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КОЖНЫЕ ПРОЯВЛЕНИЯ COVID-19 В ПРАКТИКЕ ДЕРМАТОЛОГА

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Skin Manifestations of COVID-19 Infection in the Practice of Dermatologist

Резюме

В начале 2020 года Всемирная организация здравоохранения объявила о появлении заболевания — новой коронавирусной инфекции (COVID-19). Высокая контагиозность и бессимптомная передача вируса привели к стремительному распространению инфекции и развитию пандемии. Вирус SARS-CoV-2 тропен к нижним отделам дыхательного тракта. Вместе с тем наблюдаются внелегочные проявления, в том числе высыпания на коже, которые характеризуются чрезвычайным многообразием. Некоторые авторы поражения кожи описывают как первый, а иногда и единственный симптом новой коронавирусной инфекции. Таким образом, кожные проявления должны быть тщательно оценены дерматологами при осмотре, особенно в период продолжающейся пандемии.

В статье представлено шесть клинических случаев с различными кожными проявлениями в острый период инфекции COVID-19. Первыми, к кому обратились с жалобами пациенты, были дерматологи. Высыпания на коже характеризуются многообразием и распространенностью: полиморфный васкулит, ливедо-ангиит, уртикарные, пятнисто-папулезные, папуло-везикулёзные, папуло-сквамозные элементы. Все случаи объединяет присутствие основных симптомы коронавирусной инфекции, характерных для острого периода: слабость, быстрая утомляемость, гипертермия, головная боль, миалгии, частичная или полная аносмия, агевзия.

Таким образом, в период продолжающейся пандемии обмен клиническим опытом развития кожных проявлений при COVID-19 инфекции крайне актуален. Анализ накопленных данных позволит оценить прогноз при наблюдении таких пациентов.

Ключевые слова: SARS-CoV-2, COVID-19, дерматология, кожные проявления

Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

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Abstract

In early 2020, the World Health Organization announced the emergence of the disease—a new coronavirus infection (COVID-19). High contagiousness and asymptomatic transmission of the virus led to a rapid spread of infection and reached the scale of a pandemic. It was found that the SARS-CoV-2 virus

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is pathogenic to the lower respiratory tract. At the same time, there are extrapulmonary manifestations, including skin rashes, which are characterized by an extreme variety. Some authors describe skin lesions as the first, and sometimes the only, symptom of a new coronavirus infection. Thus, skin manifestations should be carefully evaluated by dermatologists during the examination, especially during the ongoing pandemic.

This article presents 6 clinical cases with various skin manifestations in the acute period of COVID-19 infection. The first patients to complain were dermatologists. Rashes on the skin are characterized by a variety and prevalence: polymorphic vasculitis, livedo-angiitis, urticary, spot-papular, papulo-vesicular, papulo-squamous elements. All cases are united by the presence of the main symptoms of coronavirus infection characteristic of the acute period — hyperthermia, headache, fatigue, myalgia, partial or complete anosmia, ageusia.

Thus, the exchange of clinical experience of skin manifestations in COVID-19 infection is extremely relevant during the ongoing pandemic. The analysis of the accumulated data will provide an understanding of the diagnostic significance and the ability to assess the prognosis when observing such patients.

Key words: SARS-CoV-2, COVID-19, dermatology, skin findings

Conflict of interests

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ACE2 — angiotensin converting enzyme 2, BMI — body mass index, BP — blood pressure, CBC — complete blood count, COVID-19 — novel coronavirus infection caused by SARS-CoV-2, CT — computed tomography, DNA — deoxyribonucleic acid, ESR — erythrocyte sedimentation rate, HR — heart rate, PAF — platelet-activating factor, PCR — polymerase chain reaction, RNA — ribonucleic acid, SARS-CoV-2 — coronavirus that causes COVID-19

In December 2019, cases of pneumonia of unknown etiology were detected in the People's Republic of China in the city of Wuhan [1]. Later, it was found that the pneumonia was caused by a new pathogen named by the Committee on Taxonomy SARS-CoV-2, which was isolated from the lower respiratory tract of patients [2]. In early February 2020, the World Health Organization defined this disease as a novel coronavirus infection (COVID-19). The high contagiousness and asymptomatic transmission of the virus led to the rapid spread of infection and resulted in a pandemic [3, 4].

SARS-CoV-2 is a single-stranded RNA virus with surface "corona-like" proteins and belongs to the coronavirus family. This virus has tropism to the lower respiratory tract [5, 6]. The main symptoms of acute coronavirus infection include fever, cough, shortness of breath, chest congestion, headache, fatigue, myalgia, anosmia, and ageusia [6, 7]. Extrapulmonary manifestations are also observed; one of these manifestations is skin rash of vast diversity [8, 9].

