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An Unexpected Death During Oxygen-Ozone Therapy

Daniela Marchetti, M.D., and Giuseppe La Monaca

An unexpected death is described that was caused by gas embolism that occurred during oxygen-ozone (O_2/O_3) therapy administered by autohemotransfusion for psoriasis. This unusual complication suggests the necessity of investigating benefits and adverse effects of medical ozone application.

Key Words: Oxygen-ozone therapy—Gas embolism—Unexpected death.

Ozone, an allotropic form of oxygen, is primarily known for its ecological properties but also for its industrial applications and therapeutic effects.

It has been demonstrated to work on cellular metabolism by accelerating the use of glucose, improving protein metabolism, converting unsaturated fatty acids into hydrosoluble compounds, and increasing erythrocyte activity (i.e., increasing the production of 2-3 diphosphoglycerate). Ozone also has antibacterial and antiviral effects (1,2). However, inadequate ozone concentrations induce the activation of lipid peroxidation with irreversible alterations of cell membranes (3).

Medical ozone is a O_2/O_3 mixture at a low ozone concentration (from 1 to 100 μg in accordance with the types of application of ozone therapy) produced by typical generators (Fig. 1). Figure 2 illustrates the principle of a medical ozone generator. To obtain a clean oxygen-ozone mixture (free of nitric oxides), the purest oxygen must be used as the initial substance. Oxygen flow through two high voltages tubes (ozone tubes). When electrical energy is applied, some oxygen molecules (O_2) are broken down into oxygen atoms (O), which then react with other O_2 molecules to form ozone (O_3). The oxygen-ozone mixture is then conveyed through a double-jet outlet: one is used to draw the medical ozone out and the other to convert back excessive or unused ozone to pure oxygen catalytically by the destructor unit (Fig. 2).

The ozone quantity produced depends on the voltage applied, the rapidity of the oxygen flow through the discharge zone, and the space between the electrodes within the ozone tubes (4).

O_2/O_3 therapy can be administered locally by transparent plastic bags or hoods in cases of fistulae, decubitus ulcer, ulcus cruris, poorly healing wounds, and osteomyelitis. It can also applied by intramuscular, intraarticular, intravenous, and subcutaneous routes or through treatment in a body cavity (ozone enema) (4).

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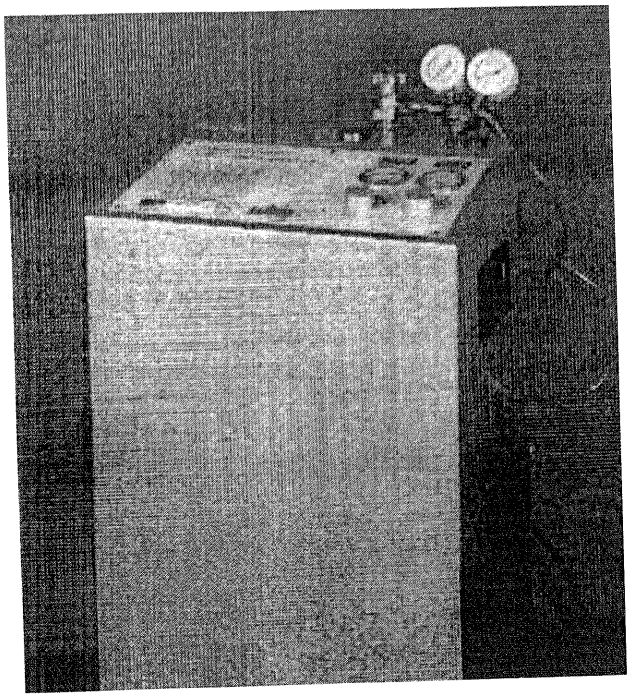

FIG. 1. Medical ozone generator.

Since 1986, the European Society of Oxygen-Ozone Therapy, based on the statistical study of Jacobs on ozone incidents (5), has forbidden O_2/O_3 endovenous injection for air embolism complication. Therefore, a widely used method is the autohemotransfusion, otherwise called major autohemotherapy (Table 1), which covers the same intravenous administration field.

O_2/O_3 therapy is indicated in various pathological situations. In the literature, there are several studies reporting its effects on allergies, arteriosclerosis, arthritis, virus infections (herpes, human immunodeficiency virus), hepatitis and cirrhosis, peripheral arterial occlusive diseases, cerebral sclerosis, and age-related degenerative retinal maculopathy. It is also used in patients with malignant tumors (6–10).

