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Ozone Therapy as a coadjuvant treatment in veterinary oncology. Case reports

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Abstract

While the therapeutic approach to cancer is complicated, it becomes a challenge for clinicians. The aim of this study was the use of ozone therapy in four oncology canine patients and the assessment of results related to the quality of life and survival thereof. We did not obviate the concomitant use of conventional treatments. Animals belonging to the following breeds: crossbred Mastiff. Mastiff. Golden Retriever and crossbred German Shepherd, were diagnosed with different types of tumours (Lymphosarcoma, Chondrosarcoma, Adenocarcinoma and Osteosarcoma, respectively). Ozone therapy was applied in treatment cycles rectally, by autohaemotherapy and by local infiltration. Concomitant use of ozone improved the quality of life and increased survival of the animals in all cases.

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Introduction

Oxidative stress (OS), and specifically the development of Reactive Oxygen Species (ROS), produces a damage on proteins, lipids and DNA that builds up during the life and results in pathological conditions such as cancer.[1] Studies directed to the elucidation and development of cancer have notably been focused on the role of ROS. [1]

The ROS's, similarly to hydrogen peroxide (H2O2), the superoxide anion ($O2^{\cdot-}$) and the hydroxyl radical ($HO^{\cdot}$) are, among other causes, responsible for the angiogenesis, the neovascularisation, the inhibition of apoptosis, the increase in pro-inflammatory cytokines, the alteration of metabolic processes[3] and the activation of NF-κ B.[1,2] Stimulation of the intracellular ROS production is considered to be the main mechanism for tumour promotion by ROS's. Simultaneously to these processes, there is a decrease in the antioxidant defence mechanism[3] and the cells become vulnerable to ROS's.

The OS that takes place in the tumour environment increases when we apply chemotherapeutic treatments. Hence, there is a worsening in the condition. This study has been designed to evaluate the efficacy of the therapy using medical ozone in the treatment of cancer, considering this therapy as a coadjuvant to conventional treatment[3].

The aim of this study is based on the benefits of said therapy. Among others, we may mention an increase in 2,3-DPG, an increase in the production of interleukin-1 and -2, of tumour necrosis factor (TNF) and of interferons, lymphocyte and immunoglobulin proliferation, an increase in prostacyclins, a decrease in tissue hypoxia level, activation of detoxifying mechanisms, an increase in the endogenous antioxidant capacity, microcirculation improvement, action on arachidonic acid and its relationship with the inflammatory cascade.[3-7]

The literature available on medicinal ozone application in cancer is becoming more and more relevant. Thus, the contributions from Schulz S (8), AliasovaAV(9), Clavo B(10), Rodríguez Y(11), Ajamimieh HH (12), Bocci V(13), Hui Chen(14), Menéndez S(15), and Goriachev ME(16), are of the utmost importance.

Materials and Methods

The oncological processes which constitute the object of this study correspond to four adult dogs of different breeds and ages.

Case 1: Multicentric prolymphoblastic lymphosarcoma, with good response to treatment with chemotherapy protocol CHOP. With this treatment, the survival average is estimated in 6-15 months.[17-20]
Case 2: Femur head chondrosarcoma T2. Slow progress. Survival is limited as a function of progress and location. Without surgical treatment, the animal is euthanized due to limp and pain within less than one year.[17 19]
Case 3: Thyroid follicular adenocarcinoma T3b N0 M0. In this case, the process is infiltrative and rapidly progressing, affecting structures such as the larynx, trachea, oesophagus, etc.. Without either surgical treatment or chemotherapy, the average survival is 6 months[17 1921]
Case 4: Metacarpal osteosarcoma T 1 M0. Rapidly growing, invasive and highly metastatic tumour. With amputation and chemotherapy, the average survival is 1 year[1719]

Ozone therapy was applied in all cases, and chemotherapy was also applied in three of them. In the case of the osteosarcoma, surgery was also applied. Ozone treatments and results thereof are described below.

The criteria established for the study are related to the application of medicinal ozone, the quality of life and the survival rate of four oncology patients having been simultaneously treated with conventional antitumour therapy and medicinal ozone therapy.

