THE IMPORTANCE OF EARLY DETECTION OF SKIN SEPSIS MANIFESTED BY GOUGEROT-RUITER TRISYNDROME

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Summary

Cutaneous sepsis is a topical issue in international research, with high mortality and high incidence of organ dysfunction, which makes it necessary and beneficial early detection of sepsis, for the rapid initiation of appropriate systemic treatment, from the first hours after diagnosis. Any type of skin infection - bacterial, viral or fungal - can cause sepsis, but the most common are bacterial infections. Vasculitis, such as Gougerot-Ruiter trisyndrome, can cause sepsis, especially if the patient has other pathologies that contribute to the onset of a complex cascade, of disturbances of several organs and systems, with their functional insufficiency.

Gougerot-Ruiter trisyndrome or allergic leukocyto-clastic vasculitis is characterized by damage to the arterioles and postcapillary venules, in the triggering of which several factors intervene (infections, drugs, auto-immune). Gougerot-Ruiter trisyndrome frequently presents as palpable purpura with elective localization in the lower half of the body, the evolution being acute, subacute, or chronic.

We present the case of a 60-year-old male patient with multiple cardiovascular, metabolic, gastroenterological comorbidities and numerous associated risk factors (smoker, overweight), who presented to the dermatology clinic for macular-papular-purpuric lesions and micronodules with a necrotic center, some isolated (abdomen, thighs), others confluent at the level of the calves in the form of painful and itchy necrotic ulcerations, with the onset of about 3 weeks, initially localized at calves and later with their extension after the thighs and abdomen. The patient did not follow topical or systemic treatment at home. Starting from the clinical and paraclinical elements, taking into account comorbidities and risk factors, the diagnosis of cutaneous sepsis was established, with vasculitis being the trigger. Elevated values of inflammatory biomarkers led to early initiation of antibiotic therapy, anticoagulant treatment, and corticosteroid therapy, which was performed in short courses and was limited by unbalanced glycemic status. The evolution was favorable, but slow, due to the inflammatory constellation of pre-existing pathologies.

The prognosis of patients with Gougerot-Ruiter trisyndrome is usually favorable, the skin damage being frequent, but the possibility of complications when there are associated pathologies must be evaluated.

Keywords: *leukocytoclastic allergic vasculitis, purpura, skin sepsis, inflammatory biomarkers.*

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Introduction

Cutaneous sepsis is a topical issue in international research, with high mortality and high incidence of organ dysfunction, which makes it necessary and beneficial to early detection of sepsis, for the rapid initiation of appropriate systemic treatment, from the first hours after diagnosis. Any type of skin infection - bacterial, viral or fungal - can cause sepsis, but the most common are bacterial infections. Vasculitis, such as Gougerot-Ruiter trisyndrome, can cause sepsis, especially if the patient has other pathologies that contribute to the onset of a complex cascade, of disturbances of several organs and systems, with their functional insufficiency. [1-3]

Gougerot-Ruiter trisyndrome or allergic leukocytoclastic vasculitis is characterized by damage to the arterioles and postcapillary venules, where deposits of immune complexes are identified by histopathological examination. [1] Goujerot-Ruiter trisyndrome is clinically manifested by polymorphic skin lesions - erythema associated with macular purpura or urticarial papules, which progress to palpable purpura and later to vesicles, micronodules or necrotic ulcerations, asymptomatic or painful, with symmetrical location, frequently in the lower limbs. [1,2] Allergic leukocytoclastic vasculitis is usually limited to the skin, with extracutaneous manifestations in less than 30% of cases. [3]

