APPLICATION OF PHOTODYNAMIC THERAPY IN COMPLEX TREATMENT OF PURULENT DISEASES OF THE HAND

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Abstract

For many years, the treatment of purulent diseases of the hand has stayed relevant. Despite the progress in modern medicine, this pathology retains its prevalence and, most importantly, is often found in patients of the working age, which determines the socio-economic importance of the search for new approaches to the treatment of purulent diseases of this localization. In the purulent surgery department of State Clinical hospital № 4, a study and treatment of two groups of patients were carried out: patients with phlegmons and felons of the hand with open management of postoperative wounds using traditional treatment methods (antibiotic therapy, immobilization, dressings with antiseptic solutions and ointments, the use of wound enzymes) and with the use of photodynamic therapy (PDT) in the postoperative period. PDT was performed on the second or third day after opening the phlegmon or felon using an ATKUS-2 semiconductor laser (AO "Poluprovodnikovye pribory", Russia) with an output power of 1 to 2 W, an operating wavelength of 660 ± 0.03 nm and an energy density between 20 and 25 J/cm^2 after application of the photosensitizer based on chlorin e_6 to the treated wound area. The article describes the technique of PDT in patients with purulent diseases of the hand. It was found that it is optimal to perform PDT as early as possible after the operation period, but not earlier than on the second day after the operation, because earlier dressing is especially painful in the absence of sutures and can lead to bleeding from a postoperative wound when the dressing is removed. The effectiveness of treatment in the studied groups was evaluated: the terms of inpatient healing in the groups were compared; the dynamics of the course of the wound process was analyzed. When comparing the results of the two groups, a significant acceleration in the healing of the postoperative wounds was noted in patients for whom PDT was used – 5 days (1.4 times) faster compared to treatment according to the generally accepted technique. The early appearance of granulations and the antibacterial effect of this procedure are noted, which significantly improves the treatment outcome for this pathology. This makes the use of PDT relevant and appropriate in the complex treatment of purulent diseases of the hand

Keywords: photodynamic therapy, purulent diseases of the hand, drainage system, photosensitizer, necroectomy.

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ПРИМЕНЕНИЕ ФОТОДИНАМИЧЕСКОЙ ТЕРАПИИ В КОМПЛЕКСНОМ ЛЕЧЕНИИ ГНОЙНЫХ ЗАБОЛЕВАНИЙ КИСТИ

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Резюме

Многие годы не теряют актуальности вопросы лечения гнойных заболеваний кисти. Несмотря на прогресс в современной медицине, данная патология сохраняет свою распространенность и, что наиболее важно, часто встречается у пациентов трудоспособного возраста, что обуславливает социально-экономическую важность поиска новых подходов к лечению гнойных заболеваний данной локализации. На базе отделения гнойной хирургии ГБУЗ ГКБ № 4 проведено исследование и лечение двух групп больных: пациентов

с флегмонами и панарициями кисти при открытом ведении послеоперационных ран при применении традиционных методик лечения (антибактериальная терапия, иммобилизация, повязки с антисептическими растворами и мазями, применение раневых ферментов) и с применением в послеоперационном периоде фотодинамической терапии (ФДТ). ФДТ выполняли на вторые-третьи сутки после вскрытия флегмоны или панариция с использованием полупроводникового лазерного аппарата «АТКУС-2» (АО «Полупроводниковые приборы», Россия) с выходной мощностью от 1 до 2 Вт, рабочей длиной волны 660±0,03 нм и плотностью энергии от 20 до 25 Дж/см^2 после аппликации на обрабатываемую раневую область фотосенсибилизатора на основе хлорина e_6.
В статье описана методика проведения ФДТ у пациентов с гнойными заболеваниями кисти. Установлено, что оптимально проводить ФДТ в максимально ранние сроки после операционного периода, но не ранее, чем на вторые сутки после операции, так как перевязка в более ранние сроки особенно болезненна в условиях отсутствия швов и может привести к кровотечению из послеоперационной раны при удалении повязки. Проведена оценка эффективности лечения в исследуемых группах: выполнены сравнение сроков стационарного заживления в группах, проведен анализ динамики течения раневого процесса. При сравнении результатов терапии отмечено достоверное ускорение в 1,4 раза (на 5 суток) заживления послеоперационных ран у пациентов, у которых применялась ФДТ, по сравнению с лечением по общепринятой методике. Отмечено раннее появление грануляций и антибактериальный эффект ФДТ, что существенно улучшает результат лечения данной патологии. Это делает применение ФДТ актуальным и целесообразным в комплексном лечении гнойных заболеваний кисти.

