DIAGNOSIS AND TREATMENT OF NECROTIZING SOFT TISSUE INFECTION COMPLICATED BY SEPSIS

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ABSTRACT

Background. The most severe and rapidly progressing tissue infections, which are accompanied by severe intoxication and sepsis, are necrotizing infections.

Material and methods. 108 patients with necrotizing soft tissue infections were examined and treated. Among them, fasciitis (83 patients), cellulitis (11 patients) and myositis (14 patients) were distinguished. Clinical, laboratory, in-depth microbiological and histological studies were used.

Results. Necrotizing soft tissue infections are characterized by microbial polymorphism without a clear correlation between the clinical course and the microbiological landscape. The impossibility of excluding the diagnosis of necrotizing soft tissue infection on the basis of the clinical picture is an indication for surgical revision of all layers of soft tissues.

Keywords: Necrotizing soft tissue infections, fasciitis, cellulitis, myositis, microbiological diagnostics, generalization of infection

INTRODUCTION

The extraordinary malignancy of the course of necrotizing infections led to the desire of researchers to associate this disease with certain microorganisms [1, 9].

In crops from foci of infection, microbial associations, which are various combinations of pathogens of wound infection, are more often found [3, 6].

Traditionally, anaerobic microorganisms play a leading role in the pathogenesis of necrotizing soft tissue infections, but in recent years there have been published works in which the legitimacy of this approach has been authoritatively questioned [4, 5, 11, 17].

Late diagnosis of the disease, underestimation of the severity of the patient's condition and, consequently, the lack of adequate comprehensive surgical treatment in a significant number

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of cases lead to the death of the patient from septic shock, sometimes before the correct diagnosis is established [10, 12, 21].

At the same time, timely diagnosis of rapidly progressive necrotizing infection is still a complex task [19, 20].

MATERIAL AND METHODS OF RESEARCH

The criteria for selecting patients in the study group were: rapid progression of the infectious process; necrotic lesions of fascia, muscles or subcutaneous tissue; absence of free purulent exudate; the extent of the lesion - more than one anatomical zone or more than 1350 sm². These criteria were met by 108 patients who were treated and examined in the surgical infection department of the multidisciplinary clinic of the Tashkent Medical Academy from 2017 to 2022.

The preliminary diagnosis of necrotizing soft tissue infections was based on the following characteristic clinical signs: cyanosis of the skin with areas of necrosis; crepitus; with dim local symptoms with a predominance of general inflammatory symptoms (oedema and infiltration of tissues, hyperemia of the skin) - pronounced general signs of an inflammatory reaction and intoxication (severe and extremely severe general condition of the patient, tachycardia, hypotension, high leukocytosis, neutrophilic shift to the left); rapid, within a few hours, the appearance of characteristic local symptoms or an increase in intoxication.

Establishing a preliminary diagnosis of necrotizing soft tissue infections was an indication for emergency surgery. The final clinical diagnosis of necrotizing soft tissue infections with an assessment of the nature, anatomical substrate and volume of the lesion was established intraoperatively after revision of the focus of infection.

Of the total number of patients studied, 62 (57.4%) were men and 46 (42.6%) were women. Patients aged 4 1 - 6 0 years (40.7%) and over 70 years (19.4%) prevailed.

In 60 (55.6%) cases, severe concomitant pathology was revealed: diabetes mellitus, postinfarction cardiosclerosis, chronic alcohol intoxication with multiple organ manifestations, and oncological diseases.

In 63 (63.6%) cases, necrotizing soft tissue infections developed against the background of damage to the skin. The progression of infection by the type of necrotizing soft tissue infections was noted after surgical treatment of abscesses and phlegmon in 12 (11.1%) cases. Trophic ulcers and gangrene of the lower extremities caused the development of necrotizing infection in 4 (3.7%) patients and bedsores in 3 (2.8%) patients.

