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Generalization of Infection in Long-Term Non-Healing Wounds

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ABSTRACT

Surgical sepsis must still be solved in the modern tanatogenetic statistical data structure. Sepsis against the background of the wound process, also known as wound sepsis, is considered the most common etiological cause of the development of this complication. Meanwhile, in the case of the development of wound infection, according to the literature, most authors pay attention to acute wounds, which, as is known, have a different pathogenetic mechanism of the course of the disease. However, in the context of the development and course of long-term non-healing wounds, there are few possible options for the generalization of infection in the literature. In this regard, our study aimed to identify the frequency of the development of clinical and laboratory signs of the systemic inflammatory response syndrome in patients with long-term non-healing wounds.

Keywords: Long-term non-healing wounds, wound sepsis, systemic inflammatory response syndrome

INTRODUCTION

According to the ICD-10 definition, long-term non-healing wounds are wounds that do not heal within the usual period of healing injuries of this type or location [T14.1. ICD-10].

Long-term non-healing wounds most often develop in patients with a burdened morbid background in the form of diabetes mellitus complicated by angio- and neuropathy, decompensated venous insufficiency, and bedridden patients for an extended period [1, 2].

The relevance of the problem of treating long-term non-healing wounds is due not only to medical significance but also to social and economic importance. Long-term non-healing wounds are a heavy burden for both patients and their family members. Due to the presence of pain, infection, loss of function in the affected area, as well as constant financial costs, not only does the quality of life decrease and the number of disabled people increases, but conditions are created for the generalization of infection, the development of surgical sepsis, and the death of the patient [3, 4].

Sepsis intensive care medicine continues to develop. Every year, the Society for Surgical Infection and Critical Care Medicine issues updated guidelines for the di-

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agnosis and treatment of sepsis, which indicates progress in the study of the fundamental mechanisms of this formidable complication and the expansion of knowledge in this field of medicine.

Today, sepsis is a dangerous disease characterized by organ dysfunction resulting from a dysregulated host response to infection [5]. The World Health Organization has recognized sepsis as a global health priority [6].

Central to the pathogenesis of sepsis is the complex interaction between the immune system and the corresponding pathogens, ranging from bacteria to viruses and fungi. However, this balanced response in sepsis is often disrupted, leading to excessive inflammation and tissue damage, a condition called "hyperinflammation" [7].

In the clinical setting, patients with sepsis often experience concomitant hyperinflammation and immunosuppression, leading to a variety of different clinical outcomes, including persistent inflammation, immunosuppression, and catabolism syndrome in critically ill patients. This dichotomous response highlights the complexity and variability of the pathogenesis of sepsis, which requires personalized therapeutic approaches [8].

The pro-inflammatory phase in sepsis, i.e., a hyperinflammatory response, often referred to as a "cytokine storm," is characterized by an intense systemic release of cytokines and other inflammatory mediators, resulting in tissue damage and organ dysfunction. This phase follows the concept of systemic inflammatory response syndrome (SIRS) but also recognizes the potential harm of non-responsive inflammatory responses.

Thus, the complexity of sepsis, combined with the individual variability of immune responses, which is influenced by health status, genetic predisposition, and infecting organisms, underscores the need for personalized therapeutic approaches in treating sepsis.

Our study aimed to identify the frequency of the development of clinical and laboratory signs of the systemic inflammatory response syndrome in patients with long-term non-healing wounds.

MATERIAL & METHODS OF RESEARCH

The material for the study was the analysis of the results of the examination and treatment of 84 patients with long-term non-healing wounds based on the clinic of the Bukhara State Medical Institute for the period 2010-2018. The criteria for inclusion of patients in the study were age over 18 years, absence of pregnancy, the patient's written consent to the studies and the presence of a long-term non-healing wound. The criteria for excluding patients from the study were age under 18 years, pregnancy, and lack of written consent of the patient to the research.

The clinical and pathogenetic variety of long-term non-healing wounds was represented by 29 (34.5%) patients with bedsores of various aetiology and localization, neurotrophic ulcers in 28 (33.3%) patients with diabetic foot syndrome and 27 (32.1%) patients with trophic ulcers of the lower extremities (mainly of the lower leg and dorsal surface of the foot) in patients after thrombophlebitis.