Some authors cite skin lesions as the first and sometimes the only symptom of novel coronavirus infection. Other investigators concluded that skin rash appeared more often in the first four weeks after the onset of the main symptoms of COVID-19 [8, 10].

The course of infection caused by SARS-CoV-2 may be asymptomatic (no main symptoms of coronavirus infection) [11]. Some authors say skin lesions may precede COVID-19 symptoms [12]. Even if there is no confirmed COVID-19 diagnosis, skin signs should be carefully evaluated by dermatologists upon examination, especially during the ongoing pandemic. The correct interpretation of symptoms can result in the earlier verification of the diagnosis.

A.S. Dvornikov et al. (2020) analyzed pathological skin changes associated with COVID-19 and divided them into seven groups; five of these groups were considered as manifestations of novel viral infection [13]. Group 1 was defined as skin vasculitis. It is thought to be directly caused by coronavirus infection, as a result of which the walls of small vessels of the dermis are damaged by immune complexes circulating in blood. Group 2 includes papulo-vesicular rash that resembles sweat rash; it develops with underlying high temperature and increased sweating for several days. Group 3 includes such skin lesions as pityriasis rosea and papulosquamous rash, which are infectious and allergic skin lesions associated with COVID-19 infection. Group 4 includes morbilliform rash. Group 5 includes toxidermia. This rash is not directly associated with coronavirus infection; it develops due to the individual intolerance of patients to certain medications. Scientists include urticaria in Group 6 of skin manifestations of coronavirus; in some cases, it can be a precursor symptom of the onset of COVID-19. Group 7 includes trophic changes in facial tissues that develop in patients due to prolonged lying in a prone position [13, 14].

The average incidence of skin manifestations in patients with SARS-CoV-2, according to different sources, ranges from 0.2% to 19.6% [7, 15]. Rash in the cases of coronavirus infection is characterized by its vast diversity; its pathogenesis is not quite clear and is poorly known [10–15]. Therefore, the awareness of professionals about such manifestations of the disease is relevant in order to reduce erroneous diagnosis and improve subsequent treatment approach. The awareness and alertness of physicians during the visit will contribute to early and timely diagnosis of the disease, which will significantly

accelerate the implementation of treatment and sanitary and epidemiological measures.

This article describes six clinical cases of skin manifestations in patients with confirmed SARS-CoV-2 infection. All patients consulted a dermatologist in the acute phase of their disease before laboratory confirmation and treatment for COVID-19.

The patients were familiarized with the stages of examination and signed informed voluntary consent for medical intervention and publication of data in scientific literature.

Case Report No. 1

Patient D., female, 72, consulted a dermatologist with complaints of swelling and rash on the skin of feet, lower legs, skin soreness in the area of rash accompanied by severe weakness, tiredness, fever up to 38°C. Rash appeared on Day 7 after reporting high temperature, weakness, and malaise. The patient took antihistamines (levocetirizine 5 mg) on her own for three days; however, her general condition continued to deteriorate: weakness increased, anosmia developed.

Life history: The patient has acute respiratory diseases once or twice a year; she is under follow-up with a diagnosis of chronic cholangiocholecystitis with mixed biliary dyskinesia, chronic gastroduodenitis without exacerbation; she has been taking ursodeoxycholic acid 500 mg in capsules before bedtime at night for three months; there is no drug intolerance.

Epidemiological history: The patient lives alone, had no contact with patients with confirmed COVID-19. She returned from Moscow a week ago.



Figure 1. Patient S., 72 years old. Polymorphic vasculitis

Objective status: Clear consciousness, active position. Satisfactory condition. Body temperature 37.2°C. Regular body type, weight 82 kg, height 165 cm, BMI 30.1 kg/m². Mucosa of the oral cavity is pink, no rash, posterior pharyngeal wall is hyperemic, tonsils are not enlarged, no dental caries, the root of tongue is coated with yellowish plaque. Vesicular breathing, respiratory rate 17/min. Heart rhythm is regular, heart tones are clear, rhythmic, heart rate (HR) 84/min, blood pressure 145/85 mm Hg on both arms, saturation 96%. Abdomen is soft, moderately painful with deep palpation in the area of gallbladder projection; liver + 0.5 cm below the costal margin. On examination, edematous inflammatory purple spots and superficial edematous papules with moderate infiltration of a brown-violet color were observed on the skin of both lower legs and feet. (Figure 1). The patient was diagnosed with polymorphous vasculitis (ICD-10: L95.9 Vasculitis limited to the skin, unspecified).