The pathological process was predominantly localized on the lower extremities - 21 (19.4%) cases, perineum and scrotum - 19 (17.6%) cases. In 41 (38%) cases, the infection spread to several anatomical zones.

Assessing the severity of the general condition of patients with necrotizing soft tissue infections, we were guided by the criteria for diagnosing R. bone sepsis developed by the Conciliation Conference in Chicago [2].

The microbial landscape was determined using a detailed bacteriological study, native smear bacterioscopy, as well as gas-liquid chromatography methods. The nature of tissue damage was revealed by histological examination of fragments.

RESULTS AND DISCUSSION

The most common laboratory sign in necrotizing soft tissue infections was tachycardia and high leukocytosis, least often there was an increase in body temperature to $38\,^{\circ}$ C and above or a decrease to $36.0\,^{\circ}$ C and below (Table 1).

Table 1
Laboratory Signs of Systemic Inflammatory Response Syndrome

Cymptoms	FORMS OF NECROTIZING SOFT TISSUE INFECTION			TOTAL	
Symptoms	Fasciitis	Cellulite	Myositis	(n=108)	
	(n=83)	(n=11)	(n=14)		
Body temperature $\geq 38^{\circ}$ C or $\leq 36^{\circ}$ C	41	5	10	56	
	(49,4%)	(45,5%)	(71,4%)	(51,9%)	
11 4 4 200	63	7	13	92 (76 0)	
Heart rate >90 per minute	(75,9%)	(63,6%)	(92,9%)	83 (76,9)	
Respiratory rate >20 times per minute or	43	5	6	54 (500()	
hyperventilation (PaCO ₂ <32 mmHg)	(51,8%)	(45,5%)	(42,9%)	54 (50%)	
Blood leukocytes >12x10 ⁹ /l or <4x10 ⁹ /l	56	6	10	72	
	(67,5%)	(54,5%)	(71,4%)	(66,7%)	
Immature forms of neutrophils >10%	58	8	8	74	
	(69,9%)	(72,7%)	(57,1%)	(68,5%)	

According to the severity of the condition and organ dysfunctions, without exception, all patients with necrotizing soft tissue infections had criteria that made it possible to establish the presence of a generalized infection in them (Table 2).

Table 2

The severity of the condition and organ dysfunctions in necrotizing soft tissue infection

	FORMS OF NECROTIZING SOFT			ТОТАТ	
FORMS OF SEPTIC COMPLICATIONS	TISSUE INFECTION			TOTAL	
	Fasciitis	Cellulite	Myositis	(n=108)	
	(n=83)	(n=11)	(n=14)		
Sepsis syndrome	55	8	9	72	
Sepsis syndrome	(66,3%)	(72,7%)	(64,3%)	(66,7%)	
C	24	3	3	20 (27.9)	
Severe sepsis	(28,9%)	(27,3%)	(21,4%)	30 (27,8)	
C 4'11-	4	0	22	6 (5 60/)	
Septic shock	(4,8%)	U	(14,3%)	6 (5,6%)	
There are no clinical signs of sepsis	0	0	0	0	
SAPS II	6	6	8	7	

Thus, pronounced signs of systemic inflammatory response and intoxication, according to accepted international criteria, allow us to regard all variants of necrotizing soft tissue infections as the cause of sepsis [8, 18].

In bacteriological examination of the discharge and biopsy specimens of wound tissues, various strains of Bacteroides were most often distinguished among obligate anaerobic microorganisms. Other obligate anaerobes were seeded in single observations. When isolating obligate anaerobes, there has always been an association with aerobic or facultative anaerobic flora. The growth of clostridia was not noted in any case. Exclusively obligate aerobes, mainly Pseudomonas aeruginosa, were found in 7 (6.5%) operated patients. In 50 (46.3%) cases, there were mono-infections, in 53 (49.1%) patients, the microflora was mixed. It should also be noted that in 5 (4.6%) cases during the bacteriological study microflora growth was not obtained. Analysis of bacteriological examination data of wound tissue discharge and biopsy specimens did not reveal correlations between various types of necrotizing soft tissue infection and the microbial landscape of the lesion (Table 3).

