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CONTENTS

ASPECTS REGARDING THE PERSONALIZED TRAINING OF THE GERMAN SHEPHERD

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Abstract

In preparing for the utilitarian work examination and in canine sports activities, those methods that ensure a more harmonious relationship between man and dog must be addressed. For the best competitive results, the training must be started at an early age, the maximum limit being 6-7 months. In order to obtain outstanding competitive results, the temperament and compartment of each dog must be taken into account in training. In case of behavioural deviations, the training must be customized and the training period must be increased.

Keywords*: German Shepherd, training*

Introduction

In the physical and mental training of a dog, the health, including good maintenance, suitable nutrition, vaccinations and regular veterinary examinations, must be taken into account.

Each specimen must be approached in a correct, regulated manner, taking into account its behavioural peculiarities. Knowing the dog's abilities and limits helps the breeder to understand how the animal perceives the surrounding reality.

The training is based on a well-established program of exercises and on the hierarchy of educational stages, starting from learning simple elements and reaching the special ones (2).

For the best competitive results, the training must be started at an early age, the maximum limit being 6-7 months, because the young dogs have a lively temperament, are more curious, more willing to investigate and take the exercises as a game (3). In the period of 8-14 months of age, fear can be imprinted, the beginning of training in this period having a low success rate. It has been observed that from the age of one year, the aggressiveness increases, especially to the males. The socialization is very important, especially in the ring, where the slightest sign of aggression leads to the elimination of the dog from the competition.

The main purpose of any breeder is to present as many specimens as possible in the "work" class. In the training for the utilitarian work exam and in the canine sports activities, those methods that ensure a more harmonious relationship between man and dog must be approached. The education of the German Shepherd

puppy begins around of three months old, with the elementary notions of discipline (pre-training) and even with the first notions of the latter (7).

The first exam which a German Shepherd can take, at the minimum of 12 months old, is the BH test or "Pet dog with socialization test". BH testing consists of (6):

– discipline test (walking on a leash, without a leash, sitting, lying down position with a long waiting for call);

– socialization test (indifference to passing an aggressive dog, next to the bicycle who honking, walking in traffic).

The race-specific work exam (Guard and Protection) includes three tests: track, discipline and attack. The participation is conditional on passing the BH test and reaching of 18 months old. The titles are awarded exclusively for the full promotion of the examination stages. The examination stages can be passed only in the order of 1 - 2 - 3 (6).

Material and methods

The biological material was represented by specimens of the German Shepherd breed, aged between 4 and 7 months. The training had an average of 2 months, including the pre-training. The pre-training consisted of short working sessions of 10 minutes. The work was done only with stimuli and rewards, without physical or mechanical constraints. The dogs have taken the BH exam at 14 months old.

From the age of 5 months, the preparation for pursuit began, using food stimuli (to increase their pleasure and interest in search).

The next stage in the preparation was the training for I.G.P. exam, consisting in tests for work, discipline and attack. The training had lasted 8 months.

In addition to preparing for the PGI, the dogs were trained for the presentation ring. The ring training was done with a "double handler", one handler being with the dog on the leash, and two people, placed in the diametrically opposite corners of the ring, communicating with the dog. In addition to pulling on the leash, the dog must learn to walk on trot (with and without a leash). The training was focused on the harmony of movement, cadence and endurance.

Results and discussions

Below are presented some case studies requiring custom preparation, taking into account behavioral problems in dogs.

When Romano Runa (Fig. 1), a 4 month old female, started the training for BH testing, it was found that she did not want to learn the presentation position (static). She had learned the other elements very quickly. Runa's temperament was analysed, and we noticed that she was energetic, very active and impatient. To correct this defect, six training sessions were performed in addition to the normal ones, the time per session remaining constant. Through a temperament-adapted training, very good results were obtained. Therefore, in 2013, in Geneva, Runa received the title of European Champion in the Junior category.

Fig. 1. *Romano Runa*

Fig. 2. *Romano Wizard*

Romano Wizard (Fig. 2), a 5-month-old male, was always running upside down, although he had no anatomical or angular defects. In this case, two collars and two leashes were used in the running training at the same time. One of the collars was for correction having small outside spikes. When Wizard lowered his

head, the leash attached to the correction collar was used. The use of the correction collar was done carefully, because the dog had to perform the exercise with pleasure. After five training sessions, the dog associated this posture with an unpleasant sensation, definitively correcting his posture. In Bucharest, in 2012, Wizard received the title of European champion in the Senior category (long hair).

Romano Picolo (Fig. 3), a 7-month-old male, began to become slightly aggressive in the presence of other males. This required an additional 30 socializing sessions. Picolo met unknown dogs in different circumstances and locations. Personalized training gave very good results, Picolo becoming, in 2013 in Geneva, European Vice-Champion in the Senior category.

Fig. 3. *Romano Picolo*

Conclusions

1. The dream of every breeder is to create a specimen that will be called CHAMPION.
2. In order to create exceptional specimens, sustained activities of selection, reproduction, breeding and education of dogs must be undertaken.
3. In order to obtain outstanding competitive results, the temperament and compartment of each dog must be taken into account in training.
4. In case of behavioural deviations, the training must be customized and the training period must be increased.

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MEDIASTINAL LYMPHOMA IN A 9 MONTHS OLD BRITISH SHORTHAIR CAT

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Abstract

Lymphoma is the most common neoplasms seen in cat. It is a malignant form of cancer that affects the lymphatic system. The anatomic sites may be represented by the gastrointestinal tract, renal, mediastinal, nasal cavity, and central nervous system or multicentric.

This case presentation follows the evolution, prognosis and response to treatment of a 9 month old British shorthair diagnosed with mediastinal lymphoma and the clinical investigation for a certain diagnosis. A special aspect of this case is the way this condition progresses. Initially, the patient shows severe signs of respiratory distress that endanger its life. The chemotherapy treatment is very well tolerated and the response is a rapid and favourable one however, the disease evolves extranodally affecting the central nervous system with the appearance of the neurological clinical signs.

Keywords: *mediastinal lymphoma, cat, PARR (lymphocyte clonality), flow cytometry, chemotherapy, central nervous system*

Introduction

Lymphoma is one of the most common types of cancers in cats, representing 90% of hematopoietic tumours (1) and 33% of all tumours diagnosed in cats (2). It is a systemic cancer caused by malignant transformation of lymphocytes, an uncontrolled clonal proliferation of lymphoreticular cells that normally come from lymphoid tissues, such as lymph nodes, spleen, and bone marrow, although they can come from any part of the body. Cats of any age can be affected, with reported cases involving patients 4 months to 19 years of age. Younger cats are more likely to develop mediastinal lymphoma and test positive for FeLV (feline leukaemia virus). Some studies have found that Siamese cats are at higher risk of developing this type of cancer (3). Male cats are more likely to develop lymphoma, often in association with a higher incidence of FeLV and/or FIV (feline immunodeficiency virus) infection.

The mediastinal form is more common in young patients with an average age of 5 years old. This involves the lymphoid structures in the thoracic cavity, respectively thymus and mediastinal and sternal lymph nodes. In 80% of the cases, this type of cancer is associated with positive testing for FeLV.

Material and methods

The patient is an intact male cat of 9 months age, British Shorthair, having a bodyweight of 4.18 kg. The owners came to the clinic for an oncology consultation.

Medical history

He was consulted by his doctor two months ago because he had an asthma-like crisis. An imaging examination (chest x-ray and abdominal ultrasound) was performed, and the presence of a soft tissue mass was discovered in the chest cavity. Additional investigations such as computer tomography (CT) were recommended, and treatment with steroid anti-inflammatory drugs was administered. Thus the general condition improved.

