VETERINARSKI ARHIV 75 (3), 273-282, 2005

Intoxication with anticoagulant rodenticide bromadiolone in a dog - a case report

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BINEV, R., P. PETKOV, A. RUSENOV: Intoxication with anticoagulant rodenticide bromadiolone in a dog - a case report. Vet. arhiv 75, 273-282, 2005.

ABSTRACT

A spontaneous intoxication caused by the anticoagulant rodenticide bromadiolone (Lanirat 0.005) in a Caucasian mountain shepherd dog at the age of 18 months is described. During its hospitalization at the Clinic of Internal Diseases, Faculty of Veterinary Medicine in Stara Zagora, clinical, laboratory, microbiological, radiological and ultrasonographic studies were performed. It was found that rodenticide intoxication was manifested by changes in the clinical status (arexia, polydipsia, hyperthermia, polypnea, dyspnea, tachycardia, pale conjunctives, liquidothorax and ascites) and in studied laboratory parameters (oligochromaemia, erythropenia, leukocytosis with neutrophilia and regenerative shift, hyperglycaemia, increased ALAT activities and prolonged PT, APTT and PIVKA).

Key words: intoxication, anticoagulant, rodenticide, bromadiolone, dog

Introduction

Pesticides are used all over the world in different branches of agriculture, industry, health care, etc. Their wide application and inadequate information about the means of their use and their toxic effects pose a real hazard for the health of both animals and humans (MARONI et al., 2000).

From the aspect of ecological agriculture the control of harmful rodents (mice, rats, field mice, etc) requires precise and adequate use of chemical means of restriction of their population. To date, the use of baits containing active substances with various composition and anticoagulant effect is the most frequent of such means (SENGALEVICH et al., 1998).

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ISSN 0372-5480
Printed in Croatia

Anticoagulant rodenticides are probably the most commonly used of such means around the world. It has been estimated that approximately 95% of all rodenticides used are anticoagulant baits (MURPHY, 2002).

Anticoagulant rodenticides are classified into two principal groups: derivatives of coumarin and indanedione. The preparations from the first group are more extensively used and provoke severe injury to vascular permeability, resulting in massive haemorrhages and the rapid death of rodents (SAMAMA et al., 2002; MURPHY, 2002; RADI and THOMPSON, 2004).

The mechanism of intoxication with coumarin anticoagulants is via a specific inhibition of blood coagulation. Vitamin K is needed for the functional synthesis of coagulation factors II, VII, IX and X. The most common vitamin K-responsive coagulopathy is anticoagulant rodenticide intoxication (ROZANSKI et al., 1999; SAMAMA et al., 2002; MISCHKE and NOLTE, 1999; MOUNT et al., 2003). Blood vessels lose their elasticity, and subsequently ruptures of large blood vessels occur, clinically manifested by massive haemorrhages and haematomes (PETRUS and HENIK, 1999; KOHN et al., 2003; LUTZE et al., 2003; MUNDEY and THOMPSON, 2003; RADI and THOMPSON, 2004). PETTERINO and PAOLO (2001) showed that anticoagulant rodenticides impair the cellular recirculation of vitamin K, causing secondary coagulopathies.

Up until now cases of intoxication with anticoagulant rodenticides and their effects have been described in cats (KOHN et al., 2003), polecats (SHORE et al., 2003), in wild animals (deer, coons, marten, eagle, owlet, hawk, etc.) with various anticoagulants such as bromadifacoum, chlorophacinone, bromadiolone and coumatetralyl (STONE et al., 1999; STONE et al., 2003).

A spontaneous intoxication with an unknown anticoagulant rodenticide in a dog has been described by BLOCKER and ROBERTS (1999); ROZANSKI et al. (1999); PETRUS and HENIK (1999); PETTERINO and PAOLO (2001); MURPHY (2002); MOUNT et al. (2003); MUNDAY and THOMPSON (2003); LUTZE et al. (2003); PETTERINO et al. (2004).

