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Сибирская язва в Российской Федерации в 2023 году: два случая из практики

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АННОТАЦИЯ

Сибирская язва представляет серьёзную проблему для здравоохранения и сельского хозяйства в России. Даже начиная с 1900 года на территории России насчитывается более 70 тысяч вспышек инфекции среди людей и животных. Адекватные ветеринарные мероприятия привели в настоящее время к резкому снижению уровня заболеваемости скота как основного источника её возбудителя. Одновременно с этим снизилась заболеваемость людей, чему в немалой степени способствует плановая иммунизация населения, подверженного профессиональному риску инфицирования. Однако, несмотря на проводимые меры, эпизоотии и эпидемические очаги сибирской язвы регистрируются ежегодно. Как следствие, достаточно часто возникают и заболевания сибирской язвой у жителей этих областей.

В работе рассматриваются особенности современного течения кожной формы сибирской язвы на основе анализа терапии больных из двух очагов сибиреязвенной инфекции в Воронежской области в августе–октябре 2023 года. Уникальность данного наблюдения заключается в возможности представить эволюцию кожных изменений при карбункулезной разновидности кожной формы сибирской язвы от ранних этапов развития язвенного процесса до практически полного выздоровления.

Ключевые слова: сибирская язва; история изучения сибирской язвы; происхождение названия болезни; классификация; варианты течения кожной формы сибирской язвы; клинический случай.

Как цитировать

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Malignant anthrax in Russian Federation in 2023: two case reports

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ABSTRACT

Malignant anthrax is a serious health and agricultural problem in Russia. Since 1900, >70,000 outbreaks of infection among people and animals have been reported in Russia. Adequate veterinary measures have led to a decrease in the level of morbidity in livestock, which is the main causative agent. Moreover, the incidence of human illness has decreased, which is greatly facilitated by routine immunization of the population exposed to occupational risk of infection. However, despite the measures taken, epizootics and epidemic foci of anthrax are registered annually. As a result, anthrax occur often among residents of these areas.

This study discusses the modern course of the cutaneous form of anthrax, which was analyzed during the treatment of patients from two foci of anthrax infection in the Voronezh region in August–October 2023. The novelty of this observation lies in the opportunity to present to readers the evolution of skin changes in the carbunculus variety of cutaneous anthrax from the early stages of ulcerative process development to almost complete recovery.

Keywords: anthrax; history of anthrax study; origin of the name of the disease; classification; variants of the course of the cutaneous form of anthrax; case report.

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INTRODUCTION

Anthrax has been, is, and in the foreseeable future will be a serious problem for healthcare and agriculture in Russia. Since 1900, more than 70 thousand outbreaks of infection among humans and animals have been registered in Russia [1]. Adequate veterinary measures have now led to a sharp decrease in the morbidity level in livestock, which is the main source of its causative agent. Simultaneously, the incidence among humans decreased, which was also facilitated by the introduction of sanitary and epidemiological surveillance at enterprises processing raw animal materials and routine immunization of the population exposed to occupational infection [1]. Despite the measures taken, epizootics and epidemic foci of anthrax are registered annually [2]. Consequently, anthrax is registered quite often among residents of these areas.

In 2022, two anthrax outbreaks were registered in the Russian Federation in two areas of the North Caucasus Federal District, namely, the Republic of Dagestan and the Stavropol Territory. In the Republic of Dagestan, at the end of March, a case of cutaneous anthrax was detected in one local resident. The infection occurred during forced slaughter of a calf (cattle), which was performed without a veterinary examination.

An epidemiological investigation showed that livestock grazing was performed on pastures common to these villages, where the soil source of infection was an old anthrax ground disposal was probably located. Because of laboratory studies conducted at the Dagestan Anti-Plague Station of Rospotrebnadzor, a culture of *Bacillus anthracis* was isolated from a clinical sample of a patient (crust of the affected skin). Using the passive hemagglutination reaction, antianthrax antibodies were detected in the patient's blood serum at a titer of 1:200. Five cultures were isolated from material from a slaughtered calf (raw meat, dried meat, skin, hoof, and excrement). At the reference center for monitoring the causative agent of anthrax (Stavropol Anti-Plague Institute of Rospotrebnadzor), specific antibodies were detected in the patient's blood serum using the indirect fluorescent antibody (IFA) method. A positive result was obtained from an allergy diagnostic test (allergotest) with anthrax allergen in vitro using flow cytometry, and the final identification of *B. anthracis* strains was performed.

In June 2022, in the Stavropol Territory, after dressing beef, a resident of Rozhdestvenskaya village fell ill with anthrax. The forced slaughter of a sick bull, not vaccinated against anthrax, was performed on her personal farm without an antemortem veterinary inspection.

The clinical diagnosis of cutaneous anthrax in the patient was established based on a characteristic clinical presentation and epidemiological history, confirmed by the results of laboratory tests conducted at the Stavropol Anti-Plague Institute of Rospotrebnadzor, namely, detection of *B. anthracis* DNA in the samples of the affected skin,

specific antibodies in a blood serum sample through IFA, and a positive in vitro allergy test using flow cytometry.

In 2022, vaccination against anthrax was performed in 66 constituent entities of the Russian Federation; 7,929 people (7,787 adults, 142 children) were vaccinated for the first time, which accounted for 97.3% of the shaped plan (8,131 people). In 71 regions, 32,101 people (31,801 adults, 300 children) were covered by revaccination. The revaccination plan (35,358 people) against anthrax was completed in 90.8% [3].

