RUPTURED ULCERATED AND INFLAMED GOUT TOPHI WITH DEEP SOFT TISSUE INFECTION OF LEFT FOOT – WHEN RHEUMATOLOGY MEETS SURGERY: A CASE TREATED WITH LOCAL OZONE THERAPY

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Abstract. *Tophaceous gout is a rare condition and chronic complication of gout due to storage of derivatives of uric acid – crystals of monosodium urate, accompanied by lipids, mucopolysaccharides matrix and proteins. Rheumatology meets the surgery in cases of rupture, ulceration and inflammation of tophi with complication with severe soft tissue infection, sepsis, large swelling, destruction of affected joints and chronic periphery neuropathy pain. Spontaneous or traumatic perforation and ulceration of tophi are rare conditions, which is why there are no rheumatology or surgical guideline for management of that condition. We present a case report of a male patient with posttraumatic perforated gout tophus and secondary soft tissue infection of left foot. He was treated with standard surgical debridement and local ozone therapy with stabilized ozonides over wound surface. The article presents a pioneer experience in the treatment of complicated tophaceous gout with topical administration of ozonated olive oil with vitamin E and shows the effect of treatment in progress.*

Key words: *tophus, gout, local ozone therapy, soft tissue infection*

Introduction

Tophaceous gout is a rare condition and chronic complication of gout due to storage of derivatives of uric acid – crystals of monosodium urate, accompanied by lipids, mucopolysaccharides matrix and proteins. The granulomatous inflammatory process is characterized by giant cell and mononuclear cells infiltration that surrounds the deposited crystals [1]. It affects patients with a long history of gout and poor control of plasma uric acid concentration. Common location of gouty tophi includes periauricular subcutaneous areas, joints, bones and soft tissues of upper and lower extremities. Rare surgical complications of tophi described are ulceration and secondary infection that may involve joints or deep soft tissues of extremities. The conservative treatment requires medication and control over the serum levels of uric acid to not to exceed 6 mg/dl with inhibitors of enzyme xanthine oxidase, together with dietary regime and changes in lifestyle: low purine food intake, stop drinking alcohol and optimizing of activities' schedule [2]. Continuously controlled and monitored levels of uric acid result in decrease of acute attacks and chronic progression to tophi formation. The prevalence of tophi formation in gouty patients may arrange between 10 to 35% [3, 4] Rheumatology meets the surgery in cases of rupture, ulceration and inflammation of tophi with complication with severe soft tissue infection, sepsis, large swelling, destruction of affected joints and periphery neuropathy. Spontaneous or traumatic perforation and ulceration of tophi is a rare condition, which is why there are no guidelines for management of the condition [1, 5]. The surgical treatment may be local debridement and evacuation of tophaceouse content with subsequent local dressings with mupirocin, colloid silver – sponge absorbable dressings and lyophilized collagen base. Indications for surgical treatment in gout patients are infection of tophi, joint movement blockage, severe pain and deformation of the joints and invalidization of the patients [6]. More severe cases with adjacent soft tissue infection required excision, curettage and local necrectomy with risk for the amputation in case of damaging of the bone due to osteomyelitis. Some surgeons use the techniques of lavage with saline solution with a good final result of shaving procedures and hydrodebridement [7]. The outcome of surgical treatment may lead to invalidization because of amputation of limb in cases with ulceration, which does not respond to generalized antibiotic treatment and lack of effect of local wound infection control by necrectomy and wound debridement. Until now in literature we do not find articles describing the usage and the final effect of local ozone therapy in cases with inflamed, ruptured or ulcerated gout tophi as a part of the complex wound healing process. Therefore, the article presents a pioneer experience in the treatment of complicated tophaceouse gout.