CBC on appointment: hemoglobin 145 g/L, RBC $5.92 \times 10^{12}/L$, color index 0.73, hematocrit 48.0%, WBC $4.56 \times 10^9/L$, neutrophils 50.9%, lymphocytes 41.5%, monocytes 4.7%, eosinophils 2.6%, basophils 0.3%, ESR 25 mm/h, platelets $307 \times 10^9/L$. Blood biochemistry: total protein 67.2 g/L, creatinine 48 $\mu\text{mol}/L$, glucose 6.4 mmol/L, urea 4.0 mmol/L, uric acid 174.9 $\mu\text{mol}/L$, total bilirubin 18.0 $\mu\text{mol}/L$, direct bilirubin 3.2 $\mu\text{mol}/L$, aspartate aminotransferase 25 U/L, alanine aminotransferase 29 U/L, total cholesterol 5.8 mmol/L, C-reactive protein 2 mg/L. Antistreptolysin O 20 IU/mL, circulating immune complexes 3.9 RU/mL (reference range: 0.0–20.0 RU/mL). Waaler–Rose test and latex test negative, microprecipitation reaction negative. Common urinalysis within normal range.

Smear from nasal and oropharyngeal mucosa for COVID-19. After receiving positive results that confirmed coronavirus infection, the patient was referred to an infectious disease specialist and hospitalized. In addition to the management of the underlying disease, the therapeutic complex included topical glucocorticosteroids in the form of 0.05% betamethasone cream. The course of the viral infection turned out to be severe; according to the computed tomography data, lung damage was more than 50%; the patient required mechanical ventilation. Positive changes regarding skin rash were seen during Week 3 of hospitalization: swelling gradually decreased, no new rash appeared, and current rash turned pale. After elimination of the etiological factor (COVID-19) on Day 37 of the disease, skin lesions regressed.

Case Report No. 2

Patient O., female, 32, consulted a dermatologist with complaints of weakness, rash on the skin of thighs, and loss of taste. From medical history: complaints of weakness, fever, and rash appeared two days ago. In the evening before the visit, the patient's temperature increased to 37.8°C. She took an acetylsalicylic acid tablet on her own. The patient denies any constant use of medications.

Life history: The patient has acute respiratory diseases 2-3 times a year; chickenpox—at the age of 5; there is no drug intolerance.

Epidemiological history: She lives with her husband, who has been in self-isolation for 7 days after returning a positive PCR test for COVID-19.

Objective status: Clear consciousness, active position, satisfactory state, body temperature 37.5°C. Regular body type, weight 61 kg, height 167 cm, BMI 21.9 kg/m². Mucosa of the oral cavity is pink, no rash, posterior pharyngeal wall is hyperemic, tonsils are not enlarged, no dental caries, the root of tongue is coated with whitish plaque. Vesicular breathing, respiratory rate 17/min. Heart rhythm is regular, heart tones are clear, HR 88/min, blood pressure 125/75 mm Hg on both arms, saturation 97%. Abdomen is soft, painless; liver does not protrude below the costal margin. On examination, pink spots of various sizes and outlines were observed that formed a bizarre reticular pattern on the skin of thighs (Fig. 2). The following clinical diagnosis was established: Livedo vasculitis (ICD-10: L95.9 Vasculitis limited to the skin, unspecified).

CBC on appointment: hemoglobin 120 g/L, RBC $4.5 \times 10^{12}/L$, color index 0.80, hematocrit 43.0%, WBC $4.6 \times 10^9/L$, neutrophils 51.8%, lymphocytes 41.5%, monocytes 5.0%, eosinophils 1.6%, basophils 0.1%, ESR 23 mm/h, platelets $300 \times 10^9/L$. Blood biochemistry: total protein 66.2 g/L, creatinine 47 $\mu\text{mol}/L$, glucose 5.4 mmol/L, urea 4.0 mmol/L, uric acid 140.9 $\mu\text{mol}/L$, total bilirubin 17.0 $\mu\text{mol}/L$, direct bilirubin 3.2 $\mu\text{mol}/L$, aspartate aminotransferase 23 U/L, alanine aminotransferase 24 U/L, total cholesterol 4.8 mmol/L, C-reactive protein 3 mg/L. Antistreptolysin O 10 IU/mL, circulating immune complexes 2.9 RU/mL (reference range: 0.0–20.0 RU/mL). Antibodies to double-stranded DNA (anti-dsDNA) 5 IU/mL (reference range: 0.0–25.0 IU/mL). Microprecipitation reaction negative. Common urinalysis within normal range.