Ozone therapy was applied by a OZONOBARIC P generator (SEDECAL, Spain). 100 mL, 60 mL, 20 mL and 5 mL syringes, 21G x 0.8 mm x 20 mm butterflies, three-way stop cocks, vaginal probes and anti-coagulant ACDA were used.

Case presentation

Case 1.

Crossbred mastiff. Intact male, weighing 52 kg and 7.5 years old.
Diagnosed in July 2013 by popliteal lymph node biopsy with multicentric prolymphoblastic lymphosarcoma, clinical stage III, substage a (without clinical symptoms) and later on with leishmaniosis in stage III by IRIS I. The animal was proteinuric.
He was treated with the CHOP protocol (Vincristine, Prednisone, Cyclophosphamide, Doxorubicin) for 25 weeks for lymphosarcoma.

5 Months after completion of the CHOP protocol, he presented non-regenerative anaemia and alterations in proteinogram. Bone marrow cytology and PCR confirmed Leishmania disease in stage III, IRIS I, proteinuria and no hypertension.

During this period of time, ozone therapy was also administered according to the following scheme: Rectal insufflations at 3 mL ozone/kg body weight, maximum 100 mL, starting with 15 or 20 µg/ mL and with increments of 5 µg/ mL every 3 sessions up to 30 or 35 µg/mL ozone, according to the scheme:

1) On 09/30/13,12/ 09/13, 02/24/14 and 06/30/14, rectal insufflation cycle consisting of 10 sessions of 100 mL vol./20-30 µg/mL. 2) On 01/26/15 and 07/13/15, rectal insufflation cycle consisting of 10 sessions of 100 mL vol./15-35 µg/ mL. 3) On 11/12/15, minor AH cycle consisting of 6 sessions at a rate of 2 sessions per week at 1 mL of blood/10 kg of body weight, with blood mixed with equal volume of ozone at a 10 -30 µg/mL concentration.

mAH application was chosen in the latter cycle due to its immunomodulating characteristics, since, although the animal was at a remission stage with respect to lymphosarcoma, leishmaniosis was still latent.

No further chemotherapeutic cycle was administered, except for the one above described. At present, this animal weighs 66 kg, his lymphosarcoma is still under remission 30 months after having been diagnosed, has an excellent quality of life and maintains an activity as expected for his age.

Case 2.

Mastiff. Intact female. 56 kg. 7 years old.
08/13 She presents a painless, poorly delimited mass at the hip joint area. The X-ray image of the femur head was compatible with neoplasia. A biopsy was performed. The result was a well-differentiated chondrosarcoma. Before the owner's unwillingness to a possible surgical intervention, a metronomic therapy was initiated, consisting of cyclophosphamide and meloxicam for a six-month period.

In 2013, 1 MAH session was applied every month for a total of 3: 1 mL of blood/kg of body weight mixed with equal volume of ozone at a 20 µg/mL concentration. And ozone was also locally applied intra- and periarticularly in the hip joint, at a volume of 40 mL of ozone and a concentration of 15 µg/mL. Along this year, her activity is normal. There is no limp.

In 2014, the animal continues her normal life. She runs and has a slight difficulty in standing up. Three further MAH sessions were applied at 1 mL of blood/ kg of body weight, with equal volume of ozone at 30 µg/mL. Local ozone infiltration at 30 µg/mL.

Given the owner's difficulty to come to the clinic, we maintained phone contact, and the animal was video recorded, just to see that her quality of life was excellent.

In March 2015, she comes with limp affecting the concerned limb. The above described therapy was applied again. She showed an improvement, but did not recover. She died in May 2015, apparently from natural causes, 21 months after diagnosis.

Case 3.

Golden Retriever. Intact female, 11 years old.
In 08/2012, the owners found a neck mass which had evolved along one month. It had grown three times its original size over that month. Cytology showed it was a follicular adenocarcinoma of the thyroid gland. The echographic image was compatible with infiltration into adjacent structures. The owners did not wish either a surgical or a chemotherapeutic therapy, hence we proposed an ozone therapy procedure.