In 2022, a tense epizootiological and epidemiological situation regarding anthrax was recorded in six neighboring countries. In Azerbaijan, three foci of infection were noted in two regions, with the disease affecting nine heads of cattle and three people. In Georgia, in August 2022, two heads of cattle died from anthrax. In 2022, at least three cases of farm animal (FA) anthrax and nine cases of human infection were recorded in four regions of Kazakhstan. In Kyrgyzstan, two anthrax outbreaks were registered in two regions with infection of one head of cattle and six people, and one presumptive outbreak of infection was detected with suspected infection of one head of cattle and three people. Two cases of livestock anthrax infection have been reported in Tajikistan. In Uzbekistan, anthrax was confirmed in a resident of the Syrdarya region. On the Ukrainian territory in the Kyiv region, five heads of small cattle (goats) died from anthrax [4].

In 2022, anthrax in people in non-CIS countries was recorded mainly in Africa and Asia. Human infections are mainly associated with eating the meat of sick and/or dead FA, contact with infected animals, and livestock products. Sporadic cases of infection in humans have also been detected in some countries in Europe, North America, and South America [3]. In the USA (Colorado), in July, two cases of human infection were confirmed because of dressing the carcasses of dead cattle [5].

As of August 31, 2023, cases (outbreaks) have been registered since the beginning of the year in five constituent entities of the Russian Federation: the Chuvash Republic, Tambov, Ryazan, and Voronezh regions among cattle and Republic of Tyva in horses) [6]. There are no grounds to believe that these are the last cases this year.

Anthrax has been known to clinicians since time immemorial; however, the variety of infection mechanisms and transmission routes, ambiguous interpretation of the main pathogenetic aspects of the disease, and variable clinical manifestations are reflected in the simultaneous existence of various classifications, each of which has both ardent adherents and opponents. For fairness, most disputes are purely theoretical because anthrax is a rare disease, and the number of real experts who have the right to express their opinion is significantly less than the number of disputants.

In general, the study of anthrax and its origin are unique in many ways. Anthrax was widely known in ancient Rus and Russia in the 18th century. It was often confused with other epizootic diseases called "cattle pestilence," "cow death," and

"cattle dieoff." The name "anthrax" appeared in Russia only in the 1780s, although the clinical symptoms of this disease were described by Russian doctors much earlier [7]. The first researchers to mention anthrax in Russia were doctors from the Kolyvano-Voznesensk factories, Abram Eshke and Nikita Nozhevshchikov. A. Eshke submitted an essay to the Medical Office titled "Brief news about Kolyvan and surrounding areas, about the diseases raging there among people and livestock, and finally about herbs growing and minerals in some places in Siberia." It describes a disease that affects livestock and people and whose clinical presentation is similar to that now defined as anthrax.

Further study of anthrax was continued by N. Nozhevshchikov, who succeeded A. Eshke as a doctor in Kolyvan-Voznesensk factories in 1758. In a report sent to St. Petersburg in 1763, he wrote: "At all the factories here and in their departments, the prescribed pestilence did not happen to people, but it happens every year in Barnaul, Kolyvan in the mines and factory departments in settlements and villages, mostly in the month of July and the first half of August, while the great heat continues, in people of both genders there is a kind of boil, similar to pestilence boils or carbuncles; here this disease is called an ulcer and a spot, and a wind-borne disease in the villages; along the Irtysh line, that is, in Yamyshevskaya, Simipolodskaya, Ust-Kamenogorsk, Biysk and other fortresses, this kind of boils is called an unknown disease"; "...back in 1715, the soldiers and Cossacks sent to build the Yamyshevskaya fortress were infected, therefore we can conclude that the aforementioned disease has been circulating in Siberia for a long time" [8]. The clinical symptoms of the disease described by N. Nozhevshchikov enabled us to believe that this was a cutaneous form of anthrax.

In 1786, the senate proposed to the medical board to send a special commission to the Chelyabinsk district to study the disease, which was causing great damage to people and livestock. The board chose the headquarters physician Stepan Semyonovich Andreevsky (1760–1818) for this purpose. From 1786 to 1789, he studied in detail the disease that was little known at that time. He collected several clinical cases, and performed a pathological autopsy. To study in detail the disease course, he conducted an infection experiment on himself. The result of his work was two reports "On Anthrax," sent to the Medical Board in 1778 and 1789. It was S.S. Andreevsky who was the first to call the disease "anthrax," considering not the place of origin of the disease but the place where he studied it [9]. In fairness, the city of Troitsk, where he performed medical activities, is located in the Chelyabinsk region, in the Southern Urals, and certainly not in Siberia.

Somewhat later, in 1790, the headquarters physician Ivan Peterson published a book in Tobolsk entitled "A Brief Description of the Disease Called in Siberia Wind or Air Ulcer," and in 1795, he sent this book to the medical board. Having approved the book, the board indicated that "this disease

was already discussed in advance by this board," probably referring to the reports of S.S. Andreevsky.

In 1792, a description of anthrax was made by the headquarters physician Mikhailo Gamaleya, who published the essay "On Anthrax and its Folk Treatment" in Perm (Fig. 1).

In 1796, based on the reports of S.S. Andreevsky, as well as the works of A. Eshke, N. Nozhevshchikov, I. Peterson, and M. Gamaleya, the medical board published a "Brief description of anthrax, containing preventive and healing means, for the benefit of the common people, selected from thorough notes and experiences sent to the Medical Board" (Fig. 2). This is a popular scientific work for several readers; therefore, the main attention was paid to information about the preventive and "healing" remedies recommended for this disease at that time. The essay indicated that in the fight against anthrax, prevention is much more important than therapy: "To achieve this goal, there are two ways of means, namely protecting and providing healing to those infected with anthrax; but as we know, it is incomparably easier to prevent the causes of anthrax than to heal those already infected with it" [7].

