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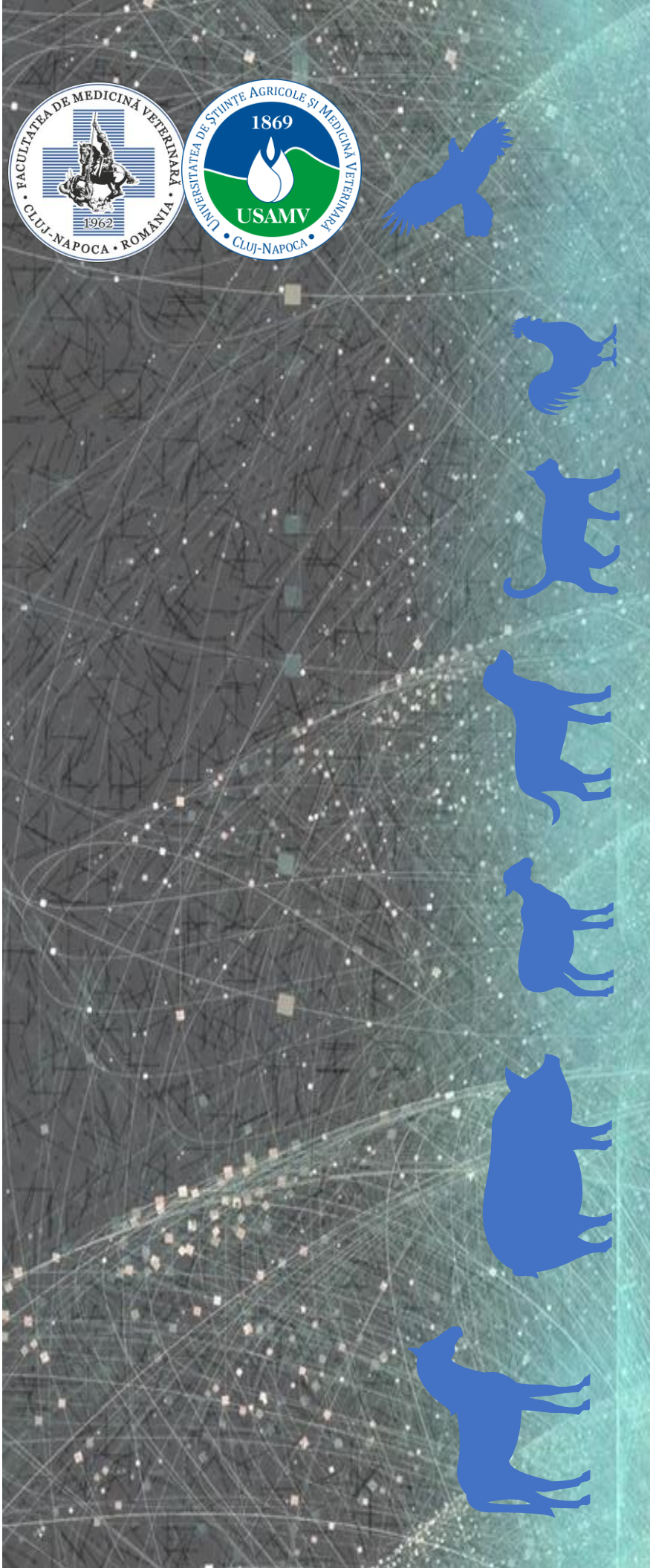

Societatea Romana Veterinara de Neurologie, Neurochirurgie si Medicina comportamentala
NEUROVET

Table of contents

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Case report

The use of Complementary medicine and Pneumo-Acupuncture to treat muscle atrophy and chronic respiratory disorders in a dog: A case report

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Abstract: A 5-year-old female Malinois dog was referred to the Faculty of Veterinary Medicine of Cluj-Napoca for complementary medicine treatment. The patient was diagnosed with severe muscular atrophy in the temporal region but also with ab-ingestis pneumonia due to improper use of the masticatory muscles. After 2 months of symptomatic therapy, partial cure of pneumonia was achieved, but the patient was left with an acute cough during the night. We decided to start a therapeutic protocol combining various Chinese therapies including acupuncture, electroacupuncture, pneumo-acupuncture and herbal therapy. The patient's condition improved considerably even after the first sessions, coughing episodes were reduced and breathing became normal. As for muscle atrophy, the results were partially improved. At the end of the treatment scheme, although the patient was not completely cured, the quality of life was significantly improved.

Keywords: canine, acupuncture, pneumo-acupuncture, muscle atrophy.

1. Introduction

In dogs, lung lesions are very similar to those seen in humans mostly characterized as interstitial pneumonia(1). A common clinical diagnosis is represented by the bacterial pneumonia and the underlying causes may include viral infections, aspiration injury and inhalation of foreign body(1). From a traditional Chinese medicine point of view, forms

of pneumonia are known as "acute febrile disease caused by Pathogenic Wind" or "invasion of the Lung by Pathogenic Heat"(2).

The atrophy of the frontal temporal muscles can have different causes which might include a low level of body fat with pronounced or rapid weight loss, exaggerated skeletal contours, progressive idiopathic atrophy, deformities due to impaired nerve function or even post-operative, also depending on the patient's age and health (3).

Pneumo-acupuncture is a Traditional Chinese veterinary medicine (TCVM) treatment that involves injecting subcutaneous air into specific acupuncture points. Large animals, such as horses, are more commonly treated with this procedure, although large dogs can also benefit. This technique is frequently used to treat Deficiency conditions like Wei Syndrome, paresthetic conditions such as suprascapular nerve paresis, facial nerve paresis, or any other local muscular atrophy(4).

Although the exact mechanism by which acupuncture improves breathing is not fully understand, evidence suggest that it may assist the relax of the muscles involved in breathing. Acupuncture has been shown to release chemicals that dilate the airways, making breathing easier(4).

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The aim of this study was to present and analyze the benefit of complementary medicine. From the author's knowledge, there are few information in the literature about this type of treatment for dogs with respiratory disorders.

2. Materials and Methods

Case description

A five-years-old, Malinois breed female dog, was presented because of respiratory disorders and progressive muscle atrophy in the temporalis region. The dog jumped on a fence and felt on her back two-months prior consult. According to the owner, the dog suffered hindlimb ataxia for the following three days after the accident, but the symptoms improved significantly after getting one dose of NSAIDs. The dog began to eat less after two weeks and experienced anorexia and muscular atrophy in the temporalis area (Figure 1). The neurological examination showed the following: the menace and palpebral reflex response were present, so were the vibrissae, oculocephalic and gag reflexes. For the auricular reflex, when we twitched the ear, the dog responded, but when we stimulated the skin on the temporalis region, the dog did not respond. We decided to pursue with the imagistic investigations.

Imagistic investigations suggested, such as radiographs and Computed tomography (CT) scan revealed lesion that correspond with late episode of pneumonia, possible aspiration (Figure 2), and on the head revealed a skull chronic fracture with thickening of the calvarium on the medial surface due to healing process. There is also a severe muscle of the temporal and zygomatic muscles (Figure 3A, B). A muscle biopsy was performed; however, it came negative for masticatory muscle myositis. The blood samples for serum chemistry profile were in normal range, except for the ALT which might have been increased because of the muscular dystrophy (Table 1), while the CBC showed a slight leukocytosis (WBC: 21.5 10ˆ9/1, N: 5.5-19.5). As a conventional therapy, the dog received antibiotics, bronchodilators, NSAID's as well as steroids, vitamins, essential amino acids, and L-carnitine for almost 3 months. After no major improvements, we decided to try also Traditional Chinese medicine to improve the breathing and the temporalis muscle.

