

Antibiogram in the biopsy of chronic venous ulcers related to sudden changes in the pain profile

J.M. PEREIRA DE GODOY

SUMMARY: Antibiogram in the biopsy of chronic venous ulcers related to sudden changes in the pain profile.

J.M. PEREIRA DE GODOY

Introduction. Chronic venous insufficiency (CVI) has an important impact on the public health system in particular due to the occurrence of chronic venous ulcers (UCV) and infections.

Objective. To evaluate cultures of biopsies of chronic venous ulcers of patients who suffered an acute change in the intensity of pain of the lesion.

Method. Antibiograms of the cultures of chronic venous ulcer biopsies of patients who suffered an acute change in the lesion with significant pain for 24 hours were evaluated. All patients were treated between 2011 and 2015 in the Vascular Surgery Outpatient Clinic of the Medical School in São José do Rio Preto. Other causes of pain such as chronic arterial insufficiency and problems with the dressings were ruled out.

Results. Positive cultures were detected in 34 of the 35 patients whose pain was resolved by antibiotic therapy.

Conclusion. Acute changes in the intensity of pain associated with chronic venous ulcers seem to be related to local infectious disease.

KEY WORDS: Venous ulcer - Infection - Antibiogram - Comorbidities.

Introduction

Chronic venous insufficiency (CVI) is a prevalent disease worldwide (1). In Brazil, this disease, in its initial form affects 53.5% and in its most severe form affects about 1.5% of the general population (2); it is more prevalent in older age groups (3). Therefore, CVI is a public health problem, and the 14th highest cause of absenteeism in Brazil.

Its etiology and pathophysiology are not yet fully understood. The main theory about the etiopathogenesis of CVI involves genetic and environmental factors that, interacting together, determine the onset of the disease. The main triggering factor is hypertension in the venous system caused by reflux or obstruction (4).

The main risk factors for the development of

CVI are advanced age, female gender, family history of the disease, constipation, obesity, number of pregnancies and lack of physical activity (5).

The symptoms of CVI vary greatly with the most common early symptoms including a feeling of heaviness and pain in the legs, especially at the end of the day. In addition, progressive edema may appear which in later stages is associated with skin irritation and pruritus. Pain becomes more serious over time and can even lead to limitations in movement.

CVI can be staged and classified, with the CEAP classification being the most used around the world; this system categorizes the disease in terms of its clinical presentation (C), disease etiology (E), anatomical site of obstruction (A) and the pathophysiology of the disease (P) (6-9).

Active venous ulcers belong to the CEAP C6 class and are in the most severe manifestation of CVI. Chronic venous ulcers (CVU) are characterized when they persist for a period of at least six weeks despite adequate therapy (10).

While the prevalence of CVU in the general pop-

Cardiovascular Surgery Department of the Medicine School in São José do Rio Preto-FAMERP and CNPq (National Council for Research and Development), Brazil

Corresponding author: Jose Maria Pereira de Godoy, e-mail: godoyjmp@gmail.com

ulation is around 1.5%, about 5% of the elderly are affected (11, 12).

There are several cellular and humoral factors associated with chronic venous hypertension that culminate in the formation of an ulcer. At sites of high venous pressure, there is a higher production of vasoactive substances secreted by endothelial cells under stress, in addition to the formation of inflammatory mediators, chemokines, increased expression of adhesion molecules and prothrombotic precursors (13).

CVU are recurrent and may persist for years (14). This significantly reduces the quality of life of patients and their relatives (15) as well as exacerbating the economic impact of the disease. In the USA, an annual cost of treating patients with CVU is estimated at up to 2 billion dollars, which is mainly related to complications of the disease (14).

Chronically open wounds are an ideal medium for bacterial growth, with colonies being found in the tissues of CVU in 80-100% of cases (16). One study identified the most common bacteria such as mainly *Staphylococcus*, *Enterococcus*, *Serratia* and *Pseudomonas* genera (17), but there are still few studies on the main pathogens involved, or on the main patterns of antimicrobial resistance associated with this condition.

The main manifestation for the suspicion of infections in CVU is pain, making this complication much more likely in patients with chronic wounds (18). The best current therapy for infections is the debridement of necrotic and devitalized tissues associated with systemic antibiotics (19) with cultures of CVU tissue often being used to guide the choice of drug (19).

The aim of the current study was, by culturing biopsy material, to evaluate the prevalence of infections in patients with CVU who suffer from sudden increases in pain.

Method

The cultures of biopsies of tissue from chronic venous ulcers and antibiograms were evaluated in patients who suffered an acute change in the pain profile of the lesion. All patients were treated in the Vascular Surgery Outpatient Clinic of the Medical School in São José do Rio Preto, Brazil, from January 2011 to January 2015.