Table 3

Frequency of isolation of pathogens of necrotizing soft tissue infection

	FORMS OF N			
MICROORGANISMS		TOTAL		
	Fasciitis	Cellulite	Myositis	(n=108)
	(n=83)	(n=11)	(n=14)	
Bacteroides spp.	4 (4,8%)	1 (9,1%)	1 (7,1%)	6 (5,6%)
Peptococcus anaerobius	2 (2,4%)	0	0	2 (1,9)
Fusobacterium necroforum	0	1 (9,1%)	0	1 (0,9%)

Streptococcus spp.	24 (28,9%)	2 (18,2%)	4 (28,6%)	30 (27,8%)
Staphylococcus aureus	21 (25,3%)	4 (36,4%)	9 (64,3%)	34 (31,5%)
Staphylococcus epidermidis	7 (7,2%)	0	2 (14,3%)	9 (8,3%)
Enterobacteriaceae	41 (49,4%)	4 (36,4%)	6 (42,9%)	51 (47,2%)
Pseudomonadaceae	5 (6,0%)	1 (9,1%)	1 (7,1%)	7 (6,5%)

In an in-depth microbiological study using gas-liquid chromatography methods, it was possible to isolate metabolites characteristic of obligate anaerobic microorganisms from all the biopsy specimens studied (Table 4). 49 (76.6%) had a combination of several anaerobes. At the same time, various, practically non-repetitive aerobic-anaerobic associations were observed. Only anaerobic microflora, in the absence of aerobic waste products, was detected only in 3 (4.7%) cases.

Table 4

The frequency of isolation of anaerobic bacteria by the method of in-depth study

MCDOODCANIGMG	FORMS OF NECROTIZING SOFT TISSUE INFECTION			TOTAL
MICROORGANISMS	Fasciitis (n=48)	Cellulite (n=7)	Myositis (n=9)	(n=64)
Peptostreptococcus anaerobius	10 (20,8%)	2 (28,6%)	3 (33,3%)	15 (23,4)
Fusobacterium necroforum	12 (25%)	1 (14,3%)	1 (11,1%)	14 (21,9%)
Actinomyces israelli	9 (19,8%)	1 (14,3%)	4 (44,4%)	14 (21,9%)
Peptococcus anaerobius	8 (16,7%)	3 (42,9%)	2 (22,2%)	13 (20,3)
Propionibacterium acnes	8 (16,7%)	1 (9,1%)	3 (33,3%)	12 (18,8%)
Peptococcus asacharolyticus	3 (6,3%)	1 (14,3%)	2 (22,2%)	6 (9,4%)
Clostridium septicum	2 (4,2%)	1 (14,3%)	1 (11,1%)	4 (6,3%)
Bacteroides fragilis	3 (6,3%)	0 (0)	0 (0)	3 (4,7%)
Veillonella	1 (2,1%)	0 (0)	1 (11,1%)	2 (3%)
Bacteroides putredinis	1 (2,1%)	1 (14,3%)	0 (0)	2 (3%)
Peptostreptococcus intermedius	2 (4,2%)	0 (0)	0 (0)	2 (3%)
Fusobacterium nucleatum	0 (0)	0 (0)	1 (11,1%)	1 (1,7%)

The ratio of anaerobic-aerobic factors of microflora (Kana/aer) in 49 (76.6%) patients was higher than 31.2%, indicating the predominance of metabolites of anaerobic microflora in the necrotic focus. In other observations, it corresponded to mixed microflora. There were no significant differences in the values of this indicator depending on the morphological substrate, the volume of the lesion and the severity of the patient's condition.