One of the most commonly used rodenticides is bromadiolone, used in the composition of the commercial preparation Lanirat 0.005. Bromadiolone is a second-generation coumarin anticoagulant. It is used at a dose of 8-10% added to a bait consisting of 100 kg ground grain, 1.5 l sunflower oil, 4 l water and 2 l Lanirat 0.005. Thus, it is used to attract harmful rodents (SENGALEVICH et al., 1998).

In the available literature there are no complete clinical and laboratory data for spontaneous intoxication with bromadiolone in dogs, which motivated our complex clinical, laboratory, microbiological, radiological and ultrasonographic studies in order to facilitate the diagnostics and the treatment of bromadiolone intoxications.

Materials and methods

On March 11, 2002 an 18-month-old male Caucasian shepherd dog from Shoumen named Spike and weighing 60 kg was referred to the Clinic of Internal Diseases, Faculty of Veterinary Medicine, Trakia University, Stara Zagora. Anamnesis revealed that a week earlier the owner noticed a symmetrical abdominal enlargement, decreased appetite, frequent urination and increased thirst. Three to four weeks previously a deratization by placement of baits containing Lanirat 0.005 in farm premises, where the dog was used as a guard, had been performed. For some time the dog was occasionally observed eating dead and dying rodents. The animal's diet normally consisted of granulated food and plenty of meat and fats. Immunoprophylactic and antihelminthic drugs were regularly administered. During the period prior to the referral, body temperature increased up to 40 °C. The dog was given antibiotics: i.m. Shotapen and 2 000 000 UI Penicillin intraperitoneally, but with no effect.

During the hospitalization clinical status was followed twice daily by checking body temperature (BT), heart rate (HR) and respiratory rate (RR), colour of mucosae, appetite, thirst, general condition, locomotor activity, sensory perception, urination, defecation, etc. applying routine clinical diagnostic methods.

At referral and at post-hospitalization days 4, 8, 12 and 16, blood from v. cephalica antebrachii was sampled for determination of haemoglobin concentration (HGB), red blood cell (RBC) counts, white blood cell (WBC) counts and haematocrit (HCT) (automated haemoanalyzer Serono-System 150+, U.S.A.), and differential WBC counts by the method of Pappenheim, erythrocyte sedimentation rate (ESR) by the method of Panchenko, Thrombin time (TT), activated partial thromboplastine time (APTT), prothrombin time (PT), protein induced by Vitamin K antagonism or absence (PIVKA) and activated clotting time (ACT) using diagnostic kits (BIOLABO, France), and a coagulometer (Amelung, Germany). The activities of transaminases ASAT and ALAT, uric acid, total bilirubin, urea, creatinine and blood sugar were assessed using an automated analyser (Reflotron Manual, Germany) using a Roche (Germany) diagnostic kit.

The course of the disease and its treatment were followed by thoracic and abdominal radiography (TUR D-800-1, Germany) and ultrasonography probe (Aloka-SSD-500, UST-5871-5).

Several punctions of the thorax (in the left intercostal spaces VII-VIII and the right intercostal spaces IV-V) and the abdomen were performed at hospitalization and post-hospitalization, on days 3, 6, 9 and 12. Physical analysis of punctate included its colour, transparency, density (using an aerometer), with a chemical analysis of the amount of protein (Esbach's albuminometer). The punctate was microscopically and microbiologically studied on McConkey agar (blood agar with 5% sheep red blood cells). The Rivolta test was applied for differentiating between transudate and exudate.

Results

The physical examination revealed pale conjunctives, decreased locomotor activity and sensory perception, rapid exhaustion, bilateral symmetrical abdominal enlargement with drooping of the ventral wall and spinal lordosis. The patient was constantly sitting up in order to ease respiration. Body temperature was 39.6 °C, heart rate 115 min^{-1} and respiratory rate – 88 min^{-1}.

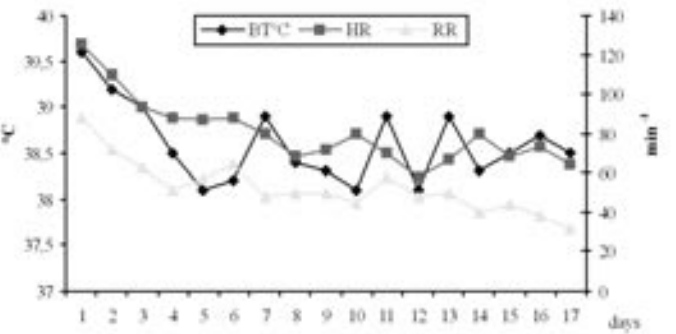

Fig. 1. Changes in body temperature (BT), heart rate (HR) and respiratory rate (RR) of a dog following intoxication with the anticoagulant rodenticide bromadiolone.