Figure 2. Patient O., 32 years old. Livedo-angiitis

Smear from nasal and oropharyngeal mucosa for COVID-19. After receiving positive results that confirmed coronavirus infection, the patient was referred to an infectious disease specialist. Outpatient treatment with self-isolation was prescribed. According to CT results, the lesion of lung parenchyma was more than 15%; the course of COVID-19 was regarded as moderate. Positive changes regarding skin rash (spots became pale pink with blurred outlines, no new ones appeared) were seen during Week 2 of treatment for the underlying disease. After elimination of the etiological factor (COVID-19) on Day 29 of the disease, skin lesions regressed.

Case Report No. 3

Patient M., male, 39, consulted a dermatologist with complaints of severe weakness, malaise, increased temperature in the evenings up to 38°C for 5 days; rash on the skin of arms accompanied by itching, loss of taste and smell. The patient linked the rash with a single intake of an acetylsalicylic acid tablet.

Life history: The patient rarely has acute respiratory diseases; chickenpox—at the age of 2; there was no drug intolerance before.

Epidemiological history: a week ago he came into contact with his neighbor who was hospitalized with viral pneumonia (COVID-19 test results unknown).

Objective status: Clear consciousness, active position, satisfactory state, body temperature 37.1°C. Regular body type, normosthenic, weight 75 kg, height 188 cm, BMI 21.2 kg/m². Mucosa of the oral cavity is pink, no rash, posterior pharyngeal wall is extremely hyperemic, tonsils are not enlarged, no dental caries. Vesicular breathing, respiratory rate 17/min. Heart rhythm is regular, heart tones are clear, HR 84/min, blood pressure 115/75 mm Hg on both arms, saturation 97%. Abdomen is soft, painless, liver does not protrude below the costal margin. On examination, heavy bright pink confluent maculopapular elements were observed in the area of hands, forearms, with a tendency to spread to the skin of shoulders (Fig. 3). Considering the complaints, the nature of the rash, and intake of acetylsalicylic acid the day before, the clinical diagnosis of maculopapular toxidermia, a moderately severe course was established (ICD-10: L27.1 Localized skin eruption due to drugs and medicaments taken internally).

CBC on appointment: hemoglobin 140 g/L, RBC $5.5 \times 10^{12}/L$, color index 0.76, hematocrit 46.0%, WBC $4.2 \times 10^9/L$, neutrophils 49.8%, lymphocytes 44.5%, monocytes 6.1%, eosinophils 1.6%, basophils 0.1%, ESR 25 mm/h, platelets $280 \times 10^9/L$. Blood biochemistry: total protein 76.3 g/L, glucose 4.4 mmol/L, urea 4.1 mmol/L, uric acid 139.0 $\mu\text{mol}/L$, total bilirubin 20.0 $\mu\text{mol}/L$, direct bilirubin 3.5 $\mu\text{mol}/L$, aspartate aminotransferase 25 U/L, alanine aminotransferase 22 U/L, total cholesterol 4.9 mmol/L, C-reactive protein 7 mg/L. Antistreptolysin O 5 IU/mL, circulating immune complexes 8.9 RU/mL (reference range: 0.0–20.0 RU/mL).