Male patients prevailed (67.9%). The mean age of the patients was 62.8±9.8 years. At the same time, long-term non-healing wounds were mainly noted among patients of mature and able-bodied age.

Among 84 patients with long-term non-healing wounds, 166 concomitant diseases were identified during the examination. Among the concomitant diseases, the most common were pathologies of the cardiovascular system (34.9%) and endocrine system (25.3%), represented mainly by diabetes mellitus. On average, there were two concomitant diseases per 1 patient.

To determine the incidence of sepsis and organ failure associated with its presence, we used the classification of sepsis according to R.C. Bone [9-13], adopted as a basis at the consensus conference of pulmonologists and intensive care physicians in the USA (Chicago) in 1991 [14]. A verified diagnosis of sepsis as a complication of long-term non-healing wounds was made by us based on clinical and pathogenetic signs proposed by the conciliation conference.

The results obtained, as they were received, were systematized in a summary unified table in Microsoft Excel and processed using Statistica for Windows (version 5.12). The significance of the differences between the samples, which were close to the norm in terms of the nature of the distribution, was established according to the parametric Student's test with a 95% reliable probability interval. The criterion for the statistical reliability of the conclusions obtained was considered to be the generally accepted in medicine value $p<0.05$.

RESULTS & DISCUSSION

When assessing the degree of generalization of infection, it was revealed that signs of systemic inflammatory response syndrome were not noted in all patients (Table).

Thus, in 33.3% of cases (28 patients), they had no common signs indicating generalization of the infection. Among them, the central part was patients with trophic ulcers after thrombophlebitis (46.4%). In other cases, the

Table. The nature of the frequency of registration of the number of systemic inflammatory response syndrome (SIRS) among patients with long-term non-healing wounds

SIRS TRAITS	Bedsores of various etiologies		Neutrophic ulcer in diabetic foot syndrome		Trophic ulcers after thrombophlebitis	
$SIRS_0$	8	28,6%	7	25,0%	13	46,4%
$SIRS_1$	9	32,1%	11	39,3%	8	28,6%
$SIRS_2$	1	9,1%	5	45,5%	5	45,5%
$SIRS_3$	9	64,3%	4	28,6%	1	7,1%
$SIRS_4$	2	66,7%	1	33,3%	-	-

variance in the frequency of recording the number of patients without signs of systemic inflammatory response syndrome turned out to be almost identical between patients with bedsores of various etiologies (28.6%) and patients with neuroischemic ulcers in diabetic foot syndrome (25%).

According to one clinical or laboratory sign of the syndrome of systemic inflammatory reaction, 28 (33.3%) patients had it. Among them, patients with neuroischemic ulcers in diabetic foot syndrome (39.3%) and with bedsores of various etiologies (32.1%) prevailed. Patients with trophic ulcers after thrombophlebitis turned out to be only 28.6%.

The most common symptoms were tachycardia (35.7% of cases) and general hyperthermia/hypothermia (28.6% of cases). Leukocytosis was noted in 7 (25%) patients, and 3 (10.7%) patients had dyspnea at rest. Leukocytosis in more than half of cases (57.1%) was noted among patients with neurotrophic ulcers of diabetic foot syndrome. A similar trend was noted in the variance of such a clinical sign as tachycardia (50%). As for the frequency of dyspnea and hyperthermia/hypothermia, in this category, variances prevailed in patients with bedsores (66.7% and 50%, respectively).

Two clinical and laboratory signs of systemic inflammatory response syndrome were diagnosed among 11 (13.1%) patients. The patients with neuropathic ulcers due to diabetic foot syndrome and trophic ulcers after thrombophlebitis were equally distributed (5 patients each) (45.5% each, respectively). Only one clinical case (9.1%) was reported among patients with bedsores of various etiologies.

The most common clinical and laboratory signs were leukocytosis/leukopenia (40.9%) and tachycardia (31.8%). Hyperthermia/hypothermia was diagnosed in 18.2% of cases, and dyspnea in 9.1% of cases.

Among patients with leukocytosis, patients with trophic ulcers due to venous insufficiency of the lower extremities prevailed (55.6%) and neuropathic ulcers of diabetic foot syndrome (33.3%). At the same time, tachycardia was equally distributed among patients of these etiological categories (42.9% each). The same variation about hyperthermia/hypothermia (50% each, respectively) was found.