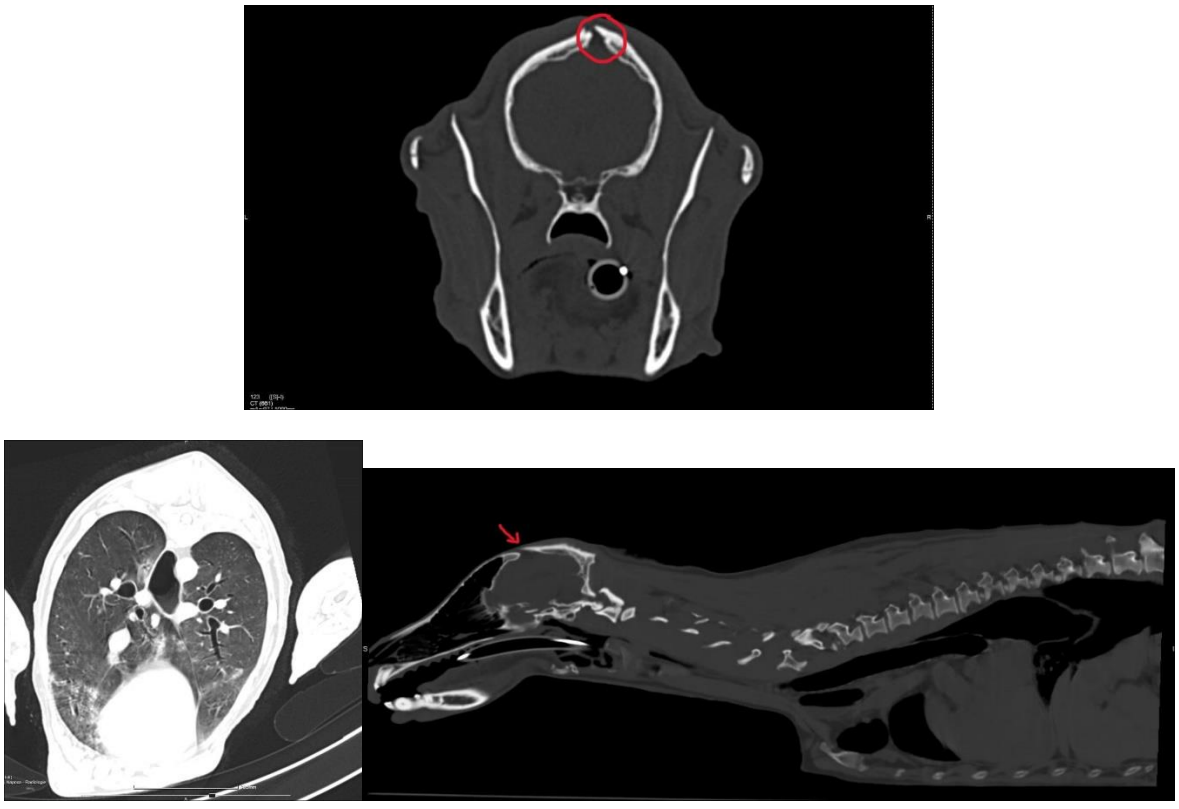

Fig. 2. CT image of a dog with diffuse pneumonia; **3A, B.** CT scan of the head showing fracture of the skull and local hemorrhage. (Original archive)

From a TCVM examination, the dog was an Earth Constitution. She was friendly with people and other dogs; she used to be active and laid-back type. According to the owner, the dog has become increasingly sleepy in recent weeks and more sedentary. The tongue was pale, wet, with cackles (Figure 4), the nose was dry, the ears and feet were cold. The cough is more sever during the night. The dog prefers cold instead of heat. The pulse was weaker on the left side. At palpation, it was sensitive to paravertebral muscle, for Bladder Meridian – BL-20/21/23.

The TCVM diagnosis was Kidney Jing Deficiency and Spleen Qi sinking with Lung Qi Deficiency.

Fig. 1. Muscle atrophy in the temporalis area (Before treatment); **Fig. 4.** Tongue is wet, thin with crackles. (Original archive)

A combination of dry-needle, electroacupuncture, pneumo-acupuncture and Herbal Chinese Medicine was performed and at least 10 weekly treatment sessions were planned (Figure 5). The treatments aimed to tonify Kidney Qi and the Spleen Meridian. The treatments were performed using sterile disposable stainless-steel Ac needles with cooper coil handle, size 0.25x0.25mm, guide tubes (Acimut) and stainless-steel Ac needles with plastic handle, size 0.16x20mm, without guide tubes (Cloud and Dragon). Dry needling (insertion at 1-1.5 cm with an intermittent manipulation of the point by twirling clockwise) and EA (40-100 Hz, 1-3V, increasing progressively for 15-20 minutes/session). Pneumo-acupuncture involved air injection, up to 5 ml into subcutaneous tissue in the temporalis region. In order to prevent air embolism, each time before injecting air, we aspirated. For the first days after the treatment, we recommended the owner to keep the dog rested for the air to diffuse without causing undue pressure on surrounding nerves and vessels.

Table 1. Blood sample – Biochemistry

ALB	3.7	2.5-4.4 g/dL
ALP	41	20-150 U/L
ALT	184*	10-118 U/L
AMY	348	200-1200 U/L
TBIL	0.4	0.1-0.6 mg/dL
BUN	18	7-25 mg/dL
CA	10.2	8.6-11.8 mg/dL
PHOS	5.1	2.9-6.6 mg/dL
CRE	0.8	0.3-1.4 mg/dL
GLU	104	60-110 mg/dL
NA+	145	138-160 mmol/L

K+	4.3	3.7-5.8 mmol/L
TP	7.3	5.4-8.2 g/dL
GLOB	3.6	2.3-5.2 g/dL
Hct	51%	30-45 %
Lac	1.8	1-3 mmol/L

3. Results

The principle of treatment was to restore smooth flow of vital energy of Spleen and invigorating the function of the Kidney Qi. The acupoints used are presented in Table 2. During each treatment, a maximum of 10 points were used, depending on the dog's reaction and status health. The acupoints were selected according to TCVM principles, by a trained acupuncturist. For the first two weeks, the treatment sessions were twice per week, and after that one time per week for the following two months.

After the first 3 sessions, the dog began to breath more easily, her cough subsided, and she was becoming more comfortable especially during the night. During each treatment we performed Pneumo-acupuncture in the ST-5, ST-7, SI-19, TH-21, GB-20.

We maintained the treatments for over two months, with significant improvement in breathing (only occasionally cough) but a mild response in muscle atrophy (Figure 6). The dog had a good appetite and began to be more active and playful, that she'd been previously.

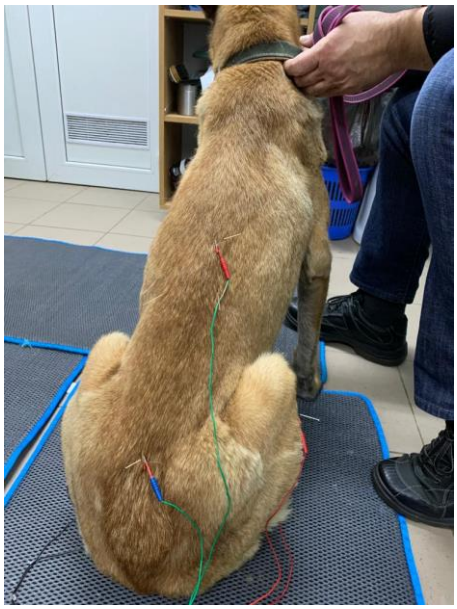

Fig. 5. Aspects during electroacupuncture treatment. **Fig. 6**. After 4 treatments. (Original archive)

We've added herbal formula Qi Performance 0.5g/10 kg twice daily for two months. We started with half a dose for the first three days to make sure there are no adverse reactions.

