

Innovations In The Treatment Of Ulcerative Skin Lesions

D.R. Khakimov^{1*}, S.Z. Obidov², Sh. F. Sadiev³, B.X. Zakirov⁴, B.R. Parpiev⁵, Sh. Khonkhadjayev⁶

^{1*,2,3,4,5,6}Republican Specialized Scientific and Practical Medical Center for Dermatovenereology and Cosmetology of the Ministry of Health of the Republic of Uzbekistan

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ABSTRACT

The article provides a review of the literature on the problem of treating trophic ulcers, which significantly worsens the quality of life of patients, often leads to death and is accompanied by large financial costs. Theories of formation and clinical manifestations are covered in detail. A clinical case of the use of platelet-rich plasma in the treatment of trophic skin ulcers.

Keywords: trophic ulcers, pathogenesis, chronic venous insufficiency, plasma saturated with platelets, PRP.

1. INTRODUCTION

In recent years, the number of people suffering from trophic ulcers (TU) has been increasing among dermatologic diseases in the world. According to the World Health Organization (WHO), trophic ulcers occur in 1-2% of the able-bodied population and predominantly in the group of people over 65 years of age, their frequency is about 34%. However, practice shows that recently it has been observed in dermatology that skin lesions located on other skin areas (body, scalp, face, etc.) are often registered. Ulcerative foci arising against the background of chronic infiltrative-inflammatory skin diseases caused by opportunistic microorganisms have a more severe, slowly healing clinical course [1,2,6,10].

There are several varieties of clinical classification of trophic ulcers.

1. According to the cause of occurrence are subdivided into:

- Ulcers due to Chronic Venous Insufficiency (CVI) of the lower extremities
- Ulcers caused by congenital and acquired arteriovenous shifts
- Ischemic ulcers
- Post-traumatic ulcers
- Neurotrophic ulcers
- Ulcers arising from common diseases
- Ulcers due to local infectious, mycotic and parasitic diseases

Venous TUs occur against the background of valve failure of superficial or perforating veins or after deep vein thrombosis [2, 10]. The pathogenetic mechanisms of trophic disorders in CVI are common and do not depend on the causes of its occurrence. In venous hypertension capillaries become tortuous, their permeability to large molecules increases and fibrin is deposited in the perivascular space. Because of this, the diffusion of oxygen and nutrients is disturbed, which contributes to ischemia and necrosis, and a decrease in colloid-osmotic pressure in this zone against the background of intravascular hypertension contributes to an increase in filtration of fluid from vessels into tissues. TU formation is preceded by such signs: edema, hyperpigmentation of the skin, muscle cramps, itching, feeling of heat, burning. They are located mainly on the medial surface of the lower third of the lower leg.

Arterial (ischemic) TUs occur in 8-12% of cases [4, 10, 13, 15]. They occur in decompensation of arterial circulation, usually in elderly men. Characteristic signs of arterial insufficiency: intermittent claudication, numbness and coldness of the limb, muscle atrophy, impoverishment of hair, dystrophic or fungal lesions of the skin of feet and nail plates, sometimes there are signs of atherosclerotic lesions of other organs and systems, more often - ischemic diseases of the heart and brain. Provoking moments can be household and industrial injuries, wearing narrow and uncomfortable shoes, hypothermia. Ulcers are usually localized in the heel area, the terminal phalanx of the big toe, on the dorsal surface of the foot, less often on the sole and anterolateral

surface of the lower third of the tibia [4, 10, 13, 15]. Ischemic ulcers are usually small in size, semicircular in shape, with sluggish granulations, dense irregular edges rising against the background of pale yellow skin, often with areas of marginal necrosis, which may extend deep with exposure of tendons and bone [4, 10, 13, 15].

Neurotrophic TUs - develop in denervated areas in patients with damage to the central or peripheral nervous system: in the neuropathic form of diabetic foot syndrome, CNS and peripheral nerve injuries, diseases accompanied by sensory peripheral neuropathy: Myelodysplasia, myelomeningocele, syringomyelia, leprosy, multiple sclerosis, amyotrophic lateral sclerosis, spinal dryness (tertiary syphilis), etc. [10]. Neurotrophic ulcers have a weak tendency to self-healing. An obligatory condition for healing is the exclusion of mechanical load on the zone of trophic disorders, for which they use full or partial unloading of the foot by walking on crutches, using orthopedic insoles and shoes, applying a removable plaster boot with a hole for care [[4, 10, 13, 15].