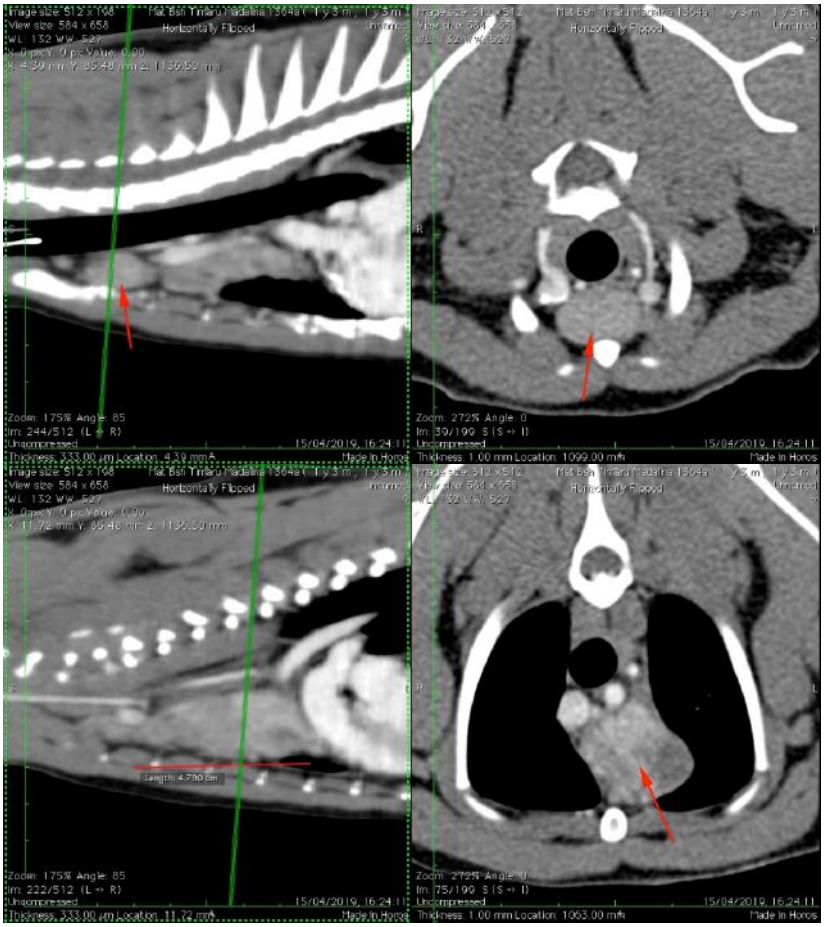

Fig. 1. *CT examination. The red arrow indicates the presence of a soft tissue mass located in the cranial thorax*

A week later, the computer tomography was performed (Fig. 1). The images confirm a tumoral mass in the cranial thorax, spread over a distance of about 5 cm, with a predominant orientation on the left side. In front of the tumoral mass, an increase in the suprasternal lymph nodes volume is observed. The CT scan shows an inhomogeneous contrast that leads to suspicion of fluid areas or necrosis. Location of tumoral mass may indicate a thymus pathology – thymic lymphoma, lymphoma, reactive or metastatic lymphadenopathy.

For the next couple of weeks, the patient receives symptomatic treatments with anti-vomiting drugs and intravenous fluids that offer improvements for a short period of time.

The general status deteriorates profoundly and quickly, with frequent vomiting (10 episodes per day). Food appetite is present, but vomiting occurs immediately after eating.

fBNP and FPL tests were performed with negative results.

Two months after the first medical evaluation, the owners came to the clinic for a specialized oncology consultation. At the time of the examination, the patient is normothermic (38.7C°). It has bright red mucous membranes, tachycardia, dyspnoea (mouth breathing, abdominal movements), tachypnea, inability to maintain a standing position, and normal palpable lymph nodes.

Radiological examination is performed to determine the stage and evolution of the disease. The images indicate a soft tissue mass located in front of the heart, which performs compression on the lung lobes, the heart, and cranial lung lobes being caudally displaced (Fig. 2).

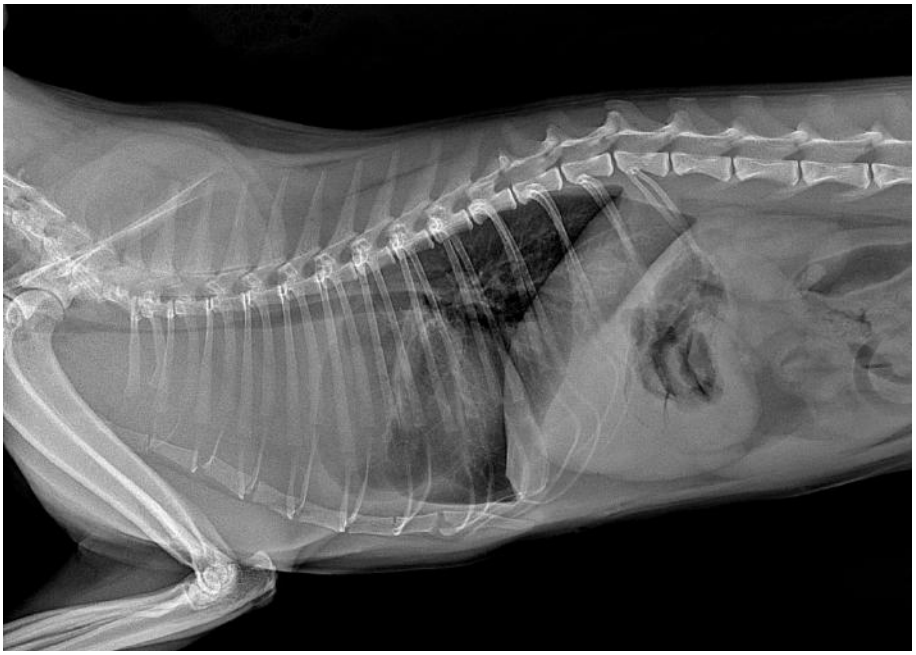

Fig. 2. *Radiological examination – thoracic cavity, right lateral exposure*

During the clinical examination, the patient develops anisocoria, difficulty breathing accentuates, and the apparent mucous membranes become cyanotic. Oxygen therapy is used for stabilization.

Ultrasound examination indicates splenic modification – it is increased in volume, the tail of the spleen makes a cranial deflection. It is homogeneous in section, and the margins are smooth. Splenomegaly can be an associated aspect of lymphoma. Eco-guided fine needle aspiration and cytological examination of the spleen are recommended. No other changes are detected in the abdominal cavity.

The major suspicion is of mediastinal lymphoma, and the differential diagnosis is thymoma.

An eco-guided sampling is performed, by fine-needle aspiration, for cytological examination and flow cytometry. This method implies sedation, using Butorphanol in a dose of 0.2 mg/kg, Diazepam – 0.2 mg/kg and, local – Lidocaine 2 mg/kg infiltrations of 5 intercostal spaces. The lateral-lateral thoracic region is sanitized, and eco-guided fine-needle aspiration is performed (Fig. 3).

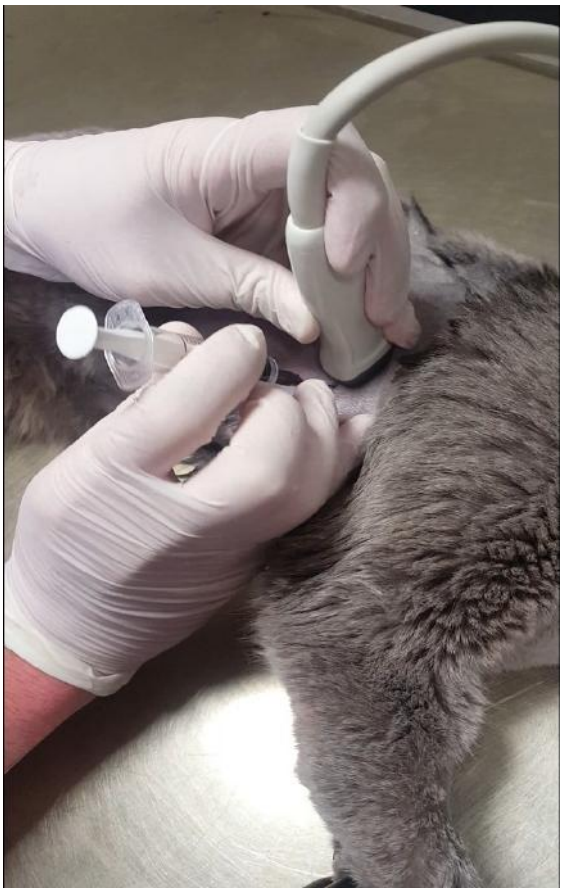

Fig. 3. *Ultrasound-guided thoracic puncture*

Flowcytometry is a modern cell analysis technique, which allows the simultaneous determination of several physical and biochemical parameters characteristic of a single cell in movement in a liquid stream. This technique can be used for peripheral blood, bone marrow, cavitary fluids, cellular aspirates (lymph nodes, liver, spleen, mediastinal mass) (4).

Sample preparation requires a tube with a red cap (without additives and without separating gel) in which 1 ml of 0.9% saline, 0.1 ml of serum from the same patient, and the content obtained in a 5 ml syringe with 22G by fine-needle aspiration are introduced (5).

Although this technique is currently experimental in cats, and the result can be influenced by the previous administration of steroidal anti-inflammatory substances and transport conditions, the owners agreed with testing.

