Case Report

jfms OPEN REPORTS

Journal of Feline Medicine and Surgery Open Reports
1–3

DOI: 10.1177/2055116916668198
jfmsopenreports.com

This paper was handled and processed by the European Editorial Office (ISFM) for publication in JFMS Open Reports

SAGE

Life-threatening haematological complication occurring in a cat after chronic carbimazole administration

Andrea Mosca and Luca Bresciani

Abstract

Case summary An 11-year-old spayed female domestic shorthair cat with a history of hyperthyroidism treated with carbimazole for 7 months was presented for a check-up after a few episodes of vomiting. The cat had been receiving prednisolone at 0.5 mg/kg PO q12h for recent pancreatitis and concurrent inflammation of liver and small intestines confirmed by biopsies. Clinical examination revealed pale mucous membranes with a capillary refill time of <2 s. Haematology showed severely decreased packed cell volume (16%), and increased prothrombin time (42 s), partial thromboplastin time (>120 s) and fibrinogen serum concentration (3.5 g/l). Morphological changes of thrombocytes in the absence of thrombocytopenia were also noted. In-saline agglutination test was positive. Abdominal radiographic and ultrasonographic examinations excluded the presence of organ abnormalities and peritoneal effusion. Blood biochemistry was unremarkable. Feline leukaemia virus and feline immunodeficiency virus tests were negative. On the basis of these findings, immune-mediated anaemia secondary to chronic carbimazole administration was suspected. Prednisolone was increased to 2 mg/kg PO q24h and carbimazole tablets were stopped. Despite close monitoring and intensive care, the cat died the same evening of admission to the hospital.
Relevance and novel information This report suggests that severe haemotoxicity may occur as a sequel of chronic carbimazole administration in cats. Routine bloodwork and accurate follow-up of cats under treatment with thyrotoxic therapy may be advisable, in order to detect haematological changes before lethal complications occur.

Accepted: 16 August 2016

Introduction

Hyperthyroidism is one of the most common endocrine disease in cats,[1] especially in middle-aged to older cats.[2,3]

Owing to concurrent geriatric problems, which are likely to increase the risk of anaesthetic-related complications, medical treatment is often preferred over surgical thyroidectomy. Serious haematological side effects are a well-known complication for patients on thyrotoxic treatment, although only two cases of methimazole-induced haemotoxicity have been reported in cats.

We report a life-threatening haematological complication occurring in a cat after chronic carbimazole administration.

Case description

An 11-year-old spayed female domestic shorthair cat weighing 5.9 kg, with a history of hyperthyroidism treated with carbimazole for the past 7 months, was presented for a check-up after a few episodes of vomiting. Total thyroxine, haematology and biochemistry were monitored routinely every 3 months. Since the beginning of the therapy, the owner had been compliant with the medication and the screening. The treatment started on carbimazole 15 mg PO q24h and the dosage was fixed accordingly with monitoring to reach a dose of 10 mg PO q24h where the cat was stable. The cat was also receiving prednisolone at 0.5 mg/kg PO q12h for

Medivet Ltd, Watford, UK

Corresponding author:
Andrea Mosca DVM, MRCVS, Medivet Ltd, Watford, Hertfordshire, Cedar Lodge, Wilbraham Road, Six Mile Bottom, Newmarket CB8 0UW, UK
Email: andrea.mosca16@gmail.com

recent pancreatitis and concurrent inflammation of liver and small intestines, confirmed with biopsies.

At presentation, the cat was alert and responsive. Its body condition score was 2/5 and the cat had gained 200 g in body weight during the previous month. Mucous membranes were pale and capillary refill time was normal. Heart rate was 164 beats per minute, with no identifiable heart murmur and the lung sounds were clear. Abdominal palpation was unremarkable. Blood was collected for a comprehensive panel and manual packed cell volume (PCV).

Abnormalities on haematology and serum biochemistry were confined to mild hypoproteinaemia (57 g/l; reference interval [RI] 60–80), mild hypoalbuminaemia (22 g/l; RI 25–46) and decreased creatinine serum concentration (69 µmol/l; RI 88–177). Serum total thyroxine was within normal limits for the species (45 nmol/l; RI 19–50 nmol/l) but borderline for a cat on treatment with carbimazole. Manual PCV was markedly low (16%). Reticulocyte count revealed a regenerative anaemia (0.17 10^9/ml) and on the blood smear red blood cells showed polychromasia and anisocytosis. Few lymphocytes appeared reactive with deeply basophilic cytoplasm and occasionally with abundant pale basophilic cytoplasm. Platelet number was adequate on the film. The in-saline agglutination test was positive. Feline leukaemia virus (FeLV) and feline immunodeficiency virus (FIV) tests were negative (IDEXX Snap Test). A coagulative panel showed that prothrombin time (42 s; RI 7.0–11.0 s), partial thromboplastin time (>120 s; RI 13.0–20.0 s) and fibrinogen serum concentration (3.5 g/l; RI 0.5–3.0) were all increased.