Congestive TUs - They are formed as a result of decompensation of cardiovascular activity, more often in the elderly and old age. Usually develop on both limbs, are multiple, extensive, have pale, flabby granulations, exuding abundantly, sometimes resembling jelly-like grayish mucus. The skin around such an ulcer is edematous, pressing on it with a finger forms a trace in the form of a hole, which slowly disappears. As cardiovascular activity improves and edema disappears, the ulcer immediately decreases in size, its edges are aligned with the bottom, and marginal epithelization appears [4, 10, 13, 15].

Diabetic TUs are the most frequent manifestation of diabetic foot syndrome (DFS). Ischemia, infection, osteoarthropathy, endotoxemia, immunologic disorders, hemostasis and microcirculation disorders also play an important role in the pathogenesis of development. The absence of pain in the area of ulcers, explained by the violation of innervation, leads to the fact that patients are very late to see a doctor. The most serious complication in this situation is infection with rapid development of wet gangrene, requiring amputation to save the limb [9, 10, 14].

Hypertension-ischemic TJA was first described by the Spanish cardiologist Martorell. Martorell syndrome in its "pure" form, as described by the author, is rare - no more than 2% of all ulcerative-necrotic lesions of the lower extremities [10]. It occurs more often in the female part of the population of the older age group (after 40 years). Prolonged hypertension leads to hyalinosis of small arterial trunks in the skin of the lower limbs, which weakens blood flow in this area of the skin. In disorders of blood microcirculation, increased permeability of the vascular membrane, formation of local microthrombosis, leading to the formation of necrosis of soft tissues are noted.

The beginning of the disease is characterized by the appearance of violet papules or red-blue areas with slight soreness, which then turn into hemorrhagic bullae. The primary cutaneous elements eventually dry up and transform into a dry necrotic scab with involvement of the skin and the upper layers of subcutaneous tissue in the pathologic process. Martorell's ulcer is usually located on the outer or posterior surface of the tibia, often on symmetrical parts of the lower leg. The ulcers are characterized by sharp painfulness both at rest and on palpation. Hypertensive ulcers, shallow, with sluggish granulations and scanty discharge, develop very slowly, but in the absence of adequate treatment their size progressively increases, often wound infection joins [6,10]. The clinical picture of the disease should be confirmed by the data of histologic examination, during which phenomena of endoarterial proliferation and subendothelial hyalinosis are found. Treatment, first of all, should be aimed at stabilizing blood pressure (BP). In local therapy in the presence of dry necrotic scab, hydrogel dressings are preferred [10].

Pyogenic TUs - arise mainly in patients from socially disadvantaged population groups against the background of nonspecific purulent diseases of soft tissues, such as pyoderma, infected wounds, skin defects arising after complicated rye, carbuncle, abscess and phlegmon. Characterized by a long and persistent course. They are multiple superficial purulent foci of round shape, covered with thick purulent plaque with a pronounced perifocal inflammatory reaction. The development of TU is usually caused by Gram-positive cocci: Staphylococcus aureus, Streptococcus sp., much less frequently by Pseudomonas aeruginosa and other Gram-negative bacilli [15].

TUs against the background of systemic connective tissue diseases - against the background of blood diseases, metabolic diseases, vasculitis, collagenosis usually have no specific signs. To recognize their nature, the diagnosis of the underlying disease is of great importance [4,8].

Radiation TUs - at first, the skin shows focal, mottled or solid pigmentation, small or large, bright red telangiectasias located in isolation or in groups. Cutaneous manifestations are accompanied by hair loss. Acute radiation skin lesions have a long course and are poorly curable. Radiation ulcers, regardless of their localization, have a great external similarity: round or oval shape, dense, uneven, ragged edges, necrotic bottom. The skin around the ulcers is changed in all cases. Ulcers penetrate deeply into the subcutaneous tissue, muscles, and often affect the bone [16].

Modern methods of treatment do not fully satisfy patients and doctors. The most important problem of dermatovenerology is that the disease is predominantly found in the working age population, etiopathogenetic mechanisms of the disease have not been fully studied, and effective treatment methods have not been developed [10,15].

Treatment of patients with ulcerative processes on the skin depends on the primary pathological process causing ulceration, general condition, concomitant diseases. Dermatologists give preference to conservative methods of therapy. Almost any genesis of trophic ulcers of the lower legs (varicose veins on the background of chronic venous insufficiency, a consequence of obliterating atherosclerosis of the vessels of the lower extremities, ulcers, symbiosis of pathogenic and saprophytic microorganisms plays an important role in the occurrence and accelerated growth of trophic ulcers [5,6,8,11,12,13].