From a TCVM point of view, the commonly applied principles of treatments are based on the relationship between Yin (vital essence) and Yang (vital function), and between the Meridians (Zang-fu organs). When it comes to pathology, there is an imbalance between the two systems mentioned above, so the relationship is replaced with an abnormal, unbalanced condition, either an Excess or a Deficiency between them.

In our case, we discuss about a Deficiency due to a chronic, long course disease with specific symptoms. The longer the course of the disease, the greater the Deficiency in the body is and more treatments or combination of techniques are needed to achieve a satisfactory result. Tonifying and Warming the body, from a TCVM point of view, involves treating the Deficiency complexes to get the Qi energy, Blood, Vital Essence, and Functions moving(2).

Table 2. Acupoints used

Local points	**GB3, ST5/6/7**
Distal points	GV6, LIV3, LI4/11, SP3/9, ST36/37, LU5/9
Association points	GV20, BL20/21/22/23/24, Bai-Hui

4. Discussion

Reinforcement of the organism consists in using different tonics, for example electroacupuncture or pneumo-acupuncture, to correct the Deficiency of vital energy in the Spleen and Lung Meridians. The most common symptoms of Spleen Deficiency are restlessness, anorexia, muscle atrophy, diarrhea, lack of energy, while the symptoms of Lung Deficiency are shortness of breath, weakness, mucous pallor**(4)**. All Chinese herbs have specific properties that are important signs of their actions. Knowing these properties and flavors helps to guide medical practice. In our case, we used the formula Qi Performance which is the modified Ba Zhen Tang (Eight-Treasure Decoction) and is a tonifying formula, commonly used to treat Qi and Blood Deficiency**(5)**. According to pharmaceutical research when this formula is used in conjunction with enteral nutrition in gastric cancer patients post-operatively, it can further promote elevation of growth hormone levels and improve both nutritional state and immune function**(6)**. In anemic mice with bone marrow depression induced by cyclophosphamide, it promotes proliferation of bone marrow cells. Huang Qi (Astragalus membranaceus) is the main herb in the formula and the tonifying effects of this herbs may be due to an increase in muscle glycogen storage and oxygen carrying capacity together with a reduction in creatine phosphate and protein metabolism, which help combat fatigue**(7)**.

The most common signs of chronic lung condition include daily coughing, shortness of breath or wheezing for more than 2 months. Often the cough can be more pronounced during the night, when the animal is quiet, and can reduce in frequency while is awake and active. In such situations, the differential diagnosis may even be heart failure, pneumonia, allergic lung disease and lung cancer**(8)**. Routine blood test results cannot be considered specific for aspiration pneumonia; however, certain abnormalities may be considered compatible with this condition. Leukocytosis or leukopenia, often with toxic changes present in neutrophils, may be seen on a CBC, but nevertheless a normal result cannot exclude aspiration pneumonia. A serum chemical profile may have normal values or specific results with a comorbidity. An interesting fact is that in Kogan et all's study**(9)**, an increase liver enzymes and a decrease in albumin levels were demonstrated in more than half of the 58 dogs diagnosed with aspiration pneumonia**(10)**.

The imagistic findings showed a chronic fracture of the skull which could be responsible for the muscle atrophy in the temporal region but cannot explain all the symptoms. Even if the CT scan did not show any tumors in the brain, we still decided to pursue for a muscle biopsy in order to exclude other disorders. The result came negative for masticatory myositis, so we did not check for muscle enzymes or inflammatory markers such as creatin kinase or canine C reactive protein. As a differential diagnosis we could have had tumors, autoimmune diseases, or inflammation of one or more components of the central nervous system. The dog also received first NSAID's and then corticosteroids, but still did not improve. Unfortunately, due to financial issue we could not pursue with any other clinical or paraclinical investigations.

Pneumo-acupuncture is a Traditional Chinese veterinary method through which air is introduced under the skin, in the subcutaneous space, to produce a pressure that might stimulate specific acupoints, as well as the muscles and nerves from the affected region**(11)**. Unfortunately, there are few information regarding the efficacy of this procedure, mostly it is mentioned in the literature its use for muscle atrophy, but we could not find relevant study to prove it. Furthermore, the fact that in our case it gave only slight improvement, we still question its efficacy. We can recommend its use for muscles with a lower degree of atrophy, as well in the acute phase of the disease.

While it is not fully understood how the mechanism of acupuncture is working to improve breathing, some researchers suggest that dry needling and electroacupuncture treatments may help to relax muscles involved in breathing**(12)**. It has also been shown that this type of treatment can release vascular and

immunomodulatory factors that distend the airways, making it easier to breath**(12)**. In our case the results were visible during each treatment we performed. Also, we cannot forget about the herbs we mentioned earlier which might also had their role in improving the breathing. In human medicine, a quite common scale used for dyspnea is the modified Borg Dyspnea Scale, which is a 0 to 10 rated numerical score reported by the patient during submaximal exercise after a period of exercise**(13)**. For animals you can see the degree of honking, coughing, inspiratory effort, or the activity status, which can be subjective, and we cannot exclude the owner's assessment of willingness to treat his dog.

The study's limitations include the lack of even more detailed investigations to establish a concrete diagnosis from the classical medicine point of view. These limitations were also due to financial reasons. Furthermore, specific blood samples (for e.g., blood gas analysis before and after each treatment session), MRI, oxygen saturation could be considered important for a good diagnosis. We suggest further studies to be done using TCVM for each pathology on a larger number of patients in order to find the optimum technique for a better outcome.

5. Conclusions

For the respiratory disorder, the patient had a good outcome, while for the muscular atrophy had a modest response. Despite the fact we were unable to cure completely the dog, we were successful in improving quality of life and dyspnea. Acupuncture and herbal medicine are effective for the treatment of chronic respiratory disorders and may be considered a complementary viable treatment.

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Data Availability Statement: The data used to support the findings of this study are included in the article.

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Conflicts of Interest: The authors declare no conflict of interest.

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Case report

Splenic hematoma and pelvic bladder in a spayed German shepherd mongrel bitch (*Canis lupus familiaris*). A case report.

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Abstract: Splenic hematomas represent the most encountered splenic benign masses in dogs (*Canis lupus familiaris*), and they are usually secondary to splenic nodular hyperplasia. In most spayed bitches with urinary incontinence (UI), pelvic bladders are a common finding. In addition, ovariohysterectomy (OHE), hormonal imbalances, and various anatomical anomalies are responsible for the onset of urethral sphincter mechanism incompetence (USMI). This case report highlights the aggravating aspect caused by a splenic hematoma to develop a pelvic bladder in a mongrel bitch, that was sterilized seven years ago. A 14-years-old spayed German shepherd was presented to the Emergency Veterinary Hospital in Cluj-Napoca, with a history of apathy, incontinence, and foul kennel smell, for several months. The diagnostic was based on anamnesis, medical history, imagistic, and routine laboratory assays. The main findings were the presence of a pelvic bladder, splenic hematoma, and chronic cholecystitis. The bitch was admitted for 14 days. Surgical intervention was required, so a splenectomy was performed. Besides the surgical management and the supportive care, the bitch also received treatment for UI with phenylpropanolamine (PPA; Propalin 5%; 1.2 mg/kg 12h PO *prn*). Three days after surgery and treatment, the bitch recovered the urinary tonus, and UI was absent. The bitch was discharged two weeks after the surgical intervention. Splenic hematomas can precipitate the development of UI by partially translocating the urinary bladder into the pelvic cavity (i.e., pelvic bladder), especially in old spayed bitches.

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Keywords: *Canis lupus familiaris*; splenic hematoma; pelvic bladder; OHE; UI; USMI.

