

CASE REPORT

Peritoneal ozone / oxygen insufflation (IPO3). Total, remission of asthenia and pain in terminal oncological patient after IPO3 cycle.

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ABSTRACT

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Pain and asthenia are difficult symptoms to control in cancer patients and greatly determine their quality of life. Conventional ozone therapy is used successfully in the symptomatic control of pain in cancer patients. We believe that the administration of ozone at high doses through IPO3 could provide an additional benefit in the control of refractory symptoms in patients with cancer.

We present a cancer patient with very poor quality of life, who was successfully treated with IPO3.

The patient is a 48-year-old woman with a history of breast cancer who has metastasis in bones, skull, liver, lung and peritoneum, with refractory symptoms. Her quality of life was limited by severe asthenia (which kept her bedridden for more than two months) and pain refractory to symptomatic treatment with opiates and corticosteroids.

The patient was treated with a cycle of rectal ozone therapy, consisting of a conditioning cycle with 15 sessions of oxygen / ozone rectally, followed by placement of a peritoneal catheter to subsequently perform five IPO3 sessions.

At the end of the treatment, all the symptoms of the patient were resolved completely, allowing the withdrawal of all the analgesic medication, returning the patient to a normal life. There were no side effects, and the beneficial effects of this IPO3 cycle were maintained for more than two months. The analysis showed reduction of the tumor and inflammatory markers during the treatment.

Ozone therapy at high doses IPO3 should be considered in cancer patients with severe symptoms and refractory to conventional treatment.

Key words:

Intraperitoneal ozone therapy, tumor asthenia, palliative treatment, complementary treatment, quality of life, pain, cancer.

INTRODUCTION AND LITERATURE REVIEW

Tumor asthenia is the most frequent symptom and difficult or impossible to control in patients with advanced cancer. Along with pain are the symptoms that strongly influence the quality of life and survival time (1).

There is no effective treatment in most cases of Asthenia. It is a lack of strength, a decline, more pronounced than a chronic fatigue syndrome. It is a state that leads patient not having any desire to move from the bed-chair, as waiting and delivered, abandoning any desire to fight. Asthenia is a set of symptoms like physical and psychic, A syndrome of tumor asthenia in advanced cancer patient, is because of tumor progression. Antitumor treatments are the main contributor to asthenia through the activation of inflammatory cytokines. Surgery, chemotherapy and Radiation can induce inflammatory cytokines and asthenia in a way related with the kind of surgery, dose and schedule of chemotherapy and dose and volume of Radiation.

Ozone therapy is a technique consisting of the administration of oxygen / ozone gas, and characterized in experimental models by various effects: antioxidant, oxygenating, immune modulator, anti-inflammatory, germicidal (2) and anti-metastatic (3).

Conventional ozone therapy is successfully used (4) in the symptomatic control of patients with cancer, being the most common routes of systemic administration, rectal insufflation and the blood route. We believe that the administration of ozone through IPO3 provides an additional benefit in the control of refractory symptoms in patients with advanced cancer (5). On the other hand, this route of administration has been shown to have anticancer effects, in vivo, in two different animal models (Schulz (3), Rossmann (6)).

We show here the case of a patient with disseminated recurrence of breast cancer, with severe deterioration of the general state due to asthenia and pain refractory to treatments, whose symptoms completely and lastingly reverted after a cycle of ozone therapy at high doses by IPO3.

CASE PRESENTATION

48-year-old woman diagnosed five years ago with stage IIIB ductal carcinoma of the breast. She underwent partial mastectomy and lymphadenectomy with subsequent adjuvant treatment with radiotherapy and chemotherapy. She discontinued chemotherapy due to severe intolerance. Since then. Four months before coming to us, he presented symptoms of progressive pain and asthenia of 6 months of evolution, with intense backache, pain in the right lower extremity, myalgias, arthralgias, headaches, intense asthenia, anorexia, weight loss, nausea and disgust. olfactory Diagnosis of metastatic recurrence in the skull, pelvis, dorsal column, femur, ribs, lungs, pleura, mediastinum and liver. During these four months of hospital stay, she did not receive chemotherapy-radiotherapy treatments. She was discharged from hospital and sent home with in-house treatment of dexamethasone, fentanyl dermal patches, oral rescue morphine, naproxen and gabapentin. With this treatment she got a partial relief of pain but no control of severe asthenia.

Analytical performed at the hospital, prior to initiation of treatments with oxygen / ozone: anemia with Hb 10.1 g/dL, hyponatremia Na 129 meq/L, steroid-secondary hyperglycemia 265 mg/dL, Ferritin 1074 ng/mL, LDH 920 U/L. CEA tumor markers 19.7 ng/mL, Ca 15.3: 99.8 IU/mL.