Ключевые слова: фотодинамическая терапия, гнойные заболевания кисти, дренажно-промывная система, фотосенсибилизатор, некрэктомия.

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Introduction

The problem of treating panaritium and hand phlegmons remains complex and relevant, despite the progress achieved by modern medical science. Among the primary patients who go to the surgeon with purulent diseases, patients with panaricia and phlegmon of the hand make up from 15% to 31% [1], 50% to 85.5% of them being people of working age. It is noted that men develop this disease more often than women [2]. Temporary disability caused by purulent diseases of fingers and hands entails economic losses which are many times higher than those related with purulent processes of other localizations.

According to the literature, 17-60% of patients with bone panaritium undergo phalange amputation. Up to 48% of minor hand injuries are complicated by suppuration, which makes microtrauma one of the leading factors in the development of a severe purulent process on the fingers and hand [1, 2].

Very often, pain in purulent inflammatory pathology of the hand is felt constantly, which leads to a serious deterioration of the patients' quality of life. Due to the violation of the function of the hand and the peculiarities of the course of the pathological process, purulent diseases of the hand result in a sharp decline in the effectiveness and quality of professional activity [3, 4].

In the surgical treatment of purulent pathology of fingers and hands, the method of choice is the one developed and implemented in the 1990s by the Department of General Surgery of the Pediatric Department of Russian National Research Medical University (under the supervision of Prof. A. P. Chadaev), the main principles of which are optimal access, adequate necrectomy and installation of a drainage and irrigation system (DIS) in the wound, with the imposition of primary stitches on the skin at the stage of surgery completion. However, in the case of extensive injuries to the hand, it is often not possible to fully close the wound defect, so there is a need for open wound management. In addition, there are a number of medical contraindications to applying DIS and maintaining a wound under primary sutures, such as bite wounds and crushed wounds [1-5]. Open management of hand wounds leads to a higher number of hospital bed days. At the same time, the risk of secondary infection increases, and there is a need for frequent dressings, which in the absence of stitches are very painful. Thus, it is necessary to find more new effective methods of treating wounds in the early postoperative period.

Photodynamic therapy (PDT), widely used worldwide for the treatment of purulent diseases, is one of the promising methods of treatment of purulent wounds of various localities [6-9].

PDT is a method of treating oncological diseases, as well as certain skin diseases (psoriasis, ichthyosis, pustular diseases, etc.) or infectious diseases, inflammatory diseases of the mucous membranes (including chronic periodontitis), based on the use of photosensitizers and laser radiation of a certain wavelength [10-16]. At the beginning of the XX century, scientists G. Raab and G. Tappeiner found that some dyes, which are harmless or slightly poisonous to infusoria in the dark, kill them very quickly in the light. This phenomenon was called the

photodynamic effect. The effect is observed only in the presence of oxygen in the environment [17, 18].

Hardly any information is found in domestic and foreign literature concerning the use of PDT in the treatment of purulent diseases of the hand.

The purpose of this work was to study the effectiveness of PDT-based treatment and traditional therapy methods for patients with purulent diseases of the hand in open management of postoperative wounds.

