# LEEK DIET MAY CAUSE HEMOLYTIC ANEMIA: A CASE REPORT IN A CAT

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## Signalement

A 7 year-old neutered female domestic shorthair cat.

## Clinical History

The cat was presented because of the ingestion of a bone. No abnormalities were noted at clinical examination, and an abdominal radiography showed the presence of a bone in the stomach. A medical treatment composed of a leek-based high fiber diet and non steroidal anti-inflammatory drugs was decided to try naturally eliminating the bone. At the following presentation, eight days later, no abnormality in the behaviour of the cat was reported by the owners.

## Clinical findings

At the second clinical presentation, the cat was bright, alert and did not present abdominal pain. The only significant clinical findings were pale mucous membranes and a slight hepatomegaly.

## Diagnostic procedures

Abdominal radiography and ultrasound suggested that the bone had been eliminated. A moderate diffuse hepatomegaly was observed. Complete blood cell count, blood film, biochemical, hemostatic and urine analyses were also performed. Results are in tables 1, 2 and 3.

Hematology results obtained with the analyzer Sysmex XT-2000iV® showed a marked macrocytic, slightly hypochromic, and highly regenerative anaemia, a moderate neutrophilia and a slight thrombocytopenia. Strongly abnormal dot plots were observed for differential white blood cell, reticulocyte and platelet dot plots (Figure 1). The main modification was observed on the PLT-O scattergrams : a new subpopulation is localized just below the red blood cell dot plot and above the platelet dot plot. On the examination of the blood smears, several signs of regenerative anemia have been seen: marked anisocytosis, moderate polychromasia, some basophilic stippling and Howell-Jolly bodies. But the most significant abnormalities on the blood smear were the presence of numerous Heinz bodies in almost all red blood cells, many free Heinz bodies at the edge of the blood smear, many ghost red blood cells, and rare blister cells (Figures 2 & 3). The abnormalities of white blood

cell morphology were the presence of some reactive monocytes, rare macrophages, and few band cells and toxic neutrophils. Moreover, numerous huge platelets clumps were seen; so the moderate thrombocytopenia was completely invalidated. A new methylene blue staining has been performed to assess the manual reticulocyte count and objectivate the Heinz bodies. The manual reticulocytes count was 2,3%, and was also lower than the automatic reticulocyte count (6,5%) obtained with the Sysmex XT-2000iV®.

Plasma biochemistry and urine analysis findings included a severe hemoglobinuria and hemoglobinemia, and a moderate increase of total bilirubin and ALAT.

*Mycoplasma haemofelis* and *Candidatus Mycoplasma haemominutum* as infectious causes for hemolytic anemia. were excluded by a negative PCR.

All these clinico-pathological findings permit to make a diagnosis of a hemolytic anemia, and the examination of the blood smear was highly suggestive of an intravascular hemolytic anemia secondary to a severe oxidative injury with formation of Heinz bodies.

**Treatment and following:**

The cat was hospitalized for five days in order to treat her and follow the clinical evolution. A palliative and supportive treatment was applied based on perfusion of NaCl 0,9 % and antioxydant drugs.

A monitoring of the hematocrit was performed during the hospitalization. It remained between 0,15 and 0,18 L/L. The cat was released 5 days after the diagnosis of the hemolytic anemia. The antioxidant treatment based on the oral administration of S-adenosyl methionine was continued for three weeks. Finally, fifteen days later, the anemia and hemoglobinuria had disappeared; the cat seemed to be cured.

**Interpretation**:

An intravascular hemolytic anemia induced by a severe oxidative injury due to a chronic ingestion of leek was highly suspected.

**Discussion & conclusion**:

Leek (*Allium porrum*) is a plant of the same family and order as onion (*Allium cepa*) and garlic (*Allium sativum*), *i.e.* Alliacaea family and Allium order. Onion and less frequently garlic are known to induce an oxidative injury in domestic animals, notably in dogs and cats, sometimes causing a hemolytic anemia [1][2][3][4][5][6][7]. In dog and cat, no case of hemolytic anemia associated with oxidative injury secondary to leek ingestion had to our knowledge been yet described. It would be logical to think that all these plants (onion, garlic and leek) should have some similar compounds which may be responsible for oxidative injury and hemolytic anemia. These toxic compounds have been particularly studied in onion because of the frequency of such poisoning in domestic animals, especially in dogs. In fact, the cat is not known to like eating food with onions or garlic, except for baby-food which can contain onion powder and is sometimes proposed to ill cats by their owners [4][5]. In onions, the toxic compounds are not completely elucidated. However, it has been demonstrated that several organosulfide compounds responsible for an oxidative injury are present, such as n-propyldisulfide, sodium n-propylthiosulfate and probably other ones [8][9][10].