Cytological examination

Diff-Quick staining is used for microscopic examination. The examined preparation is cellular rich, having a population of monomorphic cells, made up of 95% of lymphoblasts, and the rest of the population consists of medium and small lymphocytes. The cells are round or oval-shaped with small quantities of intensely basophilic cytoplasm, round or oval cell nucleus, large compared to the cytoplasm, frequent mitotic figures (Fig. 4). The cytological aspect is characteristic for mediastinal, high-grade cell lymphoma (6).

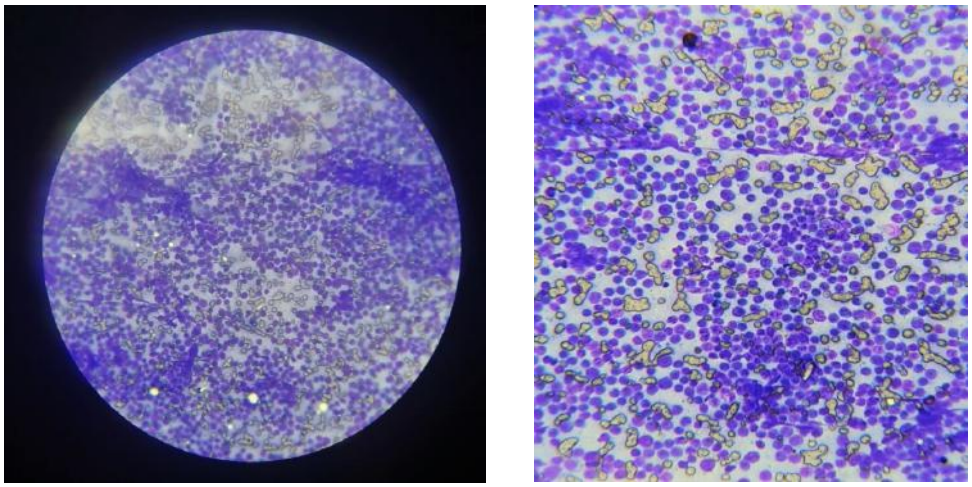

Fig. 4. *The cytological aspect of thoracic puncture, Diff - Quick staining; monomorphic cell population composed of 95% lymphoblasts*

Although most cats that develop lymphoma are positive for FeLV, in this case, the test is negative.

Blood tests reveal leukocytosis, with an increase in monocytes, lymphocytes, and granulocytes, and iron deficiency hypochromic microcytic anaemia,

represented by mild values below the physiological limit of the average concentration of erythrocyte haemoglobin and red blood cell distribution. Biochemistry shows no significant changes (Table 1).

Table 1

Modified values of haematological parameters

	Haematology	
Name	**Results**	**Reference range values**
Leukocyte	30	5-11 x 10 3/mm3
MCHC	30,3	31-36 g/dl
LDE	15,4	17-22%
LYM	9,5	1,5-4 x 10 3/mm3
MON	0,9	<0.5 x 10 3/mm3
GRA	12.1	3-12 x 10 3/mm3

Diagnosis

Evolution and clinical signs, results of imaging investigations, and cytological examination are characteristic for lymphoma. The Flowcytometry result is not conclusive in this case, but the PARR test (lymphocyte clonality test) confirms the T cell lymphoma. Phenotyping has no prognostic value for cats, but demonstrates the suspected disease, offering a precise diagnosis.

Prognostic

The literature (7-8) indicates an average survival time of 2-3 months, with the possibility of longer-term remission time. According to a research results, the average survival time of patients receiving chemotherapy (COP protocol) is 484 days (3).

Treatment

The treatment of choice for mediastinal lymphoma is multidrug, systemic chemotherapy (7, 8, 10). The purpose of this treatment is to induce remission, to slow down progression and ensure good quality of the patient's life.

In this case, the COP (High-Dose) therapeutic protocol was chosen. It consists of administration of Vincristine (0.5 mg/m2), intravenously, weekly for four weeks, then at tree week intervals; Cyclophosphamide (200mg/m2), orally, on the day after administration of Vincristine, every three weeks; Prednisone (2 mg/kg) for two weeks, then at a dose of 1 mg/kg daily.

Given that chemotherapeutic treatments are immunosuppressive, before each administration of injectable chemotherapy treatment, the blood count is performed to check the immune system's status.

Just one day after the first administration of treatment, the general condition improves, no more vomiting, breathing frequency is reduced, and breathing difficulty is no longer noticeable. So, at the next visit, in the following week, the

patient gains 200g in weight, did not showed side effects after the chemotherapy session; however, on the blood count shows mild leukopenia (WBC 4), and the characteristic values for hypochromic microcytic iron deficiency anaemia are still modified. Also, there are improvements in radiological control (Fig. 5). The established therapeutic protocol continues.

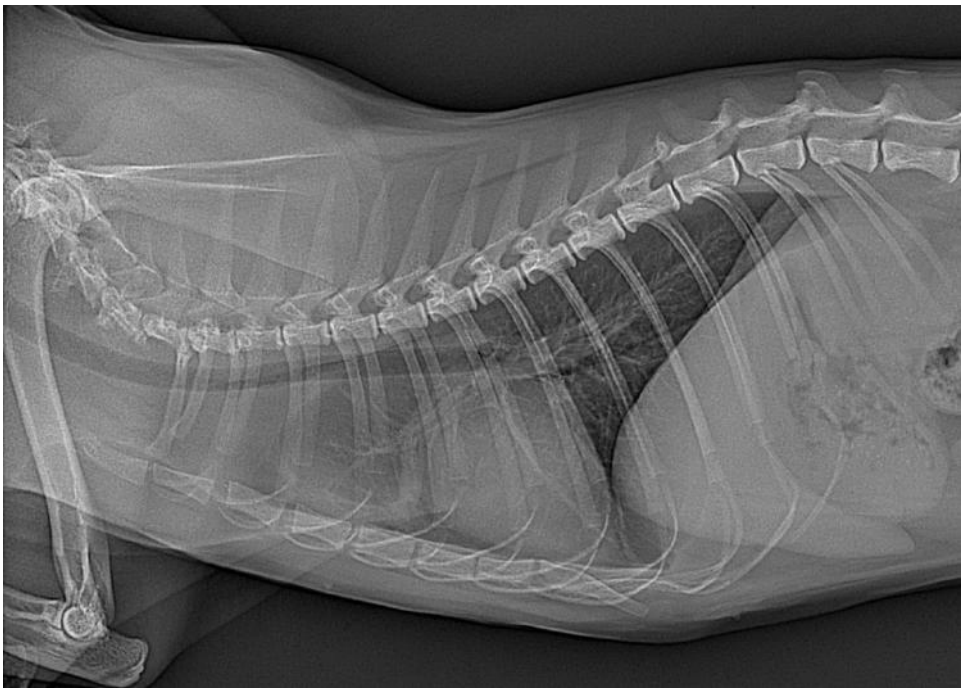

Fig. 5. *Thorax radiological examination in week two of treatment (after the first treatment of intravenous cytostatic, cyclophosphamide, and prednisone)*

The evolution is favourable, so at the next cytostatic session, he gains 250 g body weight, the blood count indicates an increase in leukocytes (WBC 6.3-physiological value), keeping LDE and MCHC below the lower limit. At the clinical examination, the patient does not show signs of disease.

During the fourth week meeting, staging is performed (complete blood count, ultrasound, and radiological examination). Biochemical analyses show no change, the parameters being within physiological limits. The blood count indicates a normal leukocyte value, and the only modifications present are the MCHC and LDE values below the physiological limit. Also, the abdominal ultrasound does not show changes, the spleen being homogeneous, regular contour, normal hilum, and the radiological appearance is improved (Fig. 6).

The next two chemo sessions are performed at three weeks intervals, and the patient is stable, having a favourable evolution. After six administrations of Vincristine, the patient is considered in remission. Literature indicates cytostatic

administration at three weeks for one year before interrupting (7, 8, 10). For reasons independent of the medical opinion, the decision was made to stop treatment with Vincristine and continue the administration of Cyclophosphamide and Prednisone.