Table. 1. Results from the analysis of thoracic punctuates obtained from a dog following intoxication with anticoagulant rodenticide bromadiolone.

Parameters	Days after the hospitalization				
	1	3	6	9	12
Amount, mL	1700	500	650	400	250
Density	1,005	1,008	1,010	1,012	1,015
Protein g%	2	2.5	2.5	3	3
Rivolta's test	-	-	±	±	±
Sediment	Plenty of erythrocytes. Polymorphonuclear leucocytes and endothel cells				

During hospitalization (Fig. 1) an elevated BT was present during the first two days, but afterwards, until the end of the follow-up, it was within physiological range (37.5-39.0 °C).

A tachycardia was observed from the first (115 min^{-1}) until the 7th (82 min^{-1}) day of hospitalization. From day 8 until the end of follow-up, RR was normalized (60-80 min^{-1}).

The pulse was strong, full, hard and rhythmic. After percussion a decrease in absolute cardiac dullness was observed, while auscultation revealed stunt cardiac tones.

Breathing at referral was with increased frequency (88 min^{-1}) difficult (with open mouth) from a costo-abdominal type, with the active participation of abdominal muscles in both respiratory phases. Percussion showed a dullness in the ventral pulmonary areas with a horizontal upper limit that moved with lifting of the front part of the body. Auscultation evidenced a bronchial respiration with moist fin bubbling rates over the limit of horizontal dullness. Underneath, respiratory sounds were poorly audible. The RR was enhanced (polypnea) for the whole period of observation (Fig. 1). The tendency towards lower RR observed during the second half of the period did not result in normalization and the values were still above physiological limits (15-25 min^{-1}).

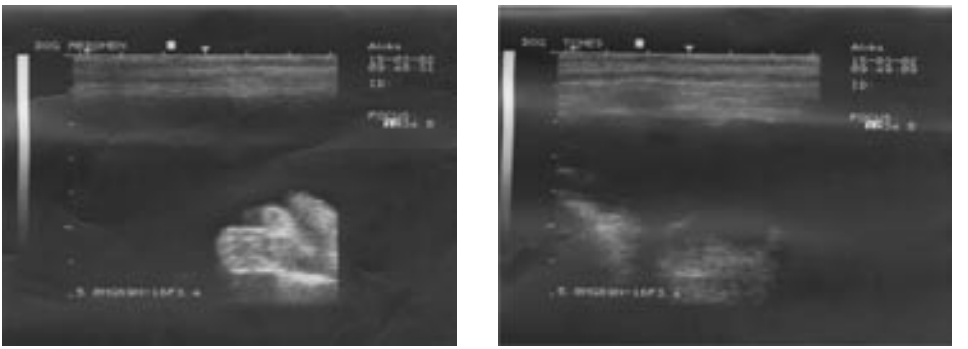

Fig. 2. Abdominal (left) and thoracic (right) ultrasonographies of a dog following intoxication with anticoagulant rodenticide bromadiolone by day 1

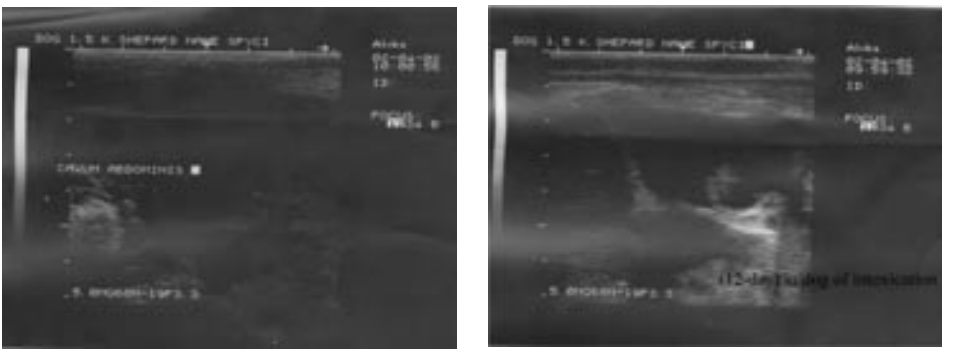

Fig. 3. Abdominal (left) and thoracic (right) ultrasonographies of a dog following intoxication with anticoagulant rodenticide bromadiolone by day 12