For decades, there was (and still is) the opinion that anthrax can occur in cutaneous, pulmonary, gastrointestinal, septic, and some other (e.g., oropharyngeal) forms (ICD-10), which is determined by the mode of infection, place of pathogen permeation, etc. [10]. However, even earlier, some authors considered the identification of such a variety of forms to be unjustified. Professor N.K. Rosenberg (1938) considered it appropriate to recognize only two main forms of anthrax, cutaneous (most common) and septic (rarer) [11]. P.N. Burgasov and G.I. Rozhkov declaimed actively against the separation of the intestinal and pulmonary forms of anthrax [12]. This situation is extremely reminiscent of a dispute about the existence of an independent form of plague such as intestinal plague. The clinical and symptomatological complex and pathoanatomical presentation are most consistent with the division into localized (most often cutaneous) and generalized, or septic and visceral forms of anthrax.

In humans, anthrax most often manifests as an infection of the external integument and is rarely complicated by anthrax sepsis; moreover, a primary generalized infection may develop, manifesting in as a pulmonary or intestinal form. In this case, a certain duality and inconsistency in the formulation obviously arises. It is both a "generalization" and an indication of the process locality ("pulmonary," "intestinal" forms). In recent years, intestinal and pulmonary forms of anthrax are still considered not as independent but as developing hematogenously, i.e., formally secondary (analog is meningococcal meningitis).

Recent research shows that with the so-called intestinal form, the process does not develop according to the seemingly obvious pattern of "enteral infection–intestinal carbuncle–lymphadenitis–generalization" but in the exact opposite way, namely, "infection–lymphadenitis–generalization–intestinal carbuncle," i.e., the pathogen does not move from the

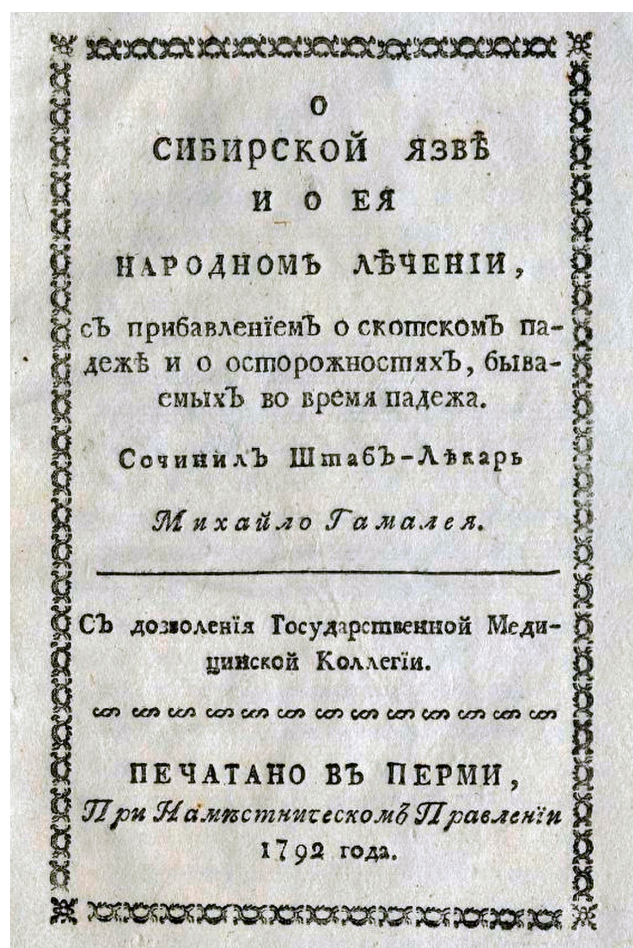


Fig. 1. Title page of Mikhailo Gamaley's essay "On Anthrax..." (1792)

intestine into the bloodstream but from the bloodstream into the intestinal lumen (Fig. 3).

Nowadays, it is advisable to distinguish between only two main forms: localized (cutaneous) and septic (generalized). Simultaneously, there is not some independent, e.g., "intestinal," form of anthrax but "a generalized form of anthrax with predominant damage to the intestines."

Naturally, generalized forms of anthrax can be primary, independent, or secondary and develop from a cutaneous (most often) lesion.

With this approach, there are no problems with determining the place of rare forms of anthrax in the classification, as the oropharyngeal form will be classified as a localized form, and the meningeal form will be classified as a primarily generalized form.

For a general practitioner, this approach is the most acceptable because it explains and eliminates all the "inconsistencies" in the epidemiological and clinical aspects that naturally arise when managing this category of patients.

However, such a seemingly "simple" form of anthrax as cutaneous has an interesting history and ambiguous (in diagnostic, prognostic, therapeutic and other terms) interpretations. In general, the term "anthrax," both in the past and at present, is used by most Russian authors to

