenia (six), monocytopenia (four), lymphocytosis (four), panleukopenia (three), eosinophilia (three), neutropenia (two) and basophilia (one).

A final diagnosis was achieved in 45/51 cases. Based on the diagnosis, the cases were grouped according to aetiology using the DAMNITV classification system and categorised as follows (some of the cases were listed in more than one category, Table 2): inflammatory/infectious 16 cases, neoplastic six cases, vascular four cases, anomalous three cases, metabolic three cases, traumatic two cases and miscellaneous 20 cases. According to classification by body system (Table 3), 13 cases were gastrointestinal, 10 cases were endocrine, five were cardiovascular, four cases were urinary, four were respiratory, three were haematological, three were musculoskeletal, two were neurological, two involved the pleural or peritoneal cavity and two were classified with miscellaneous diseases.

Outcome was known in 45/51 cases, and was unknown in six cases. One cat died and nine were euthanased as a direct consequence of their disease; the outcome was good (disease controlled or cured) in 35/51 cases. No association could be found between the severity of the thrombocytosis and outcome. Eight of the 10 cases which died or were euthanased had platelet counts of $<1000 \times 10^9$/l (ranging between 745 and 907×10^9/l), whereas counts of $>1000 \times 10^9$/l were detected in only two of these patients (1016×10^9/l and 1497×10^9/l).

Discussion

Feline quantitative platelets disorders, namely thrombocytosis and thrombocytopenia, are uncommonly reported in the literature, and no articles specifically addressing thrombocytosis in cats currently exist. Interestingly, review articles have described thrombocytopenia to be more common than thrombocytosis, both in humans and animals (Feldman et al 1988, Jain 1993). However, this is in contrast to the results of our study in cats in which thrombocytosis was more common than thrombocytopenia (4.64% versus 1.33% of cases presenting to the University of Bristol Small Animal Hospital respectively, thrombocytopenia data not shown). Thrombocytosis, in the current study, was diagnosed at a single time point for each case. It would have been interesting to have performed sequential platelet counts to determine whether the thrombocytosis was persistent, but unfortunately the retrospective nature of the study means that retrieval of such data is not possible.

Increased platelet numbers can arise due to physiological thrombocytosis, reactive thrombocytosis or essential thrombocythaemia.

Physiological thrombocytosis results from the mobilisation of platelets from body stores in response to exercise or excitement, and is characterised by a mild and transient (15–30 min) increase in platelet count that does not have clinical consequences (Jain 1993). It is hard to confirm or exclude physiological thrombocytosis as a cause of the elevated platelets counts detected in the cats in the current study. No cats had been exercised prior to blood collection, but stress

Table 2. Aetiology according to DAMNITV classification of diagnosis (some cases are listed under more than one category)

Aetiology according to DAMNITV classification	Diagnosis
Inflammatory/infectious (16)	Pancreatitis (2), oesophagitis (1), interstitial nephritis (1), gastric ulcer (1), duodenal ulcers (1), pyothorax (1), bacterial pneumonia (1), calicivirus (1), feline infectious peritonitis (1), seroma (1), eosinophilic granuloma (1), *Ollulanus tricuspis* infection (1), inflammatory bowel disease (1), middle ear polyps (1), urethral stenosis (1)
Neoplastic (6)	Gastrointestinal lymphoma (1), spinal osteosarcoma (1), lung carcinoma (1), thymoma (1), extratracheal lymphoma (1), intestinal plasma cell tumour (1)
Vascular (4)	Arterial thromboembolism (2), thromboembolic disease (1), hypertension (1)
Anomalous (3)	Congenital megaoesophagus (1), hind limb physeal separation (1), portosystemic shunt (1)
Metabolic (3)	Hepatic lipidosis (3)
Traumatic (2)	Diaphragmatic rupture (1), abdominal seroma associated with mild chronic bleeding (1)
Miscellaneous (20)	Hyperthyroidism (9), primary erythrocytosis (3), hypertrophic cardiomyopathy (2), dietary intolerance (1), idiopathic epilepsy (1), ileus post intestinal foreign body removal (1), idiopathic feline lower urinary tract disease (1), urolithiasis (1), diabetes mellitus (1)

and fear associated with hospitalisation and blood sample collection may have stimulated catecholamine-induced splenic contraction to result in thrombocytosis. However, the influence of this during sample collection could not be evaluated objectively in this retrospective study, so the presence of physiological thrombocytosis cannot be assessed.