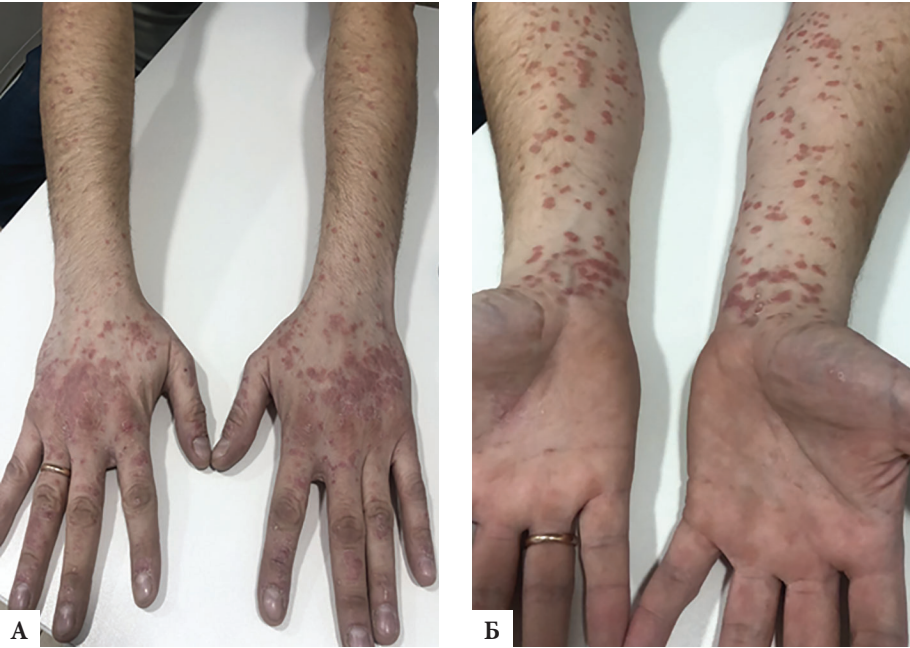


Figure 3. Patient M., 39 years old. Spotty-papular rashes on the skin of A) the back of the hands B) the forearms

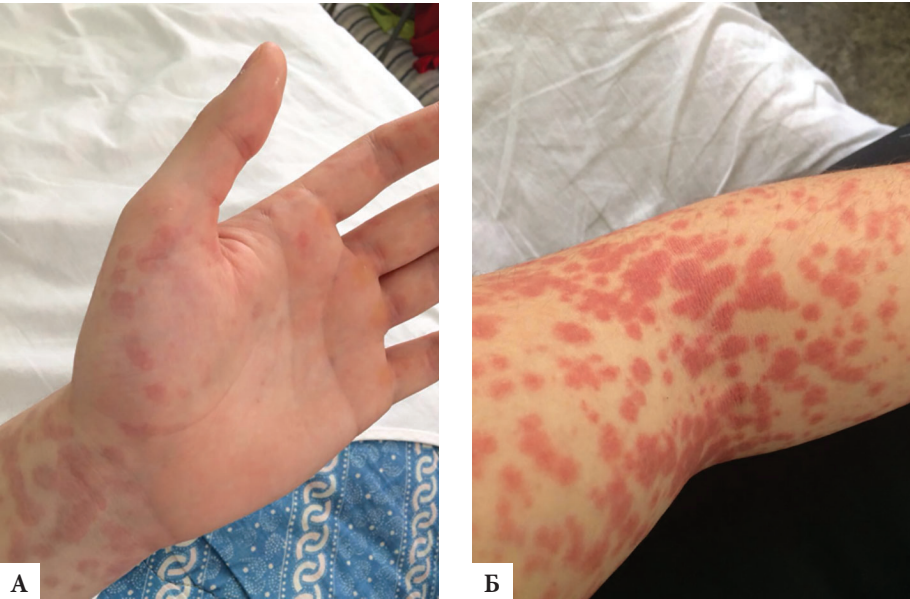


Figure 4. Patient M., 39 years old. Spot-papular rashes on the skin of A) hands B) forearms after 10 days of treatment in a hospital

Antibodies to double-stranded DNA (anti-dsDNA) 10 IU/mL (reference range: 0.0–25.0 IU/mL). Micro-precipitation reaction negative. Common urinalysis within normal range.

Smear from nasal and oropharyngeal mucosa for COVID-19. After receiving positive results that confirmed coronavirus infection, the patient was referred to an infectious disease specialist and hospitalized. According to CT results, lung damage was more than 75%. The course of COVID-19 infection was severe; the patient was on oxygen support. Sorbents were added to the management of the underlying disease: polymethylsiloxane polyhydrate (Enterosgel) for 10 days. In the course of treatment, on Day 5 in hospital, skin rash started to regress (color intensity decreased, as well as the infiltration of maculopapular elements; there was no tendency to spread along the periphery) (Fig. 4).

At the time of discharge from the hospital (Day 40 of the disease), skin lesions had regressed completely.

Case Report No. 4

Patient S., female, 23, consulted a dermatologist with complaints of weakness, sweating, and rash on the skin of the trunk accompanied by slight itching, which developed after three days of increased body temperature to 38.2°C. The patient regarded these symptoms as an acute respiratory disease, took Supradin vitamin complex and antipyretics on her own, with temporary effect. Negative epidemiological history: The patient denies contact with patients with COVID-19; she worked from home during the last 14 days and only visited a grocery store once every three days. On examination, multiple isolated papulovesicular elements with a red crown were



Figure 5. Patient S., 23 years old. Papulo-vesicular rashes on the skin of A) chest B) back

observed mainly on the skin of the back, chest, and—in a lesser extent—abdomen (Fig. 5). The clinical diagnosis of red sweat rash was established (ICD-10: L74.0 Miliaria rubra).