Full information was given to the patient and her family about the palliative objective of improving the quality of life, emphasizing that all the information we have about this treatment is based on documents and experiments on animals and not on humans, after consent in writing, we started the oxygen / ozone treatment with the following scheme: a cycle of rectal ozone therapy as conditioning prior to IPO3. Cycle of 15 sessions rectally (200 ml at the concentration of 40 µg of ozone per mL of oxygen, that is, 8 mg of ozone) every other day. The administration of IPO3 was performed according to the protocol of Dr. Siegfried Schultz (3). In summary, it consisted of the surgical placement of the peritoneal catheter followed by insufflation of 40 mL of gas mixture per kg of weight at a concentration of 50 µg/mL in the first session of the cycle, and the administration of 80 mL of gas mixture per kg of weight in the remaining four sessions. The procedures were performed daily in the operating room, under surveillance of vital signs and sedation with midazolam, propofol and fentanyl. During the five days of treatment, the intravenous antibiotic cefazolin 1 g/day was associated. At the end of each session the patient remained in the postoperative recovery room for two hours for pain control. During the rest of the day, if necessary, any regular pain killer, such as acetaminophen or ibuprofen was allowed. There were no complications or side effects related to the IPO3 sessions. The patient did not need analgesic medication after the IPO3 sessions.

The response to IPO3 treatment was very favorable, resulting in a total disappearance of pain that allowed the withdrawal of corticosteroid and analgesic medication. The conditioning phase, with rectal oxygen / ozone administration, has already produced significant but partial symptomatic improvement. However, the response was maximum after the start of the IPO3 applications, with progressive improvement from the first session and total improvement after the third session of IPO3.

The asthenia that kept her in bed during the last months, except for the fulfillment of vital needs, disappeared completely. With the suspension of morphic drugs, nausea and anorexia also subsided (reason why she had already lost 20 kg of weight), allowing the patient to resume a normal rhythm of life.

Analytically, hyponatremia and hyperglycemia were normalized after corticosteroid withdrawal.

Tumor and inflammatory markers decreased after treatment with IPO3 (Table 1) (CEA: 19.7 to 12.8 ng/mL, CA 15.3: 99.8 to 74.1 U/mL), LDH 920 to 452 U/L, Ferritin 1074 to 411 ng/mL). They gradually returned to the start values, pre IPO3, two months later. LDH remained within normal limits.

TABLE 1
Changes in blood values studied.

	BEFORE IPO3	AFTER IPO3
CEA	19,7	12,8
CA 15.3	99,8	74,1
Ferritine	1074	411
LDH	920	452

During the three weeks post-IPO3, the pain subsided completely, without the need for medication. A slight pain appeared during the next 3 weeks, which occasionally required some relief with an analgesic. At 6 weeks I return to analgesic medication prior to the onset of IPO3.

The full effects on asthenia, anorexia and general condition were maintained for a month, and gradually subsided in the following two months.

DISCUSSION AND CONCLUSION

Oxygen / ozone treatments have a varied, broad-spectrum action mechanism: they can increase tissue oxygenation, activate endogenous antioxidant enzyme systems, modulate the immune system and regulate the inflammatory-anti-inflammatory cascade, as well as being a potent germicide (2). It is easy to understand that any of these properties, by themselves, are suitable for the complementary treatment of specific diseases, but if the action is summative and joint of all these mechanisms, any disease could benefit from oxygen-ozone treatments, including cancer. The complementary treatment of cancer patients is one of the potential indications of conventional ozone therapy (2).

The antioxidant and anti-inflammatory effects of oxygen / ozone treatments are well documented, and contribute efficiently in the treatment of patients with cancer.

It has been described that oxidative stress causes antioxidant activation via Nfr2 (7) and that, precisely, oxygen / ozone treatments cause this necessary oxidative stress that sets in motion the Nfr2 pathway and consequently the activation of all endogenous antioxidant systems, thus adding a protection of healthy cells against strongly oxidative therapeutic procedures (chemotherapy, radiotherapy, surgery or hemodialysis) and diseases that cause severe oxidative stress such as cancer or diabetes, for example. At the same time, a modulation or regulation of the inflammatory-anti-inflammatory cascade occurs, modulating, via NFκβ (8), the cascade in favor of anti-inflammatory cytokines such as IL2-IL4 or IL10.

Numerous publications highlight that oxygen / ozone treatments have the ability to increase oxygen transfer to tissues, as well as tumor tissues (9). The increase of oxygen in the tumor zone causes the functional loss or deactivation of HIF-1α (hypoxia inducible factor 1 alpha). This is the fundamental switch for tumor cells to secrete vaso-endothelial growth factor (VEGF). Thus, by improving the oxygenation of the tumor territory, tumor neoangiogenesis could be potentially inhibited via deactivation of HIF-1α and VEGF (10).

On the other hand, the hypoxia of the organism and the hypoxia of the tumor environment are conditions that do not allow the immune response and anti-metastasis surveillance to be started at full capacity (11), so that the improvement of the global oxygenation allows favorable conditions for the defensive response of the immune system.