Reactive thrombocytosis occurs as a rebound response of the bone marrow to several conditions and can last days to weeks. Reactive thrombocytosis is mediated by increased plasma levels of thrombopoietin (TPO), (Jain 1993, Bourdreaux 1996, Schafer 2004, Dame and Sutor 2005), although other cytokines such as interleukin-6 (IL-6), and catecholamines, also play a role

Table 3. Diagnosis according to body system classification (some cases are listed in more than one category and more than once within the same category)

Body system origin classification	Diagnosis
Gastrointestinal (13)	Hepatic lipidosis (3), pancreatitis (2), portosystemic shunt (1), inflammatory bowel disease (1), dietary intolerance (1), *Ollulanus tricuspis* infection (1), gastric ulcer (1), duodenal ulcers (1), oesophagitis (1), congenital megaoesophagus (1), ileus (1), gastrointestinal lymphoma (1), intestinal plasma cell tumour (1)
Endocrine (10)	Hyperthyroidism (9). This includes 7 cases that were referred for further investigation of hyperthyroidism (2 of which were euthyroid and on treatment) and 2 cats diagnosed whilst at the University of Bristol, diabetes mellitus (1)
Cardiovascular (5)	Hypertrophic cardiomyopathy (2), arterial thromboembolism (2), hypertension (1), thromboembolic disease (1)
Urinary (4)	Idiopathic feline lower urinary tract disease (1), interstitial nephritis (1), urethral stenosis (1), urolithiasis (1)
Respiratory (4)	Bacterial pneumonia (1), calicivirus (1), middle ear polyps (1), lung carcinoma (1), extratracheal lymphoma (1)
Haematological (3)	Polycythaemia vera (3)
Musculo-skeletal (3)	Hind limb physeal separation (1), diaphragmatic rupture (1), spinal osteosarcoma (1)
Nervous system (2)	Idiopathic epilepsy (1), spinal osteosarcoma (1)
Pleural/peritoneal cavity (2)	Pyothorax (1), abdominal seroma (1)
Miscellaneous (2)	Feline infectious peritonitis (1), eosinophilic granuloma (1), thymoma (1)

(Chisholm-Chait 1999, Schafer 2004). Indeed IL-6 levels in humans can be used to differentiate reactive thrombocytosis (where IL-6 is elevated) from essential thrombocythaemia (IL-6 normal) (Dan 2005). In dogs and cats reactive thrombocytosis is said to most commonly occur with neoplasia, gastrointestinal and endocrine disorders, exogenous corticosteroid and vinca alkaloid treatment (Jain 1993). Other reported causes both in small animals and humans include acute blood loss, inflammatory and infectious conditions, iron deficiency and splenectomy (Davenport et al 1982, Feldman et al 1988, Dan 2005, Valade et al 2005). In agreement with previous studies (Davenport et al 1982, Feldman et al 1988, Chisholm-Chait 1999), it is likely that reactive thrombocytosis was a common cause of thrombocytosis in our study, particularly arising with inflammatory/infectious (16/51 cases) and neoplastic (6/51) conditions. Gastrointestinal signs were also commonly seen in our thrombocytosis cases (26/51) and endocrine disease was commonly represented (10/51; primarily hyperthyroidism as discussed later). In humans, the most frequent cause of reactive thrombocytosis is tissue damage following major surgery, followed by infectious disease and neoplasia (Suzuki et al 1992, Schafer 2004). The absence of apparent post-surgical thrombocytosis in the current study is probably due to the low number of post-surgery samples in the population studied. In cats reactive thrombocytosis has been reported to occur with azathioprine administration (Beale et al 1992), doxorubicin treatment (O'Keefe and Schaeffer 1992), dietary imbalances (Backus et al 1998) and a paraneoplastic syndrome (Hogan et al 1999) although similar associations were not detected in our study.

