



FEATURES OF SKIN MANIFESTATIONS IN COVID-19 AND THEIR DIAGNOSTIC SIGNIFICANCE

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✓ Resume

Etiological diagnosis of exanthemums on the background of coronavirus infection (CVI) caused by the SARS-CoV-2 virus (COVID-19) is a difficult task. This problem is especially relevant in the epidemiological period, when it is necessary to comply with the requirements for distancing and the use of personal protective equipment, including when examining the skin and oral mucosa in patients with COVID-19. Different authors distinguish different groups of skin rashes. According to British researchers, five types of rash have been identified: acral areas of erythema-edema with vesicles or pustules – pseudo-frostbite (19% of cases); other vesicular rashes (9%); urticular foci (19%); other maculopapules (47%); livedo or necrosis (6%). SARS-CoV-2 is a new, highly contagious pathogen for humans, which can spread rapidly and in any situation can have a huge impact on both health and economic and social factors.

Key words: coronavirus, clinic manifestation, , erythema

ОСОБЕННОСТИ КОЖНЫХ ПРОЯВЛЕНИЙ ПРИ COVID-19 И ИХ ДИАГНОСТИЧЕСКОЕ ЗНАЧЕНИЕ

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✓ Резюме

Этиологическая диагностика экзантем на фоне коронавирусных инфекций, вызванных вирусом SARS-CoV-2 (COVID-19), является сложной задачей. Эта проблема особенно актуальна в эпидемиологический период, когда необходимо соблюдать требования по дистанцированию и использованию средств индивидуальной защиты, в том числе при обследовании кожи и слизистой оболочки полости рта у пациентов с COVID-19. Разные авторы выделяют разные группы кожных высыпаний. По данным британских исследователей, было выявлено пять типов сыпи: акральные участки эритемы - отек с пузырьками или пустулами – псевдообморожение (19% случаев); другие везикулярные высыпания (9%); уртикарные очаги (19%); другие макулопапулы (47%); ливедо или некроз (6%). SARS-CoV-2 - это новый, очень заразный патоген для людей, который может быстро распространяться и в любой ситуации может оказать огромное влияние как на здоровье, так и на экономические и социальные факторы.

Ключевые слова: коронавирус, клинические проявления, эритема

COVID-19 KASALLIGINI TERIDA KECIШИ VA DIAGNOSTIK AҲAMIЯТИ

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SARS-CoV-2 (COVID-19) virusi tomonidan chaqirilgan ekzantema kasalligini etiologik diagnostikasi murakkab vazifalardan biridir. Ayniqsa bu muammo epidemiologik davrda dolzarb бўлиб, тери ва шиллиқ қаватларни текширишда аниқланади. Бу касалликда олимлар тери юзларида ҳар қандай турдаги тошмалар аниқланишини айтиб ўтмоқдалар. Бу тошмалар нуфакчалар, йирингчалар, қаварчиқлар, макулопапулалар, эритематоз доғлардан иборат бўлиб, атрофдагиларга тез тарқалиш хусусиятига эгадир.

Калит сўзлар: коронавирус, клиник тошмалар, эритема

Relevance

The COVID-19 pandemic is causing damage to all spheres of life (health, economic and social spheres). Today, the search for effective methods of diagnosis and treatment is particularly relevant. After the first data appeared in the literature on the features of skin manifestations of coronavirus infection, research began to search for specific skin manifestations of this disease. COVID-19 is diverse and it is still difficult to identify a specific set of symptoms, but the interest of healthcare professionals around the world is focused on this problem.

The purpose of the study. Systematization of information on skin manifestations of COVID-19 coronavirus infection from the beginning of the epidemic to 2022.

Materials and methods. Studies on skin manifestations of coronavirus infection conducted in a number of countries (Italy, China, Russia, Great Britain) have been studied. Clinical cases, articles published in the period from the beginning of the pandemic to 2022.

