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Early Diagnosis of Sepsis in Purulent-Inflammatory Diseases of Soft Tissues

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Abstract. The following work is adapted and devoted to the development of methods for the first diagnosis of infection with purulent-inflammatory diseases of soft tissues, developed against the background of diabetes, using new and traditional methods for the diagnosis of sepsis. At the same time, it was noted that early diagnosis and timely surgical treatment made it possible to reduce generalization, development of purulent-inflammatory process and mortality.
Keywords: diabetes mellitus, surgical infection, sepsis, purulent-inflammatory process, inflammation mediators.

In today's world, purulent-inflammatory diseases of soft tissues (PISD) remain a field of surgery that receives little attention from outpatient and inpatient specialists. The importance of the problem of CVID is emphasized by the fact that their frequency reaches 70% in primary referrals to general surgeons [1,12]. As part of nosocomial infections, the frequency of CVID (post-operative suppuration, post-injection complications, etc.) reaches 36%, in Russia - 24%. [2,5].

An analysis of the literature data showed that purulent-inflammatory diseases of soft tissues are the most common reason for patients seeking surgical help, since 10% of hospitalizations in the UK are patients with this pathology. In the USA, purulent-inflammatory diseases of soft tissues cause 433,000 hospitalizations per year [10,11].

The presence of concomitant pathology in the form of diabetes mellitus is of particular importance in the etiology and pathogenesis of CVD [7,8,9]. It is known that the specific changes that occur in diabetes mellitus create favorable conditions for the occurrence and progressive development of CVD. A feature of the course of CVDMT against the background of diabetes mellitus (DM) is the blurring of the clinical picture, the frequent combination of the course of the pathological process with the development of severe sepsis, multiple organ dysfunction and a high percentage of deaths [4,6,11,12]. The relevance is due to the increasing prevalence of diabetes and its numerous complications, which are the main cause of disability and mortality in people in industrialized countries. Currently, diabetes is a major problem worldwide [3.7].

Purpose of the study - to study infections and various forms of sepsis in patients with purulent-inflammatory diseases of soft tissues against the background of diabetes mellitus using new and traditional methods for diagnosing sepsis.

Materials and methods. The work is based on an analysis of the results of treatment of 73 patients with purulent-inflammatory diseases of soft tissues (PID) on the background of diabetes mellitus (DM), who were hospitalized at the Tashkent Medical Academy, multidisciplinary clinic of purulent surgery and surgical complications of diabetes mellitus of the Ministry of Health of the Republic of Uzbekistan, for the period from 2015 to 2020.

All patients, as a rule, were admitted to the clinic for urgent reasons and were subjected to a comprehensive clinical examination using modern clinical, biochemical and instrumental research methods. To identify the diagnosis, patients with CVID on the background of diabetes represented a heterogeneous group, differing in the severity of their general condition, the severity of endotoxemia and symptoms of sepsis, as well as the extent of the purulent-necrotic process and the intensity of its progression. General clinical symptoms varied depending on the cause of development of CVD, its location, the patient's condition at the time of the disease and his age.

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Results and its discussion. It is known that there is a direct correlation between the prevalence of the purulent process and the severity of the patient's condition, the degree of endotoxicosis, the incidence of severe sepsis and the prognosis of the disease. In total, HVID on the background of diabetes reached the stage of sepsis (according to the international classification of the Chicago Consensus Conference of 1992) in 57.5% of cases, accompanied by 2-4 symptoms of SIRS. In 9.6% of patients, the presence of severe sepsis was determined due to the addition of multiple organ dysfunction. 6.8% of patients were diagnosed with septic shock.

In the dynamics of the ongoing complex of treatment measures, already on the 3rd day there was a significant decrease in the number of patients with sepsis syndrome (23 patients - 33.8%) and septic shock (3 patients - 4.4%). However, against this background, the number of patients with severe sepsis increased to 9 cases (13.2%), probably due to the aggravation of the purulent-inflammatory process, and in some cases due to the resolution of the shock state of patients.

This trend was also noted on the 5th day of treatment, when there was a decrease in the number of patients with sepsis syndrome and septic shock and an increase in patients with severe sepsis. This circumstance confirmed our assumption that the recovery of patients from a state of shock is not yet a guarantee of a successful outcome of the purulent-septic process. In particular, the presence of concomitant diabetes mellitus contributes to the persistence of a burdened morbid background with severe sepsis in patients. Against the background of the treatment, a gradual decrease in the proportion of severe sepsis and septic shock is noted. Only on the 7th day of treatment, septic complications were noted in 12% of cases. They were mainly due to the presence of severe sepsis (9%) and sepsis syndrome (3%). In 58 patients, elimination of septic complications was achieved with normalization of the course of the purulent-inflammatory process.