To find new treatment options for trophic ulcers, we developed a method that includes the following components in the complex therapy: systemic and local antibiotic therapy taking into account the sensitivity of microorganisms, detoxification therapy, the use of vascular drugs (trental) for external use and PRP procedure using patient's plasma in the volume of 3.0 to 5.0 ml, which is injected around the ulcer once a week. A sterile gauze cloth moistened with activated siliceous solution (ASW - Fatiderm tonic) is also applied to the lesions for 10 days, followed by application of 5% siliceous cream (Disderm) twice daily for 30 days.

Here is a clinical case from our practice:

First clinical case

Patient A., 37 years old, was admitted to the II inpatient dermatology department of the RSSPMCDC on May 28, 2022.

Complaints on admission: ulcerative lesion on the shin of the left leg.

Subjective: pain and itching are felt.

Anamnesis morbi: considers himself sick since September 2020, when single rashes appeared on the skin of the lower limbs after surgery for varicose veins of the lower limbs. He was treated on an outpatient and inpatient basis in the Skin and Venereal Dispensary (CVD). He received systemic and local antibiotic therapy, immunotherapy. The disease progressed against the background of treatment.

Anamnesis vitae: grew up and developed in satisfactory social and living conditions, according to age. Diseases: acute respiratory infections. Allergic reactions to food and medicines were not observed. Heredity is not aggravated.

Status praesens: on admission the patient's general condition is satisfactory. No pathology was detected on the side of internal organs and systems. Body temperature is normal, BP 120/70 mm Hg. Stools and urination are regular.

Status localis: The cutaneous pathologic process presents as scattered hyperpigmented spots, nodules and ulcers on the left shin with chronic diffuse asymmetric inflammatory character. The nodules are mushy-sized and covered with bloody crusts. The size of the wound is 4 x 5 cm, covered with purulent and calcified concretions. There is localized fever around the pathologic spot. Subjectively: pain, itching. Dermographism is pink. Skin properties do not change. According to Fitzpatrick's classification the patient belongs to 3 phototypes. Dermographism is pink.



Fig.1 Patient with trophic ulcer: a - before treatment; b - 2 months after treatment

Laboratory Studies.

General blood count: Hemoglobin - 144 g/L, Red blood cells (RBK) - $5.2 \cdot 10^{12}/L$, Color value - 0.8, MCH - 27.1 pg, Hematocrit - 40.5%, Platelets - $237 \cdot 10^9/L$, Leukocytes - $5.5 \cdot 10^9/l$, Segmento nuclear neutrophils - 59,5 %, Eosinophils - 3,4 %, Monocytes - 8,2 %, Lymphocytes - 28,9 %, Erythrocyte sedimentation rate - 5 mm/hour; Biochemical analysis of blood: Glucose - 5.6 mmol/L, ALT - 31 U/L, AST - 20 U/L, Urea - 5.39 mmol/L, Creatinine - 79.3 mmol/L, Cholesterol - 5.52 mmol/L, Total Protein - 89 g/L, Rits Coefficient - 0.65, Total Bilirubin - 16.1 mmol/L, Direct Bilirubin - 3.8 mmol/L, Indirect Bilirubin - 12.3 mmol/L;

Real-time PCR for the detection of Saphylococcus spp. (MRSA): MSSA (methicillin-sensitive Staphylocococcus aureus) DNA - negative; MRCoNS (methicillin-resistant coagulnegative Staphylocococcus spp.) DNA - negative; MRSA (methicillin-resistant Staphylocococcus aureus) DNA - negative;

IL-4: 6.9 pg/mL; IL-6: 10.2 pg/mL; C-reactive protein: 10.2 mg/L; Studies for Koch's and Hansen's bacilli from skin: not detected;

Study of microflora species spectrum, colonization of skin microorganisms with determination of sensitivity to antibiotics: 46 coe st hamoliticus, with high sensitivity to Amikocin, Levofloxacin;

Analysis of urine on a semi-automatic analyzer: Quantity - 40.0 ml, Color - yellow, Transparency - transparent, Relative density - 1030, Reaction - 6.0, Urobilinoids - normal, Epithelium Flat - single, Lecocytes - 3-4, Mucus - +;

General stool analysis (G.S.A.): No pathologic changes.

Borowski's corpuscles study: not detected; IFLA - express Finacare PCT (procalcitonin) - 0.13 ng/mL;

Treatment. Patient was recommended hospital treatment with disinfection, antibacterial, vasodilating, angioprotective, local antiseptic and aniline dyes, physiotherapeutic procedures, as well as an innovative method using PRP in the volume of 3.0 to 5.0 ml, which was injected around the ulcer once a week. A sterile gauze dressing moistened with activated siliceous solution (ASW - Fatiderm tonic) was also applied to the lesions for 10 days, and then 5% siliceous cream (Dysderm) was applied with ultrasonic massage around the nidus.

