

Letter regarding “A novel bone marrow-sparing treatment for primary erythrocytosis in a cat: Onion powder”

Food for thought instead of onion powder as a treatment for erythrocytosis in cats

Dear Editors,

The precise diagnosis of erythrocytosis/polycythemia can be challenging, and its management depends on the specific cause and severity.¹⁻⁵ In a recent case report by Vasilatis et al in *Journal of Veterinary Internal Medicine*,⁶ a cat with erythrocytosis, claimed to have polycythemia vera (PV), was treated with dietary onion powder, as an oxidative hemolytic agent, for 15 months. The authors' reasoning was that it was a difficult patient to phlebotomize, and chemotherapy was not an option. We would like to comment regarding this case and the presumed effectiveness and safety of onion powder, and to express our sincere concern and caution toward recommending an oxidative hemolytic agent as treatment of any erythrocytosis.

Polycythemia vera is a now well-defined myeloproliferative disease in humans,⁵ but has never conclusively been diagnosed in cats; no acquired *JAK2* mutations have been reported in cats.^{3,4} It should be noted that cytologic and histologic examination of bone marrow is not helpful to differentiate polycythemias; all exhibit erythroid hyperplasia. One of us has had several cats with chronic persistent (up to 10 years) or transient (un-)explained erythrocytosis, and found some to have secondary causes.¹⁻³ However, we have never definitely diagnosed PV in cats, and have never seen any domestic animal with erythrocytosis develop thrombocytosis, myelofibrosis, or leukemic blast crisis as typically seen in human patients with PV.

Regarding this case report,⁶ no prior CBC results were available, leaving the actual onset of erythrocytosis unknown, and clinicopathological information provided was sparse. Renal changes were noted on initial presentation, which were dismissed, but may be responsible for excessive erythropoietin production and secondary erythrocytosis (no renal follow-up was reported). It also appears the massive erythrocytosis in the cat⁶ resolved within 5 to 15 months, suggesting a secondary cause rather than the presumed PV, which is generally persistent and progressive. Moreover, the reticulocyte count of the cat was never increased,⁶ indicating normal rather than increased erythroid production. While no obvious dehydration was observed, total protein concentrations and urinalyses were not reported, and thus a relative erythrocytosis may not have been excluded.

Hematocrits >48% are abnormal in any cat and not just >65% as stated in the report's introduction.^{4,5} This is one of the reasons

erythrocytosis is frequently overlooked in cats until late in the course of disease.¹⁻³ One phlebotomy followed by immediate hospital discharge and a scheduled reexamination only after 2 weeks for a seizing cat with a hematocrit (HCT) of 73% on presentation, as reported in this case,⁶ may be considered clinically insufficient. Frequent daily phlebotomies and supportive care are typically required early on to reduce very high HCTs to near-normal ranges and alleviate the neurologic complications.¹⁻⁴

For any cat with symptomatic or severe erythrocytosis, regular phlebotomies with sedation and skilled assistance every 2 weeks to 2 months are well tolerated similar to any blood collection from healthy feline blood donors.¹⁻⁴ Repeated phlebotomies frequently control erythrocytosis, work immediately, are generally safe, and require only PCV and total protein concentration for monitoring (no adverse drug-induced cytopenias or, as in this case,⁶ feared excessive intravascular hemolysis and oxidative tissue damage). Phlebotomy is desirable to reduce the HCT and resolve clinical signs before considering and initiating any other treatment. Periodic phlebotomies eventually induce iron deficiency (potentially associated with microcytosis and reactive thrombocytosis), slow the regenerative erythroid response, and thereby prolong the necessary phlebotomy interval to control the HCT. We have not had much luck with medicinal leeches in cats, but blaming leeches for causing seizures, as stated in their case report,⁶ is far-fetched.

Onions (*Allium cepa*), the second most frequently consumed vegetable by humans worldwide, have been recognized since ancient times for medicinal properties, for example, against cancer and thrombosis, but have never before been proposed as a treatment for PV or for that matter any other diseases. In fact, onions, besides causing teary eyes when chopped, also contain toxic compounds such as allyl and propyl sulfides, which cause hemolysis and oxidative tissue damage in susceptible animals.^{7,8} Cats are particularly prone to toxicity characterized by Heinz body anemia, because of their unique hemoglobin structure and limited drug metabolism, but cats fortunately do not fancy eating onions.