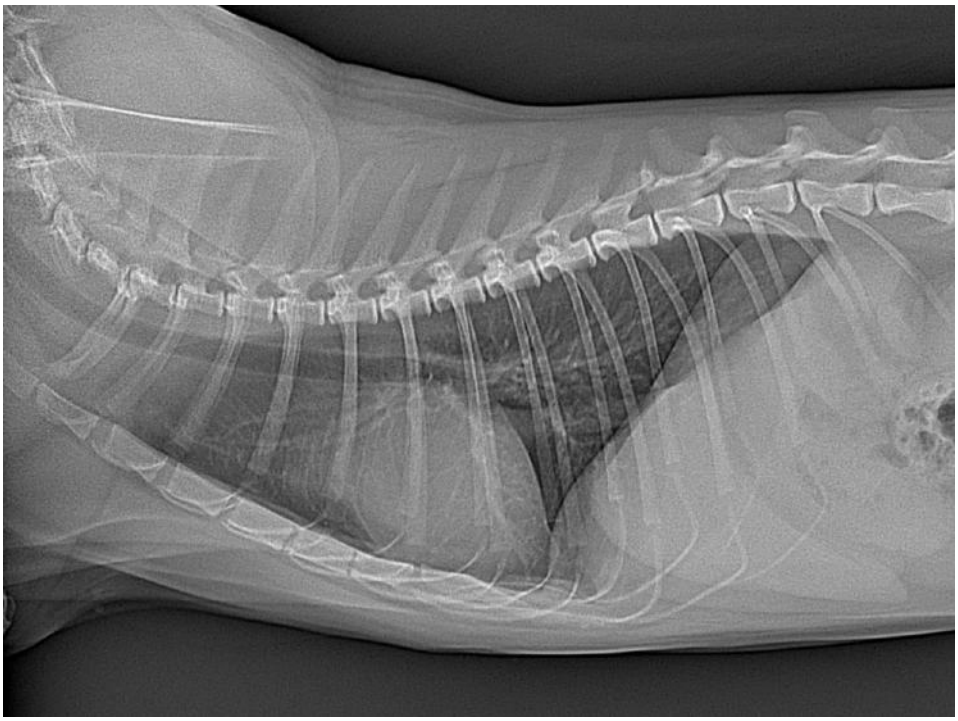

Fig. 6. *Thorax radiological examination, week 4 of treatment*

Five weeks after the last injectable chemotherapy treatment, he returns to the clinic, presenting neurological manifestations. During the last two days, he presented three episodes of neurological signs initiated by the spontaneous appearance of a muscle spasm in the anterior limb, followed by weakness, disorientation, and sternal recumbency. The duration of such an episode is 1-2 minutes, and the recovery is spontaneous and without sequelae.

Heart rate is 120 beats per minute (BPM), and respiratory rate of 40 breaths per minute (RPM). Blood tests show no changes except for MCHC and LDE.

The cardiological consultation is without any changes. However, the thorax's ultrasound and radiological examination showed a mass of soft tissue located in front of the heart (Fig. 7). We consider a possible evolution of the disease with extranodal involvement of the central nervous system, the condition considering to be classified as stage V. A study conducted at the Veterinary Faculty of Medicine from the University of Brazil showed that out of 125 cats diagnosed with lymphoma, only 12% had involvement of the nervous system (11).

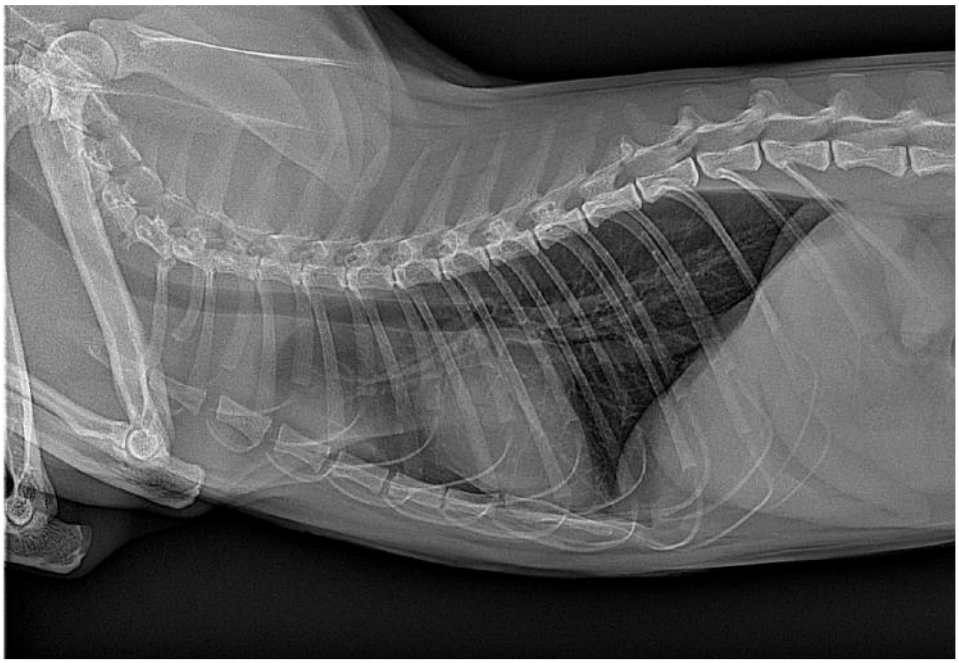

Fig. 7. *Thorax radiological examination after a five-week break in the administration of the Vincristine cytostatic. Cyclophosphamide and Prednisone were administered as usual*

A stage V evolution of the disease with extranodal involvement of the central nervous system assumes tumour cells' identification in the haematogenous marrow. Thus, ideal from the medical point of view is to perform a spinal cord puncture.

Given the disease evolution and the clinical manifestations, the L-asparaginase administration is recommended and restarts the protocol with Vincristine. The high costs of L-asparaginase administration guide the owners in the decision to refuse this substance.

The owners decide to resume the therapeutic protocol with the weekly administration of Vincristine. After the first session, the neurological signs remit, and after five weekly administrations (cyclophosphamide was kept at three weeks administration and daily prednisone), after staging, the patient is stable, considered to be in remission. We are asked to find alternative solutions for therapeutic variants that could reduce treatment costs. Thus, an attempt was made to reduce the frequency of chemotherapy administration every three weeks with the risk that the percentage of tumour cells destroyed by chemotherapy to be less than the rate of cells that multiply abnormally.

After two weeks from the last chemotherapy session, the patient presents obvious neurological manifestations, eyelid but not a pupillary reflex, bilateral miosis and episodes of hypersalivation, muscle tremors and spasm in the eyelid of the right eye, vascular fragility, heart rate of 100 BPM, respiratory rate of 25 BPM, pink apparent mucous membranes, normothermic. Vincristine is administered

again at a dose of 0.5 mg/m2 with the indication that it will need L-asparaginase if the neurological signs persist for the next 48 hours. After 24 hours, the patient no longer shows neurological symptoms.

One week later, he develops paralysis in the left anterior limb and the posterior legs, facial fasciculations, hypersalivation episodes, and hyperesthesia. Blood tests showed the parameters within physiological limits. Vincristine is administered, but this time, the improvements are partial. In the next 24 hours, the general condition improves, no longer shows hypersalivation episodes or hyperesthesia but does not fully regain the rear limb's mobility.

Forty-eight hours later, the owners decided to administer L-asparaginase, but the evolution is not favourable. Therefore, considering the patient's poor quality of life and the lack of viable and sustainable treatment, it is decided to stop the therapeutic protocol and euthanize the patient.

Conclusion

Lymphoma is circulatory cancer that affects the lymphatic system. The administration of cytostatic drugs can destroy a significant percentage of circulating tumour cells, which is why most treated patients achieve complete remissions early in chemotherapy. The periodic administration controls the abnormal cell multiplication and prevents disseminating abnormal lymphocytes by the circulatory-lymphatic route. The action of most cytostatic drugs is 7-14 days. In cases where the percentage of circulating tumour cells is reduced enough after a complete chemotherapy course, the frequency of administration can be extended to 3 weeks. In this patient's case, the advanced stage of the disease at the time of diagnosis and the lymphoma's extranodal evolution that affected the central nervous system made it impossible to administer the intravenous treatment at three weeks.

A clear and complete diagnosis in the early stages of the disease influences the prognosis and treatment response. Positive testing for FeLV does not influence chemotherapy's response but is associated with shorter average survival time. Although, in this case, the FeLV / FIV test result is negative, the sensitivity of serological tests is not high, so there is a possibility of a false-negative result. For a definite result, the use of the PCR technique is recommended.

The average survival time is also affected by the chosen therapeutic protocols. There is a possibility that if L-asparaginase were administered from the first occurrence of nervous manifestations with the administration of the COP protocol without interruption, the result would have been different, with longer average survival time.

Although the patient was in severe respiratory distress at its first visit to the clinic, the evolution and response to treatment were favourable. The survival time was five months.