1. Introduction

Urinary incontinence represents an uncontrolled or involuntary urine leakage dur ing the storage phase of micturition [1,2]. It is a common pathology in both intact (i.e., 02-0.3%) and spayed bitches (i.e., 20%) [2]. Usually, females with acquired UI suffer from USMI [3,4]. However, the pathophysiology is multifactorial but incompletely elucidated, with OHE, weight, breed, age, and anatomical anomalies as primary contributing factors [5,6]. Nevertheless, the condition comprises hormonal, structural, and functional derangements [2].

Neurogenic factors comprise low and upper motor neuron disorders; detrusor urethral dyssynergia, dysautonomia, and primary bladder atony. Non-neurogenic urinary incontinence (i.e., USMI) includes congenital disorders, detrusor hyperreflexia, anatomical or functional urethral obstruction leading to secondary bladder atony, and bladder

atony due to muscle weakness or medications [2]. Usually, all females suffer from acquired USMI. In addition, USMI and anatomical anomalies may coexist [7].

Nodular lymphoid hyperplasia (NLH) and hematomas are benign, non-neoplastic focal masses [8,9] commonly encountered as splenic or hepatic lesions in older dogs, with a reported incidence between 38-59% and account for most focal canine splenic masses [10,11]. They can also be associated with other splenic or hepatic nodules [12].

Nodular lymphoid hyperplasia is cytologically characterized as a mixed lymphoid population with medium to small lymphocytes, lymphoblasts, few plasma cells, and other cells with no signs of malignancy on smears [8].

Splenic hematomas are blood collections within the tissue, mainly in lymphoid follicular hyperplasia areas with lymphoid aggregates. The coexistence of splenic hematomas and hyperplasia is common in dogs. Usually, splenic hematomas result from NLH since it disrupts local blood flow, causing blood pooling, hypoxia, bleeding, and necrosis. Usually, dogs with splenic hematomas survive the postoperative period and have an excellent outcome [10,12–14].

In the present case, we highlight the potential of splenic masses to increase abdominal pressure on urinary bladders, causing USMI-derived UI by partially translocating the bladder into the pelvic cavity in a sterilized 14-years-old mixed German shepherd bitch.

2. Materials and Methods

2.1. Case description

A 22 kg, nulliparous 14-year-old spayed German shepherd mixed breed female was presented to the Small Animal Emergency Hospital in Cluj-Napoca with a history of apathy, weakness, polyuria (PU), and foul urinary smell kennel for several months. In addition, the owner noticed the dog urinating while sitting or sleeping on the kennel floor, and the hindlimbs were always soaked in urine. The bitch was presented to the same hospital seven years ago for sterilization. At the same time, the bitch was diagnosed with recurrent bilateral otitis (i.e., *Pseudomonas aeruginosa*) due to a food allergy. Besides the treatment received for the food allergy (Posatex, Vet Pharma Friesoythe, Germany; Enrofloxacin; Baytril, USA; and Hypoallergenic food, Royal Canin, France) and the vets' regular visits for deworming and vaccination, the bitch had no other medical history.

During the check-up, the bitch was panting (R=100), presented bilateral senile cataract, enlarged mandibular and popliteal lymph nodes, a distended and sensitive abdomen, and vulval scalding. The bitch showed normal lung and heart sounds, pink mucosae membranes, and other vital signs within the physiological limits (P=100; T=39.2^{0}C; TRC=1 "). From the cephalic *vena,* blood was collected for total solids (TS) (Element RC, Scil, Germany), a complete blood count (CBC) (VetScan, Abaxis, UK), and blood gases (Prime VET, Nova Biomedical, USA) assays.

An abdominal splenic space-occupying lesion was discovered on ultrasound (MyLabDeltaVet, Esaote, Italy); a computed tomography (CT) was recommended. In addition, an echo-guided urine sample was obtained aseptically from the urinary bladder, and a stool sample was collected for coproparasitological evaluation. The specimens were sent to the Microbiology, Pathology, and Parasitology Departments (University of Agricultural Sciences and Veterinary Medicine, Cluj-Napoca) for culture, sensitivity, sediment, cytology, and stool interpretation, respectively.

2.2. Anesthetic and CT protocol

A 20G safety IV catheter (B. Braun Melsungen, Germany) was placed on the anterior right limb, and a lactated Ringer's solution (Ringer-Lactat, B. Braun Melsungen, Germany; 10 ml/kg/h IV) was administered. The bitch was premedicated with midazolam (Dormicum 0.1%, F. Hoffmann-LA Roche Ltd., Switzerland; 0.2 mg/kg IV) and ketamine (Narkamon Bio 10%, Bioveta, Czech Republic; 1.5 mg/kg IV). Next, the dog was induced

with propofol (Propofol-Lipuro 1%, B. Braun Melsungen, Germany; 3 mg/kg IV) and maintained with isoflurane/oxygen (Isoflutek 1000 mg/g, Laboratorios Karizoo S.A., Spain) after endotracheal intubation using a 9.0 mm endotracheal tube (Well Lead Medical Co. Ltd., China). Finally, an abdominal and thoracic contrast CT scan (SOMATOM Scope, Siemens, Germany) with iohexol (Omnipaque 35%, GE Healthcare AS, Norway; 2 ml/kg IV) was performed under general anesthesia.

2.3. Anesthetic and surgery protocol

After the imagistic evaluation, it was decided to perform an exploratory laparotomy on the same day. The bitch was premedicated with pethidine (Mialgin 5%, Zentiva, Romania; 4 mg/kg IM in one dose) and midazolam (0.3 mg/ kg IV). Anesthesia was induced with ketamine (2 mg/kg IV) and propofol (2-4mg/kg IV) and was maintained with isoflurane and oxygen mixture (MAC=0.9%-1%). The dog received during the surgery a constant rate infusion (CRI) of lidocaine (Xilină 2%, Zentiva S.A., Romania; 2.4 mg/kg/h, 24h IV) and ketamine (0.6 mg/kg/h, 24h IV), in Ringer's perfusion.

Next, the bitch was placed in dorsal recumbency and was aseptically prepped on the ventral aspect of the abdomen with chlorhexidine 2% (Lifo-Scrub 2%, B. Braun Melsungen, Germany) and isopropyl alcohol (Alcool Sanitar 70%, Dual Prod, Romania). In addition, a midline abdominal anesthetic blocage was also performed with bupivacaine on the *linea alba* (Bupivacainǎ 0.5%, Infomed Fluids SRL, Romania; 1 mg/kg SC). During the surgical intervention, all the vital signs, including pulse oximetry, ECG, and capnography, were evaluated with a noninvasive multi-parameter monitor (Life Vet 8c, Eickemeyer, Germany).

A ventral midline abdominal incision was performed from xiphoid to pubis for complete abdominal exploration. The edges of the incision were protected with abdominal pads. Approximately 100 ml of hemorrhagic fluid was present in the abdominal cavity. The spleen was exteriorized and appeared larger in volume, with macroscopic structures in the parenchyma (Figure S1). The capsule was not intact. The liver also presented small reddish nodules on the surface. After the abdominal cavity was explored, the spleen was removed, and a hepatic biopsy was collected. Both specimens were rushed to the Pathology Department for further histopathological evaluation.

The blood vessels were double ligated and transected with 3-0 Polidioxanone monofilament absorbable (PDO; BioSintex, Ilfov, Romania) suture material at the splenic hilus. Next, the abdominal wall was closed in three layers. First, the aponeurosis of the *rectus abdominis* muscle was sutured with a simple interrupted pattern with 2-0 PDO (BioSintex, Ilfov, Romania) suture material; the subcutaneous connective tissue was sutured in a continuous surjet and tied with an Aberdeen knot with 2-0 PDO (BioSintex, Ilfov, Romania) suture material. Finally, the skin suture was performed with a simple “X" pattern with a 2-0 nylon (BioSintex, Ilfov, Romania) suture material. The surgical procedure lasted 45 minutes, and no complications occurred.