Materials and methods

The results of treatment of 86 patients with purulent diseases of the fingers and hands admitted to the the Department of purulent surgery of the City Clinical Hospital No. 4 of Moscow for the period from December 2017 to December 2018 were analysed. The age of patients ranged from 19 to 64 years, 78 (90.7%) of them being of employable age. Deep forms of panaritium occurred in 51 (59.3%) patients, phlegmons of the hand in 31 (36.0%), phlegmons of the hand with a transition to the forearm, in 4 (4.7%). The hand that most often (in 90% of the patients) was affected was the right hand. The most common concomitant pathologies in the patients were type II diabetes mellitus, in 10 (20%) cases, cardiovascular diseases, in 8 (16%), multiple drug use, 3 (6%), systemic lupus erythematosus, 1 patient. In terms of the causal factor, non-industrial injuries prevailed (45%), followed by bitten wounds (30%), industrial injuries (10%), post-injection phlegmons (5%), and wounds of unknown origin (10%).

Depending on the treatment method, the patients were divided into two comparable groups by age and gender, forms of the disease, and the duration of the disease before admission to the hospital. The main group consisted of 43 patients who underwent PDT after the opening of the suppurative focus; the control group consisted of 43 patients who were treated according to the generally accepted method.

All patients had a standard examination before the study, which included an assessment of clinical and laboratory data, radiography of the damaged hand, and ultrasound examination of the soft tissues of the hand. According to the indications, tetanus vaccination was administered (tetanus toxoid and tetanus serum according to the scheme), and wound components underwent bacteriological and histological examination at various times of the treatment.

At the first stage, patients in both groups were treated surgically. Purulent focus dissection, necrectomy and drainage were performed under local conductor anesthesia corresponding to the level of the infectious lesion.

Patients of the control group were subsequently subject to the standard combined treatment, which included antibacterial therapy, analgesics, daily dressings with antiseptics, physiotherapy (UHF, ultraviolet irradiation, magnetotherapy).

Рис. 1. Проведение сеанса фотодинамической терапии гнойной раны кисти
Fig. 1. Conducting a session of photodynamic therapy of the purulent wound of the hand

PDT was administered to the main group of patients in the postoperative period. A PDT session was administered as early as possible: on the second (less often on the third) day after the opening of the suppurative focus, in the context of open wound management. In the earlier postoperative period, the appointment of a PDT session is not recommended, since there is a high risk of bleeding from the wound upon the removal of the dressing; in addition, wound dressing in the first day is quite painful. The number of PDT courses varied from 1 to 2, depending on the area of damage to the hand and the dynamics of wounds cleaning.

A PDT session consisted of the following stages. A bandage with a photosensitizer based on e_6 chlorine (PS) was applied to the wound for 20 to 30 minutes. The amount of PS was calculated based on the dosage of 1 ml per 3-5 cm^2 of the treated surface. Then the wound was washed with saline solution to remove the residual PS. Activation of PS was performed immediately after the completion of the drug exposure and the removal of PS residues by light exposure to the wound surface with laser radiation with an output power of 1-2 W, at a wavelength of 660±0.03 nm, and energy density from 20 to 25 J/cm^2 (Fig. 1). The treatment was performed with "ATKUS-2" device (AO "Poluprovodnikovyie Pribory", Russia). The irradiation time for external light supply provided