Fluid therapy with Hartmann's solution (Aqupharm 11; Animalcare) was initiated.

Whole-body radiographs were performed and were unremarkable. Abdominal ultrasound and T-fast were also normal and no pericardial, pleural or peritoneal effusion were found. The liver appeared heterogeneous with no overt masses; the spleen was homogenous and small. The right kidney was 4.3 cm in length, the left one measured 3.7 cm and the architecture of both appeared normal. The pancreas was not enlarged and was surrounded by hyperechoic fat bilaterally.

Based on these results, we could rule out the most common causes of immune-mediated anaemia and conclude that the haematological disorder was secondary to chronic carbimazole administration.

Prednisolone was increased to 2 mg/kg PO q24h and carbimazole discontinued. Doxycycline was started at 5 mg/kg PO q12h with the purpose of treating an undetected *Mycoplasma haemofelis* infection. Omeprazole was also started at 1 mg/kg PO q24h to prevent gastrointestinal ulceration due to the prednisolone immunosuppressive dose.

The possibility of a blood transfusion was mentioned to the owner, who declined the procedure owing to the potential for complications. Blood pressure was measured every 2 h, while PCV was monitored every 8 h. Body temperature was maintained within normal ranges for the species by active warming. Despite close monitoring and intensive care, the cat died the same evening of admission to the hospital. Post-mortem examination was declined.

Discussion

Differential diagnoses for immune-mediated anaemia in cats include infectious, neoplastic and chronic diseases, as well as drugs and toxins.[4] In our case, the diagnostic investigations were suggestive of immune-mediated anaemia secondary to chronic carbimazole administration. Infectious diseases were excluded on the basis of the negative results for FIV and FeLV testing of serum. Furthermore, the cat was an indoor cat and had no possibility of contact with other cats.

There was no evidence of neoplastic disease, as corroborated by the ultrasonographic and radiographic findings, which failed to identify the presence of masses, organ enlargement or cavitary effusions.

A haematological disorder resulting from chronic disease cannot be completely ruled out. A chronic pancreatitis, with concurrent inflammation of liver and small intestine, was suspected on the basis of the cat's past history. However, none of the findings supported this differential diagnosis. The coagulation abnormalities detected in this cat, namely the increased prothrombin time, partial thromboplastin time and fibrinogen serum concentration,[5] together with the immunomediated origin of the anaemia, as confirmed by the positive in-saline agglutination test, seem to indicate the carbimazole toxicity as the most likely cause.

Similar cases of severe anaemia caused by methimazole were treated by discontinuing the treatment, with no re-challenge with antithyroid drugs.[6] Alongside this, it has been recommended to administer prednisolone (1–2 mg/kg PO q12–24h) and doxycycline (5 mg/kg PO q12h). In order to prevent gastric ulceration due to a high dose of prednisolone, proton pump inhibitors (omeprazole 0.5–1.0 mg/kg PO q24h) must be used. H_2-receptor antagonists (ranitidine 1 mg/kg PO q12h) can also be used to decrease pepsin and gastric acid secretions and so have a secondary efficacy.[7]

Clinical side effects typically associated with chronic carbimazole therapy include anorexia, vomiting and lethargy, but these signs are usually mild and transient, and similar to those reported with methimazole.[8] More serious side effects are reported for methimazole, such as hepatopathy, bleeding diathesis (prolonged proteins induced by vitamin K absence or antagonists [PIVKA] clotting time) and marked thrombocytopenia.[5,8] Anaemia, including aplastic anaemia, was reported by Chapman et al,[9] after 3 years of treatment, and also by Weiss in 2006.[10]

It is also of note that there may be synergistic side effects with the combination of other drugs, even if the severity is unknown.[11,12] Carbimazole is 85% protein bound,[13,14] and prednisolone is 70–80% protein bound.[15] When used concurrently, there may be a chance that carbimazole competes with this other drug for protein binding and so causes adverse side effects.[11]

Carbimazole is a well-studied thyrotoxic drug which is considered to have fewer life-threatening side effects than methimazole.[16] Although carbimazole may be better tolerated in cats than methimazole, the potential for serious adverse reactions still exists. In order to detect them, Mooney et al recommended carrying out a complete blood count every 2 weeks, at least for the first 3 months of therapy, when these reactions are most likely to occur.[16]

Owing to the rapid course of events, as well as to the severity of the condition at presentation, the cat died on the same night of admission to the hospital. A closer follow-up of the cat during carbimazole treatment could have allowed for an earlier detection of the haematological changes, in order to undertake preventive measures before lethal complications occurred.