2.4. Treatment plan

The lidocaine and ketamine CRI was continued for 24h, and the post-op protocol consisted of administration of ceftriaxone (Cefort 100%, Antibiotice, Romania; 22 mg/kg 12h IV for 10 days), metamizole (Novasul 50%, Richter Pharma, Austria; 25 mg/kg 12h IV for 3 days), gabapentin (Grimodin 300 mg/tb, Egis Pharmaceuticals PLC, Hungary; 300 mg/ administration 24h PO for 10 days), pantoprazole (Controloc 40 mg/tb, Takeda GmbH, Germany; 1 mg/kg 24h PO for 14 days), and PPA (Propalin 5%, Vetquinol, France; 1.2 mg/kg 12h PO for 14 days). After 3 days of treatment, metamizole was changed with meloxicam (Meloxidolor 2%, Le Vet Pharma, Holland; 0.2 mg/kg 24h SC for 7 more days).

3. Results

3.1. Imagistic results

Computed Tomographic findings were consistent with a large, cavitated hypoattenuating splenic space-occupying mass with a heterogenic structure with multiple fluid attenuating areas (Figure 1a,d).

The liver also had multiple hypoattenuating areas with a cyst-like structure. The gall bladder was mildly distended with hypoattenuating content (Figure 1b,e). The urinary bladder was in semi plentitude and presented with normal contrast uptake due to urine filtration and displaced caudally into the pelvic region (Figure 1c,f).

The gastrointestinal tract, alongside both kidneys, presented no pathological alterations.

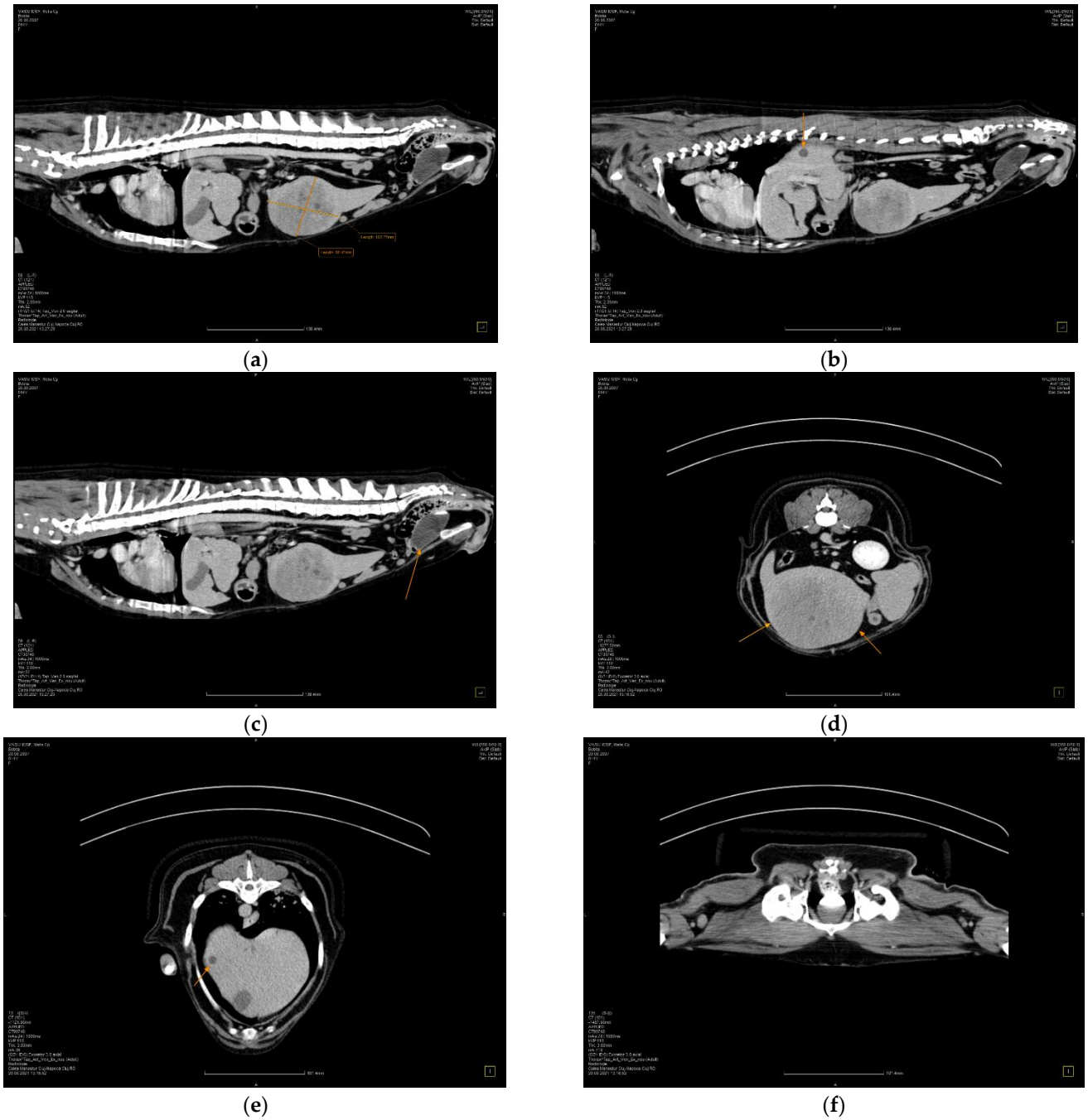

Figure 1. CT evaluation of the abdomen a, b, c: Sagittal view of the thorax and abdomen; d,e,f: axial view of the abdomen and pelvis. The reconstruction is made at different levels.

3.2. Laboratory results

Hematological assays showed the presence of hypochromic and microcytic anemia with anisocytosis and thrombocytosis. Folded levels of alkaline phosphatase (ALP), , and gamma-glutamyl transferase (GGT) confirmed the presence of cholecystitis. Cholesterol (CHOL) and lactate levels (LAC) were also folded (Supplementary Tables S1 and S2). The microbiological assays were negative; the urine sample was sterile, with no sediment or urinary cytology alterations, and the stool sample was negative.

After surgery, the anemia was accentuated, but the platelets (PLT) returned to the physiological levels, and except for ALP, alanine aminotransferase (ALT), and the globulins, all the other biochemical parameters returned within the physiological limits, including the LAC level (Supplementary Tables S1 and S2).

The histopathological evaluation confirmed the presence of splenic nodular hyperplasia (lymphoid), associated with extensive, acute splenic hematoma. The splenic mass was nodular, poorly demarcated, unencapsulated, elevating the capsule, and consisting of large blood-filled spaces (without an endothelial demarcation). The blood-filled spaces were separated by the preexistent splenic parenchyma and were focally admixed with discrete aggregates of lymphocytes organized in distinct follicular-like structures separated by a few stromal cells (occasionally demarcated by hyalinized collagen). The follicular-like structures showed typical germinal centers and consisted of a regular, stratified mixture of small and large lymphocytes with mantle and marginal zone morphologic features. Mitoses were not observed.

Within the liver, hepatic nodular hyperplasia was diagnosed. The nodular mass was well-demarcated unencapsulated, replacing the preexistent hepatic parenchyma focally and consisting of compact sheets and cords (uniform-cell hepatic plates, ≤ 4 hepatocytes thick) of hepatocytes separated by a delicate, fibrous stroma. Few foci of necrosis and extramedullary hematopoiesis (multilineage) were present. Portal spaces and mitotic figures were not observed.