Analysis of lethal outcomes in patients with CVD on the background of diabetes revealed the presence of a certain relationship with clinical and pathogenetic forms of septic complications. A total of 7 patients (9.6%) died in patients with CVD due to diabetes.

In chronological order, deaths were distributed in the following form. On the day of admission, 1 patient (1.36%) died due to progressive septic shock against the background of a severe form of CVID. Subsequently, on the 3-5th day of treatment, 5 more patients died, the cause of which in most cases was severe sepsis. Subsequently, on the 7th day of treatment, 1 patient (1.36%) died, also due to the progression of severe sepsis.

Thus, an analysis of traditional methods of treating patients with CVD on the background of diabetes revealed the frequent development of complications (42 patients - 57.5%) and mortality (7 patients - 9.6%). The dominant cause in the development of mortality was the generalization of the purulent-septic process. Based on this, it can be stated that with traditional methods of treatment for hyperventilation and diabetes mellitus, there remains a high risk of generalization of the purulent-septic process, leading to death. In this connection, it seems to us that carrying out a more detailed analysis of the development of septic complications in patients with purulent-inflammatory diseases of soft tissues against the background of diabetes mellitus will allow us to reconsider the cause-and-effect patterns of fatal outcomes of patients.

Quantitative characteristics of the dynamics of changes in septic manifestations in patients with CVD on the background of diabetes showed that upon admission of patients to the clinic, systemic inflammatory response syndromes (SIRS) - SIRS2 and SIRS3 (23.3% and 21.9%, respectively) were predominant (Table. 2). In 18 patients (24.7%) there were no signs of SIRS (SIRS0).

As traditional treatment methods were implemented, the number of patients with regression of the number of SIRS signs increased. So, on the 3rd day of treatment, the number of patients with the frequency of manifestations of SIRS symptoms was distributed as follows: SIRS1/ SIRS3/ SIRS2/ SIRS4. In 22.1% of cases, there were no signs of SIRS. On the 5th and 7th days of the traditional method, the dispersion of the distribution of patients with septic manifestations of hyperventilation on the background of diabetes was virtually identical and was distributed as follows: SIRS1/ SIRS2/ SIRS3/ SIRS4.

Thus, the analysis of the dynamics of changes in septic manifestations in patients with hypervestitis due to diabetes indicates, on the one hand, that, despite the traditional methods of treatment, even on the 5th and 7th days there is still a persistence of patients with SIRS4. On the other hand, the distribution of patients depending on the quantitative characteristics of the manifestation of septic complications dictates the need to

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evaluate the value of each of the symptoms of the manifestation of this disease. Analysis of the frequency of manifestations of individual signs of SIRS in patients in the dynamics of the course of CVID against the background of diabetes showed that upon admission, a total of 131 signs were registered in 73 patients. In total, taking into account the number of patients who did not have signs of SIRS, this figure was 87.9%. .

Table 2

Dynamics of changes in septic manifestations in patients with hyperventilation and diabetes mellitus

NUMBER OF SIGNS OF SEPSIS	DYNAMICS OF SEPTIC MANIFESTATIONS							
	On admission		3rd day		5th day		7th day	
	А.ч.	%	А.ч.	%	А.ч.	%	А.ч.	%
$SIRS_0$	18	24,7	15	22,1	23	34,3	37	56,1
$SIRS_1$	13	17,8	18	26,5	22	32,8	21	31,8
$SIRS_2$	17	23,3	13	19,1	13	19,4	5	7,6
$SIRS_3$	16	21,9	14	20,6	6	8,95	2	3,0
$SIRS_4$	9	12,3	8	11,7	3	4,55	1	1,5
ВСЕГО	73	100	68	100	67	100	66	100
Cumulative mortality over time	-	-	5	6,8	6	8,2	7	9,6

Already on the 3rd day of treatment of patients with CVD on the background of diabetes, the number of registered signs of SIRS, in absolute digital value, decreased. However, in percentage terms, this indicator did not differ significantly compared to the previous observation period. On the 5th and 7th days of treatment, the number of registered signs of SIRS in patients with CVD on the background of diabetes significantly decreased in absolute digital value by 1.7 and 3.2 times, respectively. As a percentage of the total number of recorded signs, this value was significant only on the 7th day of observation.