Contributions

Dr. Adriana Stancu (oncological evaluation, treatment, monitoring), Dr. Anca Cristea (supervisor, cytological evaluation), Dr. Daniel Lescai (performing ultrasound-guided punctures, imaging evaluation).

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DENTINOGENESIS IMPERFECTA IN A 10 MONTHS OLD CANE CORSO

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Abstract

Dentinogenesis imperfecta (DGI) is a very rare genetic dental condition characterized by enlarged pulp chambers and insufficient layer of dentin in both deciduous and permanent dentition of the affected patients. It has been reported in humans and it is usually associated with osteogenesis imperfecta. Diagnosis is based on clinical and radiological findings, but ideally histological examination and genetic tests are needed for confirmation. This is a case report of a 10 months old Cane Corso with clinical presentation of dentinogenesis imperfecta.

Keywords: *dentinogenesis imperfecta, osteogenesis imperfecta, hypoparathyroidism, Cane Corso, genetic disorder*

Introduction

Hera, a 10 months old female Cane Corso, was presented on the 15th of October 2018 for a dental consultation. She had pink teeth, a strong halitosis, the owner reported that Hera wasn't eating like she used to and she also showed signs of pain (didn't allow palpation of the mouth or conscious examination of her teeth).

Dentinogenesis imperfecta (DI) refers to an inherited condition that affects only teeth and is associated with mutations in the DSPP gene which encodes dentin sialophosphoprotein (6) and is often associated with osteogenesis imperfecta (OI).

Osteogenesis imperfecta, also known as "brittle bone disease", is an inherited disorder of the connective tissue caused by defects in type 1 collagen. This leads to low bone mass and reduced bone strength, which manifest clinically as multiple intrauterine fractures, skeletal abnormalities and death before adulthood. The clinical presentation of OI can vary from mild clinical signs to perinatal death. Most reports in domestic animals are in calves and lambs but rare cases have been previously reported in some breeds of dogs and cats. (1)

Dentinogenesis imperfecta in humans is usually associated with osteogenesis imperfecta (OI) and for OI studies have shown that it is a genetic disorder caused by mutation of one of the following genes *COL1A1*, *COL1A2*, *LEPRE1* or *CRTAP* (7).

In dogs, mutation of one of the following genes has proven to cause osteogenesis imperfecta *COL1A1*, *COL1A2*, and *SERPINH1* (10).

Material and methods

Radiographs showed a very large pulp cavity in all teeth, very thin dentin, crown fracture with pulp exposure in 304 and 404 (Fig. 2), but also an abnormal density of the cortical bone in the mandible (Fig. 1). The owner reported that the deciduous teeth had the same clinical presentation.

Fig. 1. *Radiograph of the skull left lateral – abnormal density of the cortical bone and large pulp chambers with a very thin layer of dentin*

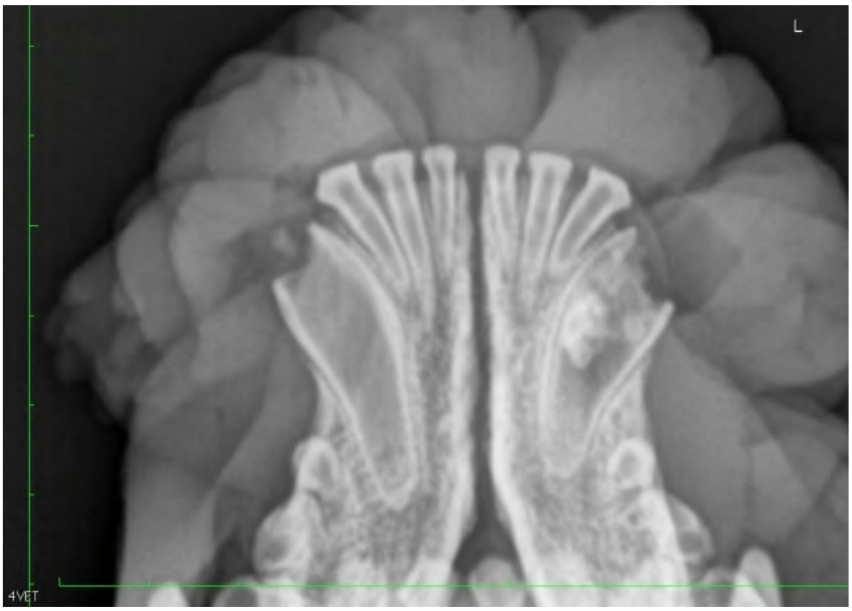

Fig. 2. *Radiograph of the rostral mandible – crown fracture with pulp exposure 304 and 404*

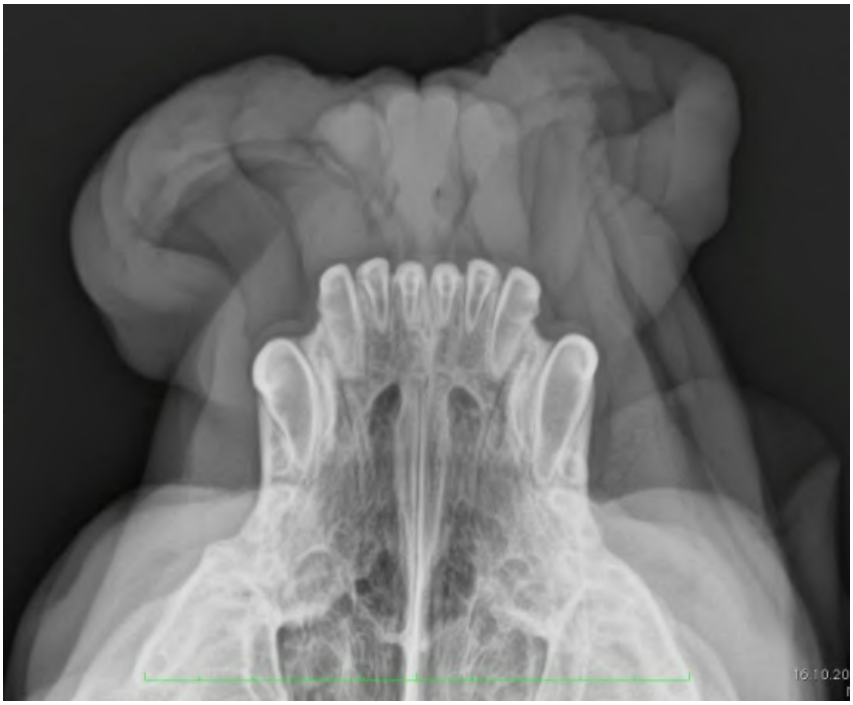

Fig. 3. *Radiograph of the rostral maxilla – large pulp chambers with a very thin layer of dentin*

The dog previously had 2 surgeries in both elbows in another clinic for bilateral elbow dysplasia. Hera is also blind with both eyes; there is no vascularization in the eyes.

Antibiotics (amoxicillin with clavulanic acid 20 mg/kg BID) and analgesia (meloxicam 0.1 mg/kg SID) were immediately started and the patient was booked for a dental procedure a week later. Haematology and routine biochemistry were normal.

The first dental examination under anaesthesia revealed 6 crown fractures with pulp exposure (109, 110, 209, 210, 304, and 404). All teeth were mildly translucent with a pink, opalescent hue. Bilateral maxillary and mandibular blocks with lidocaine 2 mg/kg were performed. We extracted 109, 110, 209, 210, 304 and 404 and tried to seal with the remaining ones. The dental extractions were very difficult, but the healing was good (as you can see in the images from the second dental procedure). The gums were sutured with PDS 3/0.

As oral homecare only chlorhexidine rinse was recommended because of the risk of fracturing the teeth when attempting to brush them. Antibiotics and pain relief medication were continued for another week after the dental procedure.