Results and discussion

"Skin changes are very often a mirror of hidden changes in internal organs" (Robert Hegglin). Often skin changes are the diagnostic key to many diseases. Skin examination should be carried out necessarily in daylight and necessarily on the whole body. The features of skin rashes, their coloring, the nature of pigmentation, the preservation of the structure of the skin surface and vascular pattern on it can give an accurate description of metabolism, its disorders.

Skin manifestations may also have diagnostic significance in coronavirus infection. In December 2019, the first cases of the new coronavirus infection COVID-19 were reported, caused by a new virus from the coronavirus group - SARS-CoV-2. In the following months, the infection spread around the globe and assumed the character of a pandemic. Initially, the clinical picture was described as an acute febrile disease with a predominant lesion of the lower parts of the lungs, cough, chest congestion and shortness of breath, severe weakness, impaired sense of smell and taste. Myalgia, nausea, vomiting, diarrhea, headaches, confusion, hemoptysis, palpitations were registered somewhat less frequently. During COVID-19, the following clinical variants can be distinguished: 1. Acute respiratory infections affecting only the upper respiratory tract; 2. pneumonia without acute respiratory failure; 3. pneumonia with acute respiratory failure and a decrease in SpO₂ level < 88% (more than 30% of patients); 4. ARDS (3-4% of patients); 5. sepsis; 6. septic (infectious-toxic) shock. According to the degree of severity, there are light (80.9%), medium-heavy (13.8%) and heavy (5.3%) forms of COVID-19. Risk factors for the severe course of COVID-19 are old age; concomitant diseases of the cardiovascular system, including hypertension; lung diseases (COPD, bronchial asthma); diabetes mellitus, metabolic syndrome and other endocrine disorders; immunodeficiency conditions: malignant neoplasms; drug immunosuppression, late stages of HIV infection and other chronic decompensated diseases.

Etiological diagnosis of exanthemums during coronavirus infection (CVI) caused by the SARS-CoV-2 virus (COVID-19) is a difficult task. This problem is especially relevant in the epidemiological period, when it is necessary to comply with the requirements for distancing and the use of personal protective equipment, including when examining the skin and oral mucosa in patients with COVID-19. It should also be taken into account that effective pharmacotherapy in CVI involves the appointment of drugs with different pharmacodynamics and pharmacokinetics. These drugs and their interactions can also lead to changes in the skin, which complicates the etiological diagnosis of skin rashes in CVI. Since the beginning of the pandemic, various clinical cases with skin manifestations in CVI have been described in the literature. To date, there are no specific skin symptoms of CVI, therefore, the study of the features of skin manifestations in CVI is an urgent task. Timely identification of skin manifestations in patients with CVI can greatly facilitate diagnosis.

Dermatological symptoms in patients with COVID-19 are very diverse, the frequency of occurrence depends on age, concomitant pathology and features of drug treatment of patients. Recalculation (2020) observed skin manifestations in 18 (20.4%) of 88 hospitalized patients in northern Italy. The author of the work focuses on the fact that 60 (40.5%) of 148 patients with a positive test for a new coronavirus infection who had already taken medications during the previous 15 days were previously excluded from the study. With the appearance of the first clinical symptoms of COVID-19, exanthema appeared in 8 (44%) of 18 patients, in the rest — after discharge from the hospital. Skin manifestations were mainly of the nature of erythematous rash (in 14 patients), in 3 patients — in the form of widespread urticaria and vesicles similar to the manifestations of chickenpox. In general, skin manifestations were most often located on the trunk and were accompanied by a slight itching, disappeared within a few days and did not correlate with the severity of the disease. The authors suggested that the above symptoms are similar to those that occur with common viral infections. Marzona A.V. et al. (2020) described a rash similar to that of chickenpox in 12