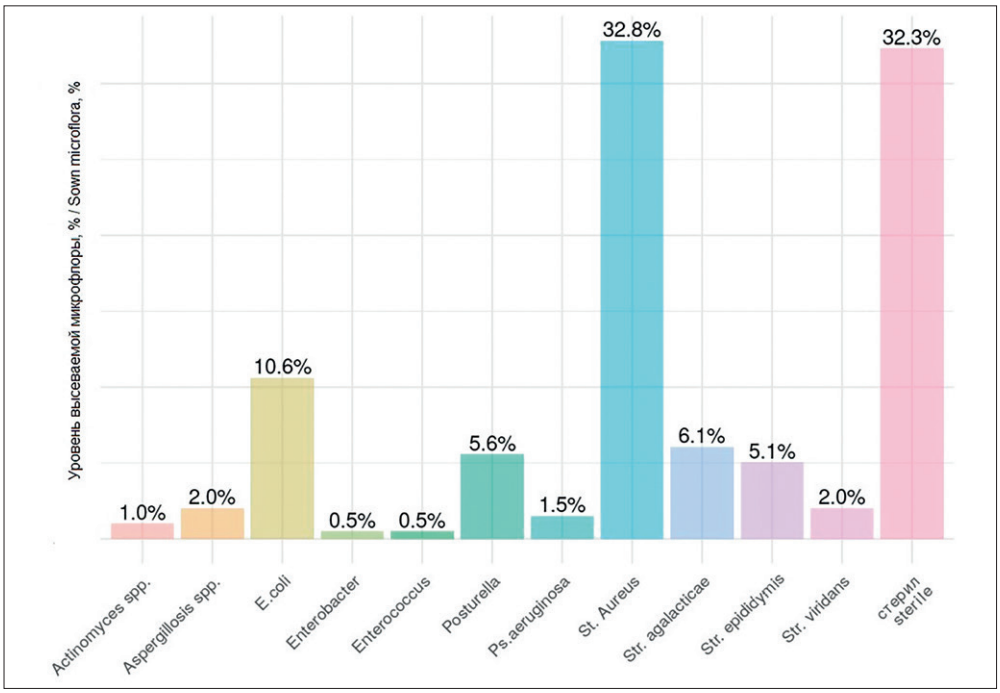

Рис. 2. Микрофлора раны при первичном посеве
Fig. 2. Wound microflora after the initial seeding

with optic fiber guides with a polished end was determined by the formula [19, 20]:

$$T\,(\text{s}) = E_s\,(\text{J/cm}^2) \,/\, P_s\,(\text{W/cm}^2),$$

where T is the irradiation time, E_s – is the required light dose (energy density), and P_s is the power density.

The cases administered PDT were observed to have a wound cleansing process, a reduction of microcirculatory disorders, and a reinforcement of previously suppressed sequential reparative processes: macrophage reaction, collagen synthesis, scarring and epithelization. Maturing granulation tissue with vertical vessels, fibroblasts, and pronounced fibrillogenesis was determined on days 6 -7. To assess the bacterial landscape of the wound, the wound contents were inoculated in a sterile test tube with a nutrient medium before and after the PDT session. The biological material was collected with a sterile cotton swab and then transferred to nutrient media in Petri dishes. Histological examination of the wound edge tissues was performed on days 2, 3 and 6 after PDT sessions in order to assess the dynamics of inflammation and determine the timing of the granulation tissue emergence.

Statistical processing of the obtained data was performed by variation statistics with the definition of Student test with 2017 Microsoft Office (Word, Excel). The mean values were compared, including the determination of measurement error and the reliability of differences in the length of hospital stay and time of wound healing between the study groups. Differences were assessed as significant at $p<0.05$.

Results

The duration of inpatient treatment of patients with purulent wounds of the hand depended on the origin of the wound, the depth of the lesion, and the time of hospitalization from the moment of the injury. In the traditional therapy group, the average duration of inpatient treatment was 13±1 days, complete wound healing was observed 17±1 days after the surgery; 30% of patients required repeated necrectomy, lavage of the purulent necrotic focus. In patients who underwent PDT in the postoperative period, the duration of inpatient treatment was 7±1 days ($p = 0.03$), and complete wound healing was observed after 12 days.

The primary bacterial seeding of wound discharge performed during surgical treatment revealed Staphylococcus aureus in 1/3 of the patients (32.8%) which was confirmed by the results of laboratory studies and coincides with earlier data from other authors [1, 2, 21]. The results of inoculations with no growth of microorganisms may be due to anaerobic microflora, which is not possible to plate with conventional methods of sample collection for inoculation.

