CASE STUDY

INFECTIONS MANAGEMENT IN VENOUS LEG ULCERS: A SINGLE CENTER EXPERIENCE

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ABSTRACT

Objectives. Chronic wounds have a prolonged period of healing due to numerous factors, including infections. Venous ulcers represent almost 80% of the lower extremity ulcerations, having a great impact on the patient's quality of life.
The objective of this study was to evaluate the presence of bacteria and the proper management in treating venous leg ulcers.
Material and methods. The study enrolled ten patients with chronic venous leg ulcers hospitalized in the Plastic Surgery Department of the Emergency Clinical Hospital "Prof. Dr. Agrippa Ionescu", during a period of six months. For each patient included in the study, we assessed the wounds culture and we started an antibiotic treatment, according to the antibiogram, which was completed by the surgical treatment of the wound.
Outcomes. Venous leg ulcers had a favorable outcome after the administration of antibiotic therapy, surgical debridement of the wound and coverage with a skin graft.
Conclusions. Venous ulcers may evolve over an extended period of time (weeks or years) and may also be associated with severe complications, such as cellulites or malignant transformation. Infections affect the healing process. Surgical debridement associated with systemic administration of antibiotics has a favorable outcome in the epithelialization of venous ulcers.

Keywords: chronic wound, venous leg ulcer, bacteria, antibiotic therapy

INTRODUCTION

A wound represents a damaged tissue caused by the destruction of a layer, usually the skin (1). Wound healing involves several steps, among which we mention the following phases: inflammatory, proliferative and remodeling. In the first 6 days of evolution of a wound, processes like vasoconstriction, coagulation, vasodilatation, chemotaxis of coagulation factors, migration of cells and cellular response of neutrophils, macrophages and lymphocytes take place. These processes correspond to the inflammatory phase. The next phase is represented by the fibro-proliferative phase, from day 4th to the 3rd week, when the matrix is formed from glycosaminoglycan and fibroblasts; angiogenesis is stimulated by the vascular endothelial growth factor and epithelialization begins (1). The last phase is the maturation or remodeling phase, from the 3rd week to the first year and it consists in the organization of the collagen fibers and in replacement of type I collagen with type III, in a ratio of 4:1 (2).

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Unlike normal wounds, healing of chronic wounds remains in the inflammatory phase and do not progress, due to different factors as: age, infections, ischemia, malnutrition, diabetes, cancer etc (3).

Skin is a host to a large number of commensals bacteria (1). When a wound appears, the bacteria contaminate it. The wounds are considered contaminated when bacteria are present in a lower number, and colonized when bacteria are multiplying, with minimal reaction from the host. Critically colonized wounds are characterized by low response of the host, while those infected are characterized by bacterial proliferation with tissue damage, with a growing host reaction. Some of the wounds become infected and so the excessive number of pathogens will affect the healing. Wound infection is defined as a quantitative culture of 10^5 bacteria per gram of tissue. This value is not so often used due to the underperformance of some laboratories. Also, the association of ischemia, diabetes and other comorbidities may reduce the threshold for detection of infection (4).

Chronic wounds are often associated with colonization of pathogenic bacteria (1). Even though some bacteria are not pathogenic, their multiple associations in chronic wounds determine an evolution to critical colonization combined with slow progression in healing (4). Some of the most frequent bacteria in chronic wounds are *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter, Escherichia coli*, *Peptoniphilusand Serratia* (1).

Venous trophic ulcers are open wounds located between the knee and the ankle that appear due to venous disease, representing 80% of the lower extremity ulcerations (5). Around 33 to 60% of venous trophic ulcers have an evolution longer than 6 weeks and so there are considered chronic venous leg ulcers (6). One of the main factors that influence and delay the healing of leg ulcers is bacterial infection (3).

The purpose of this paper was to identify the optimal treatment of infected chronic venous ulcers in order to improve the quality of life in patients with this condition.

MATERIAL AND METHODS

We enrolled ten patients with chronic leg ulcers due to venous disease, over 6 months.

The inclusion criteria were defined as venous leg ulcers older than 6 weeks. Local ethical agreement and informed consent of the patient were obtained.

At admission, usual blood tests, a bacterioscopic examination and a culture from the wound were performed. We also conducted a nutritional assessment and most of the patients with chronic wounds were suffering from protein and micronutrient malnutrition.

Empiric antibiotherapy was administered to patients with signs of severe infection as cellulites, characterized by erythema, pain, edema and warmth. The other patients received antibiotic after the interpretation of the antibiogram.

Wound dressings included silver sulfadiazine and antiseptic and the patients were advised to raise the lower extremities above the level of the heart, in order to reduce edema and to improve micro-circulation and ulcer healing.

