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Stevens-Johnson Syndrome Treated with Ozone Hemo Therapy: A Case Report

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Authors' contributions

This work was carried out in collaboration between all authors. Author LR wrote the draft of the manuscript. Authors CG, OM and NR managed the literature searches. Author GM designed the figures, managed literature searches and contributed to the correction of the draft. Author LR provided the case, the figures and supervised the work. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

We report a case of Stevens-Johnson Syndrome treated with ozone autohemotherapy. The patient had been diagnosed with Stevens-Johnson syndrome 3 months before admission to our clinic by the treating physician. There was ulceration of the buccal, nose and ocular mucosa (varying grade). Previous treatment with antiviral and anti-inflammatory drugs was done without any apparent result. The patient received a total of eight major autohemotherapies, with treatments administered every third day. We start with a first infusion of blood treated with low ozone doses followed by vitamin C 7.5 g. After the first treatment the patient showed a sudden relief of symptoms and the ulcers disappeared. The treatment was repeated to reach a stable condition and a follow up of six months showed the complete healing of the patient.

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1. INTRODUCTION

The administration of low ozone doses has been proved to be useful in several conditions linked to inflammation or to immune system disorders [1]. So far most of the clinical data regarding ozone treatment have been clearly defined by a scientific point of view only in the case of pain and disk herniation [2]. Despite this, positive effects induced by low ozone doses are commonly observed in patients suffering from rare or degenerative diseases [3,4]. Nevertheless, the scarce knowledge of its therapeutic potential by most of the clinicians make difficult or even impossible a wide cooperation among the various specialties in the aim to produce a statistical evidence of the clinical response to the ozone treatment in rare or uncommon illnesses.

Ozone, like other agents and unlike the common drugs that act on a specific receptor, induces small stress to the whole blood cells when used at low doses with the hemotherapy technique as explained below.

A recent study [5] fully explains the biochemical mechanisms and the intracellular mediators involved as a consequence of any xenobiotic interaction, making possible the evaluation of the intracellular metabolic pathways involved following a moderate oxidative stress.

In short, the stimulus of oxidative stress, in the case of ozone, is able to activate Nrf2 protein [6,7] which, moving in the nucleus, starts production, from part of target genes, of proteins that promote cell functions, strengthening the defenses, and optimizing the underlying specific function.

Stevens-Johnson Syndrome (SJS) is a severe cutaneous adverse reactions frequently caused by exposure to drugs and cause significant morbidity and mortality. The syndrome usually results from a drug reaction or previous viral infection being deadly as well as very painful and distressing [8].

SJS is defined also as a life-threatening skin condition, in which cell death causes the epidermis to separate from the dermis. The syndrome is thought to be a hypersensitivity complex that affects the skin and the mucous membranes. The most well-known causes are certain medications, but it can also be due to infections, or more rarely, cancers.

SJS usually begins with fever, sore throat, and fatigue, which is commonly misdiagnosed and therefore treated with antibiotics. In most cases, the disorder is caused by a reaction to a drug, and one drug that has come under fire lately is the cox-2 inhibitor valdecoxib (Bextra, Pfizer), which is already linked to other SJS like disorders such as Toxic Epidermal Necrolysis (TEN). There are other drugs that have been linked to SJS, and these include some other NSAIDS (non-steroid anti-inflammatory drugs), Allopurinol, Phenytoin, Carbamazepine, barbiturates, anticonvulsants, and sulfa antibiotics. The condition can sometimes – although not very often – be attributed to a bacterial infection, and in some cases there is no known cause for the onset of SJS.

SJS can affect any age group. However, also if frequently seen in young patients, it is reported that it commonly occurs in older people. This could be because older people tend to use more of the drugs associated with the disease and are therefore collectively more at risk from the disease. People that have AIDS are also at an increased risk of contracting SJS, thus confirming some impairment at the immune system level. SJS can start with non-specific symptoms such as cough, aching, headaches, and feverishness. This may be followed by a red rash across the face and the trunk of the body, which can continue to spread to other parts of the body. The mucous membranes can become inflamed and often the skin peels away in sheets. The hair and nails can also come away in some cases, and sufferers can become cold and feverish. This disease can leave the skin looking as though it has been burned, and areas where skin has flayed away can seep copiously and quickly become infected. Those suffering from severe SJS or TEN are treated in hospital, and if the cause of the problem is drug related then the drugs are stopped with immediate effect. Patients are treated intravenously to replace any lost fluids, and the skin is left to re-grow on its own. However, the chances of survival can be hit and miss depending on the level of damage and the degree of infection incurred by the patient. In less severe conditions, treatment is usually based on antiviral agents or immune suppressive therapy.

2. CASE REPORT

A 28-year-old woman previously diagnosed with SJS was admitted to our clinic after worsening skin lesions in June 2014. About 3 months before admission, steroid and antiviral treatment was initiated to treat the lesions.