Table. 2. Clinical laboratory blood examinations data of a dog following intoxication with anticoagulant rodenticide bromadiolone.

Parameters	Days after the hospitalization				
	1	4	8	12	16
Haematological parameters					
HGB g/L	82	88	98	115	122
RBC T/L	5.19	5.24	5.54	7.39	8.56
HCT %	33.3	35.7	43.4	55.3	61.1
WBC G/L	19.1	15.2	16.4	13.8	12.1
Differential wbc counts %					
Eo	0	0	1	1	0
Mm	3	5	3	4	2
St	18	25	14	13	22
Sg	70	64	65	77	62
Lym	8	6	16	5	14
Mo	1	0	1	0	0
Biochemical parameters					
Blood sugar mmol/L	6.48	6.23	6.87	5.54	4.82
Total bilirubin μmol/L	28.6	22.8	23.5	18.1	13.2
ASAT U/L	34.1	32.2	20.8	15.0	12.8
ALAT U/L	65.2	54.8	44.2	35.7	40.1
Urea mmol/L	18.8	12.4	9.6	12.8	10.2
Uric acid μmol/L	78,8	64,2	96,5	118,4	128,1
Creatinine μmol/L	148	124	109	111	94
PT s	122	84	36	18	14
APTT s	86	68	24	22	10
PIVKA s	148	96	45	32	15
TT s	18	10	14	15	10
ACT s	82	64	58	75	45

Lateral thoracic and abdominal radiographs were performed at referral, which revealed shading with a horizontal upper limit.

Ultrasonography was also performed in order to assess the amount and position of liquid in the thoracic and abdominal cavities (Fig. 2). Interpretation suggested vast anechogenic spaces (filled with liquid), contrasting with the more echogenic zones of the liver, spleen, intestines and the soft abdominal wall. A similar echogenic picture was also observed in the pleural cavity.

At day 12, a second ultrasonography was performed (Fig. 3) which evidenced a marked decrease inf thoracic and abdominal liquids.

The optimal site of thoracic punction was found using general and special methods and was located in the left VIIIth intercostal space in the zone of maximum dullness. During hospitalization, 5 thoracic punctions were performed: in left intercostal spaces VII-VIII and right intercostal spaces IV-V. The punctate had an intensively red colour and was odourless. The results of analysed punctates are presented in Table 1, showing that they were haemorrhagic transudates. The microbiologically studied was negative. Similar results showed the data of the abdominal punctates.

Laboratory parameters, assessed during the hospitalization period (Table 2), showed decreased HGB – 82 g/l, RBC – 5.19 T/l and HCT – 33.3% and increased WBC counts: 19.1 G/l. By the end of the observation those parameters returned to their physiological values. The differential WBC counts suggested neutrophilia with a regenerative shift to Mm (3-5%).

Higher blood levels were measured for blood sugar, bilirubin and ALAT. They remained elevated until the end of the hospitalization, although a tendency towards normalization was observed. Significant deviations in the levels of ASAT, urea, creatinine, uric acid and ESR were not observed during the period of study.

Prothrombin time (PT) was 122 s (reference range: 12-14 s), activated partial thromboplastine time (APTT) was 88 s (reference range: 12-16 s) and protein induced by vitamin K antagonism or absence (PIVKA) was 148 s (reference range: <25 s) at the beginning of the period of observation. Following treatment it was restored to within the reference range by day 12 of hospitalization. thrombin time (TT) and activated clotting time (ACT) was in reference range.

