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Case Report - Veterinary Medicine

Anticoagulant rodenticide poisoning in calves – case report

[*Intoxicação por rodenticida anticoagulante em bezerros – relato de caso*]

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ABSTRACT

The aim was to report two cases of accidental Brodifacum poisoning in calves on a dairy farm. The animals presented a variable clinical picture of bleeding disorders with melena, epistaxis, orthopneic position, severe dyspnea, productive cough, coarse lung crackles, and expiratory groans. The male died, the female was euthanized, and both were sent for necropsy. The anatomopathological findings revealed a predominantly bleeding diathesis in the animals. During the investigation, blood serum, liver and kidney samples were collected for toxicologic measurement, which revealed concentrations of coumarin derivatives < 0.100µg/kg in all samples. The combination of history, clinical-pathologic findings, and toxicologic results confirmed the diagnosis.

Keywords: rodenticides, poisoning, brodifacum, coagulopathies, ruminants

RESUMO

Objetivou-se relatar dois casos de intoxicação acidental por Brodifacum, em bezerros de uma fazenda de leite. Os animais apresentavam um quadro clínico variável de distúrbios hemorrágicos com melena, epistaxe, posição ortopneica, dispneia intensa, tosse produtiva, crepitação pulmonar grossa e gemidos expiratórios. O macho morreu, a fêmea foi submetida à eutanásia, e ambos foram encaminhados para exame necroscópico. Os achados anatomopatológicos revelaram, principalmente, um quadro de diátese hemorrágica nos animais. Durante o exame, foram coletadas amostras de soro sanguíneo, fígado e rins, para realização de dosagem toxicológica, obtendo-se como resultado concentrações de derivados de cumarina de <0,100µg/kg em todas as amostras. Ao se associarem o histórico, os achados clinicopatológicos e o exame toxicológico, pode-se confirmar o diagnóstico.

Palavras-chave: raticidas, envenenamento, Brodifacum, coagulopatias, ruminantes

INTRODUCTION

Rodenticides are household pest control products used to manage rodents and can be classified as anticoagulants, monofluoroacetic acid, strychnine, thallium sulfate, alphanaphthyl thiourea, and bromethalin. Approximately 95% of all rodenticides used are anticoagulant baits, and only rodenticides derived from indandione and coumarin are permitted in Brazil (Spinosa *et al*., 2008).

Anticoagulants cause severe damage to vascular permeability, resulting in massive bleeding. They work by specifically inhibiting blood coagulation because they are competitive vitamin K antagonists, which are slowly absorbed from the gastrointestinal tract and metabolised in the liver. The synthesis of clotting factors is impaired by binding to vitamin K epoxide, preventing regeneration and acting as an indispensable cofactor, with insufficient amounts for the conversion of prothrombin to thrombin, inhibiting the coagulation of the animal's blood (Yip *et al*., 2020).

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Reports of accidental poisoning by rodenticides are frequent in non-target species such as dogs and cats but have also been reported in production animals such as horses and pigs, mainly due to the increased use of these products in domestic environments (Jubb *et al*., 2016). However, reports of poisoning by rodenticides in domestic (Oliveira *et al*., 2019) and wild ruminants (Stone *et al*., 1999) are rare. Therefore, the aim is to report the clinical and pathological findings of accidental poisoning caused by the ingestion of anticoagulant rodenticides in crossbred calves.

CASUISTRY

Two mixed-breed calves were semi-intensively reared in a newly structured calf yard with only three animals of different ages, and the newborns were fed milk twice a day after being hand-milked. The history reported that a 15-day-old heifer had nosebleeds and a 10-day-old male had blackish diarrhea. In addition, the third, slightly older animal had no clinical signs.

The calves were taken to the Veterinary Hospital of the Center of Agricultural Sciences and Engineering of the Federal University of Espírito Santo. On clinical examination, they were bright, with an appetite for milk, tachycardia, tachypnea, hyperthermia, pale eye and vaginal mucous membranes and a body condition score of III (I to V). Both animals showed general bleeding disorders, with the male having melena (Fig.1A) and unilateral epistaxis, while the female had profuse hemoptysis (Fig.1B) and a pulmonary picture of respiratory distress with orthopneic position, severe dyspnea, productive cough, thick bilateral lung crackles and expiratory grunts.