Fig. 4. *Complicated crown fracture (CCF) 304 – 1st dental procedure*

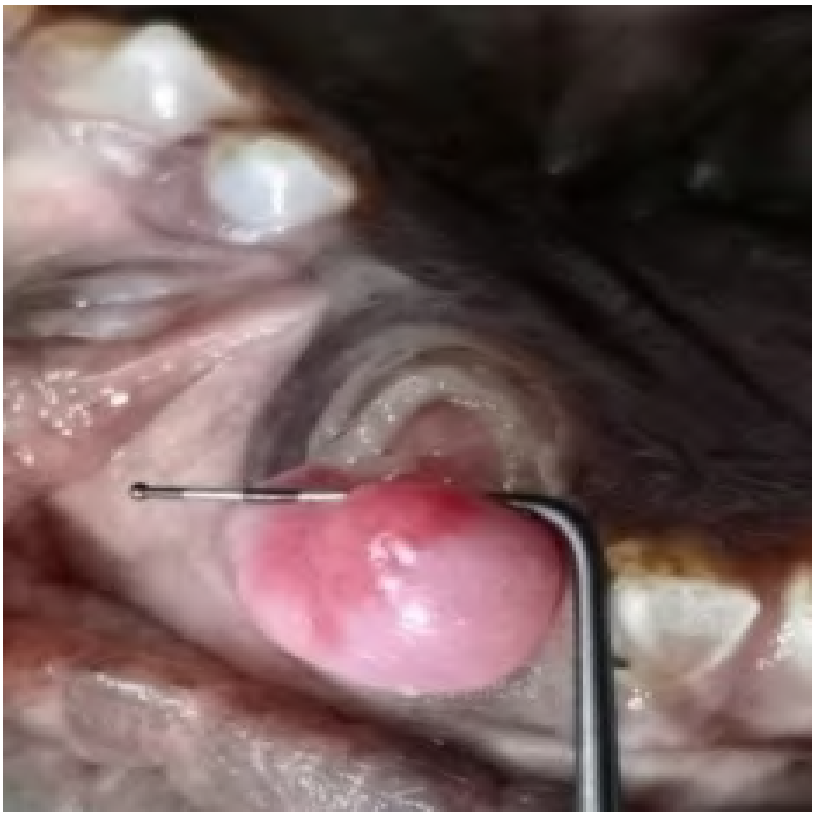

Fig. 5. *404 with CCF and pulpar granuloma – 1st dental procedure*

Fig. 6. *Dental extraction of 404 – 1st dental procedure*

Fig. 7. *Clinical view of the right mandible – 1st dental procedure*

Fig. 8. *Clinical view of the left maxilla: CCF 109 and 110 – 1st dental procedure*

At this first dental procedure (Fig. 4-8), we took a blood sample to see what the D3 vitamin, calcium and parathoyroid hormone levels were. Results showed that Hera had hypoparathyroidism (PTH level was 1.2 pg/ml, almost 16 times lower than the physiologic range) and we recommended a thyroid ultrasound, which is not available unfortunately.

Also B12 vitamin was low, so the patient received B12 supplements.

After the first procedure, the recovery was fast, the dog started eating the next day, but only very soft food.

Fig. 9. *Clinical view of the right maxilla and mandible – tooth wear of all teeth is more pronounced – 2nd dental procedure*

Fig. 10. *Clinical view of the right maxilla – 2nd dental procedure*

The second dental procedure (Fig. 9-15) took place on the 23rd of February 2019 when we performed extractions of 208 and 209 retained roots. The recovery was even better than the first one. Hera received clindamycin 11 mg/kg SID and meloxicam 0.1 mg/kg SID for 7 days. Unfortunately, a second set of radiographs was not available for this dental intervention.

Fig. 11. *Clinical view of the right maxilla – 2nd dental procedure*

Fig. 12. *Clinical view of the lower incisors that are even „pinker" then the first time – 2nd dental procedure*

Fig. 13. *Closer look of the right maxilla – 2nd dental procedure*

Fig. 14. *Left upper premolars – retained roots in 208 and 209 – 2nd dental procedure*

Fig. 15. *Left maxilla and mandible – 2nd dental procedure*

Results and discussions

The pathology of this patient is complex: dentinogenesis imperfecta, bilateral elbow dysplasia, hypoparathyroidism, blindness, B12 hypovitaminosis.

Dentinogenesis is the process of dentin production. Dentin is the second layer of the tooth that covers both the crown and the root. There are three main types of dentin (primary, secondary, and tertiary) that represent two different morphological patterns. Primary and secondary dentin have the same histological patterns and are distinguished from one another only by the time of deposition – primary dentin is deposited until root is completely formed, while secondary dentin accounts for all subsequent dentinogenesis throughout the life of the animal. If at one point dentinogenesis is disrupted, tertiary dentin is produced by the damaged odontoblasts or replacement odontoblasts from the pulp. Primary and secondary dentin have organized tubules opposed to the tertiary dentin matrix which is deposited irregularly. Tertiary dentin may have some wavy or disrupted tubules, but the majority of the matrix is amorphous and often bone□like due to entrapment of odontoblasts. This is why tertiary dentin is also called "osteodentin" (6).

In dentinogenesis imperfecta, the enamel has a normal structure, but may chip away from the underlying abnormal dentin, creating the false clinical impression of an enamel disorder. The affected teeth are often discoloured due to translucence of the abnormal dentin, lost enamel or staining as a result of pulp necrosis. The main complaint for dogs with dentinogenesis imperfecta is the fragility of the deciduous and permanent teeth with clinical consequences of multiple tooth fractures at a young age, fractures that often occur at or near the cementoenamel junction (6). The radiographic appearance includes excessively wide or narrow pulp (indicative of altered dentinogenesis), underdeveloped root

length, and/or periapical lucencies consistent with pulpal necrosis (6). Histologically, the dentin lacks a regular tubular organization and is abnormally thin, resulting in a relatively wide pulp chamber (6). In DI, the inner surface of dentin contains indistinct dentinal tubules and an artefactually detached lining layer of dysplastic odontoblasts. In normal tooth development, odontoblasts have a columnar shape and abut the deep surface of the dentin where their cytoplasmic processes extend into the tubules of the dentin (1). Differential diagnosis for dentinogenesis imperfecta: generalized enamel hypoplasia, pulpitis, attrition/ abrasion, dentin dysplasia. Given the background of association between dentinogenesis imperfecta and osteogenesis imperfecta, the possibility of a mild form of OI cannot be excluded in this case.

Hypoparathyroidism is an endocrine disorder in which the PTH levels are low, but also hypocalcaemia and D3 hypovitaminosis are present. Possible causes of the disease are diffuse lymphocytic parathyroiditis in adult dogs, destruction of parathyroids by primary or metastatic neoplasms in the anterior cervical area, and atrophy of parathyroids associated with chronic hypercalcaemia or agenesia of the parathyroid glands in pups. (8)

Hypoparathyroidism in this patient is a very odd finding taking into consideration that only the PTH levels were low and the other parameters were within normal limits. Given the age of the patient, agenesia of the parathyroids is a possibility. Although further investigations would be required as the patient had no clinical signs of hypoparathyroidism (neuromuscular excitability, tetany, weakness and intermittent tremors of individual muscle groups that progress to generalized tetany and convulsions), but there is abnormal bone density of the skull (8).

Blindness is could be a consequence of hypothyroidism (calcification of the retinal blood vessels) or it may not be related to it.

B12 hypovitaminosis was an incidental finding (B12 was tested by mistake by the referring laboratory).

Conclusions

The dental pathology in this case is a very rare congenital dental condition called dentinogenesis imperfecta or “Shell Teeth”, in which teeth have large pulp chambers and insufficient coronal dentin. The treatment of this dental disease is full mouth extractions, but given the very high level of difficulty of the extractions, we chose to extract only the fractured teeth. It may be a consequence of a congenital hypoparathyroidism, which would also explain the other pathological signs (blindness, bilateral elbow dysplasia).

The history of the patient, clinical and radiological presentation guided us well enough to the diagnosis, although it would have been ideal to have access to more investigations (thyroid ultrasound, more biochemistry parameters, histology of a tooth, PCR for identification of mutation of the DSPP gene or one of the other genes associated with OI), but unfortunately they were not available.

Given the congenital character of the disease, patients affected by it should be spayed or neutered.

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CANINE HYPOTHYROIDISM: ETIOPATHOGENESIS AND SYMPTOMATOLOGY – MINI-REVIEW

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Abstract

Hypothyroidism is the most common endocrine disorder which might occur in dogs, followed by diabetes and hypercorticism.

Primary hypothyroidism is the most common, and is the result of primary thyroid gland insufficiency associated with either lymphocytic thyroiditis or idiopathic follicular atrophy, both of which occur with an approximately equal frequency. Lymphocytic thyroiditis is considered an immune-mediated disease, while pathogenesis of idiopathic follicular atrophy is unknown.

It occurs more frequently in medium and large dogs, such as: Doberman, Irish Setter, Pinscher, Pomeranian, Spaniel, Golden Retriever, with a maximum incidence between 4-6 years (less than 2 years old) and no sex predisposition.

Clinical signs become evident after more than 75% of the gland is destroyed. These usually occur after a longer period of time (1-3 years), being a slow destructive process.

