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artículo original

Double genitourinary infection cured with medical ozonetherapy: a case report

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Ozonetherapy, HPV, urinary tract infection, ozonated oil, major autohemotherapy, vaginal ozone insufflation.

Abstract

A 44 year-old woman with chronic bacterial urinary tract infection (UTI) refractory to multiple courses of antimicrobial treatment presented with positive hybrid capture Human Papillomavirus (HPV) DNA assay on pap smear. The patient was successfully treated with systemic (Major Autohemotherapy) and local ozonetherapy (ozonated sunflower oil and ozone vaginal insufflations), with no more bladder infections and negativation of the HPV genetic test...

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INTRODUCCION

Case presentation

Herein we present a 44 year-old Caucasian woman with a 6-month history of recurrent bacterial urinary tract infection refractory to multiple courses of culture-oriented antimicrobial treatment.

She used to have monthly community-acquired *Escherichia coli* UTI. Antibiotics would only bring temporary relief of the infection. A test-of-cure urine culture performed approximately one to two weeks after completion of antibiotic therapy used to be considered to confirm clearance. However, around 15 days after the end of a course of antibiotics the discomfort would resume despite correct hygiene habits. The patient needed to take daily doses of phenazopyridine hydrochloride to have some reduction of the persistent dysuria.

The patient did not have diabetes mellitus, neurologic conditions, chronic institutional residence history, chronic indwelling urinary catheterization or other important predisposing factors for complicated UTIs. There was no history of spermicide use or frequent sexual intercourses, both also related to recurrent UTIs.

She was admitted for a UTI episode, confirmed after urine analysis and culture, showing a multisensitive community-acquired *Escherichia coli.* Her routine lab tests also showed a normal cytology pap smear and normal colposcopy, but positive hybrid capture Human Papillomavirus (HPV) DNA assay (PapilloCheck®) on her vaginal wall swab. HPV genotype 51 (high risk) was found. Since then there were no corresponding lesions in the genital area and the gynecologic examination was normal, her gynecologist did not propose any treatment and suggested watchful waiting. She would be passively followed for the development of cervical lesions.

For the recurrent UTI the treatment was as follows: 3 bladder irrigations of ozonated distilled water (250 mL of water ozonated at 50 µg/mL during 15 min). The water was injected into the bladder after normal urethral catheterization once a day during 3 days. The patient was told to hold the liquid in the bladder for the longest time possible. No antibiotics were recommended for this episode.

For the vaginal HPV she also received weekly vaginal ozone insufflations (200 mL of 20 µg/mL oxygen-ozone mixture), and ozonated oil was applied at home in the vagina twice a day. This regimen was done for 15 weeks.

She was also started on weekly treatments of Major Autohemotherapy (3,5 mg of ozone per session and 100 mL of blood) for a total of 20 sessions.

The dysuria disappeared after the first bladder irrigation. Four months after the end of the treatments the patient remains asymptomatic, the hybrid capture Human Papillomavirus (HPV) DNA assay is negative on the genital swabs and the urine analysis is normal.

Discussion

Human papillomavirus is a necessary cause for the development of carcinoma of the cervix and its precursors.[1,2,3] The prevalence of genital HPV infection has steadily increased over the past 20 years, which varies among different countries and even between different populations within countries.[4,5]

No treatment is usually indicated for asymptomatic HPV positive women without abnormalities on pap smear, even if the patient has high risk virus genotypes. This is partly due to the lack of efficient drugs against HPV. From our point of view, these women, although not ill yet, harbor a sexually transmitted virus and can spread it to partners.

Recurrent UTIs are symptomatic UTIs that follow resolution of an earlier episode, usually after appropriate treatment.[6] Recurrent UTIs include relapses (i.e., symptomatic recurrent UTIs with the same organism following adequate therapy) and reinfection (i.e., recurrent UTIs with previously isolated bacteria after treatment and with a negative intervening urine culture, *or* a recurrent UTI caused by a second bacterial isolate).[7]

Most recurrent UTIs are thought to represent reinfection with the same organism.[6] Recurrent UTIs are common among otherwise healthy young women with anatomically and physiologically normal urinary tracts.[7] Further investigations of underlying anatomical abnormalities are not routinely indicated.[8]

Escherichia coli is the predominant uropathogen (80 percent) isolated in acute community-acquired uncomplicated UTIs, followed by *Staphylococcus saprophyticus* (10 to 15 percent).[9]

In recurrent uncomplicated UTIs, reinfection occurs when the initially infecting bacteria persist in the fecal flora after elimination from the urinary tract, subsequently recolonizing the introitus and bladder.[6]

A number of host factors appear to predispose otherwise healthy young women to recurrent UTIs. These include local pH and cervicovaginal antibody changes in the vagina; greater adherence of uropathogenic bacteria to the uroepithelium; and possibly pelvic anatomic differences, such as shorter urethra-to-anus distance.