Figure 1. Calves poisoned by rodenticides. A) Blackish diarrheal feces with foul odor characteristic of melena in the male. B) Intense hemoptysis in the female.

Despite attempts of treatment, the male died in less than 24 hours, while the female was euthanized within hours of signs onset due to her deteriorating clinical condition and poor prognosis. Following the deaths, packages of brodifacoum-based rodenticide were found in other areas of the farm.

The animals were necropsied. Anatomopathological findings included coagulopathies and bleeding diathesis with moderate to intense pallor of the mucous membranes and serosa. Various degrees of hemorrhages, from multifocal to coalescent, were observed in the external mucous membranes and skeletal muscles, as well as in the internal organs.

In the cardiorespiratory system, the varying degrees of hemorrhage resulted in moderate epistaxis in the male and intense epistaxis in the female, as well as multifocal hemorrhages in the nasal turbinates. In addition to moderate hemorrhage (Fig.3A), the lungs showed diffuse congestion with multifocal atelectasis in the male and intense pallor in the female (Fig.2C), related to the blood observed in the tracheal region. In the heart, multifocal hemorrhagic lesions of varying intensity were found in the epicardium (Fig.3C), endocardium, myocardium, and at the base of the thoracic (Fig.2A), pulmonary (Fig.2B), and mesenteric arteries, as well as in the right atrioventricular valve.

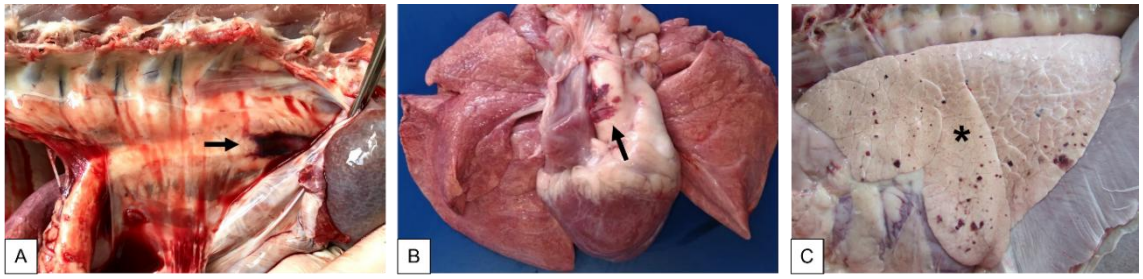

Figure 2. Macroscopic findings in rodenticide-poisoned calves. A) Photomacrograph showing intense focal hemorrhage at the base of the thoracic artery (black arrow) in the male. B) Photomacrograph showing intense focal hemorrhage at the base of the pulmonary artery (black arrow) in a female. C) Photomacrograph showing intense pulmonary pallor (*) in the female.

The liver showed both areas of hemorrhage and pallor, as well as depressed and friable areas in the medial lobe and multifocal and yellowish areas with capsular hemorrhage in the male and female, respectively. The gallbladder was distended with multifocal hemorrhages in the mucosa. The spleen of the calf showed diffuse white pulp hyperplasia, hemorrhage and hemosiderosis, while that of the female was reduced and moderately pale.

In the animals´ intestine, hemorrhages were observed at the level of the small intestine. In the ileum, hemorrhages ranged from mild to severe (Fig. 3B) with moderate mucoid content. In the colon, in addition to hemorrhage, changes in the content were seen that represented melena and hematochezia. The urinary system of the animals showed multifocal hemorrhages in the kidneys. The male showed moderate renal congestion and focal hemorrhages in the serosa of the urethral vesicle and trigone region. In the female, only moderate multifocal petechial hemorrhages were observed in the cords of the urinary bladder.

In the central and peripheral nervous system, varying degrees of hemorrhage were observed in the leptomeninges, Glasser's ganglion, and cerebellum (Fig. 3D). During necropsy, tissue fragments were collected, fixed in 10% buffered formalin, and processed by routine paraffin-embedding followed by hematoxylin-eosin (HE) staining.