In most cases, the etiology of Goujerot-Ruiter trisyndrome is unknown, but several factors are involved in the onset of vasculitis, which can be classified into two major categories: infectious (9.0-36.0%) and non-infectious, which include multiple etiologies, the most common being drug-induced (8.6-36.0%) and idiopathic (15.4-29.7%). Drugs associated with allergic vasculitis include β-lactam antibiotics, sulfonamides, thiazide diuretics, allopurinol, retinoids, non-steroidal anti-inflammatory drugs, and anti-thyroid agents. Other less common non-infectious causes include connective tissue diseases (6.4-25.0%) and neoplasms (2.3-8.0%). [3,4]

The immunoallergic mechanisms of Goujerot-Ruiter trisyndrome evolve according to the model of type III, IV, or mixed reactions, and the evolution of the disease is acute, subacute, or chronic. In acute forms the onset is sudden, with an altered general condition, with skin lesions in the form of purple spots, fluid-filled blisters clear or mixed with blood. In subacute forms, extensive necrotic ulcerations are added to the clinical picture, and in chronic forms, the rash acquires a nodular appearance. Systemic damage is rare, but should not be neglected. [1,4]

Clinical case

We present the case of a 60-year-old male patient, with a history of multiple cardiovascular comorbidities (hypertension, persistent atrial fibrillation, peripheral arterial disease stage IV, dilated cardiomyopathy), metabolic (complicated type 2 diabetes treated with insulin), gastro-enterological (hepatitis C-related liver cirrhosis) and many associated risk factors (smoker, overweight), which presents in the dermatology clinic for macular-papular-purpuric lesions and micronodules with a necrotic center, some isolated (abdomen, thighs), others confluent at the level of the calves in the form of extensive necrotic ulceration, painful and itchy, with the onset of about 3 weeks, initially localized at the calves and later with their extension at the thighs and abdomen. The patient did not follow topical or systemic treatments at home.

The general clinical examination reveals a conscious, overweight, and febrile patient.

The local clinical examination objectifies the presence of macular-papular-purpuric lesions and micronodules with a necrotic center, some isolated - abdomen, thighs (Fig.1 D, E), others confluent at the level of the calves in the form of extensive necrotic ulcerations, painful and itchy (Fig. .1 A, B). There is also ovoid ulceration, deep, with a diameter of about 5/2 cm, with irregular edges, with the base covered with cell debris, with a bleeding surface, located at the level of the amputation abutment of the right V toe and on the lateral edge. (Fig.1 C)

Paraclinical examinations revealed lymphopenia, leukocytosis, significant inflammatory syndrome, hepatic cytolysis syndrome, cholestasis, hyperglycemia, hyperuricemia, HCV antibodies present, hyper IgE, high values of D-dimers, NT-proBNP, and LDH. Tests for anti-