3.3. Post-op results

At 12 h after surgery, the bitch was bright and alert and presented a good appetite. It received small amounts of commercially canned food. Water was provided *ad libitum*. The bitch was leashed and walked 4/5 times daily with no discomfort during the walkovers.

After three days of treatment with PPA, the UI ceased, and the bitch was no longer wet on her hindlimbs. The sutures were removed 14 days after the surgical intervention, and the bitch was discharged from the hospital. The owner was instructed to continue the oral administration of PPA, following the same posological protocol, for life. The owner was also asked to give monthly feedback for the rest of the treatment, sooner if needed. A prescription for ursodeoxycholic acid (Ursofalk, Dr. Falk Pharma GmbH, Germany; 250 mg/tb, 10 mg/kg, 24h PO for 14 days) was released to treat the cholecystitis, and a hepatic diet was also recommended.

4. Discussion

In this case, we postulate that the presence of a splenic mass in a nulliparous sterilized 14-year-old German Shepherd bitch led to an increase in abdominal pressure, partially causing the urinary bladder to move from its abdominal topography into the pelvic cavity, facilitating the onset of USMI derived UI similar to the mechanism acknowledge in women where the increasing pressure of the enlarged uterus and fetal weight on the pelvic floor muscle (PFM) and the bladder throughout pregnancy [15], together with pregnancy-related hormonal changes, may lead to reduced PFM strength and their supportive and sphincteric function. In addition, these changes cause bladder, neck, and urethra mobility, leading to urethral sphincter incompetence [16–18].

In dogs, USMI is the most common cause of acquired UI (i.e., 3-5%). The frequency is influenced by gender, breed, body size, weight, docking, gonadectomy, urethral length, urethral tone, and bladder neck positioning, without any known breed predisposition [2,4,19].

Ovariectomy or OHE does not result in different continence rates; however, the risk of USMI developing increases with large breed dogs; although mixed young to middle-aged spayed females weighing more than 15 kg are typically affected, the risk decreasing every month the sterilization is postponed in the first year. However, spaying females before the onset of the first heat cycle is less likely to develop UI than those sterilized later in life. In contrast, dogs weighing less than 15 kg are less prone to develop this condition [3,5,20–22].

In adult females, USMI is the leading cause of UI [3], while in young bitches, the leading causes are various congenital abnormalities, especially ureteral ectopia [3,23]. In some breeds, including German Shepherds, USMI is encountered in juveniles and adult females [3]. In the present case, the bitch was a German Shepherd crossbreed and presented with UI about seven years after spaying intervention. To date, there is no clear correlation between the presence of USMI and the spaying age of the bitches; however, it is reported equally in both males and females [5,6,20,21].

Some reports suggest that about 89-90%% of the spayed bitches may develop USMI [3,22]; moreover, UI can occur immediately after sterilization, with the majority of the females developing USMI in the first year after OHE; however, USMI can develop even after ten years after OHE. About 75% of bitches develop USMI within three years of gonadectomy [3,6,7,20,21,24].

Urinary incontinence may be permanent or intermittent [3,7]. The exact pathophysiology of USMI is mainly unknown; however, it is multifactorial [21]. The impact of OHE on urinary tract receptor expression is controversial. There is a decrease in urethral closure pressure within one year of OHE, even in continent individuals. If the urethral closure pressure drops below a certain threshold, the sphincter becomes incompetent, and UI develops [21,25].

Moreover, about 75% of the spayed bitches that acquired subsequent USMI had at least one oestrus, and 78% presented pelvic bladders [3,26]. Interestingly, one report showed that UI was present in a bitch when oestrus would have been expected, even though the bitch was spayed [3]. Moreover, compared with continent bitches, which usually show an intraabdominal bladder neck, incontinent bitches have a shorter and dilated urethra [3,22,26]. In the current case, a pelvic bladder was also identified on the CT.

In bitches with intrapelvic bladder neck, an increase in the intrabdominal pressure will be transmitted only to the bladder. Furthermore, the intravesical pressure will rise. If the urethral resistance is poor, urine leakage can occur, as in bitches with USMI, which tend to be more incontinent whenever the intra-abdominal pressure increases [26]. Generally, UI worsens in sleeping dogs or during increased abdominal pressure episodes while barking, coughing, jumping in the owner's car, or recumbency [3,21,24]. In the present case, the owner reported that the bitch was leaking urine, especially while sleeping or laying in the kennel.

Hormonal abnormalities, mainly estrogen deficiency, may also impact sphincter incompetence; however, since not all incontinent dogs improve with estrogen supplementation, it is unlikely that estrogens alone are solely responsible for the development of USMI [21]. Urethral sphincter mechanism incompetence may also predispose to urinary tract infections [1]; however, treatment and presence of concurrent urinary pathologies, including urinary tract infections, do not influence the degree of incontinence [3,22].

There are no specific physical findings to USMI, but clinicians should pay attention to the bladder size, tone, and location. The CBC and TS are usually unaltered; however, they should be performed to rule out other concurrent pathologies. In animals with inappropriate urination, urinalysis and uroculture via cystocentesis for occult infections like cystitis or endocrinology problems like diabetes, liver failure, or other metabolic disorders, especially when dogs present PU and polydipsia (PD), are recommended. The

differential diagnostic should also assess the behavior causes of inappropriate urination. Imagistics are usually normal in dogs with USMI; however, abdominal imagistic is very important to rule out neoplastic or urinary tract calculi. If all the investigations are negative, a trial of medical therapy is acceptable for diagnostic and therapeutic. Cystometrograms and urethral pressure profiles measuring pressure along the length of the urethra are required to document decreased urethral tone [1,6,21,24,26].

Imagistics revealed the presence of cholecystitis, a splenic mass, and a pelvic bladder in the present case. The elevated PAL and GGT levels are consistent with cholecystitis. Besides the anemia and thrombocytosis, biochemistry, hematology, and urinalysis showed no other signs of occulted infections before the splenectomy. Moreover, after the surgery, the folded hepatic enzymes were caused by the hepatic biopsy.

The long-term well-being of owners and pets is affected by USMI as its etiology is multifactorial and complicated. Therefore, treatment comprises a conservative approach followed by surgical management if needed. However, irrespective of the treatment protocol, life-long management of USMI is required [21].

Sympathomimetic alpha-adrenergic agents (i.e., PPA, Ephedrine, or pseudoephedrine) and hormonal-based drugs (i.e., estrogens, testosterone, or gonadotropin-releasing hormone; GnRH) are used to treat USMI. The first category of medical substances direct stimulates the smooth muscles of the internal urethral sphincter and bladder neck, leading to an increased sphincter tone and a subsequent alleviation of UI. As urethral sphincter tone increases, UI and vulvar scalding decrease over time [1,2,4,21,25].

Usually, before surgery, most females are conservatively treated, mainly with PPA [22]. This choice is the frontline treatment of USMI and is intended for the life-long management of USMI-derived UI. Therapeutic dosages are effective between 1.5-2 mg/kg SID or BID, reaching long-term continence in bitches suffering from USMI; however, the treatment with PPA is also effective at a 1 mg/kg TID dose [1].

The clinical effect is observed in the first month of treatment. Furthermore, PPA effectively maintains continence between 90-97% of the treated bitches [1,2,21,24]. In the present case, the condition was alleviated after the first three days of PPA administration. Concurrently, the splenectomy might have also played an essential part in the liquidation of the USMI since the extra pressure exercised by the splenic mass on the urinary bladder was suppressed.

The main side effects of PPA are diarrhea and vomiting; however, cardiovascular, neurologic, and behavioral changes like anxiety, excitement, and aggressiveness may also be present secondary to an increased sympathetic tone [1,4,21]. In the present case, no such side effects were reported; however, one month after the beginning of the PPA treatment, the owner reported that the bitch presented a healthy appetite, a shiny coat, and a substantial improvement in mentation and alertness. These positive effects could be partially explained by the increased sympathetic tone and the liquidation of the anemia.