Second clinical case

Patient T., 58 years old, was admitted to the II inpatient dermatology department of the RSSPMCDC on February 19, 2021.

Complaints on admission: ulcerative lesions on the shin and foot of the right leg.

Subjective: pain and itching are felt.

Anamnesis morbi: He considers himself sick since 2019, does not connect the beginning of the disease with anything. He was treated for his disease in 1 city hospital. He received systemic and local antibiotic therapy. Against the background of the treatment the disease progressed.

Anamnesis vitae: grew up and developed in satisfactory social and living conditions, according to age. Diseases: acute respiratory infections. Allergic reactions to food and medicines were not observed. Heredity is not aggravated.

Status praesens: On admission the patient's general condition is satisfactory. No pathology was detected on the side of internal organs and systems. Body temperature is normal, BP 120/80 mm Hg. Stools and urination are regular.

Status localis: The cutaneous pathologic process presents as scattered hyperpigmented spots, nodules and ulcers on the right lower leg and foot with chronic diffuse asymmetric inflammatory character. The nodules are mushy-sized and covered with bloody crusts. The size of the wound is 5 x 6 cm, covered with purulent and calcified concretions. There is localized fever around the pathologic spot. Subjectively: pain, itching. Dermographism is pink. Skin properties do not change. According to Fitzpatrick's classification the patient belongs to 3 phototypes. Dermographism is pink.



Fig.2 Patient with trophic ulcer: a) before treatment; b) after treatment

Laboratory Investigations: General blood analysis: Hemoglobin - 136 g/L, Red blood cells (RBC) - $5.1 \times 10^{12}/L$, Color value - 0.8, MCH - 26.3 pg, Hematocrit - 39.0%, Platelets - $198 \times 10^9/L$, Leukocytes - $8.1 \times 10^9/L$, Segmento nuclear neutrophils - 61.4%, Eosinophils - 11.0%, Monocytes - 9.9%, Lymphocytes - 17.7%, Erythrocyte sedimentation rate - 6 mm/hour;

Biochemical blood test: Glucose - 5.7 mmol/L, ALT - 23 U/L, AST - 25 U/L, Urea - 5.01 mmol/L, Creatinine - 61.7 mmol/L, Cholesterol - 5.23 mmol/L, Total Protein - 80 g/L, Rits Coefficient - 1.09, Total Bilirubin - 12.5 mmol/L, Direct Bilirubin - 4.3 mmol/L, Indirect Bilirubin - 8.2 mmol/L; C-Reactive Protein: 12.1 mg/L, Highly sensitive C-reactive protein 5.0 mg/L;

Study of microflora species spectrum, colonization of skin microorganisms with determination of sensitivity to antibiotics: 43 coe st hamoliticus, with high sensitivity to Cefaperazone, Rifampicin;

Urine analysis on semi-automatic analyzer: Quantity - 20.0 ml, Color - yellow, Transparency - transparent, Relative density - 1025, Reaction - 6.5, Urobilinoids - normal, Flat Epithelium - 1-3, Lecocytes - 3-5, Mucus - ++, Oxalates - ++;

General stool analysis (G.S.A.): No pathologic changes.

Treatment: Patient was prescribed inpatient hyposensitizing, disinfectant, antibacterial, angioprotective, hepatoprotective, vasodilating, local antiseptic and aniline dyes, physiotherapeutic procedures. An innovative method of treatment PRP-therapy was also applied, using the patient's plasma in a volume of 3.0 to 5.0 ml, which is injected around the ulcer once a week and a sterile gauze napkin moistened with activated siliceous solution (ASW - Fatiderm tonic) was applied to the damaged areas for 10 days, and then 5% siliceous cream (Disderm) was applied twice a day for 30 days.

Third clinical case

Patient M., 2021, according to her mother complained of itchy pain in her back, and crotch wound, with which she was referred to RSSPMCDC.

Anamnesis morbi: The patient believes that her daughter has been ill for 4 months. She cannot attribute the onset of the illness to a specific cause. He was treated at Republican Skin Venereological Dispensary (RSVD) 2 months ago. Treatment included megacef, phenistil, linex tablets and topical mupiroban ointment. After treatment, the rash stopped growing slightly. After 5 days of treatment rash started bleeding and multiplying, rash increased in size, increased watery discharge, suppuration and pain, on this occasion went to RSSPMCDC for examination and treatment.