In our case, we cannot know the exact dose of leek consumed by the cat. We just know that there has been a chronic ingestion for eight days. The formation of Heinz bodies has been described in several diseases (diabetes mellitus, hyperthyroidism and lymphoma…) or in case of administration of drugs and exogenous molecules in cats (acetaminophen, propofol, propylene glycol, methylene blue, benzocaine or onion). We have highly suspected that it was a case of leek poisoning which had induced the severe noticed oxidative injury by exclusion of previously mentioned causes and because hemolysis has stopped after withdraw of leek administration [11].

The Heinz body is the result of clumping of denatured hemoglobin on the inner surface of the red blood cells [11]. The physio-pathological mechanism of the common formation of Heinz bodies in cat is based on the high sensitivity of feline hemoglobin to oxidant compounds because of the presence of eight cysteine sulfhydryl groups (only four in the dog) and the capacity of this one to dissociate from tetramer to dimer form more readily than in other species. The oxidation of the hemoglobin can result in Heinz body and methemoglobin formation [10]. However, hemolytic anemia is not always induced in such situation since the cat with its non-sinusoidal spleen is inefficient to eliminate the damaged red blood cells containing Heinz bodies [10]. An intravascular hemolysis occur in case of highly fragile RBC population secondary to dramatic damages on RBC membranes induced by numerous or large Heinz bodies [10].

In this clinical report, the clinical signs of the cat were similar to those described in previously published cases of onion poisoning in cats: no severe clinical signs since the cat was bright; only pale mucous membrane and hemoglobinuria were noticed at the clinical examination. The clinical signs previously described with onion poisoning were less intense in cats than in dogs, except in case of a

high dose or chronic ingestion of onion with lethargia and were weakness, pale mucous membrane, icterus, tachycardia, heart murmur, polypnea, and sometimes digestive signs [1][4][6].

The clinicopathologic findings described in our case are partially in agreement with those described in the case of onion poisoning; the hemolysis seemed to be more severe than in classical onion poisoning, since marked hemoglobinuria and hemoglobinemia were noticed. The formation of many Heinz bodies was the main significant abnormality, associated with signs of a regenerative anemia compatible with a hemolytic anemia. Heinz body formation was shown to be dose dependent in an experimental study of onion poisoning by ingestion of baby food containing onion powder [5]. This formation started within the first hours after the ingestion of onion with an immediate decrease of HCT followed by an increase in the reticulocyte count [2][4][5][6]. The anemia is not always observed in onion poisoning, except when the ingestion is chronic or massive [6]. Unfortunately, the kinetic of the anemia and reticulocyte count was not investigated in our case. Finally, eccentrocytes have been described in garlic and less frequently in onion poisoning in dogs, but these abnormal erythrocytes were not significantly observed in our case [3][7].

One of the key modifications noticed in the hematological variables in our case were abnormal dot plots given by the Sysmex XT-2000iV analyzer, and especially for the dot plot of the red blood cells and platelets. On the PLT-O scattergrams, a new subpopulation was observed, which is localized just below the red blood cells dot plot and above the platelet dot plot. The platelet count has also been distorted, but unfortunately we could not estimate the error because many huge platelet clumps were detected on the blood smear. A discrepancy in platelet count has been previously linked to the presence of many ghost cells in the case of an IMHA; the ghost cells seemed to be at the top of the platelet but included in the dot plot [12]. In our case, there were many ghost cells and especially a large number of Heinz bodies sometimes free (Figure 3). The atypical population observed on our scattergram was different from the previously described cases and could represent the free Heinz bodies according to their intermediate size observed on the blood smear. In human medicine, some fragmented RBC, like micro-spherocytosis in the case of acute burn, Heinz bodies and ghost cells was also described to disturb the platelet count measured by impedance counter and less intensively by cytometers. Moreover, spurious counts of reticulocytes has been also described in presence of Heinz bodies in human medicine [14]. In our case, we have also observed a discrepancy between manual and automatic reticulocyte counts with respectively 2.3 % and 6.5 % of reticulocytes which have been attributed to the poor separation between RBC and reticulocyte dot plots and probably the modified damaged RBC [13]. Heinz body have been reported to cause an abnormal RBC dot plot with a Technicon H-1® (Bayer) in a case of onion poisoning with baby food in a cat [4]. A hyperchromatic subpopulation of red blood cell associated with an abnormal high MCHC has been seen. This abnormality was explained by the increase of the refractive index of the red blood cells due to the presence of Heinz bodies in these cells and in suspension. In this same case report, there was an