(54.6%) of 22 patients with COVID-19. In all seven patients who underwent skin biopsy, histological data corresponded to a viral infection. Other Italian authors have suggested that exanthema, similar to chickenpox, is a rare but specific manifestation of skin symptoms associated with PCR-confirmed coronavirus infection. The authors described rashes appearing 3 days after the onset of specific clinical symptoms of COVID-19, scattered over the body, small in size, not accompanied by itching or the appearance of itching, which disappeared without scarring after 8 days. In patients with COVID-19, petechial rashes and reticular ones are also described: almost asymptomatic, randomly detected elements on the mucous membrane of the cheeks, gums, in the vestibule of the oral cavity, on the lip mucosa. Rashes in the form of spots of opal color and small, slightly towering papules, on the surface of which a transverse striation is visible (Wickham grid). Rashes similar to livedo are grouped in the form of a tree branch or a fern leaf, located against a background of hyperemic mucosa. Acroischemia: cyanosis of the fingers and toes, skin blisters and dry gangrene have been described in a number of patients from the Chinese city of Wuhan with severe COVID-19. A number of authors have reported the development of signs resembling frostbite against the background of coronavirus infection. The most frequent findings were skin formations similar to frostbite (N=402, 40.2%), spotty papular lesions (N=227, 22.7%), urticaria (n=89, 8.9%), vesicular elements (n=64, 6.4%), livedoid and necrotic lesions (N=28, 2.8%) and other undescribed skin elements and skin lesions (H=192, 19.8%). Pain and burning were registered in at least 85 cases (8.5%), itching — in 256 (25.6%) patients, the prevalence of skin manifestations of COVID-19 varied from 0.19% to 20.45%.

Based on traditional ideas about the pathogenesis of both exanthema and enanthema, rash is a focal skin reaction to the effects of the pathogen or its toxins, metabolites, arising under the influence of histamine-like substances and is implemented in a number of mechanisms, which include: • capillary dilation; • blood stasis and increased vascular permeability with the development of edema and hemorrhages; • necrosis of the epidermis and deeper layers of the skin; • dystrophic cell changes (balloon dystrophy); • formation of inflammation (serous, purulent, serous-hemorrhagic).

An expert assessment of the data from the study below was published at the end of April, 2021 in the British Journal of Dermatology. Spanish dermatologists described skin rashes that they observed in 375 patients with coronavirus infection for 2 weeks. Five types of rash were identified: acral areas of erythema-edema with vesicles or pustules – pseudo-frostbite (19% of cases); other vesicular rashes (9%); urticular foci (19%); other maculopapules (47%); livedo or necrosis (6%). Acral areas of erythema-edema with vesicles or pustules (pseudo-frostbite). These foci affecting the hands and feet may resemble frostbite (small itchy puffiness on the skin) with small red or purple spots caused by subcutaneous hemorrhages. Rashes are usually asymmetrical. They are associated with young patients, last an average of 12.7 days, develop in the late course of the COVID-19 disease and are observed with a less severe disease (when assessing the severity, hospital admission, pneumonia, admission to intensive care and mortality were taken into account). Rashes sometimes cause pain (32%) or itching (30%). Other vesicular eruptions. Vesicular eruptions were manifested by the sudden development of vesicles on the trunk, which could also affect the limbs. The vesicles were sometimes filled with blood and could become larger or more widespread. They are associated with middle-aged patients, last an average of 10.4 days, appear more often (15%) before the onset of other symptoms and are observed with moderate severity of the disease. Itching was frequent (68%). Urticary foci. The foci were pink or white swellings of the skin, usually resembling itchy blisters with urticaria. The rashes mainly developed on the trunk or spread throughout the body. In several cases, they were observed on the palms. Other maculopapules. Maculopapules are small, flat and raised red bulges. In some cases, they were located around the hair follicles, and there was also a different degree of peeling. Some of the elements were described as similar to pink lichen. Blood spots under the skin may also be present either in the form of specks /dots, or larger areas. Such rashes are associated with a shorter duration (6.8 days on average for urticular foci and 8.6 for maculopapular foci), usually appear together with other symptoms and are observed with a more severe course of COVID-19 disease (2% mortality in the sample). Itching was very frequent in urticular foci (92%) and in 57% of cases – in maculopapular. Livedo or necrosis. Livedo is the result of impaired circulation in the blood vessels of the skin. As a result, a vascular pattern appears on the skin in the form of a red or blue grid. Necrosis means premature death of skin tissue. These two symptoms reflect a different degree of vascular occlusion with narrowing or blocking of arteries that restrict blood flow in certain parts of the body (in this case, on the trunk or limbs). Such rashes are associated with elderly patients and a more severe course of the disease (mortality of 10%). However, such manifestations of COVID-19 are more variable, including transient livedo in patients with COVID-19 who did not require hospitalization. The severity of associated symptoms ranged from less severe in the case of pseudo-frostbite to the most severe in patients with Livedo's picture, who had a higher percentage of pneumonia, hospitalizations and intensive care units. The researchers noticed that some of