Anamnesis vitae: The patient grows up in satisfactory conditions. Third of 3 children in the family. Allergic conditions to food and medicines were not observed. Past illnesses: acute respiratory viral infections, influenza, chickenpox. Harmful habits: none. Denies genetic predisposition.

Status praesens: General condition of the patient is satisfactory, consciousness is clear. The skin and mucous membrane are unchanged. Lymph nodes around the ear and submandibular lymph nodes slightly enlarged, soft consistency, not enlarged. Musculoskeletal system without visible deformities. Breathing is free, through the nose. At auscultation in the lungs vesicular breathing. Heart tones clear, rhythmic. Pulse 90/min. A/D is 100/60 mm Hg. Body temperature is 36.6 C. On palpation the abdomen is soft, painless, liver and spleen are not palpated. Symptom of pulsation in the kidney area is bilaterally negative. The flow of urine and feces is smooth and regular.

Status localis: The cutaneous pathologic process is chronic, non-disseminated, asymmetric inflammatory in nature. The rash element is located on the posterior part of the body. The rash elements consist of nodules, pus, ulcers, erosions and crusts. The nodule measures 0.2 x 0.4 cm, slightly elevated above the skin surface. It is covered with pus. In some areas, the tops of the nodules are covered with erosions. The erosions are covered with serous crusts after drying. In the lumbar region there is a wound measuring 3 x 4 cm. The wound border is uneven, the wound edges are red, slightly edematous, the consistency is soft, pus is released. Other branches have ulcers measuring 0.5 x 1 cm, covered with purulent crusts. Dermographism is red. Skin properties do not change. The patient belongs to the 3rd phototype according to Fitzpatrick's classification.



Fig.3 Patient: Chronic ulcerative pyoderma: a - before treatment; b - 1 month after treatment;

Laboratory data: General blood analysis: Hemoglobin - 109 g/L, Red blood cells (RBC) - $4.54 \cdot 10^{12}/L$, Color value - 0.72, MCH - 23.9 pg, Hematocrit - 40.5%, Platelets - $414 \cdot 10^9/L$, Leukocytes - $15,38 \cdot 10^9/L$, Segmento nuclear neutrophils - 64.8%, Eosinophils - 2.7%, Monocytes - 6.1%, Lymphocytes - 26.4%, Erythrocyte sedimentation rate - 5 mm/hour;

Blood chemistry: Glucose - 5.4 mmol/L, AST - 43.0 U/L, Urea - 2.4 mmol/L, Cholesterol - 2.2 mmol/L, Total Protein - 54.0 g/L, Rits Coefficient - 1.7, Total Bilirubin - 16.7 mmol/L, Direct Bilirubin - 2.5 mmol/L, Indirect Bilirubin - 14.2 mmol/L;

Studies for Koch's and Hansen's bacilli from the skin: not detected;

Study of microflora species spectrum, colonization of skin microorganisms with determination of sensitivity to antibiotics: 70 coe st aureus, with high sensitivity to Gentomycin, Doxycycline, Cefazolin, Ceftriaxone, Cefuroxime, Cefaperazone, Ampibactum, Rifampicin, Maxifloxacin;

General stool analysis (G.S.A.): No pathologic changes.

Borowski's test for corpuscles: undetectable;

Determination of total antibodies to M.tyberculosis antigen by ELISA: 0.179;

IFLA for procalcitonin is 0.0.9 mg/mL;

Treatment: This patient was also prescribed inpatient hyposensitizing, disinfectant, antibacterial, angioprotective, hepatoprotective, vasodilating, local antiseptic and aniline dyes, physiotherapeutic procedures. An innovative method of treatment PRP-therapy was also applied, using the patient's plasma in a volume of 3.0 to 5.0 ml, which is injected around the ulcer once a week and a sterile gauze napkin moistened with activated siliceous solution (ASW - Fatiderm tonic) was applied to the damaged areas for 10 days, and then 5% siliceous cream (Disderm) was applied twice a day for 30 days.

2. CONCLUSION

Thus, ulcerative lesions on the skin and mucous membranes are not an uncommon pathology in dermatologic practice. Treatment of ulcers causes significant difficulties and requires the use of systemic and topical drugs of different pharmacological groups. PRP therapy is present various "growth factors" that promote active repair of damaged tissues. PRP therapy with platelet mass using activated ASW siliceous water - Fatiderm -150 ml (in the form of lotions) and physiotherapeutic procedure - Ultrasonic Massage (UM) with 5% siliceous cream (Disderm), which contributed to the increase of fibroblasts at the site of lesion foci and the restoration of fibrous structures of the skin and reparative regeneration of the skin.

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