Blood serum, liver, and kidney samples were also collected and previously stored in an ultra-freezer (IULT 335 D, *Indrel indústria de Refrigeração Londrinense* LTDA, Brazil) at -80°C to be sent to the analytical control laboratory for toxicological dosing using the high-performance liquid chromatography (HPLC) method. The result was concentrations of coumarin derivatives < 0.100 µg/kg in all samples.

DISCUSSION

Anticoagulant rodenticide poisoning in production animals, such as calves, is uncommon and has been described in wild ruminants (Stone *et al*., 1999). In contrast to rodenticide ingestion in calves, poisoning by coumarin derivatives has been reported in adult cattle (Oliveira *et al*., 2019), but only spontaneously through the ingestion of toxic plants containing this chemical compound. The action of fungi converts the coumarin derivatives present in plants such as *Anthoxanthum odoratum*, *Melilotus alba*, *M. altissima*, *M. indica*, *M. officinalis* into toxic coumarin (Runciman *et al*., 2002).

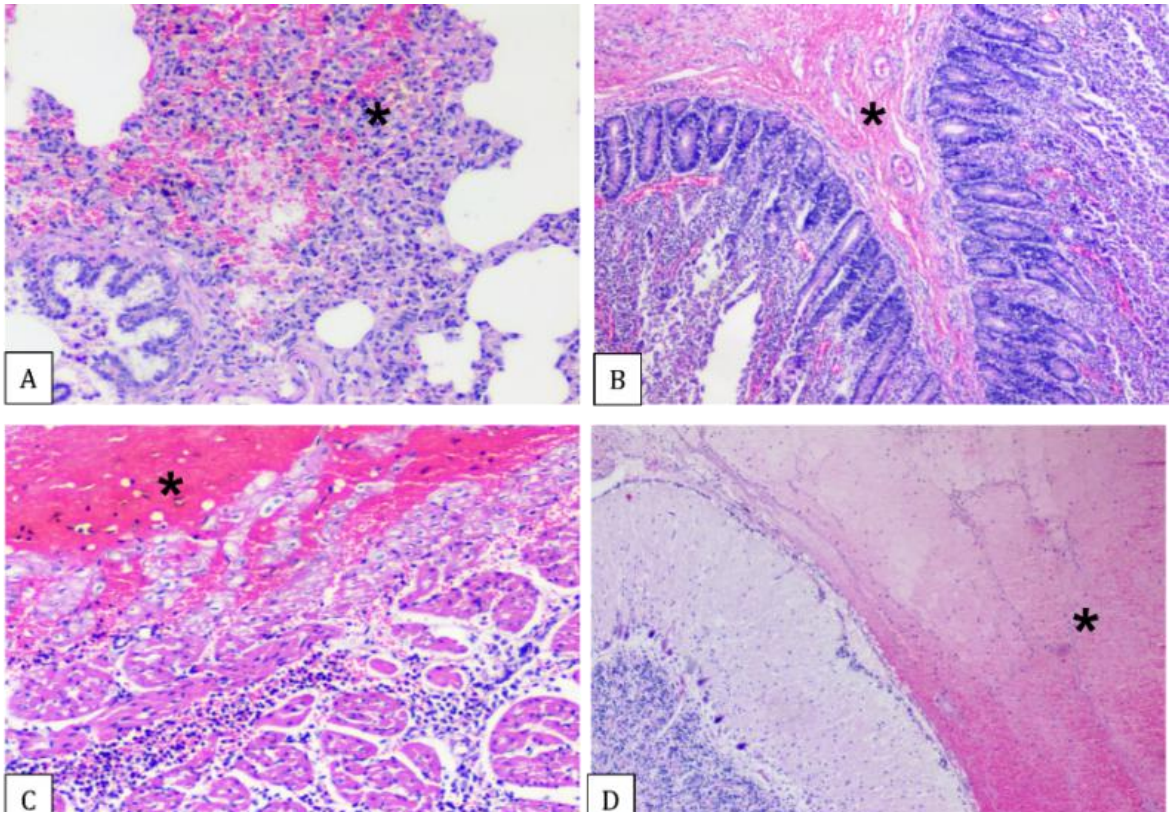

Figure 3. Microscopic findings in rodenticide-poisoned calves. A) Female lung with moderate multifocal hemorrhage (*). [B) Male small intestine with discrete extensive focal hemorrhages (*) in the submucosa and muscle. [C) Female heart with moderate multifocal hemorrhages (*) mainly in the epicardium. [HE; Obj.10x] D) Male cerebellum with intense multifocal to coalescent hemorrhages (*) mainly in the meninges.