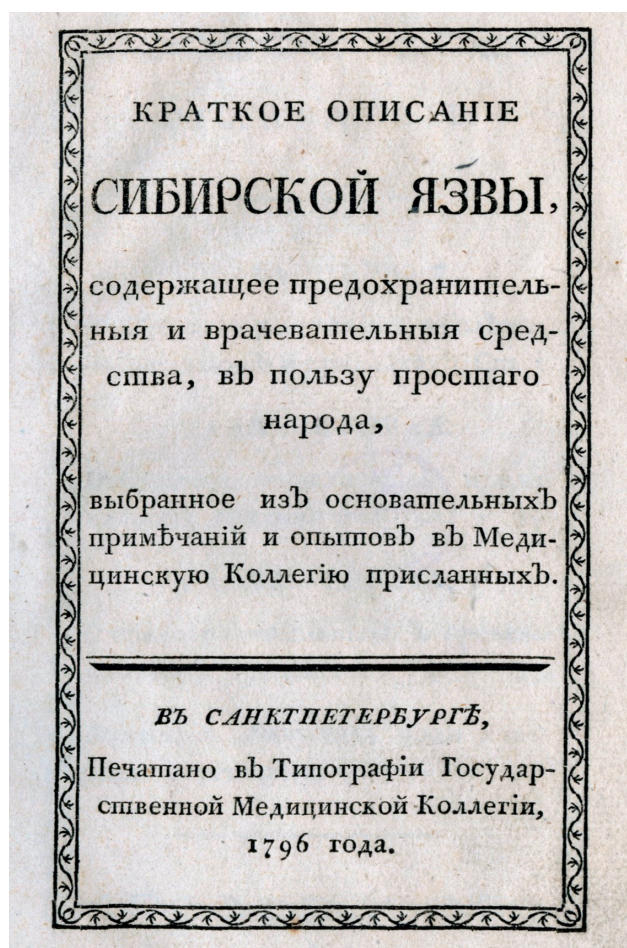


Fig. 2. Title page of the Medical Board publication "A Brief Description of Anthrax..." (1796).

refer specifically to the cutaneous form of anthrax in its most common carbunculus variety. International authors use the term "anthrax" specifically with the type of anthrax carbuncle (from the Greek *ἄνθραξ* — "coal").

Nearly all authors divide the cutaneous form of anthrax, depending on the nature of local phenomena, into several clinical variants, which has been the subject of numerous studies in both Russia and other countries. However, at present, there is neither a firmly established term for this form nor a clear, unambiguous formulation of visible skin changes [13].

The term "pustula maligna," coined by M. Enaux and F. Chaussier [14] in 1785, was initially a clinical designation for a certain form of anthrax, and one of its manifestations was a specific skin lesion.

Gradually, this original meaning of the term "pustula maligna" was forgotten and, since the beginning of the last century, was interpreted only as an unsuccessful designation of skin changes of anthrax origin [15, 16]. However, in its original meaning as a specific clinical form of the disease with its characteristics, this term was used until the midpoint of the twentieth century [17, 18].

Currently, instead of *pustula maligna* as a term denoting anthrax lesions of the skin, the term "anthrax carbuncle" is



Fig. 3. Interstitial carbuncle.

usually used, from which one of the most common types of cutaneous anthrax, the carbunculous form, gets its name. However, similar to the previous term, it has its drawbacks, the main one being that the term “carbuncle” means acute purulent inflammation of a group of hair follicles with sebaceous glands opening in them, resulting in necrosis and purulent melting of surrounding tissues.

To avoid the shortcomings inherent in the terms *pustula maligna* and *anthrax carbuncle*, E.N. Shlyakhov suggested calling skin changes “necrotic ulcers” [19]. However, this designation cannot be considered quite successful because out of the entire mass of signs characteristic of skin lesions in anthrax, only one necrosis appears in this term, which is a consequence of other, very complex pathological phenomena.

At one time, the term “anthrax” was criticized because the formation of a true ulcer represents only one of the stages in the development of skin lesions [20]. A similar evolution was noted with the other term “edema maligna,” which was introduced into medical practice by I. Bourgeois [21] in 1861. Initially, this term, like *pustula maligna*, was only a clinical characteristic of one of the forms of anthrax, which was characterized by the development of edema without the prior occurrence of skin lesions (necrosis). However, shortly after the publication of the work by I. Bourgeois, Fr. Koranyi presented data indicating the inappropriateness of isolating a variety of this cutaneous form of anthrax into a separate, independent form because all cases of anthrax edema, or, as it is sometimes called, malignant edema, are accompanied by necrosis with subsequent transition to a scab and scarring [22]. Thus, according to Fr. Koranyi, this form differed from the previous form only in its onset. M.M. Beloglazov also shared a similar point of view; he believed that there is no separate, edematous form of anthrax, but there is only a quantitative difference in the prevalence of edema, its density, skin color changes, etc., which is determined by the carbuncle location [15]. Despite these objections, most authors still identify anthrax edema as a separate type of cutaneous anthrax [16, 23–26].

In Russia, the first work that provided a brief description of the clinical forms of anthrax and gave their classification

was the dissertation of P. Bogdanov [27], which he published in 1863. The author adhered to the classification of the W.Th.I. Spinoza [28], which received general recognition at that time:

1. Carbunculous fever (febris carbunculosa)
2. Erysipelar form (erysipelas carbunculosum)
3. Pustular form (pustula maligna)
4. True carbunculous form (carbunculus magnus).

Four years later, in 1867, P. Lyubimov published a study that provided the first complete description of the clinical forms of anthrax in humans and is still of practical interest [29]. He analyzed five forms of anthrax, isolated malignant edema into a separate form, as previously described by I. Bourgeois [21], and arranged the clinical forms in order of greatest prevalence:

1. Malignant pustule (pustula maligna)
2. Carbunculous erysipelas (erysipelas carbunculosum)
3. Malignant edema (edema maligna)
4. Malignant carbuncle (carbunculus contagiosus maligna)
5. Carbunculous fever (febris carbunculosa)

P. Lyubimov examined in detail the most common first form of anthrax, a malignant pustule (carbuncle), and emphasized that the carbuncle size is usually very different, from a barely noticeable spot to a silver ruble size and more. The carbuncles also have different localizations. According to the author, carbuncles are not formed only in the scalp. Regarding disease severity and edema size, the patient did not register a proportional relationship between carbuncle size and edema area.

According to the author, carbunculous erysipelas (form 2) is quite rare. Its peculiarity is the development of not a typical carbuncle in the first days of the disease but of a peculiar inflammation of the skin, reminiscent in appearance of erysipelas with numerous blisters filled with light contents. Furthermore, the changes at the site of the vesicles after their opening are not different from the changes at the site of the lesion in malignant pustule (form 1).