Case report

We present the case of a 76-year-old male patient, Caucasian race, with a long history of gout – more than 30 years. He did not follow his rheumatologist's recommendations about diet and lifestyle. During that period, he had unfavorable metabolic control over uric acid levels. He was smoker – one pack of cigarettes daily; he drinks hard alcohol – 100/150 ml every evening. This caused predisposition to formation of multiple tophi on his hands, arms, legs and foots. He did not have relatives with gout. The last gout crisis was 14 days before the admission in Department of Surgical diseases, Medical University of Pleven. During a crisis of gout, he took no steroid anti-inflammatory drugs (NSAIDs) 75 mg/day Diclofenac sodium, Colchicine – 500 mcg, and in non-symptomatic stages Milurit (Allopurinol) 100 mg per day. He had an accident of falling in the bathroom and one of the tophi, located over the left foot, medial surface, was ruptured. After the trauma, a purulent gelatinous-hemorrhagic substance was discharged and the site of the ruptured tophus was inflamed. The patient refused to visit his physician immediately after the accident. He did not applied sterile bandages in outpatient settings. After 4 days, he presented to emergency department with severe soft tissue infection and a huge skin defect over his left foot, in the place of the ruptured tophus. The general physical examination objectively documented that the patient was in a moderate general condition, with Glasgow comma scale 14 points, body temperature 36.7ºC, blood pressure 125/80 mm Hg, pulse 86 beats per min. The patient is with normostenic body composition, weight 83 kg, height 185 cm, body mass index was normal – 24.3 kg/m^2. Abdomen was soft, non-tender and non-distended, with normal peristalsis. There were multiple tophi over his ears, arms, the both hands, knees and the feet of sizes ranging from 1 cm till 5 cm in diameter, extreme deformities of the fingers of the hands (Fig. 1a, b, c, d).

Local status over the ruptured tophus was with extreme redness, edema, swelling that propagates to the dorsal plane of the left foot and up to lower leg. The area was very painful and the motion was disturbed. The skin defect was in size 5 cm/8 cm, with lack of epidermis, the base of wound was contaminated, and wound edges were with a poor blood circulation.

The laboratory test described white blood cell count 6.3 x10^9, neutrophils – 75.4%, CRP – increased more than 8 times the upper limit – 44 ng/l, Uric acid 468 mcmol/l. Blood glucose level was in the normal range. Wound microbiology detected Staphylococcus aureus in wound secretion, susceptible for cephalosporins and lincosamides. The X- ray of the hand and feet did not show osteolytic isles or severe inflammatory damage of the bones structure, only detected deformities due to chronic storage of uric acid derivatives in tophi (Fig. 2). With X-ray of the left foot with frontal projection there were no visible destructive bone changes, only degenerative changes were described (Fig. 3).

We started the complex treatment of the patient first by surgical treatment followed by administration of systemic antibiotic Clindamycin 600 mg, three times per day in a combination with metronidazole 500 mg, three times per day as a part of therapeutic treatment.

We obtained an informed consent of the patient for surgical treatment and treatment with innovative method and informed agreement to describe the treatment and to publish the results of that innovative soft tissue infection treatment. Our research was approved by the local Ethics Committee of the UMHAT "Dr G. Stranski" – Pleven, with resolution that there were no ethical contraindications and environment for further conflicts.

The local treatment took place with innovative antibacterial formula, based on local administration of OzoilE – ozone molecules joined to olive oil vehiculum, rich of oleic acid, with combination with vitamin E. The generic formula of that content includes stabilized ozonides mixed with antioxidant vitamin E. The trade name of the products are Idrosoil Erbagil and Rigenoma spray – for "shock therapy" in severe contaminated wounds. Both products are trade marks of Erbagil, an Italian patent 0000278374, approved by the Ministry of Economic Development – the Italian office for patents and trademarks. Salvis Pharma Ltd. distributes these pharmaceutical products in Bulgaria. We used the following algorithm for local administration of ozonides: after surgical necrectomy and wound debridement we performed wound lavage with Idrozoil – a liquid detergent, rich of ozone molecules with soft cleansing effect over the tissues – for removal of wound secretions and local microflora. We used it concentrated in the first wound debridement and in solution with saline 0.9% sodium chloride in proportion 1:1 in the next surgical debridement procedures. The second step was application of Rigenoma spray and application or Rigenoma crème on the periphery of the wound. The surrounding skin was cleaned with Iodopovidone and it was not administered over the wound surface, where ozonides act, because of possibility of inaction. The final step was covering the wound surface by sterile wet gauze dressing.