Clinical signs are quite variable and depend mostly on the dog's age and the moment of occurrence of thyroid hormone deficiency. In adult dogs, the most common clinical signs are the result of decreased cellular metabolism and its effects on mental status and physical activity.

Skin, neuromuscular and reproductive disorders predominate, and rare clinical signs in adult dogs are ocular, gastrointestinal and haematological disorders, while in young dogs the main clinical manifestation is thyroid dwarfism.

Keywords: *hypothyroidism, dog, thyroiditis, clinical signs.*

Introduction

Hypothyroidism is the most common endocrine disorder that can occur in dogs, followed by diabetes and hypercorticism (6, 7, 13). Hypothyroidism has as its aetiology the deficiency of thyroid hormones. As the optimal level of thyroid hormones (T3 and T4) decreases, so does the metabolic rate (2).

The rate of hypothyroidism in dogs is between 0.2% and 0.8% and is common in medium and large dogs, such as: Doberman, Irish Setter, Pinscher, Pomeranian, Spaniel, Golden Retriever, aged between 6 months and 15 years, with a maximum incidence at the age of 4-6 years (rarely less than 2 years). There are no differences between sexes, with neutered animals (both females and males) having a higher risk of disease (2, 3, 4, 6, 9).

Although this dysfunction can be anywhere on the hypothalamic-pituitary-thyroid axis, it can lead also to thyroid hormone deficiency in >95% of clinical cases of primary hypothyroidism in dogs, that may result from self-destruction of the thyroid gland and only in 5% or less (secondary hypothyroidism) is due to TSH deficiency (pituitary or hypothalamic) (1). The two most common causes of primary hypothyroidism in adult dogs include: lymphocytic thyroiditis and idiopathic atrophy of the thyroid gland. Lymphocytic thyroiditis, probably mediated by immunity, is histologically characterized by a diffuse infiltration of the gland by lymphocytes, plasma cells and macrophages and results in the progressive destruction of follicles and the appearance of secondary fibrosis. Idiopathic atrophy of the thyroid gland is characterized histologically by loss of thyroid parenchyma and replacement with adipose tissue (4, 13).

Pluriglandular syndromes in humans are very common compared to dogs. In the literature there are data related to pluriglandular damage in dogs, such as Smith syndrome (primary hypothyroidism and primary hypoadrenocorticism) (8).

Etiopathogenesis. The causes of hypothyroidism in dogs can be multiple: tumour disorders in the hypothalamic-pituitary-thyroid axis, thyroid disorders of an autoimmune nature, genetic disorders and iatrogenic disorders.

Tumours with hypothalamic location influence the production of TRH (Tireotropin realeasing hormone) – *tertiary hypothyroidism*. Tumours at the pituitary level influence the production of TSH – *secondary hypothyroidism* or at the thyroid level influence the secretion of T3 and T4 – *primary hypothyroidism*. It should be noted that 75% of dogs with thyroid tumours have T3 and T4 values within normal limits (3, 13).

Thyroiditis in dogs is usually *autoimmune,* although molecular and immunological pathogenesis has not been fully elucidated. Due to the absence of fibrosis and inflammation, it is unclear whether follicular atrophy is a distinct syndrome or is the effect of thyroiditis. Antithyroglobulin antibodies are present in 36-50% of dogs (13).

Genetic disorders – congenital hypothyroidism (cretinism). The genetic predisposition to thyroiditis has been described in the Beagle and Barzoi breeds. It can be primary, produced by iodine deficiency, thyroid dysgenesis or dishormonogenesis, but also secondary, by TSH and TRH deficiency (3).

Iatrogenic hypothyroidism can be found after the application of long-term treatments with high doses of iodine, antithyroid drugs and in thyroidectomies (3). In adult dogs, a spontaneous form of hypothyroidism is the result of a progressive autoimmune process, leading to lymphocytic infiltration and the disappearance of thyroid follicles. The so-called idiopathic forms, in which the thyroid is atrophied, without inflammatory infiltrate is considered to be the end result of an autoimmune disorder (9).

Clinical symptoms. Many functional disorders have been reported and associated with hypothyroidism, with the aetiology of reduced basal metabolism, manifested by reduced mental function, lethargy, exercise intolerance, associated with weight gain without increased appetite (10). Skin, neuromuscular and reproductive disorders predominate.

Weight gain in some dogs, without an increase in appetite, may be the first sign of hypothyroidism.

Dermatological signs have a frequency between 60-80% in dogs with hypothyroidism. Frequently, in this condition, there is a thinning of the hair on different areas of the body, often alopecia being symmetrical bilaterally, not itchy. The areas initially affected by hair loss are those that have greater frictional wear, such as the tail and the cervical area (2, 5).

Hyperkeratosis is a common condition in hypothyroidism, which is characterized by an increase in the corneum layer of the skin. Hyperpigmentation is more common in areas with alopecia, as well as in the dorsal portion of the nose and the distal portion of the tail, commonly found in dogs with hypothyroidism. Sometimes only the tail is affected, with the appearance of a "rat's tail". In humans, the nails detach from the nail bed (onycholysis), the process being described in patients with hypothyroidism. Oncolysis in dogs with hypothyroidism is uncommon (4, 13).

Mixedema can also develop due to the accumulation of glycosaminoglycans and hyaluronic acid in the dermis and subcutaneous. These substances bind considerable amounts of water, which leads to noticeable thickening of the skin. Mixedema is located predominantly in the region of the face and forelegs, expressed by thickening of the facial folds and lowering of the eyelids, imposing a sad face on the animal (4).

Neuropathies are common in middle-aged adult dogs, usually in large breeds, and often without specific clinical signs of hypothyroidism. Hypothyroidism is associated with polyneuropathy. Peripheral neuropathies can also affect cranial nerves that cause abnormalities such as tilting of the head, facial nerve palsy, strabismus, nystagmus, facial tenderness, laryngeal paralysis, muscle weakness with crawling limbs while walking and sometimes myalgias, limping. Neurological signs are present in 7.5% of cases of hypothyroidism in dogs. *Neuromuscular signs* are due to demyelination and axonopathy, accumulation of mucopolysaccharides in the perinerium and endonerium, atherosclerosis and hyperlipemia (11, 12). The clinical manifestations of animals with central nervous system damage are represented by ataxia, walking in a circle, sometimes vestibular syndrome (4, 9, 11).

Reproductive disorders in males are manifested by testicular atrophy, oligospermia and azoospermia, and in females by disruption of the oestrous cycle ("quiet" heat, prolongation of anoestrus, prolonged bleeding during oestrus – blood hypocoagulability) – infertility, abortion, sometimes galactorrhea (1, 4).

Eye damage is not common in hypothyroidism, but high blood cholesterol and circulating fat can sometimes lead to corneal dystrophy. This lesion is usually represented by a small white spot on the surface of the eye. Other eye signs are corneal ulcer, dry kerato-conjunctivitis, anterior uveitis and various retinopathies (4).

Cardiovascular symptoms are discovered after the electro-cardio-graphic examination (ECG) where there is a decrease in the amplitude of the R wave, bradycardia and atrio-ventricular block, even atrial fibrillation (4). Myocardial

infiltration with mucopolysaccharides or impaired vasodilatory capacity of the coronary artery, possibly secondary to elevated alpha-adrenergic activity or atherosclerosis, may be a prolonged impairment of cardiac function (7).

Haematological damage. The results of blood tests, respectively of the hemogram, of the biochemical examination, as well as the urinary analysis can support a diagnosis of hypothyroidism and exclude other diseases. Mild non-regenerative anaemia and hypercholesterolemia can occur in 35-75% of hypothyroid dogs (4). Anaemia due to a reduction in erythropoietin, following a reduction in serum T4 levels, as well as decreased intestinal absorption of iron, folic acid and vitamin B12. Hypercholesterolemia is always present, mainly due to the role of thyroid hormone in stimulating lipid synthesis, mobilization and degradation of liver lipase and lipoproteins, as well as on low-density liver lipoprotein (LDL) receptors (2). Reduced lipolysis causes moderate weight gain and hyperlipidaemia, while reducing the degradation of cholesterol to bile acids quickly leads to hypercholesterolemia and promotes the development of atherosclerosis (10). Uncommon abnormalities include slight increases in alkaline phosphatase, alanine aminotransferase, and creatinine kinase.

The main signs and symptoms *after parturition*, which may suggest a thyroid condition (hypothyroidism), include an enlarged fontanelle (which must be closed at birth), hypothermia, hypoactivity, difficulty sucking and abdominal dysthymia (6).