Form 3 is characterized by the appearance of edema without obvious warning signs. The swelling increases very quickly, covers a large area, but is rarely dense, even in the center. After 3–4 days, blisters are usually found at the site of edema, which quickly open, and necrosis subsequently develops in their place. This form is usually very severe, often with a lethal outcome, and during recovery, rough scars remain at the site of necrosis.

Form 4 (malignant carbuncle) is distinguished not only by clinical signs but also by the route of infection. Form 4, according to P. Lyubimov, develops when infected through the gastrointestinal or respiratory tract. In this form, simultaneously with the appearance of a carbuncle in any body part, “general phenomena” develop with a lethal outcome, usually after 1–4 days. According to the clinical course, routes of infection, and outcome, form 4 is close to form 5 carbunculous fever (apoplectic anthrax). It is peculiar for its rapid course without carbuncle formation.

If we translate the dissertation and classification of P. Lyubimov into modern (Russian) language, we will obtain the forms of anthrax such as localized (resp. cutaneous — carbunculous, bullous, and edematous) and generalized (intestinal, pulmonary, and septic). As the saying goes, comment is needless for Ecclesiastes said, “What has been will be again, what has been done will be done again; there is nothing new under the sun” (Bible. Book of Ecclesiastes or Preacher).

In this study, we review the characteristics of the modern course of cutaneous anthrax based on an analysis of the treatment of patients from two foci of anthrax infection in the Voronezh region in August–October 2023.

DESCRIPTION OF THE CASES

Case report 1

Patient P., born in 1971, registered and living in the Voronezh region, Paninsky district, received inpatient treatment at the Voronezh City Clinical Hospital of Emergency Medical Care No. 8 (VCHEMC No. 8) from August 18, 2023, to September 29, 2023.

On August 10, 2023, P. performed the slaughter of FA (1.2-year-old heifer) at the homestead. He had three heads of cattle (a cow, a 1.2-year-old heifer, and a 4-month-old bull), 17 pigs, and chickens in the household. The cow was vaccinated against anthrax, whereas the heifer and bull were not. He performed the slaughter because “the heifer was upset.” It was also revealed that a pig died on August 19, 2023 (the cause was not established).

The patient lives at home with his sister and nephew (examined and healthy). He did the slaughter, and his sister helped him (she held the cow by the horns). After slaughter, the meat was taken by resellers (found through an advertisement in the newspaper) and sold without proper veterinary control at one of the markets in Voronezh. The skin and bones of the slaughtered animal were thrown into the rear yard.

Patient P fell ill on August 14, 2023. His temperature rose to 37.7°C–39.4°C, and a spot papule ulcer appeared on the right hand and right shoulder. On August 17, 2023, an ulcer appeared on the left index finger, hand, and forearm, with persistent fever up to 39.8°C, and noted burning sensation in these places. The ulcer on the left forearm was independently treated with chlorhexidine. He first sought medical help at the Paninsky District Hospital on August 17, 2023, was examined by a surgeon and a dermatologist, was diagnosed with allergic dermatitis, and desensitizing therapy was recommended. The next day, August 18, 2023, he returned to the district hospital again because his temperature did not decrease. He noticed an increase in the ulcer size on the left forearm with the formation of a black scab. He was examined by a dermatologist and an infectious disease specialist. The patient was remotely consulted by telephone with the chief

external specialist in infectious diseases of the Voronezh Region Health Department, and cutaneous anthrax was suspected. The patient was referred to Voronezh Medical Center VCHEMC No. 8.

On August 18, 2023, at 4:23 p.m., Patient P. was admitted to the infectious diseases building of VCHEMC No. 8 with signs that did not exclude cutaneous anthrax. He was hospitalized in the anesthesiology and intensive care unit. Biological material was promptly collected for laboratory testing (blood, contents of ulcers, washings from the surface of the ulcer, scab, and blood).

Upon admission, the patient’s condition was severe. He had clear consciousness. His skin was flesh-colored, with normal moisture. On the skin of the upper extremities in the area of the dorsal surface of the right hand, an ulcer with necrotic contents in the center with a diameter of 6–7 cm was identified on hyperemic and swollen skin. Similar ulcers were noted on the index finger of the left hand (up to 2 cm), outer surface of the left forearm (up to 7–8 cm in diameter), outer surface of the right forearm (up to 3 cm), and outer surface of the right shoulder (2 cm in diameter) (Fig. 4).



Fig. 4. Patient P. Multiple anthrax carbuncles on both arms, day 3 of the illness.

The upper limbs up to the middle of the shoulder were swollen. The swelling had a gelatinous consistency and was painless on palpation. Axillary lymphadenitis on both sides was up to 2.5–3.5 cm and was sensitive to palpation. Visible mucous membranes were of normal color and moist. The tongue was clean and moist. Nasal breathing was free. The oropharyngeal cavity was calm and clean. His body temperature was 37.9°C. The chest was regular and symmetrical. Percussion above the surface of the lungs revealed a clear pulmonary sound in both lungs. The respiratory rate was 16 per minute. Pulse (heart rate) was 91 beats per minute, rhythmic, with moderate volume and tension. Blood pressure was 142/93 mmHg. Saturation was 96% (without oxygen support). The abdomen was soft and painless on palpation. The liver and spleen were not palpable. CVA tenderness in the lumbar region was negative on both sides. Urination was free and painless. Defecation was regular, with formed stool.

The necessary treatment (400 mg ciprofloxacin two times a day for 14 days + 200 mg doxycycline two times a day for 10 days) was prescribed. The disease course was moderate. The temperature has returned to normal since August 20, 2023.