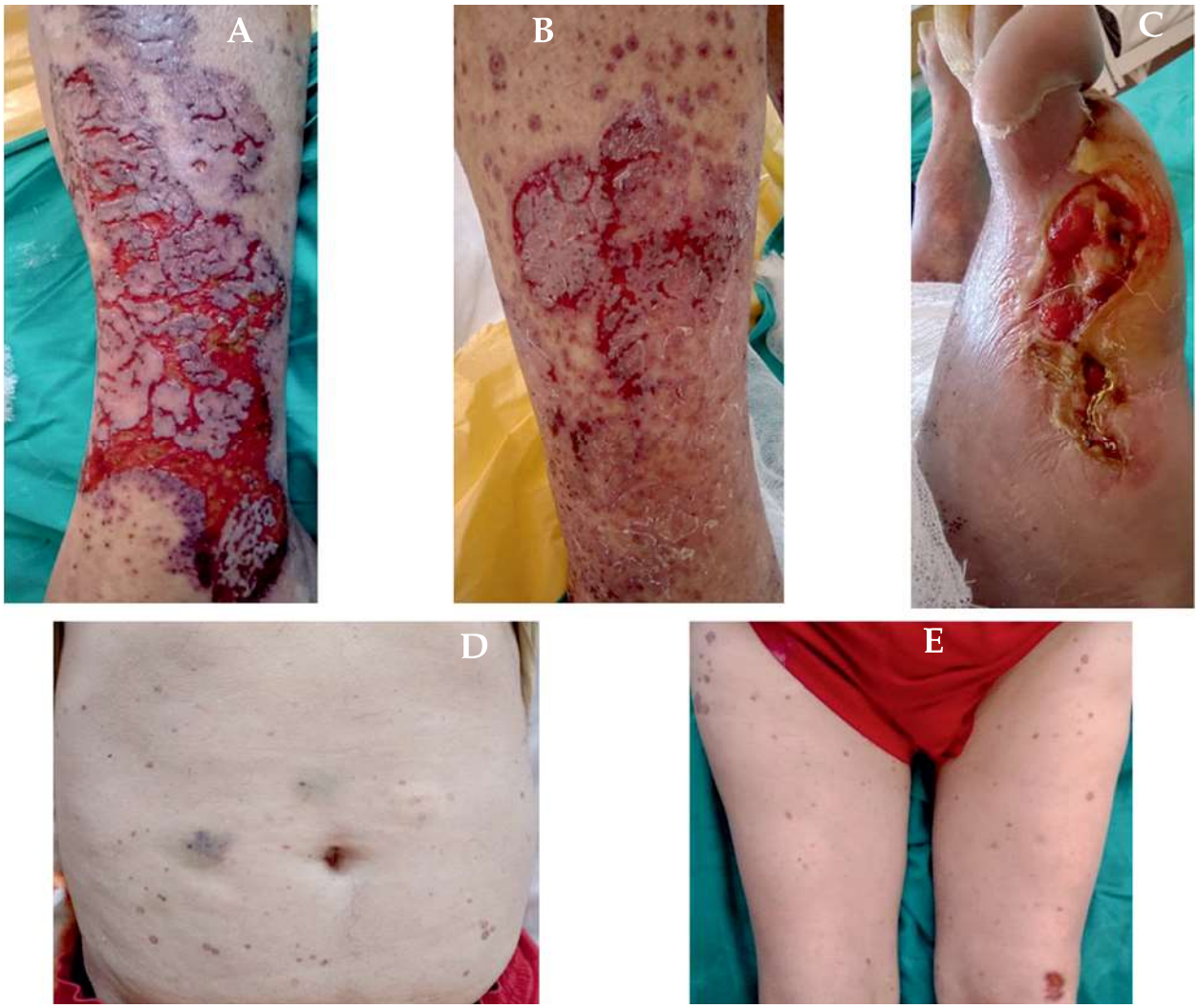

Figure 1. Clinical aspects observed at the time of presentation in the dermatology clinic.

nuclear antibodies (ANA), anti-neutrophil cyto-plasmic antibodies (ANCA), anti-double-stranded DNA (dsDNA) antibodies, anti-phospholipid antibodies were negative; cryo-globulins were absent; complement C3-C4 fractions, protein electrophoresis, urinalysis, and tumor markers showed normal values; sero-logical tests for syphilis and HIV were negative. SARS CoV2 RT-PCR testing and chest radiographs ruled out a possible COVID-19 infection. Bacteriological examination of leg ulcerations secretion and amputation abutment ulceration of V right toe revealed superinfection with S. aureus with positive blood cultures. Internal medicine, cardiology consultation, and investigations such as abdominopelvic ultra-sound and Doppler ultrasound of the lower limbs were performed, which ruled out a specialist emergency. During the hospitalization, a punch biopsy was performed at the level of necrotic ulcers, and the histopathological examination revealed an angiocentric inflam-matory process associated with leukocytoclasia (disintegration of neutrophil nuclei - "nuclear dust"), endothelial cell edema, extravasation of erythrocytes, and fibrinoid necrosis, confirming the diagnosis of leukocytoclastic vasculitis.