Discussion

Anticoagulant rodenticides impair the cellular recirculation of vitamin K causing secondary coagulopathies, inhibits blood coagulation and affects blood vessels via an analogous mechanism (BLOCKER and ROBERTS, 1999; PETRUS and HENIK, 1999; MUNDEY and THOMPSON, 2003; KOHN et al., 2003). This explains haemocirculatory disorders manifested by accumulation of haemorrhagic transudate in thoracic (liquidothorax) and abdominal cavity (ascites) (RADI and THOMPSON, 2004), observed by us. It could be

presumed that the simultaneous decrease of RBC counts, haemoglobin (normochromic anemia) and haematocrit values occurred as a consequence of blood loss. The observed leukocytosis and hyperthermia are probably caused by immunodeficiency, which in turn resulted in some kind of infection (KATARANOVSKI et al., 2003). Immunodeficiency is a consequence of long-term anaemia and hypoxia, as well as liver injury (RADI and THOMPSON, 2004). The large amount of thoracic transudate is most likely responsible for the collapse of the compressed pulmonary parenchyma and for the signs of respiratory insufficiency: polypnea, dyspnea, and costo-abdominal type of breathing. The tachycardia is a compensatory mechanism for oligochromaemia, erythropenia and pulmonary insufficiency. Hyperglycaemia, bilirubinaemia and increased ALAT activity are other signs of the toxic effect of anticoagulant rodenticides on liver parenchyma. It could be accepted that the same toxicodynamics are also valid for bromadiolone intoxication.

Treatment. Throughout the period of hospitalization (days 1-15), 300 mL 20% glucose, 5 mL 10% vitamin C, 5 mL 20% coffein natricum benzoicum intravenously and 3 mg/kg body weight vitamin K_1 subcutaneously were administered once daily. Medication therapy was extended by intramuscular administration of 12 mL Lincomycin-Spectinomycin 5/10 (50 mg lincomycin hydrochloride and 100 mg spectinomycin dihydrochloride in 1 mL injectable solution) (Alfasan-Woerden, Holland) every 24 hours for 10 days; 20 mg Furosemide (in 2 mL injectable solution) every 12 hours for 3 days, followed by oral application of 40 mg Furosemide tablets twice daily for 10 days, and 5 g urotropin (hexamethylentetramin) once daily for 7 days.

The punctions of thoracic and abdominal cavities were followed by intrathoracal or intraperitoneal administration of 10 mL vitamin AD_3E, (vitamin A 15000 UI, vitamin D_3 20000 UI and vitamin E 0.01 g), 1 mL gentamicin (40 mg/mL), 5 mL 1% novokain (1 g procaine hydrochloride in 100 mL, VetProm, Radomir, Bulgaria) and 1 mL dexamethasone (2 mg dexamethasone disodium phosphate in 1 mL; Alfasan-Woerden, Holland).

After a 3-week therapy, the clinical and the laboratory status of the patient was within reference ranges and the dog was discharged from the clinic as cured.

Anticoagulant rodenticide toxicosis is a potentially fatal condition, but it may be treated successfully if diagnosis is made quickly and appropriate therapy is instituted.

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Received: 17 January 2003
Accepted: 5 May 2005

BINEV, R., P. PETKOV, A. RUSENOV: Trovanje antikoagulantnim rodenticidom bromadiolonom u psa - prikaz slučaja. Vet. arhiv 75, 273-282, 2005.

SAŽETAK

Opisano je trovanje antikoagulantnim rodenticidom bromadiolonom (Lanirat 0,005) u kavkaskog planinskog ovčara u dobi 18 mjeseci. U tijeku njegova liječenja provedene su kliničke, laboratorijske, mikrobiološke, radiološke i ultrazvučne pretrage. Trovanje se očitovalo promjenama u kliničkoj slici (areksija, polidipsija, hipertermija, polipneja, dispneja, tahikardija, bljedoća spojnica, likvidotoraks i ascites). Od laboratorijskih pokazatelja ustanovljena je oligokromemija, eritropenija, leukocitoza s neutrofilijom i regenerativnim promjenama, hiperglikemija, povećana aktivnost ALAT i produženo PT, APTT i PIVKA.

Ključne riječi: trovanje, antikoagulant, rodenticid, bromadiolon, pas