Ephedrine or pseudoephedrine can also be of aid. However, these medical substances have an efficacy of only 25-75% and may show adverse effects such as panting, hyporexia, and lethargy [1,21].

Oestrogens (i.e., Estriol) alone or combined with alpha-adrenergic drugs may be necessary to reach continence in some affected females. However, estrogens are not side-effect-free since vulvar hyperplasia, vaginal discharge, and even pyometra are reported [1,21,25]. A combination of GnRH analogs and PPA are also used; however, the treatment is effective for no more than six months [1].

In male dogs, testosterone may be considered if they do not respond favorably to the PPA treatment; however, side effects are also reported in this category of drugs [1,21,25]. Moreover, the use of methyltestosterone (0.32-1.27 mg/kg PO SID twice a week or *eod*) in spayed bitches, may be more effective than in castrated male dogs, with excellent responses between 2 to 4 weeks; however, it seems that the tapper off the testosterone dose has a negative impact on incontinence [27].

The main reasons owners decide to start surgical treatment are represented by poor response to medication (i.e., 17%), progressive unresponsiveness to PPA administration

(i.e., 48%), presence of side effects associated with PPA therapy, and owner preference for surgical treatment rather than medical approach (i.e., 29%) [22].

In refractory patients, the following treatment options are mainly surgical and include minimally invasive urethral occluders, urethral bulking, urethropexy, cystourethropexy, and colposuspension, or surgically inserting a hydraulic artificial urethral sphincter (HAUS) [2,7,21,28].

The HAUS placement represents a relatively novel approach. It is implemented in animals where medical management or other surgical approaches are ineffective. To date, the HAUS system is believed to provide the best long-term results for the surgical treatment of bitches with refractory UI, with most dogs achieving complete continence with few reported complications and no other medical treatments needed [5,6,28]. Nevertheless, the overall prognosis for USMI is typically good with long-term therapy [21].

The nonmalignant splenic masses are usually identified in 7-14 years dogs; however, nonmalignant and malignant splenic masses can coexist in the same individual [10]. In affected dogs, 17-50% of splenic masses are hematomas and account for the majority (i.e., 46%) of the benign splenic masses [9,29–31]. In comparison, splenic and hepatic nodular hyperplasia is accounted for with a prevalence of about 44% and 38%, respectively [9].

Usually, in dogs, splenic hematomas are secondary to underlying splenic disorders, such as NLH, and are less commonly a consequence of trauma [10,12,13]. For example, in a case series, a fall on the stairs is the only trauma-related splenic hematoma event reported in dogs; however, whether a splenic mass existed prior to the traumatic event or not is unknown [14]. In the current case, the hematoma was identified in a 14-year-old spayed bitch, and the owner reported no trauma.

Grossly splenic hemangiosarcomas and hematomas are indistinguishable during clinical examination, during surgery [10,14,32], and to some extent, even imagistic evaluation poses limitations [10,12,13]; moreover, it is possible that what initially is thought to be a splenic hematoma may be cancer. Thus histologic diagnosis is mandatory since the risk of misdiagnosis is high (i.e., 11%) [14]. The histological evaluation of the specimens sent to the Pathology Department confirmed the presence of NLH.

The most affected dogs are the German shepherds (i.e., 11.3%) and Labrador retrievers (i.e., 6%), with splenic NLH, with or without hematomas, as the most diagnosed benign splenic mass (i.e., 86%); moreover, 46% of the animals being spayed bitches, with a mean age at the time of splenic removal of ten years [14,33].

Interestingly, about 7.6% of dogs with splenic masses die in the perioperative window. However, only 1% of these dogs die during hospitalization [31]. The leading underlying causes of death are uncontrolled hemorrhage (i.e., 24.4%), Portal system thrombosis (PST; i.e., 22%), Pulmonary thromboembolism (PTE; i.e., 9.8%), pneumonia (i.e., 9.8%, each) or, Disseminated intravascular coagulation (DIC; i.e., 7.3%) [31].

Gender, splenic mass volume, elevated ALP levels, hemorrhagic peritoneal effusion, anemia, body weight, transfusion coagulopathy, palpable masse, and metastasis are the main parameters evaluated for the survival of dogs diagnosed with splenic hematomas [14]. In addition, marked preoperative thrombocytopenia, anemia, and the development of intraoperative ventricular arrhythmias are risk factors for perioperative death in dogs with splenic masses [31]. However, besides the presence of a distended and sensitive abdomen, increased ALP levels, and anemia, no other risk factors had been identified in the perioperative window in the current case.

Prompt surgical interventions increase life expectancy after splenectomy in dogs with benign splenic masses [29,30]. In cases with splenic hematomas, the overall median survival is 647 days after surgery, up to 3287 days (i.e., 2-9 years) [14]. To date, at 219 days after splenectomy, the owner reports positive feedback. In addition, the health status of the bitch had much improved, with no reported side effects whatsoever.

To the author's knowledge, this is the first case report where a pelvic bladder, and consecutive USMI, are associated with a splenic hematoma in a nulliparous sterilized mixed German Shepherd bitch. Therefore, splenic masses should be considered predisposing factors for UI development, consecutive to USMI, especially in old, spayed bitches.

Supplementary Materials: Figure S1: The gross aspect of the splenic hematoma in a 14-years old spayed mixed German Shepherd bitch, after splenectomy, Table S1: Pre-operatory and post-operatory biochemical and hematological values, Table S2: Pre-operatory and post-operatory blood gases values (i.e., venous blood).

Author Contributions: Conceptualization, data curation, writing, review, and editing IV; Patient monitoring, anesthesia, surgery, CAO, ANA, VNO, and IM; Imagistics RP, AR; Post-op treatment AR, MV, EMM, and IV; Histopathologic examination and interpretation FT. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: This research was conducted according to the national (Legea 43 din 2014) and European (Directiva EU 63/2010) legislation regulations regarding animal protection and welfare for scientific purposes. The owner was informed that the outcomes of this case report would be published and gave its verbal consent for publication. Accordingly, ethical review and approval were waived for this study, as standard procedures were implied.

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Communication

Etiopathogenetic mechanism in dogs with syringomyelia

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Abstract: Syringomyelia (MS) is a condition characterized by the development of cavities in the parenchyma of the spinal cord (sirinx). Cavalier King Charles Spaniel (CKCS) dogs have a high incidence of Chiari malformation. The breed was born in 1928, from dogs of the King Charles Spaniel breed, a favorite dog of royal and noble families, with the aim of recreating a dog similar to the one present in the portraits of King Charles II, during the restoration period. The CKCS breed is native to the United Kingdom, being composed of small brachycephalic specimens - toy, a distinctive feature of the breed being the flattened and miniaturized appearance of the head (Rusbridge & Knowler, 2003).

Syringomyelia is a topical and real interest topic in canine neuropathology, representing the topic of numerous researches, both due to the many unknowns of the evolution of the diseases, and the fact that at present there is no effective treatment.

Keywords: Central nervous system, genetic predisposition, CT exam, behavioral changes, nervous symptoms

1. Introduction

In dogs, the etiology of syringomyelia is not fully known, but in the case of Cavalier King Charles Spaniel and Griffon de Bruxelles, syringomyelia may occur as a result of gene modification. BMP 3 (bone morphogenetic protein 3) is the gene responsible for regulating the harmonious development of the skull and spinal cord, so that the extreme brachycephalic conformation of these breeds is associated with Chiari malformation and syringomyelia. Two chromosomal loci were identified - CFA 22 and CFA 26, which are

associated with the presence of a reduced volume of the caudal cranial fossa and with the modified orientation of the caudal cranial fossa, characteristic of Chiari malformation and syringomyelia [1] (Miller & Zachary, 2017), [2] (Schoenebeck, et al.,2012).