Iron deficiency is a commonly reported cause of reactive thrombocytosis in both humans and dogs (Stockham and Scott 2002, Schafer 2004). The pathogenesis of the thrombocytosis is unknown (Dan 2005), although increased levels of thrombopoietic cytokines may be involved. Unfortunately, blood iron profiles were not available for the cases in the current study as evaluation of iron stores in cats is difficult and so is not routinely performed. Feline serum ferritin measurement is not available in the United Kingdom and as healthy cats do not always store iron in their bone marrow, bone marrow evaluation is not a reliable method to assess iron stores in cats (Stockham and Scott 2002). Interestingly, six of the cases in the current study did have clinical signs of bleeding which had been ongoing for at least 2 weeks. It is possible that iron deficiency was present in some of these cases but concurrent haematological abnormalities (microcytosis, hypochromasia) suggestive of iron deficiency were not present in these cats and they were not anaemic. Evaluation of their mean corpuscular volumes and mean corpuscular haemoglobin concentrations did not show these parameters to be at the low end of the reference interval either. Additionally all of the six cats recovered without receiving iron supplementation. Thus, we feel that it is unlikely that iron deficiency was responsible for the thrombocytosis seen in these cases, although this remains unproven without the ability to evaluate their iron status accurately. However, iron availability is reduced during inflammation (Deicher and Hörl 2006), and this may well play a role in the pathogenesis of inflammation-associated thrombocytosis.

In humans, reactive thrombocytosis is most frequently recognised in hospitalised children less than 2 years old. This association between young age and thrombocytosis is thought to arise due to the higher circulating TPO concentrations and increased sensitivity of megakaryocytic progenitor cells to TPO in children (Dame and Sutor 2005). In our study 25.4% of the thrombocytosis cases were younger than 1 year of age, with no disease category being over represented in this group. It is, therefore, possible that thrombocytosis is more common in younger cats because of similar mechanisms to those reported in children. Measurement of TPO concentrations in younger cats would be useful to further investigate this hypothesis. However, confirmation of the presence of an association between thrombocytosis and young age would require evaluation of the age distribution of all cats presenting to the University of Bristol Small Animal Hospital to compare with that of the thrombocytosis cases. Unfortunately, these data were not available.

Essential thrombocythaemia is an uncommon myeloproliferative disease, rarely reported in cats (Feldman et al 1988, Hammer et al 1990, Chisholm-Chait 1999). No cats with essential thrombocythaemia were definitively diagnosed in the current study. However, three cats with thrombocytosis were diagnosed with primary erythrocytosis in the current study. In humans, essential thrombocythaemia can occur as part of the disease polycythaemia vera (Schafer 2004), thus resulting in concurrent erythrocytosis and thrombocytosis. It is possible that the three cats in our study had a similar syndrome, although this has not yet been reported in cats.

In our study, thrombocytosis was found in association with a diagnosis of hyperthyroidism in nine cases (17.6%), although in two of these cases thyroxine levels were normal at the time that thrombocytosis was detected, as a result of pre-referral treatment with methimazole. These nine cats represent 13.2% of the 68 hyperthyroid cats seen with in our hospital during the time period of our study. The high incidence of concurrent thrombocytosis and hyperthyroidism in our study population is in contrast with data from a previous study (Sullivan et al 1993), where 14% of the 21 hyperthyroid cats evaluated were thrombocytopaenic, but none had thrombocytosis. None of the thrombocytopaenic cats seen during our study period were hyperthyroid (data not shown). In humans, hyperthyroidism can be associated with an increase in thrombopoiesis, as demonstrated by an increased number of reticulated platelets (Stiegler et al 1998) and it is possible that a similar mechanism exists in cats.

To the authors' knowledge, the incidence of concurrent haematological abnormalities and thrombocytosis has not been evaluated in previous studies. Lymphopenia was the most common abnormality seen in association with thrombocytosis (33.3%) for which no other underlying condition could be found (eg, FIV/FeLV infection, glucocorticoid and chemotherapeutic treatment). Lymphopenia is commonly seen in sick cats, often without the other components of the stress leukogram, thus it is perhaps not surprising that a high incidence of lymphopenia was seen in this group of thrombocytotic cats. It is a limitation of this current study that it was not possible to evaluate a control group for the incidence of haematological abnormalities in cats with normal platelet numbers, so definitive associations cannot be confirmed.

We conclude that thrombocytosis is a relatively common haematological abnormality in a feline referral population. It is most commonly reactive and associated with gastrointestinal and endocrine conditions or inflammatory/infectious and neoplastic disease. The overall outcome for cats with thrombocytosis in this study was good and furthermore the outcome was not influenced by the degree of thrombocytosis.

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