He was discharged with clinical recovery as an outpatient on September 29, 2023, after scab shedding (according to SP 3.3686-21 "Sanitary and epidemiological requirements for the prevention of infectious diseases").

The final diagnosis at discharge was 22.0 Anthrax, cutaneous form, without complications. The patient spent a total time of 42 days in the infectious diseases hospital. The dynamics of the skin manifestations of anthrax are presented in Figs. 5–10.

Further examination was performed.

Multislice computed tomography of the chest (CMSCT) dated September 18, 2023, showed no CT signs of focal or infiltrative changes.

A coagulogram dated August 18, 2023, revealed an activated partial thromboplastin time (aPTT) of 43.1 s, a prothrombin index (PTI) of 98.6%, D-dimer level of 1,138.6 ng/mL, and fibrinogen of 5.5 g/L.

A coagulogram dated September 26, 2023, revealed aPTT of 33 s, PTI of 86%, D-dimer of 106 ng/mL, and fibrinogen of 3.6 g/L.

INF to Tr. Pal. was negative (August 18, 2023), AT/AG HBs was negative (August 18, 2023), HVC was negative (August 18, 2023), and HIV was negative (August 18, 2023).

Complete blood count (CBC) dated (August 18, 2023) revealed Hb of 152 g/L, erythrocytes of $4.86 \times 10^{12}/L$, platelets of $136 \times 10^9/L$, leukocytes of $8.2 \times 10^9/L$, stab of 3%, segm. Of 79%, eos. of 1%, lymph. of 15%, mon. of 2%, and erythrocyte sedimentation rate (ESR) of 80 mm/h.

CBC dated September 26, 2023, revealed Hb of 134 g/L, erythrocytes of $4.56 \times 10^{12}/L$, platelets of $237 \times 10^9/L$, leukocytes of $6.6 \times 10^9/L$, stab of 1%, segm. of 68%, eos. of 2%, lymph of 28%, mon. of 1%, and ESR of 30 mm/h.

A common urinalysis (CUA) dated August 18, 2023, revealed the following: transparency, transparent; color, light yellow; reaction, 5.5; protein, 1 g/L; leukocytes, 0 in the field of view; erythrocytes, 0.6; density, 1,030.

A CUA dated September 26, 2023, revealed the following: transparency, transparent; color, light yellow; reaction, 5.5; protein, none; leukocytes, 75 per field of view; erythrocytes, 0.3; density, 1,030.

A biochemical blood test dated August 18, 2023, revealed the following values: aspartate aminotransferase (AST), 94 U/L; alanine aminotransferase (ALT), 172 U/L; glucose, 8.4 mm/L; urea, 6.0 mm/L; creatinine, 0.072 μ m/L; total bilirubin, 8.0 μ m/L; lactate dehydrogenase (LDH), 506 U/L; total protein, 69 g/L; albumin, 41 g/L; ferritin, 526 μ g/L; C-reactive protein (CRP), 200.0 mg/L; and procalcitonin (PCT), <0.5 ng/mL.

A biochemical blood test dated September 26, 2023, revealed the following: AST, 27 U/L; ALT, 49 U/L; glucose, 5.3 mm/L; urea, 4.7 mm/L; creatinine, 0.078 μ m/L; total bilirubin, 5.0 μ m/L; LDH, 244 U/L; total protein, 70 g/L; albumin, 45 g/L; ferritin, 300 μ g/L; CRP, 18.0 mg/L; PCT, <0.5 ng/mL.

An electrocardiogram dated September 6, 2023, showed no signs of acute coronary pathology.

Ultrasound examination of the abdominal organs on September 18, 2023, revealed ultrasound signs of diffuse changes in the liver and pancreas.

In the biomaterial of the patient (samples of the affected skin, such as wound contents, vesicle contents, wound lavage, and wound scab) sent to the reference center, a polymerase chain reaction (PCR) study revealed *B. anthracis* DNA (Study No. 821–842 dated August 19, 2023, at the Stavropol Anti-Plague Institute of Rospotrebnadzor) with Ct on the green channel of 24.18–31.56 and Ct on the yellow channel of 21.69–28.23.

In the remaining samples (soil from a pasture, wash off from an ax, wash off from a rope, cattle skin, litter, and grass from pasture), DNA of the anthrax pathogen was not detected.

In the blood serum of Patient P, using the indirect method of fluorescent antibodies (an additional study method of the reference center for monitoring the anthrax pathogen using an experimental test system produced by the Stavropol Anti-Plague Institute of Rospotrebnadzor), specific antibodies to the anthrax pathogen were not detected.

During allergy diagnostics with anthrax allergen in vitro using flow cytometry in a blood sample from Patient P, the intensity of CD63 expression on basophils was 1.1% (negative result).

On August 20, 2023, PCR determination and bioassay on laboratory animals registered positive results when examining animal biomaterials (skin).

An emergency regimen was introduced in the region by Decree of the Governor of the Voronezh Region dated August 20, 2023, No. 144-u, "On the establishment of restrictive measures (quarantine) for anthrax disease in certain territories of the Paninsky and Novousmansk municipal districts of the Voronezh Region," until November 16, 2023.



Fig. 5. Anthrax carbuncles on the dorsum of the right hand; day 3 of the illness.



Fig. 6. Anthrax carbuncles on the dorsum of the right hand; day 7 of the illness.



Fig. 7. Anthrax carbuncles on the dorsum of the right hand; day 16 of the illness.



Fig. 8. Anthrax carbuncles on the dorsum of the right hand; day 29 of the illness.



Fig. 9. Anthrax carbuncles on the dorsum of the right hand; day 41 of the illness. The scab was rejected on the 40th day of illness.