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2. Receptivity

Syringomyelia (MS) are commonly diagnosed in Cavalier King Charles Spaniel and Griffon de Bruxelles breeds, but are also found in other brachycephalic breeds, including: Chihuahua, Maltese Bichon, Pomeranian, Pug, French Bulldog, Yorkshire terrier, Boston terrier, but and their mestizos (Dewey, et al., 2005) (Rusbridge, 1997).

Syringomyelia are rarely diagnosed in cats, however recent studies have indicated the presence of MS in cats, especially in brachycephalic breeds.

In the literature, syringomyelia has rarely been described in other animal species, especially in horses and calves, in most cases being a congenital disease, not being correlated with MC (Chiari-like malformation).

3. Etiopathogenesis

One of the most common causes of syringomyelia (MS) is Chiari-like malformation (MC), secondary to volume mismatch between the caudal cranial fossa

(too small) and brain tissue (too large), altered CSF (**c**erebrospinal fluid) circulation, and subarachnoid space compression (Freeman, et al., 2014) (Rusbridge, 2014). In addition to MC, syringomyelia can also be associated with many pathologies that cause CSF obstruction. However, it is unclear why only some dogs diagnosed with Chiari-like malformation (MC) develop MS and others do not. Other causes besides MC that can lead to syringomyelia are CSF obstruction (neoplasms), trauma, constrictive lesions of the spinal cord or space-occupying processes in the spinal cord. In a study conducted in 2013 [3] (by Driver et al.) in dogs with and without MS, pulsation cerebellar was assessed during the cardiac cycle using magnetic resonance imaging. These findings support theories of the pathogenesis of syringomyelia secondary to Chiari malformation in human medicine, highlighting the similarities between canine and human patients.

There can be many factors that influence the pathogenesis, among which we list intracranial hypertension, blood-brain barrier disturbances, imbalance between CSF production and absorption, or insufficiency of extracellular fluid absorption or drainage (Hemley, et al., 2012).

5. Physiopathology of syringomyelia

Due to the underdeveloped caudal cranial fossa, its small volume cannot fully encompass brain tissue. This abnormality leads to the herniation of the cerebellum, thus obstructing the flow of cerebrospinal fluid (CSF) through the foramen magnum (FM), and the CSF pressure exerted on the CNS (central nervous system) is inconsistent CSF flow disturbance as well as pressure variations seem to play an important role in development of syringomyelia. Cerebellar herniation appears to be a component of MS. (Fig.2). It is common in cases of MS, but the presence or size does not anticipate the formation of MS. An explanation by which herniation cerebellar contributes to the pathogenesis of MS is that obstruction of CSF channels occurs in the foramen magnum, but there must be other predisposing factors. (Cerda-Gonzalez, et al., 2009b) (Lu, et al., 2003).

Another important factor included in the pathogenesis of MS is CSF circulation. Changes in speed, turbulence and disturbances in CSF circulation can lead to the formation of intramedullary cavities. A high rate of CSF flow recorded in the foramen magnum along with a lower rate of CSF flow in the cervical vertebrae C2-C3 are considered predisposing factors in the formation of MS.

Intracranial pressure is higher than in the cervical portion of the spinal cord, so when there are rapid increases in pressure, CSF converges to the cervical region. Inside the spinal cord, the pressure tends to increase faster in the lumbar region than in the cervical area, further favoring CSF movement toward the cervical portion of the spinal cord. (Rusbridge, et al., 2000) (Kirberger, et al., 1997)

Due to the direct link between MS and CSF circulation disturbances, the size of the cerebral ventricles correlates with the size of the medullary cavities.CKCS dogs diagnosed with MC and MS have smaller jugular foramen (jugular hole) compared to CKCS patients diagnosed only with MC. Because of this, the venous shaft at the level of the jugular hole is reduced and associated with a small cranial base, leading to increased venous pressure and reduced absorption of CSF, predisposing factors in the formation of intramedullary cavities. (Rusbridge, et al., 2009a) (Schmidt, et al., 2012).

Another cause of reduced CSF absorption is low sinus volume in CKCS patients diagnosed with MC and MS. Reduced venous sinus volume leads to increased intracranial pressure and secondary to improper CSF reabsorption.

3. Discussions

The pathophysiology of syringomyelia is still unclear, several theories are exposed in the literature. However, the full mechanism is not fully understood, and has been the subject of intense research in recent years. It is important to note that the tubular formations in the spinal cord parenchyma, which does not involve the central medullary canal, are defined as syringomyelia (sirinx), while hydromyelia is defined as a dilation of the central canal of the spinal cord. These two cavities can communicate with each other, but it is difficult to highlight this communication. In the early stages, the cavities are located dorsally and laterally by the central medullary canal, in the gray matter. The medullary tissue around the cavities is edematous. If syringomyelia is causing signs and symptoms that interfere with the life of animal, it is recommended a treatment based on Gabapentin at 10 mg/kg orally every 8 to 12 h as a primary treatment for several symptoms like: neck and back pain on palpation, abnormal scratching, episodes of sudden vocalizing or in advanced stages is necessary surgery. The goal of surgery is to remove the pressure the syrinx places on your spinal cord and to restore the normal flow of cerebrospinal fluid. This can help improve the symptoms and nervous system function (Fig. 1).

4. Conclusion

Overall, the prognosis for CM/SM-affected dogs depends on the severity of clinical signs and on the response to medication. Chiari-like malformation and syringomyelia is a progressive condition in those dogs that are affected clinically. Some dogs will need constant dose adjustments to adequately treat their symptoms. Unfortunately, some dogs afflicted with severe and disabling pain do not respond to medical management and are surgical candidates.

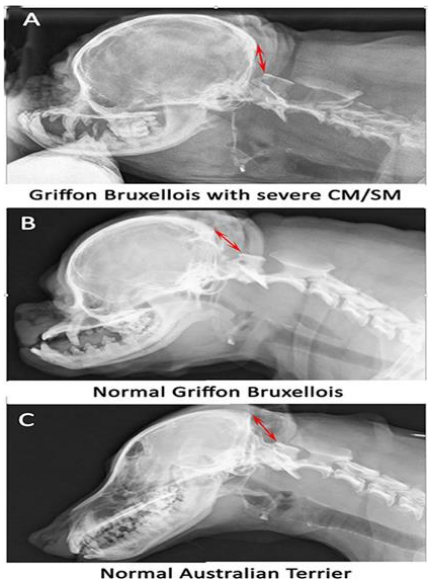

Fig.1 Differences between a healthy dog and a dog with Syringomyelia (https://www.frontiersin.org/articles/10.3389/fvets.2018.00280/full)

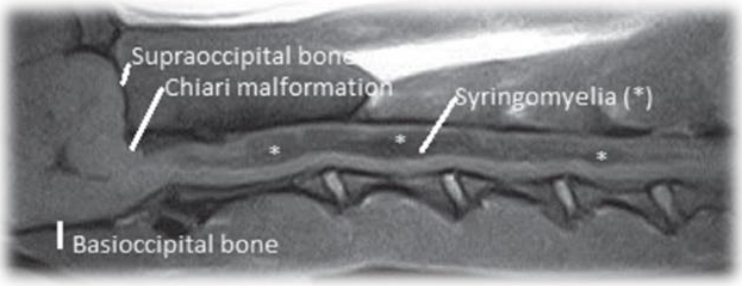

Fig. 2 Chiari malformation and Syringomyelia seen on a CT image (https://www.vin.com/apputil/content/defaultadv1.aspx?id=5328340&pid=11349&print=1)

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