In order to assess the presence and degree of generalization of the inflammatory process, we assessed changes in the blood serum levels of diagnostic markers of sepsis (procalcitonin, proinflammatory cytokines IL-1b, IL-6 and tumor necrosis factor) in patients during the course of CVD with diabetes (Table 3)

A study of markers of generalization of the inflammatory process in patients with hyperventilation and diabetes mellitus showed a stable change in their level over the course of treatment. The level of procalcitonin in the blood serum, which averaged 17.15±5.4 ng/ml upon admission of patients to the clinic, was more indicative of the significant presence of sepsis. At the same time, in the dynamics of treatment of patients, this indicator, although it decreased to 4.1±0.98 ng/ml on the 7th day of the study, its level was on average 82 times higher than normal values.

Changes in the concentration of pro-inflammatory cytokines in the blood serum of patients with CVD on the background of diabetes in the dynamics of their treatment were not unambiguous. The highest values stood out for the pro-inflammatory cytokine IL-6, which, upon admission of patients with CVD and diabetes, exceeded the values of IL-1b and TNF-α by an average of 1.7 times.

Over time, on the 3rd and 5th days of treatment, the pro-inflammatory cytokine IL-6 increased relative to the first period to 38.3±7.4 pkg/ml. At the same time, the 7th day of the study was characterized by a decrease in this marker compared to the initial values by 1.5 times.

A similar trend of changes, albeit in a short-term range, was also detected in relation to the pro-inflammatory cytokine IL-1b. The decrease in this indicator on the 7th day of treatment was significant (2.3 times) compared to the initial values. At the same time, the dynamics of changes in the concentration of the pro-inflammatory cytokine TNF-α was characterized by stable values on the 3rd and 5th days of treatment compared to the period when patients were admitted to the clinic. The decrease in this indicator on the 7th day of treatment was as significant as in the case of previous proinflammatory cytokines (almost 2 times).

In general, it should be noted that the changes we identified in the content of pro-inflammatory cytokines in the blood of patients with DVT on the background of diabetes confirmed the well-known data on their role in the generalization of infection. However, the persistence of high values under the condition of treatment for 5 days indicated a discrepancy in conclusions between the presence of a septic complication

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and its type. In this regard, it seems necessary to us to analyze the level of change in diagnostic markers of sepsis in the blood depending on the type of its manifestation.

The nature of changes in the average value of markers for diagnosing the generalization of infection in patients during the course of CVID against the background of diabetes showed an ambiguity in the trend of changes (Table 4).

Table 4

The nature of changes in the average value of markers for diagnosing the generalization of infection in patients with CVID on the background of diabetes, M±m.

TYPE OF SEPTIC MANIFESTATION	MARKER OF INFECTION GENERALIZATION			
	PCT (ng/ml)	IL-1b (pkg/ml)	IL-6 (pkg/ml)	TNF-α (pkg/ml)
Without sepsis n=31	1,99±0,09	7,4±1,12	14,4±2,1	3,15±0,52
Sepsis syndrome n=30	4,75±0,57*	17,85±2,4*	33,9±9,4*	12,3±0,98*
Severe sepsis n=7	17,75±5,2*	19,2±1,54*	44,2±10,4*	27,9±1,4*
Septic shock n=5	34,5±2,8*	33,53±8,4*	54,7±12,4*	42,4±5,2*

Note: * - the value is significant in relation to the same indicators, provided there are no signs of SIRS ($p<0.05$);

The level of procalcitonin in patients with non-septic hypervestitis was 39.8 times higher than normal values (0.05 ng/ml), which was probably due to the peculiarity of the course of this pathological process in patients with diabetes mellitus. In the subgroup of patients with CVD, complicated by sepsis syndrome, there was a 95-fold increase in procalcitonin in the blood serum compared to normal values. At the same time, compared to the previous group, this figure was only 2.4 times higher. Severe sepsis, and especially septic shock, were characterized by the highest values of procalcitonin levels in the blood serum in patients with CVD and diabetes, exceeding control values by 355 and 690 times, respectively.

Thus, the concentration of procalcitonin in the blood of patients with hyperventilation and diabetes mellitus increases in proportion to the severity of the infectious process. Local inflammatory foci are not accompanied by a significant release of procalcitonin into the blood (the average procalcitonin level was 1.99±0.09 ng/ml). In the presence of generalized infection, a procalcitonin level of more than 2 ng/ml is typical (the highest procalcitonin level was observed in a patient with septic shock - 34.5±2.8 ng/ml). Accordingly, the procalcitonin test has a high diagnostic potential and is recommended for routine use in a modern hospital.