Fig. 10. Anthrax carbuncles on the dorsum of the right hand; day 63 of the illness.

From September 5 to 6, 2023, four patients from the Bogucharsky district of the Voronezh region were admitted to the infectious diseases department (medical center) of the VCCHEMC No. 8 with signs that did not exclude cutaneous anthrax. Biological material was promptly collected for laboratory research at the Center for Hygiene and Epidemiology in the Voronezh Region and at the Stavropol Anti-Plague Institute of Rospotrebnadzor. The results of the preliminary epidemiological investigation revealed an infection outbreak that arose in the Batovka village, Bogucharsky district, where on the personal farm of individual entrepreneur B, a heifer died on September 01, 2023, and its meat was subsequently sold (without veterinary control).

Further, after contact with meat purchased from the abovementioned farm, from September 6 to 7, 2023, four more patients were admitted.

All patients were diagnosed with a cutaneous form of the disease of moderate severity. All patients received antibiotic therapy (400 mg ciprofloxacin two times a day intravenously for 14 days + 200 mg doxycycline two times a day for 10 days), according to clinical recommendations. After scab shedding, all patients were discharged from the hospital under the supervision of outpatient specialists at the primary healthcare facility.

Case report 2

On September 7, 2023, patient K, born in 1976, registered and living in the Voronezh region, Bogucharsky district, Boguchar, came to the Bogucharsky District Hospital with signs of the disease that did not exclude anthrax.

The anamnesis revealed that on August 29, 2023, patient K bought meat from a reseller in an unauthorized place, without checking for information about veterinary control. The patient cut the meat for storage (she had cuts on the fingers of both hands during cutting) and did not eat it. On September 2, 2023, itching and redness appeared on the middle finger of the right hand and on the fingers of the left hand on September 3, 2023. On September 6, 2023, a skin element with an area of necrosis formed. The patient started taking antibacterial drugs on her own (she took 200 mg of doxycycline in the evening) and made an alcohol compress on both middle fingers.

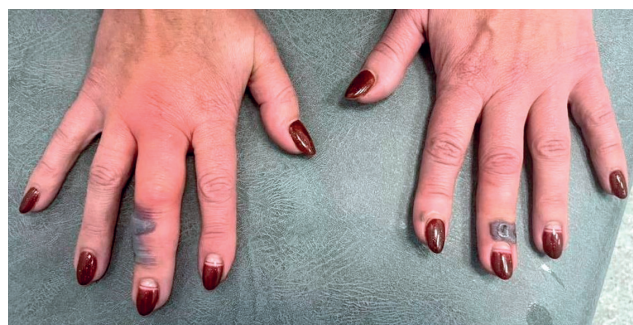


Fig. 11. Multiple anthrax lesions on the skin of both hands. Swelling of the hands.

On September 7, 2023, patient K sought medical help from an infectious disease specialist at the Bogucharsky District Hospital. She received remote consultation over the telephone from the chief external specialist in infectious diseases of the Voronezh Region Health Department. With suspicion of a cutaneous form of anthrax, the patient was referred for hospitalization to the Medical Center of VCCHEMC No. 8.

She lives with her husband, and he has no signs of the illness. According to preliminary information, the beef was purchased by a reseller in the village of Batovka, Bogucharsky district, where anthrax cases were detected.

On September 07, 2023, at 15:47, patient K was admitted to the infectious diseases building of the VCCHEMC No. 8 with signs that did not exclude cutaneous anthrax. She was hospitalized in box No. 9 of the anesthesiology and intensive care unit. Biological material was promptly collected for laboratory testing (blood, contents of ulcers, washings from the surface of an ulcer, scab, blood, and swab from the throat and nose).

Upon admission, her condition was moderately severe. She had clear consciousness. The skin was flesh-colored, with normal moisture. Black scabs with a light rim were observed on the third finger of the right hand with a diameter of 2.5 cm, on the third finger of the left hand with a diameter of up to 3 mm and up to 2 cm, on the second finger of the left hand up to 5 mm, and on the first finger of the left hand up to 5 mm (Fig. 11).

Severe swelling of the hands was noted. Axillary lymphadenitis on both sides measured up to 2–3.5 cm and was sensitive to palpation. Visible mucous membranes were of normal color and moist. The tongue was clean and moist. Nasal breathing was free. The oropharyngeal cavity was calm and clean. The body temperature was 37.0°C. The chest was regular and symmetrical. Percussion above the surface of the lungs revealed clear pulmonary sounds in both lungs. The respiratory rate was 18 per minute. Pulse (heart rate) was 80 beats per minute, rhythmic, with moderate volume and tension. Blood pressure was 120/80 mmHg. Saturation was 99% (without oxygen support). The abdomen was soft and painless on palpation. The liver and spleen were not palpable. CVA tenderness in the lumbar region was negative on both sides. Urination was free and painless. Defecation was regular, with formed stool.

The necessary treatment (400 mg ciprofloxacin two times a day for 14 days + 200 mg doxycycline two times a day for 10 days) was prescribed. The disease course was moderate.

She was discharged with clinical recovery as an outpatient on October 02, 2023, after scab shedding (according to SP 3.3686-21 "Sanitary and epidemiological requirements for the prevention of infectious diseases").

The final diagnosis at discharge was 22.0 anthrax, cutaneous form, without complications.

The patient a total time of 25 days in the infectious diseases hospital. Further examination was performed.

CMSCT dated September 7, 2023, showed no CT signs of focal or infiltrative changes.

A coagulogram dated September 7, 2023, revealed aPTT of 36 s, PTI of 82%, D-dimer of 475 ng/mL, and fibrinogen of 3.9 g/L.

