

УДК 616.99

Coinfection of Congo-Crimean hemorrhagic fever and various infectious diseases

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Introduction. Crimean-Congo hemorrhagic fever, caused by Crimean-Congo hemorrhagic fever virus, is endemic in Africa, Asia, and Europe, but epidemiology and epizootiology is only rudimentarily defined for most regions [1]. The virus transmitted to humans by the bites of infected ticks *Hyalomma* spp. [2]. With Crimean-Congo hemorrhagic fever, both a mild febrile disease can be observed and it can progress to a severe and often fatal hemorrhagic shock responsible for multiple organ failure in humans and animals [2]. One of the actively developing areas of scientific research at the moment is to determine the association of this virus with various diseases as one of the possible causes of the development of severe forms of the disease. The aim of this study is to review the current literature on the presence of coinfection of Congo-Crimean hemorrhagic fever with various infectious diseases.

Comparative analysis of the epidemiological situation of the Congo-Crimean hemorrhagic fever in Kazakhstan and India according to official statistics.

Foci of Congo-Crimean hemorrhagic fever are widespread and cover the territory of two continents – Eurasia and Africa, in a total of 46 countries. In Europe, the circulation of the virus was detected in Bulgaria, Greece, Hungary, Yugoslavia, Portugal, Turkey. There are foci in the south of the Russian Federation, in Moldova, Ukraine, Armenia, Azerbaijan, a case of the disease has been identified in Georgia, in the south of France it is known from serological data. In Asia, foci exist in Pakistan, Afghanistan, Iraq, Iran, India, the United Arab Emirates, Kazakhstan, Kyrgyzstan, Uzbekistan, Tajikistan, China. On the African continent, foci of Congo-Crimean hemorrhagic fever are known in Senegal, Nigeria, Kenya, Uganda, Egypt, Tanzania, Ethiopia, South Africa, Mauritania, Zimbabwe, Central African Republic, Upper Volta, Burkina Faso, etc. [2,3]. In the Kazakh Soviet Socialist Republic (Kazakh SSR, today's Kazakhstan), the first reported cases of Congo-Crimean hemorrhagic fever were recorded in 1948 [3]. A total of 801 Congo-Crimean hemorrhagic fever human cases (101 deaths) were identified as having occurred from 1948 through the end of 2021 [3]. In India, the first case of Congo-Crimean hemorrhagic fever was registered in March 2011 in the Sirohi district of

Rajasthan, bordering the state of Gujarat [4]. For the period 2019, 5 cases of the disease are reported, including 3 deaths in Gujarat [5].

Features of the pathogenesis of the Congo-Crimean hemorrhagic fever

In the mechanism of pathogenesis of Congo-Crimean hemorrhagic fever, local and generalized damage by a highly pathogenic virus of the endothelial vascular system, closely interrelated with a violation of the immune response of the macroorganism, with their subsequent decrease against the background of antiviral etiotropic therapy, elimination of the virus, is determined as a key factor) [6]. The apoptotic pathways of the macroorganism are also being studied, which can limit the replication of the Congo-Crimean hemorrhagic fever virus, since the replication of the virus can induce apoptosis, and the enzyme caspase - 3, activated during apoptosis, can cleave the nucleoprotein of the Congo-Crimean hemorrhagic fever virus and inhibit the replication of the virus [7]. The main attention during the pandemic was focused on COVID-19, but cases of Congo-Crimean hemorrhagic fever were recorded, there were variants of a combination of both infections. These two nosologies in the development of the pathological process have some similarities: the etiological factor is the RNA containing the virus; the incubation period is from 2-14 days; there is a febrile reaction, a predominant lesion of the intima of the vessels leading to the development of sepsis, multiple organ failure syndrome with an unfavorable outcome. Predicting possible complications based on the dynamics of clinical and laboratory changes in order to determine more effective management and treatment tactics is an important help for practitioners. Various aspects of the pathogenesis of COVID-19 and Congo-Crimean hemorrhagic fever have not yet been fully studied and continue to be studied at a deeper level, using materials on the molecular genetic diversity of viruses as an etiological factor of the disease [7].

The course of Congo-Crimean hemorrhagic fever and other infectious diseases in the case of coinfection.

The literature describes cases in a patient with Congo-Crimean hemorrhagic fever with COVID-19 coinfection. He was treated with favipiravir because he had several positive results of PCR tests for COVID-19. COVID-19 infection is a new viral disease mainly of the pulmonary system, characterized by fever, cough, myalgia, shortness of breath, darkening of the "frosted glass" type and multiple infiltrates on CT of the chest organs, lymphopenia, hyperferritinemia, increased CRP and D dimer levels [8,9]. According to some researchers, a combined course of Congo-Crimean hemorrhagic fever and brucellosis in regions endemic to the diseases is also possible [10]. Two of these diseases are common among people living in rural areas and engaged in animal husbandry. Since brucellosis in most cases manifests itself with nonspecific clinical symptoms similar to other

diseases, in this regard, there are many errors with the correct diagnosis. There are reports in the literature about the co-infection of the Congo-Crimean hemorrhagic fever, the joint course of which led to a fatal outcome [11,12]. Since the symptoms of malaria and Congo-Crimean fever are similar and include chills, headache, myalgia and sometimes abdominal pain, vomiting, cough, flu-like syndrome or anemia due to hemolysis, differential diagnosis can cause difficulties. A rare case of coinfection with Crimean-Congo hemorrhagic fever and visceral leishmaniasis in a 14-month-old girl is also described [13].

Conclusion. Thus, in endemic areas, both for Congo-Crimean hemorrhagic fever and for malaria, brucellosis, visceral leishmaniasis and in the era of the Covid-19 pandemic, there may be a one-time infection of patients with them and their combined course is observed, therefore it is extremely important to take into account both infections in differential diagnosis. We recommend that practical healthcare workers keep in mind about the co-infection of Congo-Crimean hemorrhagic fever and other infectious diseases.

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