the skin manifestations associated with COVID-19 are common and can have many causes, this applies, in particular, to maculopapules and urticary foci. By themselves, they do not help in establishing a diagnosis. Livedo and necrosis, on the other hand, are quite rare foci, and most often they appeared in elderly and severe patients. However, it is difficult to say whether such foci are caused directly by COVID-19 or they are only an indicator of complications. For this reason, one should be very careful when trying to independently diagnose COVID-19 based on skin symptoms; after all, skin rashes and other skin foci are quite common phenomena, without being a specialist, they are difficult to differentiate. A team of researchers led by Professor N.N. Potekhaeva identified seven groups of skin rashes in patients with COVID-19 coronavirus infection, depending on their etiology and mechanisms of development:

1. Skin angitis. They are caused directly by a coronavirus infection, against which the walls of small vessels of the dermis are affected by circulating immune complexes in the form of deposits with infectious (viral) antigens. Special forms associated with COVID-19 infection include acrovasculitis.

2. Papulo-vesicular rashes. Papulo-vesicular rashes (of the type of miliaria or eccrine sweating) occur against the background of subfebrility with multi-day increased sweating in patients. Unlike the classical course, miliaria are characterized by the vastness of skin lesions.

3. Papulo-squamous rashes and pink lichen. They are infectious and allergic skin lesions associated with COVID-19 infection. A clinical feature of pink lichen in coronavirus infection is the absence of a "maternal plaque".

4. Measles-like rashes. With COVID-19 infection, these rashes resemble in their clinical characteristics the rashes that occur with measles, and thus indicate pathogenetic proximity to other viral exanthemes.

5. Toxidermy. They are not directly related to coronavirus infection and are a consequence of individual patient intolerance to certain medications.

6. Urticaria. Depending on its origin, the disease can have a twofold character. On the one hand, urticaria rashes may be a harbinger of the onset of COVID-19 infection or occur together with its first symptoms. On the other hand, urticaria often develops due to drug intolerance and in this case belongs to one of the clinical manifestations of toxidermia. The acral location of blisters against the background of COVID-19 infection can also be attributed to the specific features of urticular skin lesions in this viral disease.

7. Artificial lesions. Artificial lesions are the result of forced prolonged stay of patients in the pronation in order to improve respiratory function.

Conclusion. Although skin rashes may be one of the first manifestations of COVID-19 infection, they are of a very diverse morphological and pathogenetic nature, therefore they cannot serve as a fully evidence-based basis for clinical diagnosis. Further dynamic observations of the course of skin manifestations in COVID-19, accumulation of clinical cases and experience in order to analyze their diagnostic and prognostic significance are needed.

SARS-CoV-2 is a highly contagious pathogen for humans that can spread rapidly and in any environment can have a huge impact on both health and economic and social factors. The consequences of COVID-19 can affect long after the resolution of the pandemic and lead to the emergence of new methods of management of dermatological patients.

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