A coagulogram dated September 28, 2023, revealed an aPTT of 36 s, PTI of 80%, D-dimer of 519 ng/mL, and fibrinogen of 3.2 g/L.

INF to Tr. Pal. was negative (September 09, 2023), AT/AG HBs was negative (September 9, 2023), HVC was negative (September 9, 2023), and HIV was negative (September 9, 2023).

CBC dated September 7, 2023, revealed Hb of 149 g/L, erythrocytes of $4.93 \times 10^{12}/L$, platelets of $189 \times 10^9/L$, leukocytes of $13.5 \times 10^9/L$, stab of 4%, segm. of 69%, eos. of 1%, lymph. of 22%, mon. of 4%, and ESR of 20 mm/h.

CBC dated September 28, 2023, revealed Hb of 148 g/L; erythrocytes of $5.0 \times 10^{12}/L$, platelets of $211 \times 10^9/L$, leukocytes of $8.5 \times 10^9/L$, stab of 1%, segm. of 49%, eos. of 1%, lymph. of 45%, mon. of 4%, and ESR of 20 mm/h.

CUA dated September 7, 2023, revealed the following: transparency, transparent; color, light yellow; reaction, 5.5; protein, none; leukocytes, 75 per field of view; erythrocytes, 0.3; density, 1,015.

CUA dated September 28, 2023, revealed the following: transparency, transparent; color, light yellow; reaction, 5.5; protein, none; leukocytes, 0 in the field of view; erythrocytes, 0.3; and density, 1,030.

A biochemical blood test dated September 7, 2023, revealed AST of 29 U/L, ALT of 28 U/L, glucose of 6.9 mm/L, urea of 3.4 mm/L, creatinine of $0.045 \mu\text{M}/L$, total bilirubin of $12.8 \mu\text{M}/L$, LDH of 469 U/L, total protein of 74 g/L, albumin of 44 g/L, ferritin of $63 \mu\text{g}/L$, SRP of 20.0 mg/L, and PCT of $<0.5 \text{ ng}/\text{mL}$.

A biochemical blood test dated September 28, 2023, revealed AST of 22 U/L, ALT of 20 U/L, glucose of 4.9 mm/L, urea of 4.0 mm/L, creatinine of $0.071 \mu\text{M}/L$, total bilirubin of $6.8 \mu\text{M}/L$, LDH of 294 U/L, total protein of 73 g/L, albumin of 47 g/L, ferritin of $128 \mu\text{g}/L$, SRP of 0.0 mg/L, PCT of $<0.5 \text{ ng}/\text{mL}$.

Electrocardiogram dated September 07, 2023, showed no signs of acute coronary pathology. Ultrasound examination of the abdominal organs on September 18, 2023, showed ultrasound signs of diffuse changes in the liver and pancreas.

In the patient's biomaterial (samples of the affected skin such as lavage from a woundscan of a wound) sent to the reference center, a PCR study revealed *B. anthrax* DNA (research No. 473B dated September 07, 2023, at the Stavropol Anti-Plague Institute of Rospotrebnadzor). In the remaining samples (throat and nasal swabs and blood), DNA of the anthrax pathogen was not detected.

During hospital stay, photographs were taken of the dynamics of skin manifestations of anthrax, which was continued in the outpatient setting. The results are presented in Figs. 12–15.



Fig. 12. Anthrax carbuncle on the right middle finger; day 10 of the illness.



Fig. 13. Anthrax carbuncle on the right middle finger; day 14 of the illness.

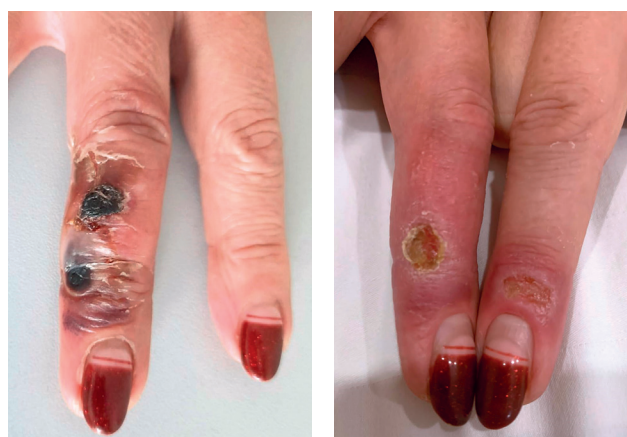


Fig. 14. Anthrax carbuncle on the right middle finger; day 20 of the illness.



Fig. 15. Rejection of the crust on the middle fingers of both hands; day 30 of the illness.

DISCUSSION

The uniqueness of this study does not consist in the description of a rather ordinary situation when, to paraphrase slightly the classic, the strictness of Russian sanitary rules and regulations, including veterinary ones, were

compensated by the optionality of their implementation. The questions of why the cattle were not vaccinated against anthrax, why all the rules for slaughtering livestock were violated, and how the meat of a sick animal ended up on the city market without appropriate inspection are beyond the scope of the issues considered in this study. In this case, the infectious disease service was at its best. Thanks to the high professionalism of infectious disease specialists, it was possible to make the correct diagnosis immediately when patients contacted them, which not only determined the subsequent adequate treatment approach and allowed to avoid possible adverse outcomes but also forced the entire sanitary and epidemiological service to work and prevent the emergence of new cases.

CONCLUSION

The authors consider their main merit to be presenting to readers the evolution of skin changes in the carbunculous form of cutaneous anthrax from the early stages of ulcerative process development to near-complete recovery. We have

not come across similar cases in the available literature or on the Internet. The print version of the article presents only the most significant stages in the evolution of skin manifestations of anthrax, whereas in the electronic version of the journal, the dynamics are traced in more detail.

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