It was recommended to avoid overheating, implement sanitary and hygiene measures (baths with zinc-containing shower gel, ironing underwear and bed linen with a hot iron before use), zinc-containing cream on skin lesions.

Smear from nasal and oropharyngeal mucosa for COVID-19. After receiving positive results that confirmed coronavirus infection, the patient was examined by an infectious disease specialist. The course of infection caused by SARS-CoV-2 was mild; there was no evidence of lung damage. Skin rash regressed after 2 weeks of treatment.

Case Report No. 5

Patient V., male, 48, consulted a dermatologist with complaints of skin rash that developed on Day 4 of low-grade fever accompanied by mild occasional itching. The patient also noted weakness, loss of taste, nasal congestion, and muscle pain. The patient took no treatment on his own.

Life history: The patient has acute respiratory diseases 2-3 times a year; there is no drug intolerance.

Epidemiological history: a week ago, the patient accompanied his relative suspected of COVID-19 to the hospital (coronavirus test results are not known).

Objective status: Clear consciousness, active position. The condition is satisfactory. Body temperature 37.1°C. Regular body type, normosthenic, weight 90 kg, height 168 cm, BMI 31.9 kg/m². Mucosa of the oral cavity is pink, no rash, posterior pharyngeal wall is hyperemic, tonsils are not enlarged, no dental caries, and the root of the tongue is coated with yellow plaque. Vesicular breathing, respiratory rate 17/min.

Heart rhythm is regular, heart tones are clear, HR 86/min, blood pressure 145/85 mm Hg on both arms, saturation 96%. Abdomen is soft, painless, liver does not protrude below the costal margin. Heavy, bright red teardrop-shaped papules were observed on the skin of the chest, abdomen; more on the back, buttocks, arms; less on legs, 3 to 10 mm in diameter, prone to peripheral growth, covered with delicate scales. Face with no rash, nail plates are not affected. Scraping the papules revealed symptoms typical for psoriasis: “stearic stain,” “terminal film,” and “bloody dew” (Fig. 6). A clinical diagnosis of guttate psoriasis was established (ICD-10: L40.4 Guttate psoriasis).

CBC on appointment: hemoglobin 140 g/L, RBC $4.2 \times 10^{12}/L$, color index 1.00, hematocrit 46.0%, WBC $4.0 \times 10^9/L$, neutrophils 50.2%, lymphocytes 44.8%, monocytes 8.0%, eosinophils 0.9%, basophils 0.1%, ESR 20 mm/h, platelets $250 \times 10^9/L$. Blood biochemistry: total protein 79.3 g/L, glucose 5.9 mmol/L, urea 5.1 mmol/L, uric acid 110.0 $\mu\text{mol}/L$, total bilirubin 18.0 $\mu\text{mol}/L$, direct bilirubin 2.5 $\mu\text{mol}/L$, aspartate aminotransferase 35 U/L, alanine aminotransferase 28 U/L, total cholesterol 5.9 mmol/L, C-reactive protein 10 mg/L. Antistreptolysin O 5 IU/mL, microprecipitation reaction negative. Hepatitis B surface antigen (HBsAg) not found, total antibodies to hepatitis C virus (anti-HCV) not found. Common urinalysis within normal range.

Smear from nasal and oropharyngeal mucosa for COVID-19. After receiving positive results that confirmed coronavirus infection, the patient was referred to an infectious disease specialist and hospitalized. According to computed tomography results, lung damage was more than 70%, the course of COVID-19 infection was severe, the patient was on oxygen support.

Topical glucocorticosteroid agents in the form of 0.05% betamethasone cream were added to the