abnormal basophil cytogram, which displayed a population of cells which seemed to be smaller particles than leukocytes and present in a large number: these particles had been highly suspected to be the many Heinz bodies [4]. A similar observation was done on the WBC/BASO and on the DIFF dot plots (Figure 1) with an abnormal down shift of the dot plots. This was highly suspected to be related to Heinz bodies and ghost cells.

As a conclusion, practitioners should be aware of the possible toxicity of leek before prescription of a high fiber diet based on leek to facilitate the elimination of foreign bodies. Leek ingestion should not be recommended especially in ill cats, at least if their disease is classically related with an oxidative injury.

**Table 1: Hematology results obtained with the Sysmex XT-2000iV® (Sysmex)**

| Analytes | Data | Reference Interval |
|---|---|---|
| HGB (g/dL) | 5.7 | 8.0-14.9 |
| RBC (.$10^{12}$/L) | 3.4 | 5.5-10 |
| HCT (L/L) | 0.18 | 24-45 |
| MCV (fL) | 52.1 | 40-55 |
| MCH (pg) | 16.8 | 13-17 |
| MCHC (g/dL) | 32.2 | 30-36 |
| PLT (.$10^{9}$/L) | 285 | 300-800 |
| WBC (.$10^{9}$/L) | 22.31 | 5.5-19.5 |
| Neutrophils (.$10^{9}$/L) | 19.6 | 2.5-12.5 |
| Lymphocytes (.$10^{9}$/L) | 1.56 | 1.5-7.0 |
| Monocytes (.$10^{9}$/L) | 0.67 | 0.0-0.85 |
| Eosinophils (.$10^{9}$/L) | 0.22 | < 1.5 |
| Reticulocytes (/L) | 209 100 | < 110 000 |
| PCR analysis (*Mycoplasma haemofelis* and *Candidatus Mycoplasma haemominutum*) | Negative | Negative |