Pro-inflammatory cytokines IL-1b, IL-6 and TNF-α also tended to significantly increase, but less pronounced than procalcitonin. In particular, the pro-inflammatory cytokine IL-1b in patients with sepsis syndrome increased by 2.4 times compared to normal values. In severe sepsis, this figure was 2.6 times higher, and in patients with septic shock – 4.5 times higher ($p<0.05$).

In a study of the pro-inflammatory cytokine IL-6 in patients with sepsis syndrome, the excess of its normal values in the blood plasma of patients with CVD on the background of diabetes was 2.3 times, and in severe sepsis – 3.1 times. The maximum value of this indicator was noted in patients with septic shock (the excess of this indicator above normal values was 3.8 times).

The pro-inflammatory cytokine TNF-α responded to changes in the septic type of complication more significantly than previous indicators. In all cases of the development of septic complications in patients with hyperventilation and diabetes mellitus, the order of manifestation of the severity of the pathological process was noted. In sepsis syndrome, this indicator exceeded normal values by 3.9 times, in severe sepsis – by 8.9 times, and in septic shock – by 14.5 times.

A separate analysis of changes in the content of procalcitonin in patients with hyperventilation and diabetes mellitus, depending on the type of septic manifestation, showed that during all periods of the study a characteristic distribution of the dispersion value of this indicator was noted (Table 5). Septic shock was characterized by the highest values of procalcitonin content in the blood serum, which ranged from 30.2±2.5 ng/ml to 39.7±3.1 ng/ml. On average, the level of procalcitonin in the blood in patients with septic shock was 34.5±2.8 ng/ml. At the same time, in patients with severe sepsis this indicator averaged 17.75±5.2

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Date of Publication:24-11-2023

ng/ml. The level of procalcitonin in the serum of patients with sepsis syndrome varied in the range from 2.1±0.1 ng/ml to 6.9±0.15 ng/ml.

Regarding the category of patients who had no signs of septic complications, the average value of procalcitonin in the blood serum during all periods of the study was 1.99±0.09 ng/ml, which indicated the generalization of the inflammatory process with the erasure of its clinical signs. That is, in other words, against the background of the absence of generally recognized signs of systemic inflammatory response syndrome, in patients with CVID on the background of diabetes, there was an increase in the level of procalcitonin in the blood serum to a level indicating the presence of generalization of the infection.

Proof of our judgment can be provided by data on the dynamics of changes in the level of procalcitonin in the blood serum in patients who did not have signs of SIRS. On admission, the level of procalcitonin in the blood serum was 0.5±0.09 ng/ml; on the 3rd day it decreased to 0.2±0.03 ng/ml. On the 5th day of treatment, the level of this indicator reached normal values (0.05±0.0012 ng/ml) and remained so on the 7th day of observation (0.04±0.001 ng/ml).

In general, confirming the above conclusions, it should be noted that the level of procalcitonin, which is the main marker of generalization of infection, in patients with CVD on the background of diabetes exceeded control values even in the presence of clinical signs of SIRS. This circumstance was typical in the early stages of treatment. In subsequent periods of treatment, clinical and laboratory data on the manifestations of SIRS and the level of procalcitonin were similar in expressing the pathological essence of the process.

The concentration of the pro-inflammatory cytokine IL-1b in patients with CVD on the background of diabetes upon admission to the clinic varied from 10.4±0.15 pg/ml to 32.8±9.84 pg/ml. The average value of this indicator during this period was 21.02±0.32 pkg/ml (Table 6). Analysis of changes in the concentration of the pro-inflammatory cytokine IL-1b depending on the type of septic manifestation was distributed in decreasing order from septic shock to signs of sepsis syndrome. In septic shock, the average concentration of the proinflammatory cytokine IL-1b was 33.53±8.4 pkg/ml. In patients with severe sepsis, the average level of the proinflammatory cytokine IL-1b was 19.2±1.54 pg/ml. In the case of examination of patients with signs of sepsis syndrome, the level of proinflammatory cytokine averaged 17.85±1.49 pkg/ml. It should be noted that in cases where there were no signs of SIRS in patients upon admission to the clinic, the level of the proinflammatory cytokine IL-1b was 10.4±0.15 pkg/ml. At the same time, despite the general trend in the dynamics of a decrease in this indicator to 4.1±0.1 pkg/ml on the 7th day of treatment, the 3rd day was still characterized by relatively high digital values (9.8±0. 24 pkg/ml).