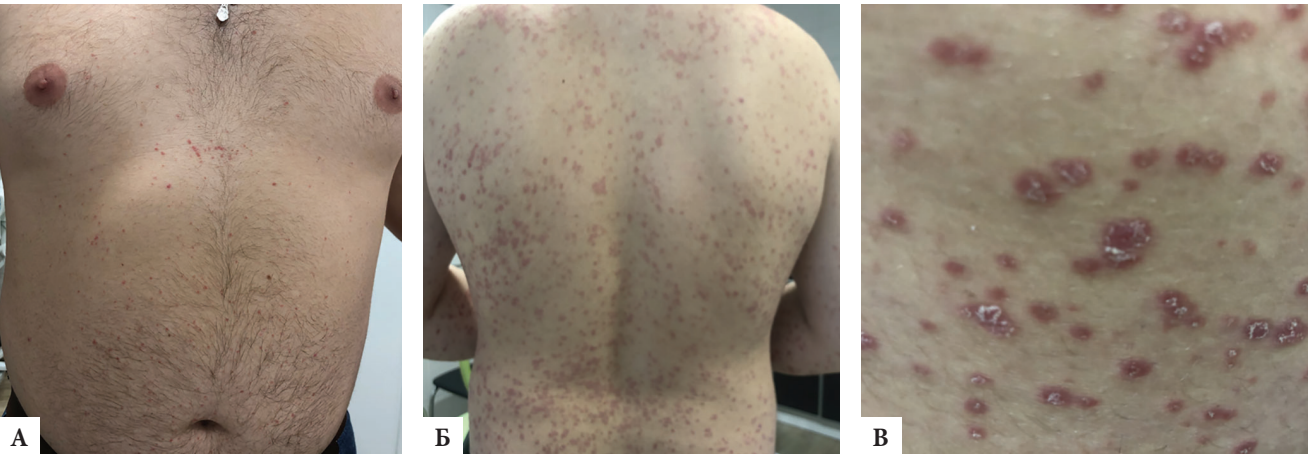


Figure 6. Patient V., 48 years old. Papulo-squamous rashes on the skin A) abdomen Б) back B) macro photography of elements

management of underlying disease. In the course of treatment, on Day 15 in hospital, skin symptoms regressed: no new rash appeared; current rash stopped growing, peeled off heavily, its infiltration and brightness decreased.

At the time of discharge from the hospital (Day 40), skin lesions had regressed completely.

Case Report No. 6

Patient M., female, 26, consulted a dermatologist with complaints of skin itching accompanied by bright pink rash. The first elements appeared 11 days ago on the skin of hands. Temperature increased to 37.6°C and there was loss of smell for about a week. The patient thought it was associated with high consumption of chocolate (1 chocolate bar per day). The patient took antihistamines on her own for a week with temporary positive effect.

From life history: The patient has acute respiratory diseases 1-3 times a year; chickenpox—at the age of 2; there is no drug intolerance.

Epidemiological history: her husband was hospitalized with confirmed COVID-19 three weeks ago.

Objective status: Clear consciousness, active position. The condition is satisfactory. Body temperature 37.1°C.

Regular body type, normosthenic, weight 65 kg, height 168 cm, BMI 23.0 kg/m². Mucousa of the oral cavity is pink, no rash, posterior pharyngeal wall is hyperemic, tonsils are not enlarged, no dental caries, the root of the tongue is coated with yellow plaque. Vesicular breathing, respiratory rate 18/min. Heart rhythm is regular, heart tones are clear, HR 82/min, blood pressure 135/85 mm Hg on both arms, saturation 97%. Abdomen is soft, painless, liver does not protrude below the costal margin. Examination of the skin of the trunk, upper and lower extremities revealed multiple confluent urticaria up to 3 cm in diameter (Fig. 7). A clinical diagnosis of acute idiopathic urticaria was established (ICD-10: L50.1 Idiopathic urticaria).

CBC on appointment: hemoglobin 140 g/L, RBC $4.7 \times 10^{12}/L$, WBC $4.6 \times 10^9/L$, neutrophils 52.2%, lymphocytes 36.8%, monocytes 10.0%, eosinophils 0.9%, basophils 0.1%, ESR 24 mm/h, platelets $270 \times 10^9/L$. Blood biochemistry: total protein 70.0 g/L, glucose 5.6 mmol/L, serum urea 5.2 mmol/L, uric acid 102.0 $\mu\text{mol}/L$, total bilirubin 16.0 $\mu\text{mol}/L$, direct bilirubin 2.0 $\mu\text{mol}/L$, aspartate aminotransferase 25 U/L, alanine aminotransferase 22 U/L, total cholesterol 4.9 mmol/L, C-reactive protein 12 mg/L. Antistreptolysin O 15 IU/mL.