In all cases, the morphological picture in the preparations of the skin, subcutaneous fat, skeletal muscles and fascia obtained from the focus of inflammation was characterized by widespread necrotic tissue changes. The exudate contained a small number of polymorphonuclear leukocytes and stratified necrotic tissues. Circulatory disorders manifested themselves in the form of plethora, stasis and sludge phenomenon in the vessels of the microvasculature. In fibrinoid necrosis of the artery walls, perivascular focal haemorrhages were noted. There has always been a pronounced interstitial oedema of the surrounding tissues.

Differential diagnosis of necrotizing soft tissue infection at an early stage of the disease in some cases presented certain difficulties. Among the diseases accompanied by the development of extensive foci of soft tissue necrosis, rapidly progressive inflammation, and systemic inflammatory reaction syndrome, the following definition can be distinguished.

Prolonged compression syndrome, like a surgical infection, in a significant number of patients is accompanied by a rather severe general condition, intoxication, and often multiple organ failure [15]. There is also a pronounced swelling of the limb, abundant exudation from wounds, necrotic muscle damage, and, consequently, skin changes caused by it, such as hyperemia, cyanosis, and bullae. In addition, large areas of deep-lying necrotic tissues serve as an excellent breeding ground for the development of various microorganisms, so it is almost impossible to completely eliminate the development of necrotizing soft tissue infection [13].

In such situations, we started intensive therapy based on the principles of treatment of both necrotizing soft tissue infection and prolonged compression syndrome. If, against the background of conservative treatment, a positive trend was noted for several hours - stabilization of the general condition, the absence of progression of local symptoms of inflammation - then the disease was regarded as a syndrome of prolonged compression, and the operation was performed only after the final stabilization of the patient's condition and demarcation of necrosis. With the ineffectiveness of intensive care, an increase in swelling of the limb, and the development and increase in renal failure, we resorted to emergency surgical intervention, during which we established the final diagnosis. With a characteristic picture of necrotizing soft tissue infection, radical surgical intervention was performed. In the absence of total necrosis of soft tissues, the detection of "mosaic" myonecrosis, secondary necrotic foci against the background of a large volume of visually healthy tissues, we performed surgical treatment of the wound, recommended for prolonged compression syndrome, which consists in the wide opening of all

fascial cases, if necessary, supplemented by necrectomy. Fasciotomy was combined with separation, revision and drainage of intermuscular spaces and muscle cases

Necrotic changes in soft tissues, similar in appearance to necrotizing infection of soft tissues, were observed with infringement of hernias of the anterior abdominal wall with phlegmon of the hernial sac. At the same time, a routine physical examination of the patient with the identification of symptoms of infringement of the hernial sac made it possible to clearly differentiate this disease [14].

Extensive necrotic changes were also observed in patients who were injected with various drugs and narcotic drugs. These patients had a variety of external manifestations, such as oedema, dysfunction of the affected limb, and hyperemia of varying intensity. Given that the administration of these drugs, as a rule, occurred without observing the rules of asepsis, it was not possible to exclude the infectious nature of the necrotic process [7]. However, due to the fact that in both cases the situation required immediate surgical intervention, the diagnostic error did not cause serious negative consequences for patients.

The intraoperative picture of necrotic lesions of chemical origin in a number of cases corresponded to necrotic myositis with its inherent extensive muscle necrosis. The spread of the necrotic process and the change in laboratory parameters occurred slowly, therefore, the general condition of patients remained satisfactory for a long time, and there was no systemic inflammatory reaction.

In the first hours after the onset of skin changes, certain difficulties in differential diagnosis were presented by various hematomas that outwardly resembled a necrotizing infection of soft tissues. As with surgical infections, an increase in the size of the focus of hyperemia and cyanosis due to the spread of blood poured into the subcutaneous tissue occurred quite quickly. In some observations, blisters also appeared on the skin. The task was complicated in cases where patients, being in a state of alcohol, or drug intoxication, as well as due to somatic severity, could not accurately indicate the presence of an injury that preceded the disease. In the absence of other clinical manifestations indicating the presence of a surgical infection, in these situations, we carried out dynamic monitoring of the patient for several hours. The absence of an increase in local changes, as well as clinical and laboratory signs of intoxication, made it possible to exclude necrotizing infection of soft tissues. In other cases, it was necessary to resort to performing a diagnostic incision with a revision of all layers of soft tissues.