As for patients with bedsores, it should be noted that one patient had 2 clinical and laboratory signs of a systemic inflammatory response syndrome, leukocytosis and tachycardia.

We identified three clinical and laboratory systemic inflammatory response syndrome signs among 14 (16.7%) patients with long-term non-healing wounds. More than half (64.3%) of them were patients with bedsores. In 28.6% of cases (4 patients), these were patients with neurotrophic foot ulcers due to diabetes mellitus, and in 7.1% of cases (1 patient), with trophic ulcers due to chronic venous insufficiency of the lower extremities.

The analysis of clinical and laboratory signs of variance was mainly manifested by a combination of hyperthermia/hypothermia (33.3%) and tachycardia (31%) with the presence of leukocytosis/leukopenia (26.2%) or dyspnea (9.5%). They were mainly diagnosed among patients with pressure ulcers. For example, leukocytosis/leukopenia among patients with long-term non-healing wounds in 72.7% of cases was noted among patients with bedsores of various etiologies. Such a situation was

also noted in the presence of dyspnea (75%), hyperthermia/hypothermia (64.3%) and tachycardia (53.8%), which was apparently due to the initially combined damage to soft tissues.

Only in three (3.6%) patients with long-term non-healing wounds did we identify four clinical and laboratory signs of systemic inflammatory response syndrome. These were among patients with bedsores of various etiologies (2 patients) and neurotrophic ulcers in diabetic foot syndrome (1 patient).

Often, the generalization of the infection manifested itself in the form of chronic sepsis with organ dysfunction, which could occur under the mask of the pathology of the affected organ. An example is the following clinical case:

Patient U.S., born in 1963, # 2864/513, came to the nephrology department of our clinic after a long period of examination and treatment in other hospitals with a diagnosis of chronic pyelonephritis in the acute stage. The main complaints were pain in the lumbar region, frequent urination, periodic hyperthermia, palpitations, and pronounced general weakness. The patient has been suffering from long-healing ulcers of the right foot and lower leg for 2 years, which appeared after thrombophlebitis of the deep veins of the lower extremities (figure). He received treatment on an outpatient and inpatient basis. The wounds were periodically covered with a necrotic crust.

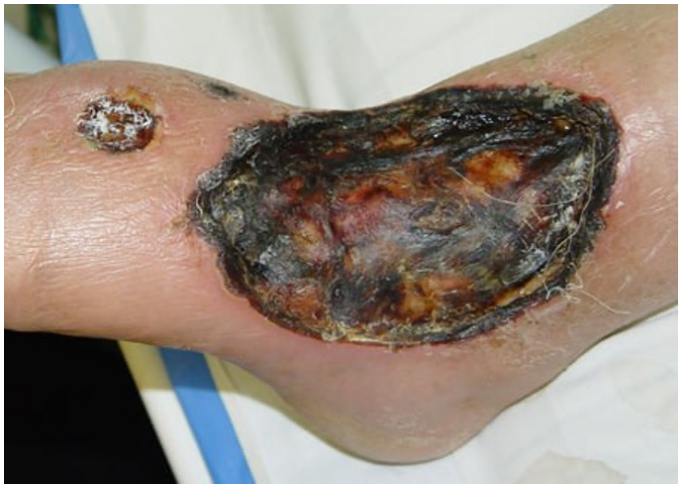

Figure. Trophic ulcers of the lower extremities in the patient presented in the description of this clinical example

Over the past month, the patient has developed swelling of the lower extremities and free fluid in the abdominal and pleural cavities, weight loss. Ultrasound revealed diffuse changes in the kidneys, moderate splenomegaly, and hydracalcinosis. Chest x-ray showed left-sided exudative pleurisy. Over the past two weeks, the patient's cervical and submandibular lymph nodes have enlarged. Blood tests revealed hypoproteinemia (39 g/l), dysproteinemia, an increase in alkaline phosphatase up to 143 U/l, urea up to 18.3 mmol/l, creatinine up to 82 μmol/l, leukocytosis up to 16x10^9/l, thrombocytosis – 488x10^9/l, erythrocytes 4.7x10^{12}/l, haemoglobin – 78 g/l. Bacteriological wound culture identified Staphylococcus aureus in titer 10^9; urine culture revealed Staphylococcus aureus in titer 10^7. The results of hemaculture are negative. The diagnosis was established: post-thrombophlebitic syndrome complicated by trophic ulcers of the right tibia and foot. Chronisepsis with kidney damage. Pyelonephritis.