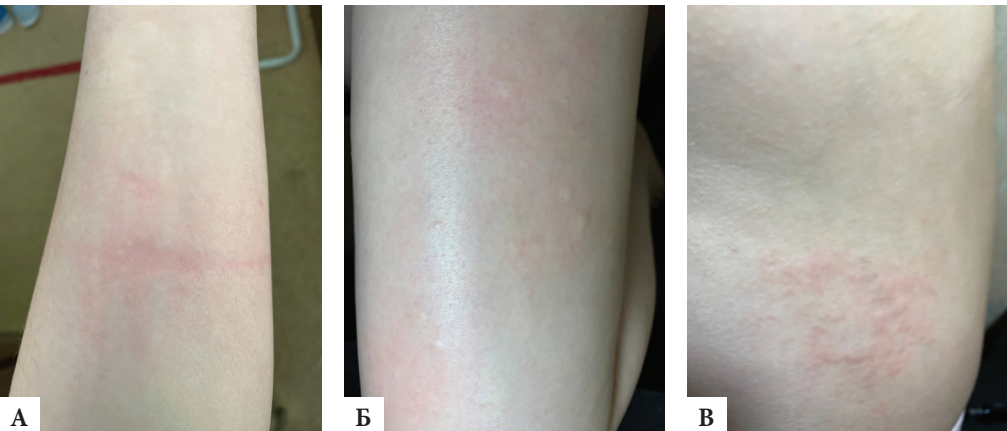


Figure 7. Patient M., 26 years old. Urticaria. Blisters in the area of A) left forearm Б) right thigh B) torso

Microprecipitation reaction negative. Hepatitis B surface antigen (HBsAg) not found, total antibodies to hepatitis C virus (anti-HCV) not found. Common urinalysis within normal range.

Smear from nasal and oropharyngeal mucosa for COVID-19. After receiving positive results that confirmed coronavirus infection, the patient was referred to an infectious disease specialist and hospitalized. According to computed tomography results, lung damage was about 40%. The course of COVID-19 infection was assessed as moderate.

In the course of treatment (including systemic glucocorticosteroids), on Day 5 in hospital, urticaria completely regressed.

Discussion

Back in 2004, in their work on the study of ACE2 protein distribution in tissues, which is the functional receptor for SARS coronavirus, Hamming I. et al. wrote that vascular abnormalities and inflammatory changes in various organs, including the skin, may be associated with the systemic toxic effects of immune responses caused by SARS-CoV infection [16].

Today, many authors consider the development of papulosquamous rash as an infectious and allergic skin lesion associated with COVID-19 infection, i.e., paraviral dermatosis. Skin vasculitis is probably directly caused by coronavirus infection, as a result of which the walls of small vessels of the dermis are damaged by immune complexes circulating in the blood [14]. Magro C. et al. (2020) reported an inflammatory thrombogenic vasculopathy with deposition of C5b-9 and C4d complement components in both involved and unchanged skin. Also, co-localization of COVID-19 spike glycoproteins with C4d and C5b-9 in interalveolar septa and skin microvasculature was observed in two clinical cases. The authors concluded that a subgroup of patients with severe COVID-19 may have a catastrophic microvascular injury syndrome mediated by the activation of complement pathways and an associated procoagulant state [17]. Potekaev N.N. et al. (2020), based on their experience and analysis of literature data, argue that there is a probable causal relationship between skin vasculitis and COVID-19 infection as a result of damage to small vessels of the dermis by circulating immune complexes, activation of complement pathways and the procoagulant environment [14].

Demopoulos C. et al. (2020) argue that a common pathogenetic link for all clinical varieties of urticaria is the increased vascular permeability of the microvasculature and the development of acute edema around these vessels due to the increased level of histamine and other inflammatory mediators (PAF; cytokines released by activated mast cells) in serum, which leads to vasodilation and plasma extravasation [18]. It was also demonstrated that it was the sharp increase in the level of PAF, the most powerful trigger of platelet activation and thrombus formation, that stimulated perivascular activation of mast cells and caused pneumonia in patients

with COVID-19 followed by severe acute respiratory syndrome at the end of the disease [18]. It is probably the sharp increase in the PAF level in several patients with the onset of COVID-19 that induces the development of acute urticaria. Therefore, urticaria-like rash may be the first symptom of COVID-19.

The skin rash described here, which develops at the onset of COVID-19 (in the acute period of the disease before laboratory confirmation of infection and treatment), varied in its clinical presentation and developmental mechanism. However, these skin manifestations have one thing in common—the beginning and the end of these skin processes coincided with the course of SARS-CoV-2 infection. In several cases, sweat rash (associated with high fever and increased sweating for several days) and toxidermia (due to the patient's individual intolerance to acetylsalicylic acid) are not directly related to coronavirus infection. Other clinical cases of skin vasculitis and urticaria described are most likely to be included in the symptom complex of COVID-19. The case of papulosquamous rash is considered an infectious and allergic skin lesion associated with COVID-19. In their article, Gisondi P. et al. (2021) justifiably concluded that the polymorphism of skin manifestations in cases of COVID-19 can be due to a variety of underlying pathogenetic mechanisms [11].

Conclusion

Sharing clinical experience in the analysis of skin manifestations in patients with COVID-19 is extremely relevant during the ongoing pandemic. Evaluation of the accumulated information allows determining the diagnostic and prognostic significance of skin symptoms in patients with COVID-19.

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