In one case, in acute pancreatitis, we observed the appearance of ecchymosis around the navel, due to local toxic vascular damage - a symptom of Grunwald. As with necrotizing soft tissue infection, there is an increase in the symptom of a systemic inflammatory reaction. In this regard, in order to avoid delayed diagnosis, a diagnostic incision is often the only way to exclude surgical infection of soft tissues in this situation.

Local manifestations of limb ischemia in obliterating atherosclerosis, arterial thrombosis, and diabetic foot syndrome may be similar to changes in necrotizing soft tissue infection [16]. The slow increase in local symptoms, the absence or non-severity of other physical and laboratory signs, and the characteristic anamnesis make it easy to distinguish this group of diseases from a necrotizing soft tissue infection [1].

Manifestations of systemic vasculitis during the initial examination can cause diagnostic alertness [7]. Various changes in skin colouration, soft tissue necrosis, as well as muscle pain, and impaired limb function, make us think about a surgical infection [2,16,20]. In such cases, the presence of rheumatic diseases in the anamnesis, damage to several parts of the body at the same time, and the absence of rapid progression and characteristic laboratory changes speak in favor of the immune, rather than the infectious nature of the process [17].

Thrombophlebitis of the saphenous veins of the lower extremities, as well as necrotizing infections of soft tissues, can begin with the appearance of pain, moderate oedema of the affected limb, increasing dim hyperemia, characteristic spots, and an increase in body temperature [2]. Symptoms of thrombophlebitis develop quite quickly, however, unlike necrotizing soft tissue infection, there are practically no signs of a systemic inflammatory reaction, which makes it possible to exclude a surgical infection with a thorough examination.

In post-injection ileofemoral phlebothrombosis, after administration of narcotic and psychotropic substances into the inguinal region, as well as in rapidly progressive necrotic processes, there is pain, moderate swelling of the limb, and non-intensive, without clear boundaries, hyperemia may be observed [18]. In some cases, the muscles become "wooden", resembling necrotic myositis. The situation is complicated by the fact that anamnestic data do not help to carry out differential diagnosis, since there is always a source of infection and damage to the skin. In addition, the diagnosis of ileofemoral phlebothrombosis alone does not exclude the presence of necrotizing soft tissue infection. In such cases, it is necessary to focus on the patient's condition, and laboratory data, and, if necessary, resort to a diagnostic incision.

We also observed the occurrence of crepitus tissue after operations on the abdominal organs during the restoration of intestinal motility, puncture of the pleural cavity, and laparoscopy. In all cases, this symptom was not accompanied by the appearance of any skin changes, as well as negative dynamics in the general condition of patients.

In erysipelas, despite the presence of oedema and hyperemia in the focus of infection, and in some cases bullae, differential diagnosis usually does not present any particular difficulties: unlike necrotizing infection of soft tissues, in this disease, hyperemia, as a rule, is quite intense, bright, bullae are filled with a clear liquid [15]. The disease in most cases is accompanied by a rise in body temperature to 40 0 C and above with chills, More often than with necrotizing soft tissue infection, there are phenomena of regional lymphadenitis and lymphangitis.

In patients of the intensive care unit, we observed the appearance of oncotic oedema, visually resembling a necrotizing soft tissue infection. In addition to external manifestations, there were no other signs that make it possible to suspect necrosis of soft tissues with this symptom.