Table 6

The nature of changes in the content of the pro-inflammatory cytokine IL-1b (pkg/ml) in the blood serum of patients during the course of hyperventilation with diabetes, M±m.

TYPE OF SEPTIC MANIFESTATION	DYNAMICS OF THE DISEASE			
	On admission	3rd day	5th day	7th day
Without sepsis, n=31	10,4±0,15	9,8±0,24	5,4±0,11	4,1±0,1
Sepsis syndrome, n=30	18,5±2,14	18,5±2,45	17,4±1,98	17,0±1,55
Severe sepsis, n=7	22,4±3,18	20,4±2,87	18,5±1,45	15,4±1,13
Septic shock, n=5	32,8±9,84	42,7±8,41	25,1±1,24	-

Note: * - the value is significant in relation to the indicators upon admission of patients to the clinic ($p<0.05$).

It should be noted that in this case, despite the absence of clinical signs of generalization of infection in patients with DVT on the background of diabetes, the study of a proinflammatory cytokine indicated the opposite phenomenon. Another feature in the change in the concentration of the pro-inflammatory cytokine IL-1b in patients with CVID on the background of diabetes is an increase in its level on the 3rd day of treatment in the case of the development of septic shock, which, apparently, was associated with the use of additional aggression in the form of COHO .

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The concentration of the proinflammatory cytokine IL-6 in patients with CVD on the background of diabetes upon admission to the clinic varied from 10.2±0.49 pkg/ml to 54.5±12.8 pkg/ml (Table 7). It should be noted that an increase in the concentration of IL-6 was observed with the severity of the septic manifestation.

The moderate increase in this marker of generalization of infection on the 3rd and 5th days of the traditional method of treatment remained unchanged on the 7th day of the study. The addition of multiple organ dysfunction and septic shock to the septic complication of hypervestitis due to diabetes mellitus against the background of high values of the proinflammatory cytokine IL-6 in the blood serum was characterized by stable digital data.

The nature of changes in the content of the pro-inflammatory cytokine TNF-α in the blood serum of patients during the course of hyperventilation with diabetes showed a marked difference between the types of septic complications (Table 8).

In patients with sepsis syndrome, the level of the proinflammatory cytokine TNF-α varied from 12.0±0.58 pg/ml to 12.5±0.98 pg/ml. In patients with severe sepsis, this indicator ranged from 26.4±1.44 pkg/ml to 28.5±1.47 pkg/ml. The most pronounced changes were noted in patients with septic shock. In this category of patients, the level of the pro-inflammatory cytokine TNF-α in the blood serum was significantly high and ranged from 40.7±5.8 pg/ml to 43.8±5.4 pg/ml.

Table 8

The nature of changes in the content of the pro-inflammatory cytokine TNF-α (pkg/ml) in the blood serum of patients in the dynamics of the course of hyperventilation with diabetes, M±m.

TYPE OF SEPTIC MANIFESTATION	DYNAMICS OF THE DISEASE			
	On admission	3rd day	5th day	7th day
Without sepsis, n=31	2,7±0,45	2,8±0,52*	3,7±0,12*	3,4±0,1*
Sepsis syndrome, n=30	12,4±1,24	12,5±0,98*	12,4±0,55*	12,0±0,58*
Severe sepsis, n=7	28,4±2,85	26,4±1,44*	28,5±1,47*	28,4±2,5*
Septic shock, n=5	42,7±10,4	43,8±5,4*	40,7±5,8*	-

Note: * - the value is significant in relation to the indicators upon admission of patients to the clinic ($p<0.05$).

Thus, our study showed that diagnostic markers of generalization of the inflammatory process, along with signs of SIRS, have informational value, which, undoubtedly, can be used in assessing the effectiveness of therapy and preventing the development of sepsis. At the same time, a feature of the course of purulent-inflammatory disease of soft tissues in patients with diabetes mellitus is the erasure of clinical signs of generalization of infection in the presence of reliable laboratory data on indicators such as procalcitonin and proinflammatory cytokines IL-1b, IL-6, TNF-α. In this regard, it seems to us that in order to objectify the diagnostic value of these laboratory methods for assessing the patient's condition, the development of integrated methods is required, which in turn will make it possible to unify the system of diagnostic and treatment algorithm.

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