Patients with a diagnosis of chronic venous ulcer were enrolled in this study if the pain of the lesion increased acutely from one day to the next and remained for at least 24 hours. Patients with ulcers not related to CVI were excluded from this study. During the visual examination of the ulcers, no significant hyperemia was observed, but the edges of the lesions became irregular in all patients selected for biopsies (Figure 1).

All patients were submitted to biopsies and cultures of the material were requested. Initial treatment consisted of topical dressings of silver sulfadiazine with cerium. In case of normalization of pain while awaiting the result of the culture, patients were not prescribed systemic antibiotics. Those who did not improve with this dressing received specific antibiotics with resolution of the pain being seen within two to three days.

The design of this study was submitted to and approved by the Ethics Committee in Medicine School of Sao Jose do Rio Preto-FAMERP number #CAAE: 54868116.9.0000.5415/2016.

Descriptive statistics were used to compare events with the unpaired t-test being used to compare ages. An alpha error of 5% (p-value < 0.05) was considered statistically significant.

Results

Thirty-five patients were submitted to biopsies. Twenty-four of the patients were females, with a mean age of 56.64 years and 11 were males, with a mean age of 57.63. There was no significant difference between the mean ages of the men and women (unpaired t-test: p-value = 0.8). Thirty-four of the 35 cultures of the biopsies were positive and only one was negative. Multiresistant bacteria were detected in the cultures of five (14.2%) biopsies.

Discussion

The present study evaluated the possibility of infections being the main cause of sudden changes in the profile of pain related to CVU. These patients were being treated and initially had no strong pain. However, suddenly, from one day to the next, they began to feel intense pain and required pain relievers.

There was no change in the type of dressing and no ischemic condition was identified, but the characteristic of the wound changed with the edges becoming irregular. Biopsies of tissue from ulcers of 35 patients were performed with cultures for bacteria being positive in 34. Several studies report the association of pain with infection, but no study was found that specifically correlated pain with acute infection (2, 5).

During the visual examination of the ulcers, no significant hyperemia was observed, but the edges of the lesions became irregular in all patients selected for biopsies (Figure 1).

Chronic venous ulceration may be associated with arterial insufficiency, one of the differential diagnoses of pain in these patients. Inadequate dressings may contribute to pain, but in this study, the dressings remained the same before and after the onset of intense pain. Therefore, sudden increases in pain is a warning of possible infection.

Another fact to be considered is that 5 of the 35 patients were infected by multiresistant agents and needed hospitalization for antibiotic therapy. There-

fore, a biopsy is important to identify infections and schedule antibiotic therapy.

Another characteristic that drew attention was that there was no hyperemia at the edges of the ulcers but there was within the lesion, thus configuring a more localized condition. These patients received topical dressings with silver sulfadiazine and cerium; no systemic antibiotic was prescribed in cases where the pain improved while awaiting the result of the culture. This strategy can be used to avoid systemic antibiotic therapy.

The quality of life of these patients is already affected because of the chronicity of CVI with the presence of an ulcer with pain being just another aggravating factor (15). The rapid resolution of pain with the use of analgesics until the infection is controlled is critical.

The characteristics of the lesion such as the presence of cellulite, maceration of the edges, granulation of the wound, eczemas, pruritus, purulent exudation and odor constitute the main aspects to be analyzed at each dressing. Each of these aspects may suggest some complication in the evolution of the wound and serve as a warning.

A number of therapeutic possibilities are described in the literature, in particular local treatments such as substances to stimulate granulation and the use of an Unna boot that aims to treat the venolymphatic circulation. In this way, a more specific approach can be used for each wound, depending on different factors such as the size of the ulcer, infection, presence of necrotic material, etc.

Infection and pain force the patients to rest, a condition that limits their ability to work, affecting their economic and social status, and places a burden on the healthcare system. Hence, prevention and the treatment of venous ulcers as early as possible can reduce absenteeism from work.

Conclusion

The acute change in the profile of pain related to CVU may be associated to a local infectious disease.

Conflict interest

The Authors declare that there is no conflict of interest regarding the publication of this paper.



Figure 1 - Lesions became irregular.