Oxygen / ozone has germicidal properties but we can not assure that this guarantees an aseptic administration of IPO₃, given the ozone's ways of action. That is why the maximum aseptic measures should be kept and we advise all patients to associate antibiotics. Ozone has a direct antitumor effect in vitro on cancer cells (12), but an antitumor effect has also been demonstrated in vivo in animals treated with ozone peritoneally. Ozone has a direct antitumor effect in vitro on cancer cells (12), but an antitumor effect has also been demonstrated in vivo in animals treated with ozone peritoneally .

In 2008, Siegfried Schultz published in the International Journal of Cancer (5) the first results with IPO₃ in the treatment of VX2 tumors or of squamous cells implanted in the ear of New Zealand white rabbits with regional and distant metastases (lung). of total cure in 50% of the animals treated with IPO₃. Here, a strong stimulation of white cells, especially neutrophils and NK cells, as well as an increase in the active metabolites of prostacyclin, which is known to be a potent antimetastase agent (13), already stand out as a probable antitumor mechanism. There is also activation of interleukin 2 (IL2). They saw that the peritumoral infiltration of IL2 (18) and subsequent infiltration of VX2 tumor cells blocked the success of the tumor implantation. This led them to carry out a second study with the 6 cured rabbits. These rabbits were divided into two groups of 3, one of the groups was subjected to immunosuppression with cyclosporin A and dexamethasone. The two groups were infiltrated again, in both ears, cells of the VX2 tumor. The result was that only in the immunosuppressed group, the appearance of VX2 cancer occurred in 4 of the 6 ears. In the non-immunosuppressed group none of the 6 ears had tumor. Therefore, it can be deduced that IPO₃ acts as a preventive and blocker of new tumor implantations through immune mechanisms and cytokine release, among which, undoubtedly, IL-2 is one of them.

Subsequently, in 2014, Rossmann and Bette (Clinical Cancer Research) (14) confirm the results obtained by Schultz's work, reporting 70% cures on the same experimental model, demonstrating how the IPO₃ achieves a strong tumoricidal response and that it is due to also to a strong lymphocyte stimulus, especially CD3 lymphocytes. And that this response can be transferred adoptively to other animals blocking the implantation of new tumors. Confirming also the upward activation of prostacyclin and other cytokines. In September-2018, Bette-Rossmann (15) and colleagues report another new mechanism of action of IPO₃, the blockade of the epidermal growth factor receptor (EGFR).

The ozone therapy, by conventional routes, in some patients, the potential improvement of symptomatology related to tumors and the side effects of chemotherapy and / or radiotherapy can be offered, also improving the efficacy of these treatments. This case shows us a much more intense and rapid efficiency and effectiveness of ozone therapy in high doses administered by IPO₃. Our experience in the complementary treatment with ozone / oxygen in cancer, in which we use different routes of administration, such as rectal or blood, made us aware of a clear difference in the beneficial effects, both subjective and objective, when using the IPO₃. Undoubtedly, studies are needed to know the extent of this substantial improvement and corroborate our observation: complete remission of severe and refractory symptoms to conventional optimized therapy.

The IPO3, is applied regularly in veterinary medicine. The innocuousness of this technique has been described by Springmann (16). The potential of ozone to prevent the development of tumors, including antitumor capacity, as demonstrated in the regression of tumors after their implantation and metastatic spread is described in the works and has been demonstrated by Schulz (4), and corroborated by Rossmann (14) and Bette (15), who described the immunological mechanisms responsible for this activity. Recently, a member of our group, C. Peirone (6), described antitumor activity in vivo in a different experimental model.

In humans, the use of this technique was first described at the at the middle of the 20th century for the treatment of abdominal inflammatory pathology (17). The first use of the IPO3 for the treatment of patients with cancer was published in 2012 by members of our group (4).

We describe the total disappearance of pain and asthenia after treatment with IPO3. This improvement must be understood within a context of a strong anti-inflammatory effect through the potential mechanisms that ozone / oxygen has. This improvement suggests the implementation of ways of action still to be clarified, that are activated under the influence of high doses of oxygen / ozone, as is the case we describe, producing the resolution of refractory symptoms to conventional treatments. The IPO3, not only proved innocuous and reasonably tolerable, but also managed to avoid the damaging effects of corticosteroid therapy. The improvement of analytical parameters could reveal a direct effect on tumor development and should be evaluated in future studies.

We believe that IPO3 should be considered as a adjuvant rescue treatment in cancer patients with severe symptoms refractory to conventional treatment. The case of our patient and in view of symptom-free time, treatment with IPO3 should be cyclical and repeated periodically, so trials and studies are needed to confirm that the rate of cancer progression could be slowed down, helping the healthy chronification of the disease and therefore a longer survival time associated with a better quality of life.

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