A three-day course of trimethoprim/sulfamethoxazole is the current standard therapy, with three days of trimethoprim or a fluoroquinolone (i.e., ofloxacin, norfloxacin, or ciprofloxacin) being equally effective. The antimicrobial susceptibility profile for uropathogens in a community should guide treatment decisions.[10]

Continuous antimicrobial prophylaxis for six to 12 months reduces the rate of UTIs during the prophylaxis period, with no difference between the six-month and 12-month treatment groups after cessation of prophylaxis.[11]

Although conventional treatment is based on antibiotic use, the impact of such drugs on the microbiota, immune response should not be minimized. Antibiotic-induced disruption of the microbiota and immune homeostasis can lead to multiple diseases.[12]

Ozone has the capacity to inactivate bacteria, viruses, fungi, yeast and protozoa.[13-20] When applied externally in a form of gaseous mixture or in ozonated solution (oil, water or saline) it produces direct oxidative effect on the microorganism membrane. Ozone can destroy practically all kinds of bacteria, viruses, fungi and protozoa. Gram-positive bacteria and capsular viruses having a lipid bio-layer are particularly sensitive to oxidation.[20,21,22]

Ozone has been used to treat gynecological infections or genital inflammatory conditions, such as colpitis, bacterial vaginosis, adnexitis, endometritis, parametritis and pelvioperitonitis. In dermatology ozone has successfully treated acneiform eruptions, furunculosis, pyodermia, herpes, psoriasis and mycosis.[20]

A recent report showed efficacy, safety and the low cost treatment of skin verrucas, usually caused by HPV, with ozonetherapy.[23]

The use of ozone is based on its oxidative, antiseptic and bactericidal properties. Ozone inactivates bacteria and fungi through oxidation of the phospholipids and lipoproteins in a much less time compared with chlorine. It is also very effective in destroying viruses and carcinogenic agents, which in most cases are not killed by usual chemicals used for water purification. Being able to destruct smell-creating substances, ozone came to be used as deodorant agent.[20]

Our patient had a high risk HPV genital infection against which no good treatments were available. Pap cytology is limited since it detects the symptoms but not the cause for cervical cancer, which is a persistent infection with carcinogenic human papillomavirus (HPV). It has now been firmly established that infection with high-risk papillomavirus (HPV) types is the primary cause of almost all cervical cancers.

She had been using antibiotics for recurrent UTI, without definitive resolution. In order to avoid more disruption of the body microbiota with such drugs, we opted to use ozone, which has the property to eliminate microbes and dissolve bacterial biofilms without the risk of microbial resistance.

Consequently we decided to recommend ozonetherapy, due to its microbial, immune-enhancing properties, anti-inflammatory and analgesic effects, favoring tissue healing.

The use of therapeutic ozone concentrations provides bactericidal effect which indirectly activates the non-specific defense system (phagocytosis activation, enhanced synthesis of cytokines-interferons, interleukin tumor necrotic factor) as well as components of cellular and humoral immunity.[20,24-26]

Anti-inflammatory effect is revealed in ozone capacity to oxidize the compounds containing double bonds, the arachidonic acid (20:4) and its derivatives - prostaglandins, in particular. These biologically active substances participate in the development and sustaining the inflammatory process. Besides, ozone regulates metabolic reactions in tissues at the place of inflammation and resolves pH.[20]

Ozone analgesic effect is provided by oxidation of the products of albuminolysis, the so-called algopeptides. They act on the nerve endings in the damaged tissue and determine the intensity of pain response. To add to that, analgesic effect is also caused by normalization of antioxidant system and accordingly, by the decrease in the amount of toxic molecular products of lipid peroxidation on cellular membranes, that modify the function of membrane-inbuilt enzymes, which participate in ATP synthesis and in maintaining the vital activity of organs and tissues.[20]

Conclusions

Although orthodox medicine has provided a variety of topical and systemic anti-infective agents, some of them have become scarcely effective owing to antibiotic- and chemotherapeutic-resistant pathogens or simply due to primary inefficacy. For more than a century, ozone has been known to be an excellent disinfectant that nevertheless had to be used with caution for its oxidizing properties. Only during the last decade it has been learned how to tame its great reactivity by precisely dosing its concentration.

This case report demonstrates the bactericidal, virucidal, antinflamatory and analgesic effects of ozone used to treat both a bacterial and a viral infection. We used the 3 fundamental forms of application of ozone: (1) ozonated water, (2) ozonated vegetable oil, and (3) oxygen/ozone gas mixture.

More studies should be implemented for both types of infection. Ozonetherapy might be a good solution for the increase of antibiotic-resistant germs. Also, it might be effective as a primary care approach to reduce the transmission of HPV and the prevalence of HPV induced-cancers.

A longer follow up will be needed to confirm the long term benefits of ozone in this case. However, we believe we were able to bring quick and persistent comfort and the clearance of a high-risk oncogenic virus, thus reducing the chances of transmission and tissue damage.

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