The microbiological study of intraoperative inoculations before PDT produced the following data: *Staphylococcus aureus*: 32,8%; *Streptococcus agalacticae*: 6,1%; *Streptococcus epididymis*: 5,1%; *Streptococcus viridans*: 2,0%; *Esherichia Coli*: 10,6%; *Enterobacter*: 0,5%; *Enterococcus*: 0,5%; *Posturela*: 5,6%; no growth: 32,3% (Fig. 2).

In part of the inoculations, the associated microflora was found to be *Candida albicans* (10.4%).

The antimicrobial effect of PDT was revealed by bacteriological research: in the inoculations produced after the completion of PDT courses, the growth of microorganisms detected during primary bacteriological studies was absent in all observations.

According to the clinical findings and the histological data, on the 2nd and 3rd days after PDT, the wound became cleared of purulent necrotic masses, and on the 5th day, granulation tissue appeared. Visual examination found that the amount of discharge from the wound in patients after PDT significantly decreased, the hyperemia of the wound edges and edema decreased by day 2 after the course of PDT, the quantity of fibrinous overlay was significantly lower than in patients of the control group, and the use of wound enzymes was no longer required.

After PDT, an analgesic effect was observed in all patients, which was expressed in a significant decrease in pain syndrome when subjectively evaluated on the standard pain scale. During the second dressing in both groups, the pain syndrome was 8-9 points, and immediately after the PDT session, the indicator decreased to 5-6 points and then progressively decreased to 1 point as assessed during dressing on the 5th day. In patients who did not undergo PDT, the pain syndrome on the 5th day remained at the level of 4-5 points.

The advantages of using this technique in the treatment of purulent wounds of the hand can also include the absence of additional destructive tissue lesions in the wound, the possibility of affecting deeply located tissues.

After PDT, amputation of the affected phalanges or repeated necrectomy were not required. During PDT, there was almost no bleeding during subsequent dressings.

No allergic reactions to the introduction of PS were observed. During the PDT session, the patient experienced no pain syndrome. No hyperthermia and no local inflammatory reaction were observed during the PDT session and after it.

As an example of the effective use of PDT in the treatment of hand phlegmon, we present the following clinical observation.

Patient K., 42 years old.

He was hospitalized in the Department of purulent surgery of the City Clinical Hospital No. 4 from December 5 to December 11, 2017 with a diagnosis of phlegmon of the back of the left hand.

Complaints on admission: pain in the left hand, hyperthermia.

According to the patient, 3 days before admission, he injured his left hand in a fight, and a day later he noted signs of inflammation. He was hospitalized in a purulent surgery unit. On admission: hyperthermia 38.9°C, state of moderate severity.

The clinical findings at admission (Fig. 3a): the back of the left hand is swollen, hyperemic, in the projection of the third intermetacarpal space, a wound of 2.0x4.0 cm in size is observed, with pronounced perifocal edema and hyperemia. Palpation of the back of the hand discovered a sharp pain, and a fluctuation was determined. Movements in the third and fourth metacarpophalangeal joints are limited and painful. Regional lymph nodes are not enlarged.