As this clinical case has shown, a sluggish inflammatory process in a long-term non-healing wound has led to kidney damage in the form of sluggish urological diseases. At the same time, as is known, in chronic wounds, the inflammatory phase becomes very long, which ultimately leads to poor and delayed healing [15]. Several features characterize persistent inflammation in such wounds. Macrophages can be one of the keys to the possible generalization of infection, which is essential in developing methods for predicting this formidable complication of long-term non-healing wounds [16].

CONCLUSION

Analysis of the distribution of patients depending on the number of clinical and laboratory signs of the systemic inflammatory response syndrome, based on the criteria for diagnosis, allowed us to identify the presence of generalization of infection in 28 (33.3%) patients. At the same time, among patients with bedsores and neurotrophic ulcers of diabetic foot syndrome, they turned out to be the most numerous (41.4% and 36.7%, respectively). Often, the generalization of the infection manifested itself in the form of chronic sepsis with organ dysfunction, which could occur under the mask of the pathology of the affected organ. As the clinical example shows, a long-term disease, accompanied by a non-specific clinical picture, requires the obligatory exclusion of the bacteriological factor in developing this complication. In this case, a sluggish inflammatory process in a long-term non-healing wound led to kidney damage in the form of sluggish urological diseases. We were dealing with chronic sepsis, which manifested itself not only with signs of systemic inflam-

matory response syndrome but also with organ dysfunction.

Conflict of interest – The authors declare no conflict of interest.

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Ethical issues—The authors state that all ethical issues were resolved within the framework of protocols approved by the Republican Bioethics Committee, allowing the implementation of these studies.

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UZOQ MUDDATLI BITMAGAN YARALARDA INFEKTSIYANI GENERALIZATSIYASI

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Milliy bolalar tibbiyot markazi, Toshkent, Uzbekiston

ABSTRAKT

Jarrohlik sepsis statistik ma'lumotlarning zamonaviy tanotogenetik tuzilishida hal qilinmagan muammo bo'lib qolmoqda. Yara sepsi deb ham ataladigan yara jarayoni fonida sepsis ushbu asoratning rivojlanishining eng keng tarqalgan etiologik sababi hisoblanadi. Ayni paytda, yara infektsiyasining rivojlanishida adabiyotga ko'ra, ko'pchilik mualliflar ma'lum bo'lganidek, kasallikning patogenetik mexanizmiga ega bo'lgan o'tkir jarohatlarga e'tibor berishadi. Shu bilan birga, uzoq muddatli shifo topmaydigan jarohatlarning rivojlanishi va davomida, adabiyotda infektsiyani umumlashtirishning mumkin bo'lgan variantlari kam. Shu munosabat bilan, bizning tadqiqotimizning maqsadi uzoq muddatli bitmagan yaralari bo'lgan bemorlarda tizimli yallig'lanish javob sindromining klinik va laboratoriya belgilari rivojlanish chastotasini aniqlashdan iborat edi.

Kalit so'zlar: uzoq muddatli bitmagan jarohatlar, yara sepsisi, tizimli yallig'lanish javob sindromi

ГЕНЕРАЛИЗАЦИЯ ИНФЕКЦИИ ПРИ ДЛИТЕЛЬНО НЕЗАЖИВАЮЩИХ РАНАХ

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АБСТРАКТ

Хирургический сепсис остается далеко нерешенной проблемой в современной танотогенетической структуре статистических данных. Сепсис на фоне раневого процесса, известный также как раневой сепсис, считается наиболее частой этиологической причиной развития данного осложнения. Между тем, в случае развития раневой инфекции по данным литературы большинство авторов уделяют внимание острым ранам, которые, как известно, имеют иной патогенетический механизм течения заболевания. Однако в условиях развития и течения длительно незаживающих ран, возможных вариантов генерализации инфекции в литературе описано мало. В связи с этим, целью нашего исследования явилось выявление частоты развития клинико-лабораторных признаков синдрома системной воспалительной ответной реакции организма у больных с длительно незаживающими ранами.

Ключевые слова: длительно незаживающие раны, раневой сепсис, синдром системной воспалительной ответной реакции