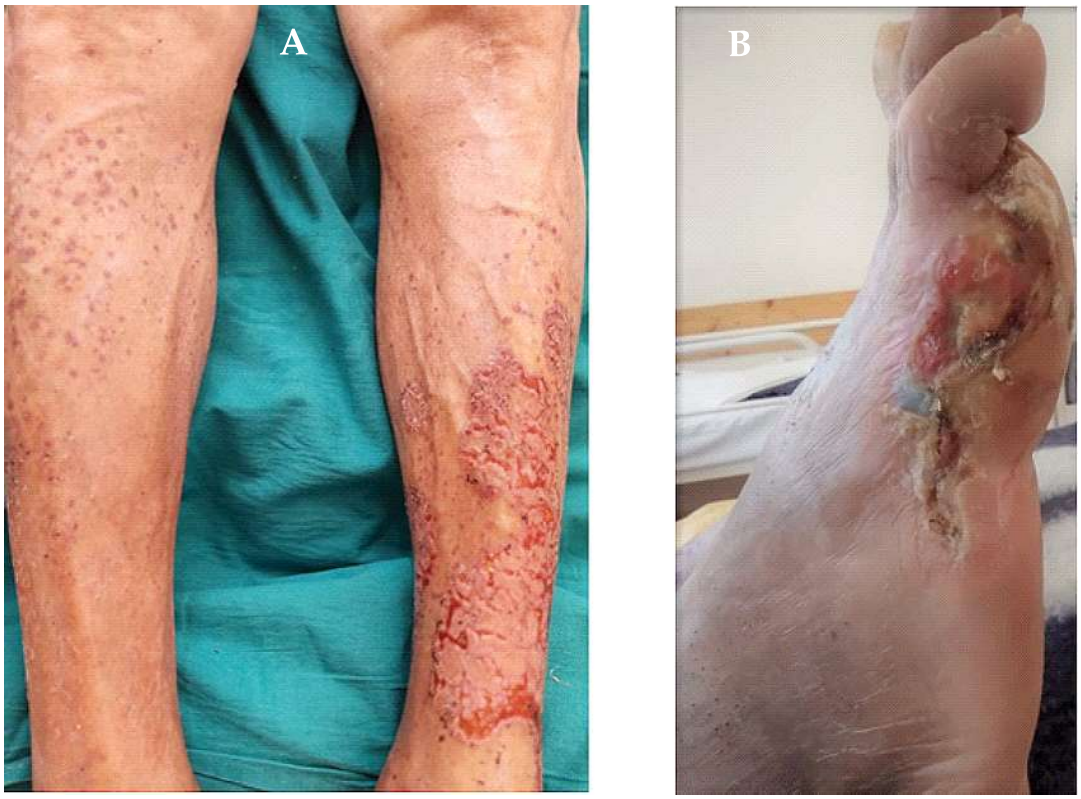

Figure 2. Clinical aspects observed at the time of discharge.

Corroborating the clinical and paraclinical data, taking into account comorbidities and risk factors, the diagnosis of cutaneous sepsis was established, the triggering factor being vasculitis. Elevated values of inflammatory biomarkers (presepsin, procalcitonin, C-reactive protein) led to the early initiation of antibiotic therapy (Ceftriaxone 1 g at 8 hours, iv) and anti-coagulant treatment (Enoxaparin 0.4 ml x 2, sc). Also, treatment with analgesics, venotonic, venotrophic, antihistamines, and short-term corticosteroid therapy was initiated, the latter being limited by the patient's unbalanced glycemic status. For the lesions on the calves, antiseptic solution was applied, followed by epithelializing ointment with antibiotic alternative with dermatocorticoid and cream with 1% silver sulfadiazine, and for the amputation abutment ulceration was initially applied iodoform, later continuing with hydroactive dressing of calcium alginate and epithelializing ointment with antibiotic. The evolution was favorable, but slow, due to the inflammatory constellation of pre-existing pathologies.