Surgical treatment was started in patients refractory to conservative therapies (Fig. 1). Debridement was necessary to remove necrotic tissue and bacterial burden (Fig. 2). After debridement and antibiotic therapy, a new bacterioscopic examination and culture were performed. In cases with negative cultures, a new surgical procedure was scheduled and the ulcer was covered with a split thickness skin graft (Fig. 3). Protein and caloric deficits were replaced by the addition of micro-nutrients.

RESULTS

Within the study group, 50% of patients were at the first hospitalization and 50% of them came from other medical centers. Initial treatment in those admitted from other medical centers had failed.

FIGURE 1. *Nonhealing chronic venous ulcer*

FIGURE 2. *Venous ulcer after surgical debridement*

The most frequently encountered germ was *Staphylococcus aureus*, found in six out of ten patients, four of them being resistant to Methicillin. In patients at the first admission, only one germ was identified on the wound, *Staphylococcus aureus* in three cases, *Enterococcus faecalis* and *Enterococcus faecium* (each in one case). The other half of patients with previous hospital admissions had at least two pathogens isolated

FIGURE 3. *Venous ulcer covered with a split thickness skin graft (5 days after surgery)*

from the wound: *Staphylococcus aureus* associated with *Klebsiella pneumonie* or *Escherichia coli* and *Pseudomonas aeruginosa; Proteus mirabilis* associated with *Escherichia coli, Pseudomonas aeruginosa* with *Klebsiella oxytoca* and *Morganellamorgani* or *Enterecoccus faecalis* with *Stenotrophomonas maltophilia*. These pathogens had multiple antibiotic resistances, targeted antibiotics for a long period of time being required.

As an empirical antibiotic for clinical infected ulcers associated with cellulitis, was used a second-generation cephalosporin that was in some cases subsequently changed based on the result of the antibiogram. In *Staphylococcus aureus* infections, the most frequent used class of antibiotics, based on the antibiogram, were the fluoroquinolones. In cases where multiple pathogens were isolated, Polymyxin E was associated with fluoroquinolones (Ciprofloxacin), with a second-generation cephalosporin (Cefuroxime) or with an antibiotic from the glycylcycline class (Tigecycline). The median period of time of antibiotic administration was 7 days. After two days from the end of antibiotic treatment, a new culture was obtained. If this culture was sterile, the patient was scheduled for a new surgery and the wound was skin grafted. Before this second

surgery, trying to maintain a hemoglobin higher that 8 g/dl and total serum proteins more than 4,5 g (to promote skin graft integration), hemoleucogram and total serum proteins were screened. If the culture was positive, a new antibiotic therapy was started taking into consideration the result of the drug susceptibility test.

DISCUSSIONS

Chronic wounds are predisposed to bacterial infections. Venous ulcers are included in this category, especially due to tissue hypoxia (3). This impairs the action of leucocytes on bacteria by lowering the "oxidative burst" (4).

Bacteria affect the wound in different ways. One of the most harmful ways is the maintaining of the inflammatory response with secretion of toxins and proteases, which destroy the growth factors and impairs wound healing through a creation of proteinaceous debris like a pseudoeschar (4). Another way of affecting healing is through biofilm, an association of bacteria embedded within a self-produced matrix. This biofilm becomes resistant to host immune response, topic antimicrobial agents and antibiotics triggering an inflammatory response. This places the wound in a prolonged inflammation that determines secretions of cytokines and proteases with degradation of wound tissue (7). Wound culture in these cases have limitations because many of the pathogens contained in the biofilm cannot be isolated, and often a molecular method is necessary (8).

Usually, every decrease of a wound rate of healing should be considered infected, a bacterioscopic examination and culture being necessary. There are also some others suggestive signs of wound infection present in our enrolled like pain, increased edema, increased discharge, change of aspect and smell of the drainage (7).

Usually systemic antibiotics are not necessary, but a local treatment which includes opening the wound, debridement and proper cleaning is mandatory (5). Antibiotics are administered in wounds with a good perfusion and in infected wounds associated with cellulitis, acute decreased healing or increased pain (1).

In our study, the antibiotic was chosen according to patient's wound vascular status, leukocyte and kidney activity and was administered empirically until the antibiogram result was ready. The choice was based, as in other studies, on the grade of infection and on the epidemiological data (9,10). Usually mild infections were caused by Gram positive cocci, especially *Staphylococcus aureus,* while moderate infections had pyogenic Gram positive cocci and in some cases also Gram negative bacteria. Mild and infected wounds were treated empirically with a Gram positive cocci antibiotic and severe infections with a broad spectrum antibiotic, due to their polymicrobial etiology.

The appropriate route of administration was parenteral and was changed to oral when the patient stabilized.

CONCLUSIONS

Infection plays an important role in delaying chronic wounds healing. The presence of biofilm decreases the activity of topical or systemic antibiotics and it is correlated with a poor prognosis.

The administration of systemic antibiotics is very important to be based on the antibiogram and not to be extended over a long period of time. Surgical debridement is an important part of the venous ulcer management, lowering the bacterial load and biofilm and empowering the antibiotics activity.

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