**Figure 1: Sysmex XT 2000iV cytograms from the blood sample of the cat**

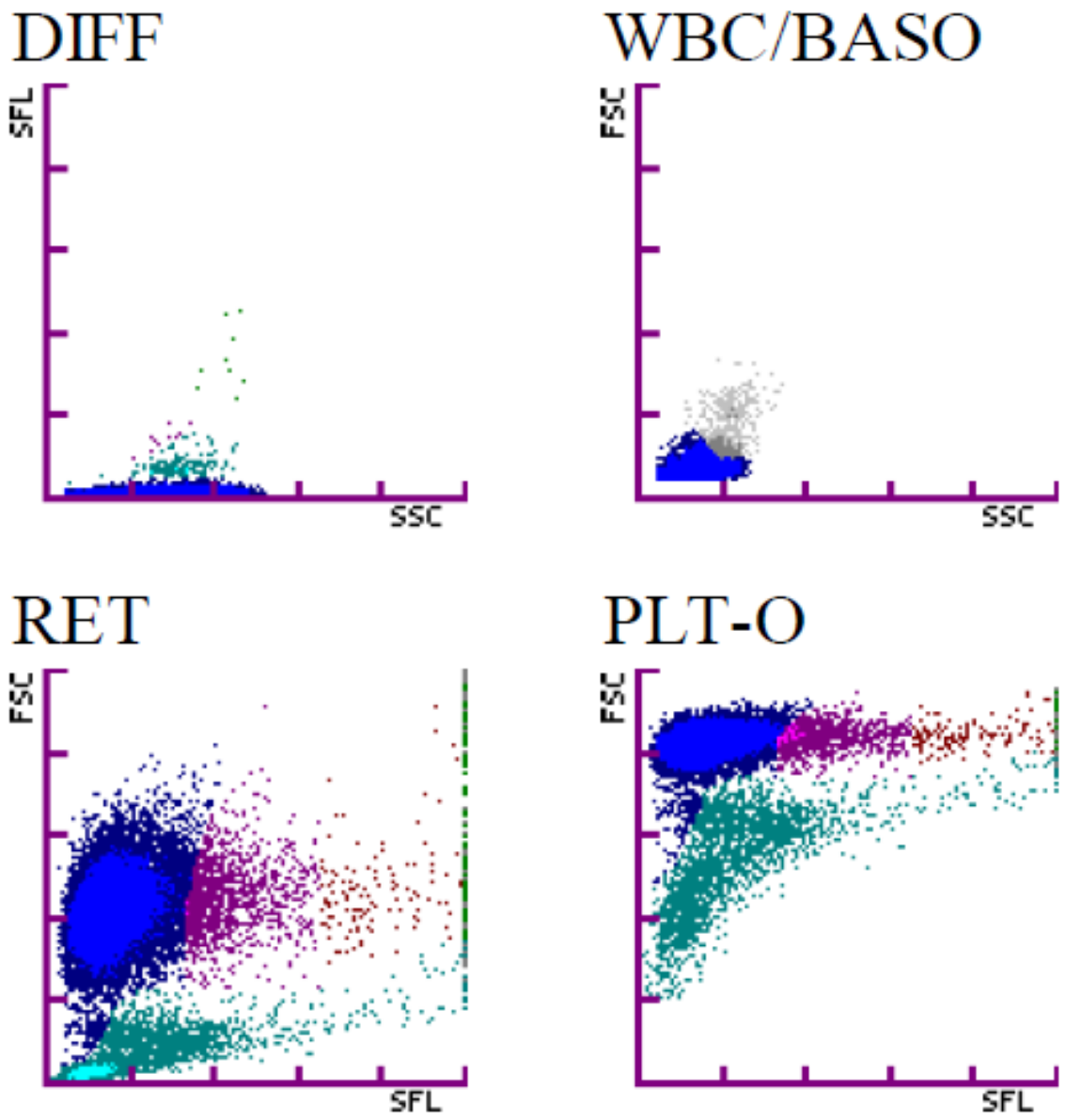

**Figure 2: Picture of the blood smear edge (x 1000, oil, modified May-Grünwald Giemsa stain). Black arrow: Heinz Bodies; white arrow: pycnocytes or free Heinz bodies**