Fig. 1a. Left hand with tophi



Fig. 1b. Right hand with tophi



Fig. 1c. Left knee with tophi

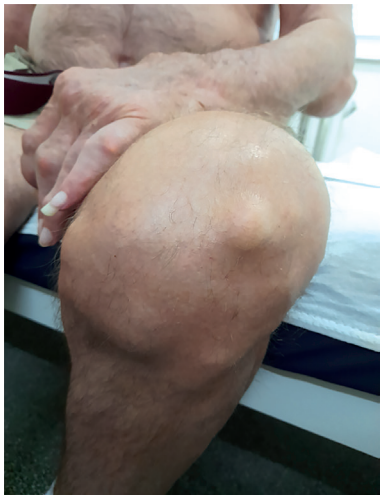
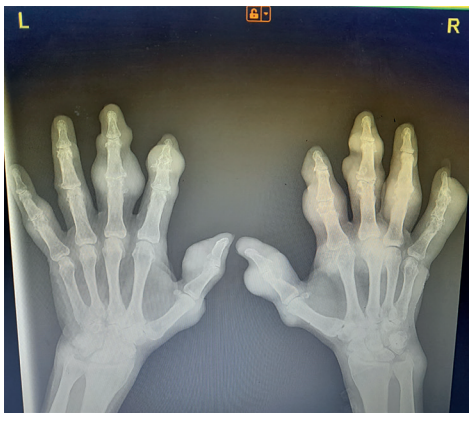


Fig. 1d. Right knee with tophi



a



b

Fig. 2. X ray of the hands



Fig. 3. X ray of left foot

We repeated these steps in every day scheduled procedures and documented the wound healing process in dynamics. The results are shown on Fig. 4a, b, c , d.

We observed better wound healing process with reduction of local edema; erythema and necrotic places were successfully replaced by isles of granulation tissue and nascent epithelization.

The patient was discharged on the 5th day after admission with negative microbiological results for any microbes, normalized levels of C-reactive protein and lack of febrility, with improved active movement in left foot, after active rehabilitation in the department. The patient was consulted with rheumatologist and permanent treatment for gout with febuxostat 120 mg per day was prescribed.

The uric acid level on discharge was normal – 390 mcmol/ l, wound was sterilized and there were no microbial agents from microbiological verification in the end of treatment, with normal leukocyte and CRP levels.

Discussion

Foot, ankle and Achilles tendon are the most usual places of deposition of monosodium urate and tophus formation of lower leg. The first metatarsophalangeal articulation was exposed to damaging due to uric acid crystals deposition and changes in architecture of that joint. The point of maximum tension and body weight stress is just this place of the foot, together with the fifth metatarsophalangeal joint and calcaneus. Arthritis, chronic pain, its exacerbation and tophus formation lead to impaired movements and disability due to severe chronic pain.

Surgical procedures in complicated gout tophus are a part of non-pharmacological treatment of complicated gout and tophus. It aims to manage the inflamed and ruptured tophi, to prevent their complications as ulceration and pain exacerbation ant to improve movements and quality of life. In 2016, Poratt et all. performed a study and metaanalysys over surgical treatment of lower leg in gout patients [8]. There are variety of surgical interventions over the soft tissues as wound debridement, curettage and closure of huge skin defects by flap grafts and procedures over the bones and articulation-arthroscopy for removal of uric acid crystals; arthrodesis. The effect of surgical treatment may vary from reduction of attacks to different complications as persistence of regional pain, impaired wound healing process with focal necrosis, rebound of infection and amputation due to sepsis [8]. The systematic reviews do not highlight just one surgical method to be of choice in complicated tophi, and we do not find arti-



Fig. 4a. Day 1 of treatment



Fig. 4b. Day 6 treatment



Fig. 4c. Day 10 of treatment



Fig 4d. Day 15 of treatment

cles describing the method of local ozone therapy as a non-pharmacological and surgical local treatment in ulcerated or perforated or inflamed tophi in gout patients.

The secret of ozone therapy in tissue recovery from severe infections is the molecular formula of ozonides: a chemical product of the reaction between ozone molecules and the oleic acid originated in the olive oil base. An OzoilE formula is unique for ozonated oils. It is established by special ozonation process, patented as an original chemical reaction between the ozone molecules oleic acid molecules and vitamin E in specific pressure and temperature condition. The patented OzoilE formula consist of stable ozonides with vitamin E acetate (Fig. 5) [9, 10].