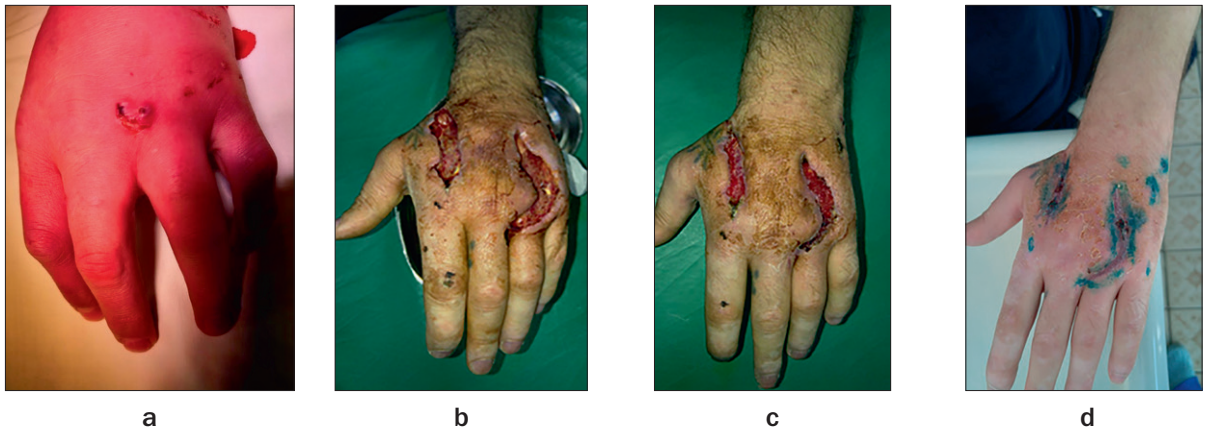

Рис. 3. Клиническая картина флегмоны левой кисти:
a – до операции;
b – после некрэктомии и вскрытия флегмоны;
c – через 2-е сут после проведения ФДТ;
d – на 12-е сутки после операции (амбулаторный этап лечения)

Fig. 3. The clinical picture of the phlegmon of the left hand:
a – before the operation;
b – after the necrectomy and phlegmon autopsy;
c – 2 days after the PDT;
d – on the 12th day after the operation (outpatient treatment)

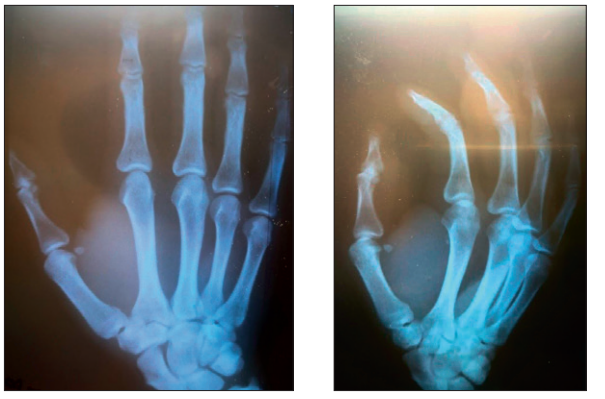

Рис. 4. Рентгенограмма при поступлении (а и б – разные проекции)
Fig. 4. X-ray upon admission (a and б – different projections)

The x-ray of the hand dated 05.12.2017 (Fig. 4) shows no destructive or traumatic changes of the bone.

The ultrasound of the soft tissues of the left hand performed at admission showed an infiltration of tissues, with many accumulations of liquid.

The clinical and laboratory data were as follows: leukocytosis: up to 25,000 g/l, RBC: 4.04 million, hemoglobin: 136 g/l, hematocrit-38%, left shift in neutrophil band cells, ESR: 35 mm/h, blood glucose level: 5.2 mmol/l. On the day of admission, the patient underwent surgery, including incisions and necrectomy. However, in the postoperative period, inflammatory phenomena persisted, as well as purulent discharge from the wound, edema of the back of the hand, hyperthermia up to 38.3 C° (Fig. 3b).

Inoculations from the wounds found *Staphylococcus aureus* and *Escherichia coli* sensitive to the 3rd and 4th generation cephalosporins.

On the 2nd day after the operation (07.12.17), the patient was prescribed PDT with PS based on e_6 chlorine with an exposure of 15 min. The wound was irradiated with ATKUS-2 device for 4.5 minutes at a laser power of 2 W, a wavelength of 660±0.03 nm, and an energy density of 25 J/cm^2. During the session, the patient noted a tingling sensation in the area of the wound. After the session, the patient noted a decrease in pain, and the visual inspection after the completion of the PDT session showed that the amount of discharge from the wound decreased.