Absolutely no increase in Heinz bodies while supplemented with onion powder was documented in the cat of their report,⁶ and only rare (<1%) Heinz bodies were observed throughout the entire 15-month period. This is inconsistent with the claim that oxidative hemolysis was induced by onion powder. The authors of the case report⁶ were dosing

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onion powder at the lowest dose the owner could dispense with food (which sounds archaic compared to the practice of compounding) and estimated that 1.2% dietary onion powder was administered, although the actual amount may have been lower. Experimentally, as little as 0.3% onion powder caused 5% Heinz bodies, and 1.5% to 2.5% onion powder caused 25% to 35% Heinz bodies.⁸ Because onion powder causes a strong linear, dose-dependent Heinz body response, 1.2% onion powder would have been expected to cause approximately 15% Heinz bodies within 2 weeks. Without an increase in Heinz bodies, there is no evidence to support any effect of the onion powder on erythrocytes. Furthermore, no reticulocytosis, hyperbilirubinemia, and other evidence of hemolysis was observed at any time point, despite a nearly 20% decrease in HCT within 10 days of treatment. The authors of the case report⁶ suggest there was intravascular hemolysis, but dietary onion-containing supplements produce a slower oxidative process causing Heinz body anemia primarily by erythrophagocytosis rather than intravascular hemolysis, which, if sufficient to reduce the HCT, would be expected to cause visibly hemolyzed plasma, increased mean cell hemoglobin and mean cell hemoglobin concentration, hemoglobinuria, and reticulocytosis. Thus, the dose of onion administered was (luckily) likely too small to cause hemolysis. Since the HCT normalized, it is likely the onion supplementation could have been stopped. Additional follow-up evaluation after ceasing onion powder supplementation might have been revealing.

It should be noted that high doses of onions, whether given experimentally or inadvertently, can cause acute intravascular hemolysis in susceptible animals, but fortunately, cats appear resistant to hemoglobin-induced nephropathies. Oxidative cell damage beyond the well-defined hemolytic effects of onions is more difficult to assess, but could be harmful due to cats' limited metabolism and when exposed long term, as proposed in this case report.⁶

"Dark pink" mucous membranes are hard to visualize but may indicate methemoglobinemia, which was not measured in this case as a cause. While ingestion of onion powder by cats has been associated with only a slight increase in methemoglobin concentration (<1%),⁸ hereditary (congenital) methemoglobinemia, typically caused by methemoglobin cytochrome b₅ reductase deficiency, has been frequently overlooked in companion animals. In contrast, cherry red mucous membranes may indicate carbon monoxide intoxication and occasionally can be chronic.

In conclusion, besides PV, other primary or secondary causes may have led to erythrocytosis in the cat of their report.⁶ While onions can cause hemolysis with Heinz bodies, they were not observed in this case.⁶ Thus, the onion dose administered was likely too low, and the cat recovered on its own. While onions are an integral part of the diets of humans, they can be toxic to companion animals and livestock and are not a treatment. We hope we provided some food for thought to not recommend and not to use onion supplementation as treatment for PV, for erythrocytosis of any cause, or frankly, for any illness in any species.

Urs Giger^{1,2}

Mary M. Christopher³

¹School of Veterinary Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA

²Vetsuisse Faculty, University of Zürich, Zürich, Switzerland

³School of Veterinary Medicine, University of California, Davis, Davis, California, USA

REFERENCES

1. Hasler A, Giger U. Polycythemia. In: Ettinger SJ, Feldman EC, eds. *Textbook of Veterinary Internal Medicine: Diseases of the Dog and Cat*. 5th ed. Philadelphia, PA: WB Saunders; 2000:203-206.
2. Giger U. Polycythemia. How I diagnose and treat polycythemia. 42nd World Small Animal Veterinary (WSAVA) Congress, 25-28 September, 2017, Copenhagen, Denmark.
3. Hasler AH, Giger U. Serum erythropoietin values in polycythemic cats. *J Am Anim Hosp Assoc*. 1996;32:294-301. doi:10.5326/15473317-32-4-294
4. Darcy H, Simpson K, Gajanayake I, et al. Feline primary erythrocytosis: a multicentre case series of 18 cats. *J Feline Med Surg*. 2018;20:1192-1198. doi:10.1177/1098612X17750333
5. Spivak JL. Polycythemia vera. *Curr Treat Options Oncol*. 2018;19(2):12. doi:10.1007/s11864-018-0529-x
6. Vasilatis DM, McGill JE, Gilor C. A novel bone marrow-sparing treatment for primary erythrocytosis in a cat. *J Vet Intern Med*. 2021;35:1977-1980. doi:10.1111/jvim.16194
7. Yamato O, Kasai E, Katsura T, et al. Induction of onion-induced haemolytic anaemia in dogs with sodium n-propylthiosulphate. *Vet Rec*. 1998;142:216-219. doi:10.1136/vr.142.9.216
8. Robertson JE, Christopher MM, Rogers QR. Heinz body formation in cats fed baby food containing onion powder. *J Am Vet Med Assoc*. 1998;212:1260-1266.