The ozone therapy is based on the local tissue effect of ozone molecules – antioxidant effects, immunomodulation. The stable ozonides inhibit cyclooxygenase and lipoxygenase activity, and the result is decreasing of production of prostaglandins. Ozonides stimulate activity of monoamine oxidase (MAO) and diamine oxidase (DAO) to decrease production of histamine and serotonin. This leads to decreasing of local redness, capillary permeability and tissue edema [11, 12] Local ozone therapy may affect the local microcirculation, improving of the oxygen metabolism in the cells, improving of mitochondrial function and increasing of production of adenosine triphosphate (ATP). The soft tissue regeneration is stimulated by ozonides with stimulation of production of several growth factors – the epidermal (EGF), transforming growth factor-beta (TGF-beta), fibroblast (FGF) and vascular-endothelial (VEGF) growth factors. All these growth factors stimulate proliferative stage of tissue regeneration with collagen fibers synthesis, neoangiogenesys and epithelization [13, 14]. Antibacterial and antifungal effects of ozonides are realized by hydroperoxides – active oxygen radicals, which destruct the microbial wall due to oxidative stress. Antibacterial effect of ozonides without any tissue toxicity or evidence for allergy reactions make them preferred for a local advanced and enhanced treatment strategy with possibility for shortening the antibiotic course duration. With that antibacterial activity, ozone therapy helps preventing of changes in body and local microbiome, induced by antibiotic treatment. The olive oil component in ozonides prevents wound dehydration and has therapeutic effect over irritated skin: it reduces local discomfort, protects the epidermis and preserves elasticity of the skin [15]. A systemic review over effect of topic ozone therapy in chronic wounds and ulcers in diabetic patients and patients with chronic arterial insufficiency do not report any adverse events or complications.[16, 17] On investigation over 10 patients with gout and hyperuricemia, the application of systemic ozonated autohemotherapy leads to increasing of creatinine clearance rate and decreasing of pain according visual analogue scale (VAS) score. The most effective and safe dose for ozone was accepted 20 μg/ml for ozonated autohemotherapy [18]. The study on the effect of ozonetherapy in gout in experimental study over rats models concluded that intraperitonealy administered ozone therapy reduces statistically inflammatory process in acute stage of the disease [19]. Unfortunately, we did not find any information or any results of effect of local administration of ozone therapy in complicated gout tophi in the literature. Surgical treatment, alone, for gout tophi is associated with postoperative complications, especially in septic patients or patients with comorbidities, associated with history of chronic and untreated gout – hypertension, diabetes mellitus and chronic arterial diseases. In a cohort study on 45 patients, 53% of operated patients had delay of wound healing because of a post-surgical complication. Prevention of all possible complications includes improved control over the serum levels of uric acid by proper medication by rheumatologists [20, 21].

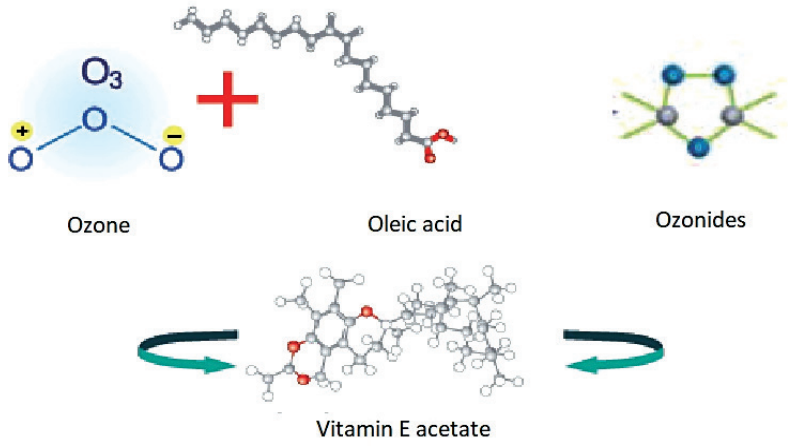


Fig. 5. Ozonides molecule structure [12]

Conclusion

Ozone therapy is an emerging treatment strategy that acts via complex mechanisms, including antioxidant effects, immunomodulatory capacity, and modulation of local microcirculation. In literature, we did not find any article about the application of local ozone therapy in patients with complicated tophi and soft tissue infection

due to gout. We are pioneers in surgical treatment of complicated rheumatological diseases and we report the effect of standard surgical methods and innovative pharmaceutical products in complicated wound healing. Our experience with treatment of complicated tophus with local ozone therapy is a novel method and we are the pioneers in application of ozonides in tophaceous gout. Topical ozone therapy is a new and useful method for treatment of complicated gout tophi.

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