In the tissue sample taken from the wound edge before PDT, there are foci of necrosis and tissue edema (Fig. 3b). On the first day after the PDT session, a decrease in inflammatory phenomena was noted at histological examination; on the second day, fresh granulations were visualized in the wound, and no purulent discharge was detected (Fig. 3c), which was also confirmed by the results of inoculation of the wound content.

In the Department, the patient received analgesic therapy and daily aseptic dressings. Physical therapy was not administered.

The patient's condition at discharge was satisfactory. The postoperative wound was without signs of inflammation, the bottom of the wound was covered with red coarse granulations, there was no discharge, the wound

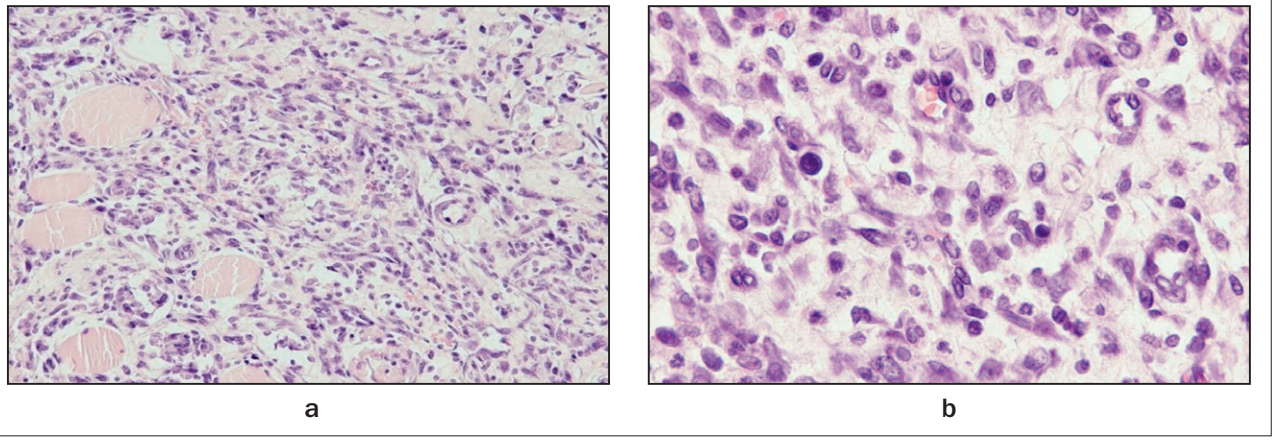

Рис. 5. Биоптат ткани, взятой из края раны пациента К. (окраска гематоксилином и эозином):
а – до курса ФДТ: фрагменты некротически измененных мышечных волокон и фибринозно-лейкоцитарного слоя; отек, полнокровие сосудов глубоких отделов раны, островки формирующейся грануляционной ткани (увеличение х120);
b – на вторые сутки после курса ФДТ: макрофаги и отдельные неориентированные фибробласты вблизи сосудистых элементов (увеличение х200)
Fig. 5. Tissue biopsy taken from the edge of the wound of patient K. (stained with hematoxylin and eosin):
a – before the PDT course: fragments of necrotic altered muscle fibers and fibrinous-leukocyte layer; edema, vascular congestion in the deep sections of the wound, islets of forming granular tissue (magnification x120);
b – on the second day after the PDT course: macrophages and individual non-oriented fibroblasts near vascular elements (magnification x200)

became completely clean. The edges of the wound are without inflammation, with signs of epithelization. The patient was discharged for outpatient treatment on the 5th day after the surgery. Plastic surgery to close the wound defects was not required, as the wounds healed (Fig. 3d).

Conclusion

The developed method of the use of PDT in the complex treatment of purulent diseases of the hand with open wound management has a positive effect on the course of the wound healing process, helps to accelerate purification and reduce the healing time of wounds by 1.4 times, reduces the duration of inpatient treatment by 1.8 times compared to the traditional method, and contributes to good functional results. The new method of PDT use improves the immediate and long-term results of patients treatment, which is of great socio-economic significance.

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