In some cases, various skin diseases can mimic a necrotizing soft tissue infection by external manifestations [4, 18]. Severe maceration against the background of oedema of the trunk and limbs, often with non-compliance with the rules of personal hygiene, is sometimes complicated by fungal infections, as well as superficial necrosis of the skin. These changes, as a rule, occur in obese patients and are localized on the scrotum, perineum and inguinal folds, which is why it is necessary to carry out a differential diagnosis with Fournier's gangrene. As with most of the other sufferings described above, the study of anamnesis (duration of the disease, previous skin diseases), laboratory data and, if necessary, dynamic observation make it possible to exclude necrotizing infection in such patients.

The similarity with necrotizing soft tissue infection in the clinical picture of other infectious and non-infectious diseases and complications is due to the same immediate causes of the appearance of certain external symptoms, such as ischemia and necrosis of deeper tissues, venous thrombosis in the focus of inflammation, toxic damage to capillaries and nerves, inflammation of regional lymphatic vessels, hair follicles, etc.

In all groups of clinical observations, complex treatment of necrotizing soft tissue infection was carried out according to a single scheme consisting of active surgical treatment of foci of infection and multicomponent intensive care.

In the course of surgery, the nature of the lesion of soft tissue structures by the infectious process was visually determined. All operated patients had soft tissue oedema. Swelling and necrosis of fascia, except in cases of necrotizing fasciitis, was often found in necrotic myositis in 11 (78.6%) patients, while this symptom was not characteristic of necrotic cellulite. Discharge of dirty grey or black colour was noted in most cases of necrotizing fasciitis 71 (85.5%), while exudate of the colour of "meat slops" was more characteristic of myositis. At the same time, with necrotic cellulitis, there was often only a change in the colour and consistency of adipose tissue with sequestration of areas of various sizes and scanty turbid discharge.

All patients underwent radical surgical treatment with a focus on surgical infection. Surgical intervention was performed immediately, or, with unstable hemodynamics, after a brief intensive anti-shock preoperative preparation in the intensive care unit or directly on the operating table.

The operations were performed exclusively under anaesthesia. Linear incisions were made over the entire area of the lesion, and necrectomy was within visually healthy tissues. By all means, they performed a revision of muscle masses, individual muscles, as well as adjacent intermuscular, paravasal and perineural tissue. Radical necrectomy was not performed only in the immediate vicinity of large vessels (popliteal, inguinal, axillary regions, retroperitoneal space and neck). In the case of total lesions of all soft tissue structures of the limbs, in 12 (11.1%) cases, they were amputated within healthy tissues without applying a tourniquet and suturing the stumps. The operation was completed by applying gauze dressings with water-soluble ointments. In the postoperative period, local treatment of wounds was carried out, making dressings with water-soluble ointments, if necessary, staged necrectomy.

Multicomponent intensive care, starting from the moment of admission, included infusion therapy with correction of water-electrolyte balance, systemic antibiotic therapy, and nutritional and immune therapy with mandatory glycemic control.

In order to reduce the massive loss of proteins, water and electrolytes, as well as to prevent secondary infection, to reduce the duration of treatment, the wound surface was closed as early as possible using autodermaplasty with a split skin flap, combined plastics, plastic surgery with local tissues, dermotension. The mortality rate in our observations was 30 people (27.8%).

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CONCLUSION

The bacteriological examination is an informative method for assessing the microbial landscape and guidelines for the selection of targeted antibiotic therapy. The analysis did not reveal the dependence of the clinical picture of necrotizing soft tissue infection on the isolated pathogen.

The differential diagnosis of necrotizing soft tissue infection should be carried out with a number of infectious and non-infectious lesions. If there is still a suspicion of a necrotizing infection, surgical revision of all layers of soft tissues is indicated.

Complex surgical treatment of necrotizing soft tissue infection should be started immediately after the diagnosis is established according to the uniform principles of active surgical treatment, without waiting for the identification of the pathogen and obtaining the results of other objective research methods.

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7328

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