Discussions

The key component in the etiopathogenesis of leukocytoclastic allergic vasculitis is the deposition of immune complexes in the postcapillary venules, which activate the complement cascade, with the production of chemotactic factors for leukocytes and the expression of adhesion molecules. As a result, neutrophil chemotaxis occurs, with the release of enzymes and reactive oxygen species, with the aim to eliminate antigens. This produces an intense reactive inflammatory process, with increased permeability of blood vessels and extravasation of erythrocytes. [1,4]

In the present case, prolonged antigenic stimulation and the immunological status of the patient, it is believed that it would have contributed to the appearance of sepsis having as substrate leukocytoclastic vasculitis.

Sepsis is a dreaded complication in dermatology, being an important cause of morbidity and mortality, which requires the early introduction of antibiotic therapy and rebalancing measures. Sepsis is the body's systemic inflammatory response to an infectious injury, associated with organ dysfunction. The systemic inflammatory response (SIRS) is defined by the presence of two or more of the following criteria: fever (> 38 degrees) or hypothermia (< 36 degrees), polypnea (respiratory rate > 20/ minute), tachycardia (heart rate > 90 bpm), leukocytosis or leukopenia. Sepsis is defined by the presence of criteria for SIRS, associated with clinical and microbiological data highlighting infection. [5,6]

The frequency, etiology, and evolution of sepsis in a dermatology department were evaluated in a study conducted in 2004-2006 on a group of 860 patients (Asati et al.), which showed that 103 patients (12%) had met the criteria for systemic inflammatory response syndrome (SIRS), and 40 patients (4.65%) had sepsis. The skin conditions encountered in most patients with sepsis were bullous dermatoses (42.5%), erythroderma (25%), and toxic epidermal necrolysis (22.5%). Severe sepsis was identified in 17 patients (42.5%) and 15 (37.5%) of them died. The most common isolating agent was methicillin-resistant *S. aureus* (99; 25.9%), followed by *Acinetobacter* spp. (52; 13.6%), *Pseudomonas* spp. (40; 10.5%), methicillin-sensitive *S. aureus* (33; 8.7%) and *Klebsiella* spp. (22; 5.8%). [7]

Optimal management for leukocytoclastic allergic vasculitis is not mentioned in the literature, but therapeutic success is influenced by early diagnosis and treatment. [8] Treatment is determined by the etiology and extent of the disease. When vasculitis is the manifestation of infection, treating and eliminating the infection is essential. If vasculitis is the manifestation of a systemic vasculitic process, treatment will be influenced by the severity of damage to internal organs and requires a combination of cortico-steroids and immunosuppressants. [4,8] The onset of sepsis in the context of vasculitis requires the early introduction of empirical antibiotic therapy and later according to the antibiogram, and in severe cases, corticosteroid therapy may be combined to reduce symptoms, cutaneous lesions, for faster recovery and a lower risk of recurrence. The combination of anticoagulation is recommended for patients with a history of deep vein thrombosis, pulmonary embolism, chronic venous insufficiency, obesity, and bedridden patients. [4,8,9]

In cases of leukocytoclastic allergic vasculitis limited to the skin, the prognosis is favorable. For cases where systemic seizure and sepsis set in, the prognosis is less favorable, with complete remission being obtained within 6 months to 1 year, in only half of the affected patients. [10,11]

Conclusions

The prevalence of skin sepsis has increased significantly in different parts of the world, and the main challenge in addressing skin sepsis remains early diagnosis and management.

Patients admitted to dermatology departments, undergoing immunosuppressive therapy or systemic corticosteroid therapy, and with severe skin barrier alteration, require close monitoring, as sepsis occurs in these patients.

Sepsis with a cutaneous starting point as a complication of vasculitis is a dermatological emergency, which requires in addition to topical and systemic treatment specific to vasculitis, hydro electrolytic rebalancing measures, control of decompensated pathologies, and dynamic monitoring of biological parameters.

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Conflict of interest
NONE DECLARED

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