Conclusions

Life-threatening side effects, occasionally reported with methimazole in cats, may occur also with carbimazole. Routine bloodwork and accurate follow-up of cats under treatment with thyrotoxic therapy may be advisable, in order to detect haematological changes before lethal complications occur.

Funding The authors received no financial support for the research, authorship and/or publication of this article.

Conflict of interest The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

References

1 Peterson ME, Randolph JF and Mooney CT. **Endocrine diseases**. In: Sherding RD (ed). The cat: diseases and clinical management. 2nd ed. New York: Churchill Livingstone, 1994, pp 1403–1506.
2 Peterson ME, Kintzer PP, Cavanagh PG, et al. **Feline hyperthyroidism: pretreatment clinical and laboratory evaluation of 131 cases**. *J Am Vet Med Assoc* 1983; 183: 103–110.
3 Peterson ME and Turrel JM. **Feline hyperthyroidism**. In: Kirk RW (ed). Current veterinary therapy IX. Philadelphia: WB Saunders, 1986, pp 1026–1033.
4 Mitchell K and Kruth S. **Immune-mediated anemia and other regenerative anemias: feline IMHA**. In: Ettinger SJ and Feldman EC (eds). Textbook of veterinary internal medicine. 7th ed. Toronto: Saunders Elsevier, 2010, pp 768–769.
5 Randolph JF, DeMarco J, Center SA, et al. **Prothrombin, activated partial thromboplastin, and proteins induced by vitamin K absence or antagonists clotting times in 20 hyperthyroid cats before and after methimazole treatment**. *J Vet Intern Med* 2000; 14: 56–59.
6 Daminet S, Kooistra HS, Fracassi F, et al. **Best practice for the pharmacological management of hyperthyroid cats with antithyroid drugs**. *J Small Anim Pract* 2014; 55: 4–13.
7 Kohn B, Weingart C, Eckmann V, et al. **Primary immune-mediated hemolytic anemia in 19 cats: diagnosis, therapy, and outcome (1998–2004)**. *J Vet Intern Med* 2006; 20: 159–166.
8 Peterson ME, Kintzer PP and Hurvitz AI. **Methimazole treatment of 262 cats with hyperthyroidism**. *J Vet Intern Med* 1988; 2: 150–157.
9 Chapman E, Johnston L and Graham P. **Treatment of feline hyperthyroidism with 2.5 mg thiamazole (methimazole): efficacy and safety**. Proceedings of the 15th ECVIM-CA Congress; 2005 Sept 1–3; Glasgow, UK. pp 218–219.
10 Weiss D. **Aplastic anemia in cats – clinicopathological features and associated disease conditions 1996–2004**. *J Feline Med Surg* 2006; 8: 203.
11 Tesseromatis C and Alevizou A. **The role of the protein-binding on the mode of drug action as well the interactions with other drugs**. *Eur J Drug Metab Pharmacokinet* 2008; 33: 225–230.
12 Kratochwil NA, Huber W, Müller F, et al. **Predicting plasma protein binding of drugs: a new approach**. *Biochem Pharmacol* 2002; 64: 1355.
13 Frénais R, Burgaud S and Horspool LJI. **Pharmacokinetics of controlled-release carbimazole tablets support once daily dosing in cats**. *J Vet Pharmacol Ther* 2008; 31: 213–219.
14 Peterson ME and Aucoin DP. **Comparison of the disposition of carbimazole and methimazole in clinically normal cats**. *Res Vet Sci* 1993; 54: 351–355.
15 Lowe AD, Campbell KL and Graves T. **Glucocorticoids in the cat**. *Vet Dermatol* 2008; 19: 340–347.
16 Mooney CT, Thoday KL and Doxey DL. **Carbimazole therapy of feline hyperthyroidism**. *J Small Anim Pract* 1992; 33: 228–235.