Ozone treatment is used in Germany, Switzerland, and in Eastern Europe. In Italy, O_2/O_3 therapy is considered an experimental treatment for chronic venous insufficiency, peripheral arteriopathies, ischemic ocular diseases, and chronic hepatitis B and C.

The case that we present concerns an unexpected death caused by an unusual complication that occurred during oxygen-ozone therapy administered by autohemotransfusion for psoriasis.

CASE REPORT

In February 1996, a 20-year-old woman suddenly lost consciousness during her 31st oxygen-ozone treatment by autohemotransfusion. Resuscitation was unsuccessful.

A chest radiograph (24 hours after the death) demonstrated gas in the right and left cardiac chambers and in the main vessels (Fig. 3). The autopsy was performed 48 hours after the death. The body was that of a well-developed and well-nourished young woman (body weight: 60 kg; crown-heel length: 160 cm) with some distinctive lesions of psoriasis on her arms, legs, and anterior thoracic surface. No other external findings were observed except for two acupuncture signs on her left arm and one on the right side of the neck.

First, the brain was examined, with care taken to double clamp the middle cerebral, basilar, and vertebral arteries before cutting them through. The remaining clamps were removed after the brain had been submerged in water. This procedure revealed some bubbles. The brain was kept in 10% buffered formalin. The section, performed 10 days later, showed petechial hemorrhages, especially in the white matter.

To gain access to the chest, the ribs were cut, starting from the second costal cartilages to save the epiaortic vessels. After clamping the aorta, the caval veins, and the trachea before sectioning, the heart was removed, together with the lungs and neck organs. Then they were all placed in water,

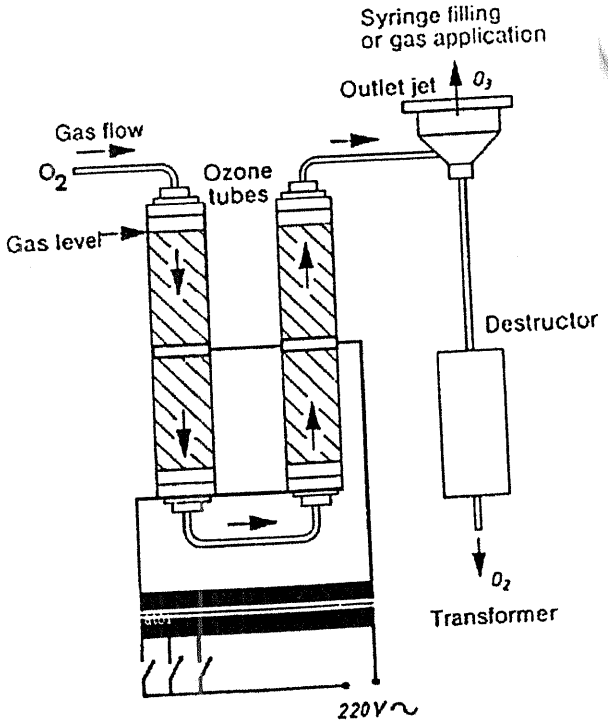

FIG. 2. Schematic diagram of the principle of a medical ozone generator.

TABLE 1. *Technical recommendations for autohemotherapy according to the Italian Scientific Association for Oxygen-Ozone Therapy guidelines*

Transparent medical plastic bags for hemotransfusion must be partially emptied from anticoagulant in proportion to the amount of blood venous collection (about 150 cc).
One of the needles connected to the plastic bag is replaced by a 19-G butterfly to avoid a double injection.
150 cc of blood is extracted from a peripheral vein and collected in the plastic bag that must be weighted before and during the blood drawing.
Connecting tube is clamped and detached from the butterfly that is left in vein and employed for physiologic solution infusion to save vascular access.
Ozone/oxygen mixture at the desired concentration is extracted from medical ozone generator and injected in the plastic bag through the connecting tube.
When the desired quantity of ozone/oxygen mixture is obtained, the connecting tubing is definitively closed.
The plastic bag is gently shaken and then joined to a second connecting tube.
This second tube is connected to the butterfly needle, and the blood is slowly reintroduced (50–60 drop/min).
After every application, the quantity of blood and ozone employed must be registered.

and some air bubbles emerged after the clamps were released.