For 7 consecutive sessions, the tumour mass was infiltrated with ozone at a concentration of 30 µg/mL and rectal insufflations were carried out at a rate of 3 mL of ozone/kg of body weight at 20 µg/mL. Two weeks after the first application, the tumour had decreased by 20% of its original size at the right upper quadrant. Three further infiltrations were made in October, November and December using the same protocol as above.

The tumour size remained the same until the end of the animal's life. The animal enjoyed an excellent quality of life until death, which occurred during sleep. She lived for 7 months since diagnosis.

Case 4.

Crossbred German Shepherd. Neutered male, 35 kg, 8 years old.
In January 2012, he presented forelimb limp and pain on palpation of the metacarpal area. He was administered meloxicam, with poor results. An X-ray was taken which evidenced a third metacarpal bone lesion compatible with a fissure. Due to limp and pain worsening, a biopsy was performed with the result of multinucleated giant cell osteosarcoma. The entire limb was amputated.

After surgery, the stump showed inflammation, reddening and pain. Ozone was intra-lessionally infiltrated at a concentration of from 8 to 15 µg/mL, together with 3 rectal insufflations at a dose of 3 mL ozone/ kg body weight and at a concentration of 15 µg/mL. The symptoms subdued after 3 applications. Immediately after surgery discharge, a chemotherapeutic treatment was initiated consisting of Carboplatin at 300 mg/m^2, with a single application every 3 weeks for a total of 5 sessions.

Simultaneously to the chemotherapeutic sessions, rectal insufflations were administered at a ratio of 6 sessions for each one of carboplatin. We started at a dose of 3 mL ozone/kg body weight at a concentration of 20 µg/mL for the first two cycles, and increased this dose to 25 µg/mL for the third and fourth and to 30 µg/mL for the fifth cycle.

During Carboplatin treatment, neutropenia occurred between the first and second applications, but it did not preclude application of the next cycle. In fact, there was a quick recovery, with a three-fold increase in leucocyte number and with hematic values within normal along all that period and up to now.

In September 2012, a metronomic therapy was initiated with meloxicam and cyclophosphamide. It was maintained for a few months until the animal developed haematuria and polyuria. The symptoms were compatible with iatrogenic haemorrhagic cystitis. Echography confirmed the inflammatory process, ruling out other conditions. Said therapy was withdrawn and irrigations were made with ozonized water and ozone was insufflated at a concentration of 15 µg/mL on three occasions, one each week, together with conventional therapy. The animal's process subdues from the second application. Rectal insufflation was simultaneously applied at a concentration of 20 µg/mL for 7 sessions.

Since the end of 2013 and up to now, the animal has undergone 4 cycles per year, one every three months, each cycle consisting of two weeks of rectal insufflations. Protocols in the last two years were coordinated, with RI application for two consecutive weeks starting with a dose of 3 mL ozone/kg body weight, no more than 100 mL, at 20 µg/mL, and every three sessions it was increased to 5 µg up to 30 or 35 µg/mL.

Four years have passed since diagnosis. His quality of life is excellent. He has gained weight up to 40 kg on some occasions, to the point that he had to lose weight. His activity (running, jumping) is even higher than the average for a 12-year-old crossbred German Shepherd.

General discussion

Oncological disease therapy represents a big challenge to the medical practitioner. The plurality of factors to be taken into account when trying to treat such processes entails that no scientifically supported contribution should be discarded.

In veterinary medicine, in addition to the above mentioned factors we must consider that quite often we lack the appropriate means to make a good diagnosis and the lack of the owner's collaboration in order to apply a good treatment. As can be seen from the above-disclosed cases, the desired treatment could not always be applied within the appropriate terms. Due to all these circumstances, ozone therapy has become of great help and has come to fill that therapeutic void. In the above cases, we have observed that quality of life and survival are better than the average when compared with those of conventional treatments.

As clinicians, we can apply our knowledge and observe such promising results as above disclosed, but they are to be supported by research. We may logically expect that, if we could combine the best conventional therapies with ozone therapy, the results would be excellent; this experience is an indicative sample of the results obtainable in veterinary medicine.

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