References

1. Carriazo MG, de las Heras CG, Vázquez PM, Solís MR. Estudio de la insuficiencia venosa crónica mediante ecografía Doppler y realización de cartografía venosa. *Radiología*. 2016;58(1):7-15.
2. Vuylsteke ME, Thomis S, Guillaume G, Modliszewski ML, Weides N, Staelens I. Epidemiological Study on Chronic Venous Disease in Belgium and Luxembourg: Prevalence, Risk Factors, and Symptomatology. *European Journal of Vascular and Endovascular Surgery*. 2015;49(4):432-439.
3. Rossi FH, Volpato MG, Metzger PB, Beteli CB, Almeida BLD, Rossi CBO, Izukawa NM. Relationships between severity of signs and symptoms and quality of life in patients with chronic venous disease. *Jornal Vascular Brasileiro*. 2015;14(1):22-28.
4. Pereira de Godoy JM, Braile DM, de Fátima Guerreiro Godoy M. Lymph drainage in patients with joint immobility due to chronic ulcerated lesions. *Phlebology*. 2008;23(1):32-4.
5. Dimakakos E, Syrigos K, Scliros E, Karaitianos I. Prevalence, risk and aggravating factors of chronic venous disease: an epidemiological survey of the general population of Greece. *Phlebology*. 2013;28(4):184-190.
6. Rabe E, Pannier F. Clinical, aetiological, anatomical and pathological classification (CEAP): gold standard and limits. *Phlebology*. 2013;27(suppl 1):114-118.
7. Radak DJ, Tanaskovic SZ, Vlajinac, HD, Marinkovic JM, Maksimovic MZ. Relationship Between Pain and CEAP C Categories of Chronic Venous Disease. *Angiology*. 2015; 0003319715613179.
8. Belczak CE, de Godoy JM, Belzack SQ, Ramos RN, Caffaro RA. Obesity and worsening of chronic venous disease and joint mobility. *Phlebology*. 2014 Sep;29(8):500-4. doi: 10.1177/0268355513492510. Epub 2013 May 31.
9. Eklöf B, Rutherford RB, Bergan JJ, Carpentier PH, Gloviczki P, Kistner RL, Perrin M. Revision of the CEAP classification for chronic venous disorders: consensus statement. *Journal of vascular surgery*. 2004;40(6):148-1252.
10. Mosti G, De Maeseneer M, Cavezzi A, Parsi K, Morrison N, Nelzen O, Rabe E, Partsch H, Caggiati A, Simka M, Obermayer A, Malouf M, Flour M, Maleti O, Perrin M, Reina L, Kalodiki E, Mannello F, Rerkasem K, Cornu-Thenard A, Chi YW, Soloviy M, Bottini O, Mendyk N, Tessari L, Varghese R, Etcheverry R, Pannier F, Lugli M, Carvallo Lantz AJ, Zamboni P, Zuolo M, Godoy MF, Godoy JM, Link DP, Junger M, Scuderi A. Society for Vascular Surgery and American Venous Forum Guidelines on the management of venous leg ulcers: the point of view of the International Union of Phlebology. *Int Angiol*. 2015 Jun;34(3):202-18.
11. Souza Nogueira G, Rodrigues Zanin C, Miyazaki MC, Pereira de Godoy JM. Venous leg ulcers and emotional consequences. *Int J Low Extrem Wounds*. 2009 Dec;8(4):194-6. doi: 10.1177/1534734609350548.
12. Chi YW, Raffetto JD. Venous leg ulceration pathophysiology and evidence based treatment. *Vascular Medicine*. 2015;20(2):168-181.
13. Comerota A, Lurie F. Pathogenesis of venous ulcer. In *Seminars in Vascular Surgery*. 2015;28:(1)6-14.
14. Rasmussen JC, Aldrich MB, Tan IC, Darne C, Zhu B, O'Donnell TF, Sevick-Muraca EM. Lymphatic transport in patients with chronic venous insufficiency and venous leg ulcers following sequential pneumatic compression. *Journal of Vascular Surgery: Venous and Lymphatic Disorders*. 2016;4(1):9-17.
15. Souza Nogueira G, Rodrigues Zanin C, Miyazaki MC, Pereira de Godoy JM. Quality of life of patients with chronic venous ulcers and socio-demographic factors. *Wounds*. 2012 Oct;24(10):289-92.
16. O'Meara S, Al-Kurdi D, Ologun Y, Ovington LG, Martyn-St James M, Richardson R. Antibiotics and antiseptics for venous leg ulcers. *Cochrane Database Syst Rev*. 2014;1(1).
17. Rhoads DD, Wolcott RD, Sun Y, Dowd SE. Comparison of culture and molecular identification of bacteria in chronic wounds. *International journal of molecular sciences*. 2012;13(3):2535-2550.
18. Reddy M, Gill SS, Wu W, Kalka SR, Rochon PA. Does this patient have an infection of a chronic wound? *JAMA*. 2012;307(6):605-611.
19. O'Donnell TF, Passman MA, Marston WA, Ennis WJ, Dalsing M, Kistner RL, Stoughton J. Management of venous leg ulcers: Clinical practice guidelines of the Society for Vascular Surgery® and the American Venous Forum. *Journal of Vascular Surgery*. 2014;60(2):3S-59S.