The visceral pleura appeared to be intact. Examination of the heart revealed a patent foramen ovale of no hemodynamic relevance. Ventricles, atria, coronary arteries, and valves appeared to be normal. Frothy blood was found in the pulmonary artery and in the aorta.

The macroscopic examination of the remaining organs didn't show pathological findings.

Histologically, there were no specific changes except for unstained vesicles adjacent to the cerebral capillary and arteriolar intima. Similar unstained vesicles had also been observed in perivascular spaces, as well as annular hemorrhages. Edema, endoalveolar hemorrhages, and focal emphysema were present in the lungs.

No toxicological abnormalities were found in the blood, urine, and bile. Unfortunately, we could not take air samples by external heart puncture to determine oxygen/nitrogen ratio by chemical analysis (11,12).

DISCUSSION

Several literature reviews exist dealing with gas embolism as a potential complication of medical and surgical treatment (13–30) but, to our knowledge, it has never been reported in relation to O_2/O_3 therapy by autohemotransfusion.

To avoid infact from ozone endovenous injection, autohemotherapy requires blood collection from the patient, treatment of it by medical ozone in a plastic bag that has already been disconnected from the venous system, and then the reinjection of the blood by a second connection (Table 1).

In our case, chest radiography and pathological findings indicated death to be caused by a paradoxical air embolism from a congenital heart abnormality (patent foramen ovale). The arterial shunt could have been caused by an inversion of intera-

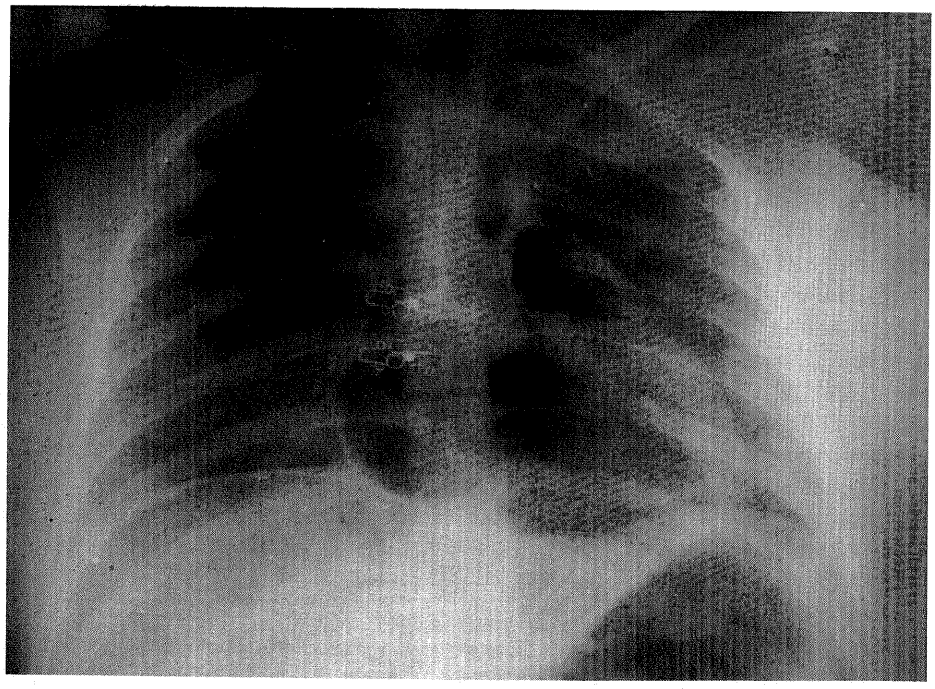

FIG. 3. Chest radiograph shows gas in right and left cardiac chambers and in the main vessels (pulmonary artery and aorta).

trial pressure gradient for the amount of gas introduced and/or its flow rate (in experimental research on dogs, a fatality rate of 100% was obtained with 7.5 ml of air/kg injected in 5 seconds or less) (31).

Thus, investigation of the scene did not give enough information on the gas volume or the flow rate used, but made us suspect an unsuccessful disconnection of devices from the patient's venous circulation. None of the instruments required to detach the plastic bag from the peripheral vein before ozone addiction, nor those that are necessary for blood reinjection, were found at the scene of death (Table 1).

Another aspect that has to be considered is the lack of conformity of the medical ozone treatment to the Italian trial recommendations, which do not accept this treatment for psoriasis in accord with the scientific literature.

For this reason, our case could be legally considered to be an incorrect medical ozone administration.

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