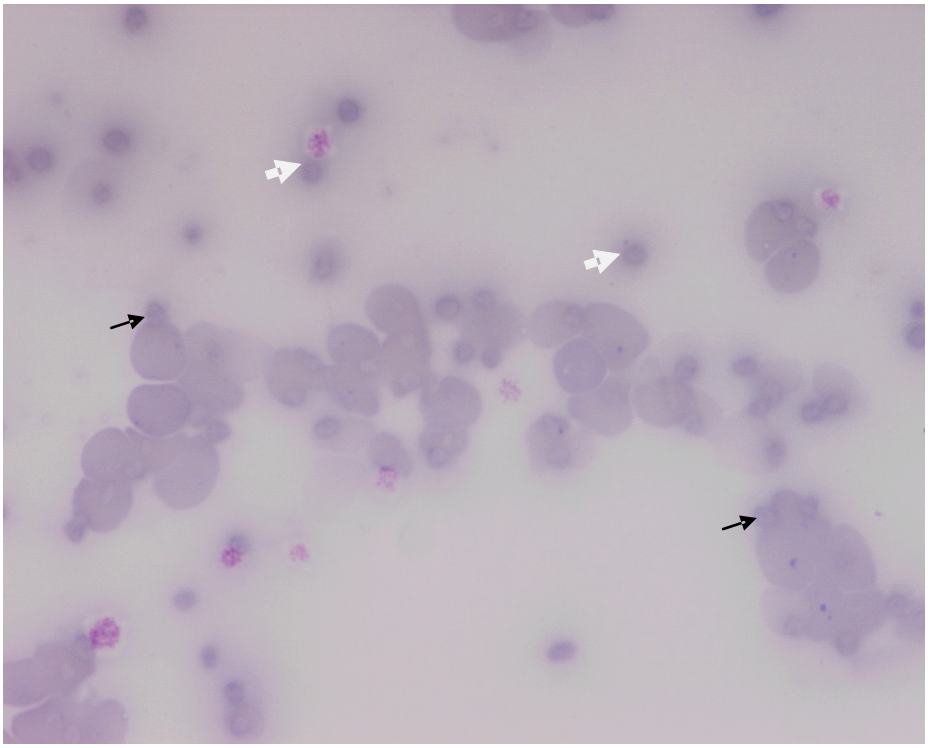

**Figure 3: Picture of the blood smear (x 1000, oil, modified May-Grünwald Giemsa stain). Red arrow: blister cell; black arrow: Heinz Bodies**

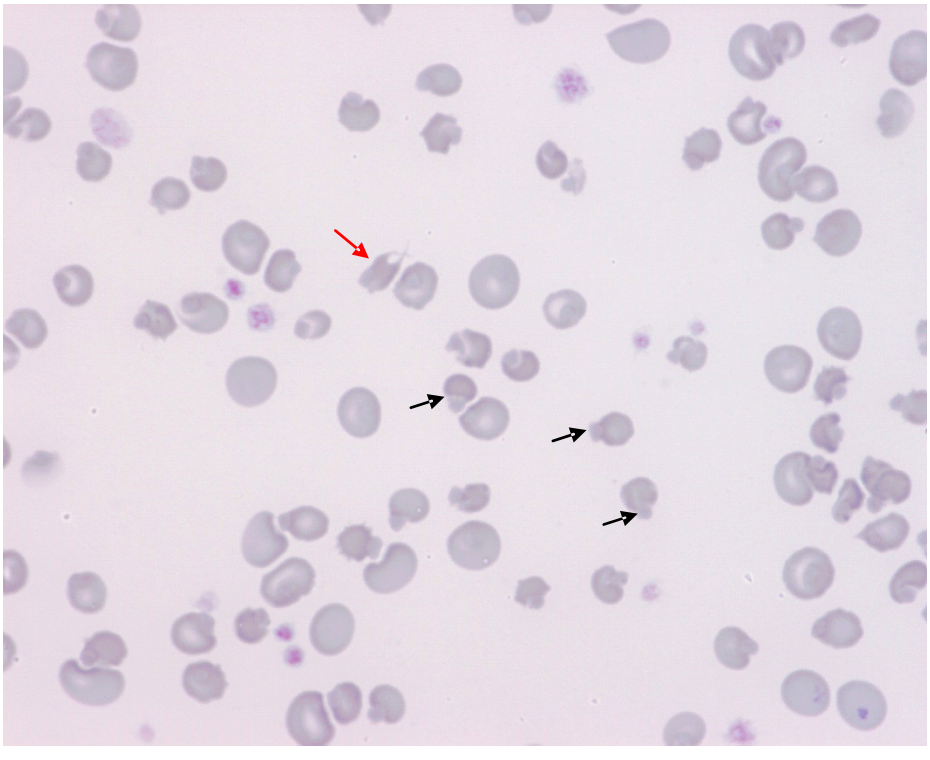

**Table 2: Urine analysis results**

| Analytes | Data | Reference Interval |
|---|---|---|
| Source | cystocentesis | - |
| Color | Dark red | Clear yellow |
| DU | 1.025 | 1.030-1.060 |
| Sediment | Neg | < 5 cells / 40 PF |
| Dipstick | Unreadable | - |

**Table 3: Biochemistry results on plasma obtained with VetTest® (Idexx Laboratories)**

| Analytes | Data | Reference Interval |
|---|---|---|
| Color of the plasma | Red | Clear |
| Creatinine (µmol/L) | 56 | 27-186 |
| ALT (U/L) | 146 | 20-100 |
| PAL (U/L) | 21 | 10-90 |
| Total Bilirubin (µmol/L) | 13.0 | 1.7-9.9 |
| Total Protein (g/L) | 75 | 50-82 |
| Albumin (g/L) | 30 | 22-44 |

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