Many clinical cases of bleeding disease have been reported in cattle exposed to dicumarol in moldy sweet clover (*M. alba*) (Runciman *et al*., 2002). However, these signs usually develop after weeks of repeated exposure. However, this prolonged exposure does not occur with rodenticides because they are more active compounds, and accidental exposure is generally short term, with the potentially toxic and clinically relevant dose (LD50) of dicumarol being 541 mg/kg body weight, whereas the LD50 of warfarin is 58 mg/kg body weight (Berny *et al*., 2006).

Newborns are more susceptible to intoxications such as the one described in this report due to their curiosity (Pedroso *et al*., 2009), low vitamin K reserves (Jubb *et al*., 2016), lack of odor and pleasant taste due to the sucrose content (Valchev *et al*., 2008), and in the case of ruminants, their nonfunctional rumen (Spinosa *et al*., 2008). The intoxication found in calves was also described as suspicious by Berny *et al*. (2006) and observed in piglets (Amaral *et al*., 2015).

Experimental diphenadione poisoning in neonatal and adult cattle showed that younger animals that still not have a functional rumen were more likely than adults to develop clinical signs of anticoagulant poisoning due to the non-destruction of anticoagulant compounds in the rumen, which would explain the lack of signs in other animals in the herd and in the other young but older animal in the calf yard (Spinosa *et al*., 2008).

The clinical changes of a hemorrhagic nature found in the rodenticide-poisoned calves in this report are due to the accumulation of blood in the cavities through the passage of mucous membranes and are consistent with cases found

in the literature in horses (Mcconnico *et al*., 1997) and pigs (Amaral *et al*., 2015).

The severity of spontaneous hemorrhage, characterized by epistaxis, melena, and hematuria, depends on the toxicity, amount, and type of compound ingested, as well as the animal's body condition and vitamin K bioactivity (Jubb *et al*., 2016). The onset of clinical signs after ingestion may take several days or be acute, or the animal may die suddenly without prior signs. If the bleeding is severe, anemia and weakness may develop, as well as dyspnea due to hypovolemia and hemothorax (Brito *et al*., 2005).

The macroscopic and microscopic findings observed in the animals associated with the hemorrhagic diathesis were similar to those described by Amaral *et al*. (2015) in piglets intoxicated with coumarin derivatives, as well as the signs found by Brito *et al*. (2005) in an outbreak of intoxication in adult cattle in confinement. The anatomopathological findings showed changes typical of intoxication by anticoagulant rodenticides, and the cause of death was cardiorespiratory collapse due to the numerous hemorrhages found in vital organs such as the CNS, heart, and respiratory system as a result of vasodilation with a drop in blood pressure and consequent cardiac tamponade (Jubb *et al*., 2016).

Anticoagulant rodenticides are often used in livestock facilities to control rodents attracted to grain and feed piles. Usually, the toxic principle responsible for poisoning is brodifacoum, due to its greater toxicity and its presence in the composition of the vast majority of rodenticides (Valchev *et al*., 2008). Therefore, due to the packaging of rodenticides (Rigon GS®, brodifacoum 0.005%, Rogama, Brazil) in pellets found elsewhere on the farm, it is believed that the application of rodenticides in the environment without proper technical knowledge caused the animals to be exposed to the principle (Spinosa *et al*., 2008).

The presence of coumarin derivatives in liver, kidney and blood serum (<0.100 µg/kg) observed in this report has also been found in adult cattle, in serum (Runciman *et al*., 2002), in rumen, reticulum, omasum, and abomasum contents, liver and kidney (Brito *et al*., 2005), and in pigs, in stomach contents, liver and kidney (Amaral *et al*., 2015). However, the concentration of coumarin found in tissues is often not described in the literature, as usually only traces are found, which can be explained by the fact that insufficient quantities are sent and qualitative rather than quantitative dosages are carried out (Brito *et al*., 2005). In horses, clinical reports of brodifacoum intoxicated animals have reached plasma concentrations of 0.05 to 0.18µg/mL (Mcconnico *et al*., 1997), which are within the linear range of the analytical method used in this study.