As the puppy with hypothyroidism ages, the head becomes relatively large and coarse, and the tongue becomes wide and thick, the torso wide and the legs short, accompanied by cretinism. It is frequently associated with prolonged persistence of puppy hair, alopecia, delayed tooth eruption and persistence of baby teeth until adulthood, sometimes goiter (4).

The radiographic examination of the spine and long bones reveals a delay in the maturation of the skeleton and vertebral bodies, abnormally short, which can even lead to compression of the spinal cord. In the case of long bones, the appearance of the ossification centres, as well as of the epiphyseal growth cartilages is delayed. Epiphyseal dysgenesis can also be associated with scattered ossification outbreaks, giving the epiphysis a granular appearance. When the disease is not detected in time, the physical appearance of the vertebral bodies and long bones remain open (unfinished and growing) until the age of three or four years (1).

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COMPARATIVE ONCOLOGY – AN INTEGRAL PART OF THE NEW *ONE HEALTH* CONCEPT

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Abstract

Globally, the remarkable progress of scientific research and biotechnology, doubled by improving living conditions, has led to human well-being and increased life expectancy. However, in contrast to this positive evolution, the health challenges are constantly increasing, induced by the appearance of more and more diseases with uncontrolled evolutions. Due to this fact, the new global medical concept One Health *has been established in order to bring together the concerns of specialists in all fields regarding health, including food, nutrition and occupational, with the primary direction of Primary Life Prophylaxis.*

As an integral part of this One Health *concept, comparative oncology comes together as a unitary whole to bind all the knowledge gained by human, veterinary and experimental medicine on the aetiology, evolution, diagnosis and therapy of cancer, thus creating a corollary on this serious disease of the 21st century. Starting from this desideratum, in this paper we present some of the reasons why the association of human medicine with veterinary medicine is a step forward in the fierce fight against neoplasia.*

Keywords*: One Health, comparative oncology, canine tumours, human oncology*

Introduction

One Health is a new medical approach that recognizes that human health, animal health and ecosystem health are inextricably linked. It seeks to promote, improve and protect the health and well-being of all species by strengthening collaboration between human beings, veterinarians and all other professional categories with a role in health (1, 2).

The concept is not new, the recognition that environmental factors have an impact on health dates back to antiquity when the Greek physician Hippocrates

(460 BC-370 BC) promoted the fact that public health depends on a clean environment (6). In the mid-1800s, Dr. Rudolf Virchow recognized the link between veterinary medicine and human medicine. He defined the term "zoonosis" to describe a disease that can be transmitted from animals to humans and actively supported veterinary medical education.

The use of the *One Health* concept, in its full form, occurred recently in 2003, in connection with Ebola and haemorrhagic fever, when William Karesh stated that "Human or livestock or wildlife health can't be discussed in isolation anymore. There is just one health. And solutions require everyone to work together at all different levels" (5).

In 2004, the World Health Organization (WHO), the Food and Agriculture Organization (FAO) and the World Organization for Animal Health (OIE) implemented the *One Health* concept in their strategic plans, WHO defining it as "an approach regarding the development and implementation of programs, policies, legislation and research in which several sectors communicate and collaborate to achieve better public health outcomes" (WHO, 2017).

In Romania, the *One Health* concept started in 2015 with the founding of the *One Health – New Medical Concept Association, Romania*. It was extended in 2019, when the *One Health Institute of Comparative Medicine* was created, within the Romanian Academy of Medical Sciences, whose main objective is the primary prophylaxis of diseases in humans, by corroborating and disseminating information on aspects of global pathology, within the chain of living environment - occupational - nutrition and feeding - animal pathology - humans (Fig. 1).

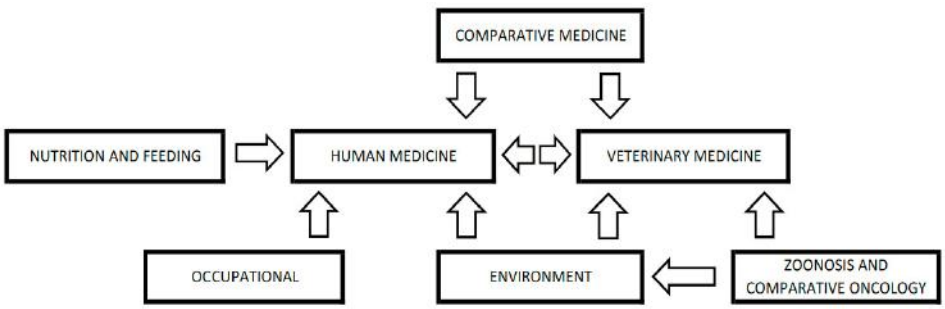

Fig. 1. *Components of the One Health concept*

Comparative Oncology – an integral part of Comparative Medicine

Comparative medicine is a fundamental part of the new *One Health* medical concept with major implications in translational and biomedical research of human and animal pathology (3, 7), pointing the most important medical advances of humanity (8).

The basic components of Comparative Medicine are ZOONOSIS and COMPARATIVE ONCOLOGY.

Comparative oncology comprises a cross-disciplinary approach that has recently gained significant importance due to the strong anatomical and physiological similarities between mammals and humans, especially dogs, which have been used for a long time in both preclinical drug testing as a toxicological model and more importantly, in the study of pathogenesis (the study of cancer-related genes and proteins) and cancer therapy (8-15).

The spectrum of cancers observed in dogs is as diverse as the one observed in human patients. There are many similarities, such as: spontaneous appearance of tumours, immune system reactivity, comparative histological and genetic aspects, response to chemotherapy, tumour heterogeneity, metastasis, tumour recurrence / resistance, etc. (4). Thus, specialized studies demonstrate this fact on tumours such as osteosarcoma, melanoma, non-Hodgkin's lymphoma, leukaemia, prostate carcinoma, breast carcinoma, lung carcinoma, head and neck carcinomas, soft tissue sarcomas and bladder carcinoma (Fig. 2) (8).

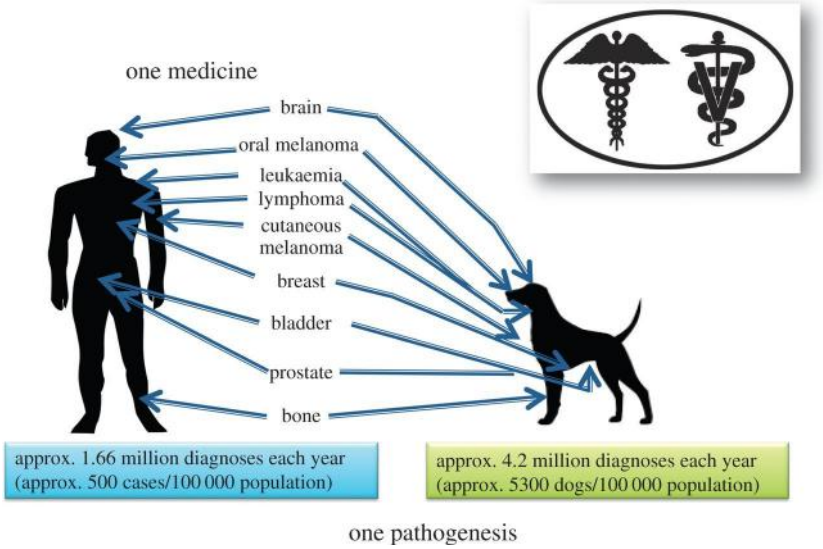

Fig. 2. *Remarkable similarity between human and canine cancers location* (17)

Also, an element not to be neglected, which is also supported by the *One Health* concept, is represented by the quality of the canine species to function as a bio-sentinel of cancer in a family. From our own observations, we identified two situations that we consider important, namely:

1) in many families in which people with cancer have been diagnosed, especially breast neoplasms, over time, the pet of the canine species, has also developed a similar breast cancer;

2) on the other hand, when in a family, the canine pet had a form of cancer, in a variable period, one or more cancer diseases also appeared in the members of the respective family.

At first glance, one could speak of a possible interspecies transmission of cancer, but, in reality, it is an identification, in the same area, of some onco-inductive etiological factors, which affect both humans and the animals with which they cohabit (16).

Conclusions

1. *One Health* – A Health for People, Animals and the Environment – is the new global medical concept that requires the effective cooperation of specialists in the fields that implies health, but also in related fields, to find the best solutions for a safe and comfortable future, in within a constantly changing biodiversity.

2. In broad practice, the existence of a single medicine, conferred by the new global *One Health* concept, offers oncology the opportunity to better understand the pathogenesis and therapy of cancer in the human and animal world, due to the interspecific similarity of the disease.

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