Despite the pharmacological treatment the skin lesions showed no improvement and the patient contacted the emergency department of our clinic. The patient had no history of chronic obstructive pulmonary disease or asthma and she did not consume alcohol.

On admission, the patient's blood pressure was 130/85 mm Hg, pulse 65 beats per minute, respiratory rate 20 breaths per minute, and oxygen saturation was 99% under room air. There were bullae and multiple skin eruptions involving the oral and nasal mucosa (Fig. 1).

We suggested stopping the steroid and antiviral administration and, after the informed consensus from the patient, we started a blood treatment using low ozone doses and vitamin C. Major Auto-Hemotherapy (AHT) was performed with Ozonosan® Bottles and ozone. Ozone was generated from medical-grade oxygen (O_2) using electrical corona arc discharge, by the O_3 generator (Model Ozonosan Alpha Plus, Hansler, GmbH, Iffezheim, Germany), which allows the gas flow rate and O_3 concentration to be controlled in real time by photometric determination, as recommended by the Standardization Committee of the International O_3 Association [9].

Briefly, blood was drawn from the patient, exposed to the same volume of oxygen or ozone and re-injected into the blood stream [7]. The amount of blood used was standardized to 1.3 multiplied by the Body Weight (BW) of the patient. After the re-infusion of the ozonated blood, 7.5 g of vitamin C in 50 ml saline was administered to the patient (Pascorbin®, Pascoe).

Three days after her admission, despite improvement of the skin lesions, we decided to follow with the same therapy twice a week for three weeks. A complete recovery of buccal lesions was evident since after the first treatment (Fig. 2).

After a follow up of six months the patient was evaluated for her actual status and the improvement was definitely assessed (Fig. 3).

Fig. 1. Buccal lesions before treatment

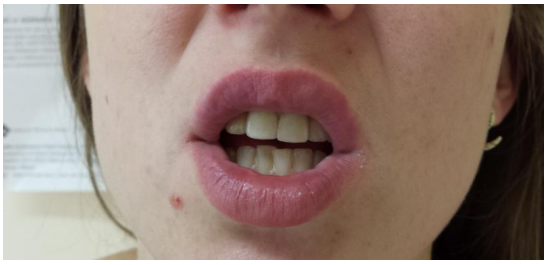

Fig. 2. Buccal mucosa after the first treatment

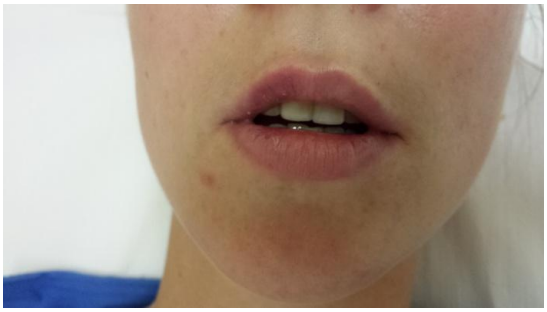

Fig. 3. Six months after the end of the ozone treatment

3. DISCUSSION

SJS and TEN, rare variants of severe adverse cutaneous drug reactions, are characterized by more or less extensive painful erythematous macules evolving to epidermal detachment and mucous membrane erosions resulting from massive apoptosis of epithelial cells [10].

The pathogenesis of SJS is not fully understood but is believed to be immune-mediated [11] and this was the reason that suggested the use of oxidative therapy which is reported to modulate the function of our immune system [12].

Indeed ozone, in contact with blood components (serum component and cells membrane), generates oxidative bio-products that, entering in

the cell cytosol, can modulate some sub cellular pathways. The expression of proteins that collectively could favor the cell function and modulate the immune functions is going to be finally outlined [7,13].

Differential diagnoses for SJS include autoimmune bullous dermatoses, acute generalized exanthematous pustulosis, erythema multiforme, disseminated fixed bullous drug eruption and staphylococcal scalded skin syndrome.

Even if most of the above conditions are usually triggered by herpes simplex infections, but rarely by drug intake, SJS is mainly drug-induced.

Herpetic ulcers are smaller with regular borders than ulcers associated with SJS. The presence of a temporal relationship between the drug intake and onset of the disease excludes the possibility of any infectious aetiologies. Anyway, in our case the patient had been submitted to steroid and antiviral treatments only. Furthermore, the patient went to our observation with a previous SJS diagnosis and her situation appears to be not so severe requiring immediate hospitalization.

This was the main reason why we started, with the consensus of the patient, the treatment of ozone by mean of AHT that, as reported above, it is known to modulate both immune system and cytokines [14].

4. CONCLUSION

The clinical observation described in this case report, suggests that oxidative therapy by mean of low ozone doses (ozone hormesis or ozohormesis) could be helpful and considered as a valid complement to the pharmacological assessment in conditions where immune system is weak or unbalanced [3].

CONSENT

All authors declare that 'written informed consent was obtained from the patient for publication of this case report and accompanying images.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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