Microbiota, Biochemical Environment and Clinical Management of Neuropathic Ulcers

Miguel Ángel Acosta Benito*, and Silvia Estrada de la Viuda
Madrid’s Public Health Service, Universidad a Distancia de Madrid (UDIMA University), Spain

Abstract

Post traumatic neuropathic ulcers are similar to those in patients with diabetes mellitus. The different biochemical and microbiological conditions in the various strata of the ulcers suggest that there is a relationship between microorganisms that appear in each stratum and those biochemical conditions which may be decisive in treatment.

We present the case of a woman with post-traumatic neuropathy that has a foot ulcer in which Morganella morganii, Pseudomonas aeruginosa, E.coli and Streptococcus agalactiae are isolated. Exclusively mechanical handling is decided. Antibiotic treatment is not administrated due to the resistance generated by interactions between microorganisms and the physical and biochemical environment in the different levels of depth of the wound, because it avoids healing.

It is necessary to study the preference of different organisms for each stratum of the wound, the biochemical interactions and the immune regulation that occurs in them to understand the evolution of neuropathic ulcers and improve their treatment.

INTRODUCTION

Neuropathic leg ulcers are a frequent entity for primary care physicians, surgeons and other specialists. They are produced by changes in the pressure on the region affected, and usually require long treatments with a slow progression of the disease and frequent complications. Poly microbial nature of infections and certain immunological and biological mechanisms that establish stratification at various levels according to the deep of the ulcer are the causes of this progression. We present a case of a woman with posttraumatic sensory neuropathy who developed an ulcer, in order to discern about these mechanisms.

CASE PRESENTATION

We present a case of a 31-years-old woman with 20-pack-year smoking, and not alcohol consumption. She suffered a car accident in November 1999 with complex pelvic fracture, right hemithorax, left sacroiliac dislocation, comminuted fracture of the right sacral wing, isquiopubian bilateral fractures, pubis diastasis, and fractured right iliac blade and transverse L5 process. She has been operated on multiple occasions due to these problems.

She follows treatment with a continuous subcutaneous infusion pump and intrathecal catheter amounting to T11 (4% bupivacaine 10 ml and 2% Morphine 10 ml), 800 mg carbamazepine, oxycodone 80 mg, and clonazepam 2 mg each eight hours, oral contraceptives, hidroaltesona 20 mg each 12 hours, and morphine rescues if breakthrough pain.

The patient comes in to the primary care center presenting an ulcer in the right heel with a year of evolution, which has been treated by podiatrist without improvement. There is an ulcerated lesion in the calcaneus, whitish, with hyper keratotic border, with no signs of infection, and bone seen. It is not painful on palpation. It has appeared in the member affected by neuropathy after the accident (electromyogram: severe multiple root injury in the right leg). It is treated from the start with silver sulfadiazine and is derived to plastic surgery. Gammagafry discards osteomyelitis.

A first crop of ulcer material is performed and shows Morganella morganii, Pseudomonas aeruginosa, E. coli and Streptococcus agalactiae. Plastic surgery service decides not to treat with antibiotics and an ulcer debridement is performed. The cures are performed again by washing and application of silver sulfadiazine.

One month after surgery a sample of the ulcer is taken again and shows Psuedomonas aeruginosa, Enterococcus and...
Osteoarthritis is a risk factor for the appearance of postsurgical neuropathic ulcers. The appearance of neuropathic ulcer is related to decreased sensitivity and pressure changes in the patient’s foot. Risk factors for the occurrence of these ulcers include the presence of previous minor injuries, history of long-term ulcers and wide variation in the number of daily footsteps [2].

Neuropathic ulcers secondary to trauma share the pathophysiologic mechanism of neuropathic ulcers of patients with diabetes mellitus, which are much more frequent. That is why the microbiota of both types can be similar. Most frequent bacteria’s found in diabetes ulcer are *Staphylococcus aureus* and *Pseudomonas aeruginosa* [3]. However, the characteristics thereof vary depending on the characteristics of the ulcer. Deep and long-standing ulcers have a greater amount of anaerobes and proteobacteria. *Staphylococcus* is more common in shallow and short-lived ulcers. *Streptococcus*, meanwhile, are more prevalent in diabetic patients [4]. It is possible, therefore, that the microorganisms present in each type of ulcer involved in its evolution and can be related to the previous patient co morbidity.

*Pseudomonas aeruginosa* is a bacterium that can colonize neuropathic ulcers, and there is no dear consensus on the first-line antibiotic therapy to be used. It produces severe and complicated infections, and features a wide antibiotics resistance [5]. However, the most common strains in chronic ulcers are firmicutes or enterobacteria (40 %), Proteobacteria (24%) and *actinomycetes* (19%). In each ulcer, maybe, there are different kinds of bacteria in each level of depth of the lesion, which generates a different metabolic environment in these levels [6].

Recent works have shown there are mechanisms of apoptosis that slow and impede tissue repair in case of ulcers. In the case of skin ulcers, these mechanisms employ the extrinsic pathway of apoptosis. The increase in the production of tumour necrosis factor alpha (TNFα) is associated with an increased activation of this pathway through the Fas ligand and with caspasas [7] intervention.

It has been shown that in patients with severe infections there is a modulation of macrophages and monocytes that modifies the inflammatory response and the production of TNFα. Studies in mice indicate that the immune response to infection is modulated, so that patients can express an increased production of TNFα and reactive oxygen species that facilitates tumour necrosis and complicates the healing of the cutaneous ulcer [8].

The previously described association between the various layers of a skin ulcer and the presence thereof of a different biochemical and microbiological [6] environment may be the cause of polymicrobial infections and resistance to the action of antibiotics.

Biofilms created by bacteria in each of the layers increase the resistance to antibiotics, and make necessary that, as in our case, the treatment of ulcer needs of mechanical treatments, both chemical or with debridement. Breaking the biofilm improves the healing and the prognosis [9].

The case presented is a practical example that involves the factors discussed. The presence of multiple microorganisms isolated from the ulcer studied, arised from neuropathy, and the slow response to surgical management suggest that the relations of the biochemical conditions generated from the interaction between bacteria and biochemical environment are behind the clinical response to treatment and the evolution of the ulcer.

It is necessary to continue the study of these biochemical interactions and immune regulation in relation to the individual’s response to stress and pressure against the colonizing organisms. New therapeutic targets will try to regulate inflammatory activity to improve immune response and decrease apoptosis, so the virulence of local infection can decrease.

REFERENCES