It is imperative to conduct a differential diagnosis with other clinical entities that can cause hemorrhagic conditions in ruminants, such as lacerations of major vessels, abomasal ulcers, disseminated intravascular coagulation, congenital factor, and platelet deficiency, *Pteridium* sp. poisoning, ophidian accidents, and sulfaquinoxaline ingestion (Jubb *et al*., 2016).

CONCLUSIONS

The suspicion of anticoagulant rodenticide poisoning was based on anamnesis and the clinical-pathological findings, which were confirmed by the toxicologic examination of the tissues. The lack of reports in the literature, both accidental and experimental, on this type of intoxication in ruminant herds, as well as the lack of quantification of rodenticide concentrations, make early diagnosis difficult due to the scarcity of literature on the actual toxicity in non-target animals, limiting correct therapy and making this clinical condition potentially fatal.

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REFERENCES

AMARAL, A.F.; JÜHLICH, L.M.; TAKEUTI, K.L. *et al*. Surto de intoxicação por cumarínico em leitões de maternidade. *Acta Sci. Vet*., v.43, p.1-3, 2015.

BERNY, P.J.; ALVES DE OLIVEIRA, L.A.; VIDEMANN, B.; ROSSI, S. Assessment of ruminal degradation, oral bioavailability, and toxic effects of anticoagulant rodenticides in sheep. *Am. J. Vet. Res*., v.67, p.363-371, 2006.

BRITO, M.F.; SEIXAS, J.N.; JABOUR, F.F. *et al*. Sobre um surto de envenenamento por derivado de dicumarínico em bovinos. *Pesqui. Vet. Bras*., v.5, p.143-149, 2005.

JUBB, K.V.F.; KENNEDY, P.C.; PALMER, N. *Pathology of domestic animals*. 6.ed. Philadelphia: Saunders, 2016. v.3, p.264.

MCCONNICO, R.S.; COPEDGE, K.; BISCHOFF, K.L. Brodifacoum toxicosis in two horses. *J. Am. Vet. Med. Assoc*., v.211, p.882-886, 1997.

OLIVEIRA, M.C.; RAMOS, A.T.; CUNHA, I.M. *et al*. Enfermidades de bovinos e ovinos diagnosticadas no Estado do Tocantins. *Acta Sci. Vet*., v.47, p.1676, 2019.

PEDROSO, P.M.; BANDARRA, P.M.; BEZERRA JUNIOR, P.S. *et al*. Intoxicação natural e experimental por *Nerium oleander* (Apocynaceae) em bovinos no Rio Grande do Sul. *Pesqui. Vet. Bras*., v.29, p.404-408, 2009.

RUNCIMAN, D.J.; LEE, A.M.; REED, K.F.M.; WALSH, J.R. Dicoumarol toxicity in cattle associated with ingestion of silage containing sweet vernal grass (*Anthoxanthum odoratum*). *Aust. Vet. J.*, v.80, p.28-32, 2002.

SPINOSA, H.S.; GÓRNIAK, S.L.; PALERMO-NETO, J. *Toxicologia aplicada à veterinária*. São Paulo: Manole, 2008, 346p.

STONE, W.B.; OKONIEWSKI, J.C.; STEDELIN, J.R. Poisoning of wildlife with anticoagulant rodenticides in New York. *J. Wildl. Dis*., v.35, p.187-193, 1999.

VALCHEV, I.; BINEV, R.; YORDANOVA, V.; NIKOLOV, Y. Anticoagulant rodenticide intoxication in animals–a review. *Turk. J. Vet. Anim. Sci*., v.32, p.237-243, 2008.

YIP, L.; STANTON, N.V.; MIDDLEBERG, R.A. Vitamin K1 treatment duration in patients with brodifacoum poisoning. *N. Engl. J. Med*., v.382, p.1764-1765, 2020.